Making Healthcare Safer III: A Critical Analysis of Existing and Emerging Patient Safety Practices

Agency for Healthcare Research and Quality

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Structured Abstract

Objectives: To review and summarize the evidence for selected patient safety practices (PSPs) and factors important to their successful implementation and adoption.

Data sources: Searches of computerized databases for articles in peer-reviewed publications and in the gray literature.

Methods: The full project team took part in some or all of the following six-step report process:

1. Development of conceptual framework
2. Identification, selection, and prioritization of harm area topics
3. Identification, selection, and prioritization of patient safety practices
4. Literature searches
5. Review of the evidence
6. Report development

To conduct the literature searches, the project team identified PSP-specific search terms and ran them for every PSP in the MEDLINE and CINHAL databases, filtering for English publications only between 2008 and 2018. Across the PSPs examined, there was wide variation in the rigor of studies included in the evidence reviews. Individual authors decided the minimum threshold of quality for including specific studies given the state of the field for each PSP. We aimed to apply the criteria drawn from the Evidence-based Practice Center "Methods Guide for Effectiveness and Comparative Effectiveness Reviews" on strength of evidence derived from GRADE. To the extent possible, authors for each review indicated the strength of evidence by practice, outcome, and/or setting.

Results: The five major threats to safety that were addressed include medication management issues, healthcare-associated infections, nursing sensitive events, procedural events, and diagnostic errors; and the report covers 47 PSPs in 17 specific harm areas. The PSPs were chosen for inclusion in the report based on the high-impact harms they address and interest in the status of their appropriateness for use. While the team was going through the process of selecting PSPs to address specific harm areas, it became evident that several cross-cutting contextual factors should also be reviewed. These cross-cutting practices are improving safety culture; teamwork and team training; clinical decision support; person and family engagement; cultural and linguistic competency; staff education and training; and data monitoring, audit, and feedback.

Conclusions: The amount of published research in patient safety has exponentially grown since the last AHRQ "Making Health Care Safer" report was published in 2013, albeit with publications varying in quality. PSPs that are more well-established are now being investigated in light of emerging harms, such as the applicability of infection-prevention-related PSPs to address the threat from multidrug-resistant organisms. Similarly, emerging PSPs are being investigated for use to address well-established harms, such as the use of clinical decision support to reduce diagnostic errors. It is clear that a wide range of factors impact the effectiveness of PSPs with respect to their ability to prevent harm.

Contents

ES. Executive Summary

ES.1 Background/Introduction

The Making Health Care Safer reports from the Agency for Healthcare Research and Quality (AHRQ) have had an important role in reducing harm and improving the safety and quality of care for patients. The reports—providing an analysis of the evidence for various patient safety practices (PSPs)—have served as a source of information for multiple stakeholders, including healthcare providers, health system administrators, researchers, and government agencies. The reports have also identified contextual factors that contribute to successful PSP implementation. The reports have helped to shape national discussion regarding patient safety issues on which providers, payers, policymakers, and patients and families should focus attention.[1,2]

Since the second report was published in 2013, there have been many improvements in patient safety. Building on the success of PSPs in inpatient settings, AHRQ is seeking to support a culture of safety across the healthcare continuum, including in nursing homes, home care, outpatient, and ambulatory settings, and during care transitions. Making Healthcare Safer III has made strides in transitioning from a predominantly acute care PSP review to include PSPs from other settings and during transitions. The scope of this report has also expanded to match emerging themes and strategic goals championed by the U.S. Department of Health and Human Services, including addressing the opioid crisis and emerging health risks (e.g., multidrug-resistant organisms), and overall directives to "put patients first" and to reduce provider burden and burnout.

The Making Healthcare Safer III report project team, composed of Abt Associates and IMPAQ International, began its work by developing a new conceptual framework that does the following: (1) puts the patient in the center; (2) acknowledges that patients are constantly exposed to potential harms; and (3) proposes patient safety approaches that mitigate patients' past and future vulnerabilities. We have thus taken an approach that is both holistic (considering the whole patient through the continuum of care) and targeted (focusing on what harms are relevant to a particular patient at a particular point in care). Additionally, by following the patient, this framework includes harms during movement between settings and harm risks from existing vulnerabilities and disparities. Starting from the new conceptual framework, we organized the report by "harm areas." This is intended to make the report easier to access for all patient safety stakeholders, who will be able to quickly locate topics of interest and importance to their particular needs and circumstances.

ES.2 Objectives

The purpose of the Making Healthcare Safer III report is to create a source of information on practices that can improve patient safety across a variety of settings and stakeholders. For this report, patient safety practices are defined as "discrete and clearly recognizable structures or processes used for the provision of care that are intended to reduce the likelihood and/or severity of harm due to systems, processes, or environments of care."[3] A PSP may have varying degrees of evidence to support its ability to prevent or mitigate harm or its use in specific contexts.

ES.3 Methods

The methods by which the full project team—including AHRQ and the patient safety and clinical experts on the Advisory Group (AG) and Technical Expert Panel (TEP)—completed the report are outlined in Table ES.1.

Table ES.1: Six-Step Process to Developing the Making Health Care Safer III Report

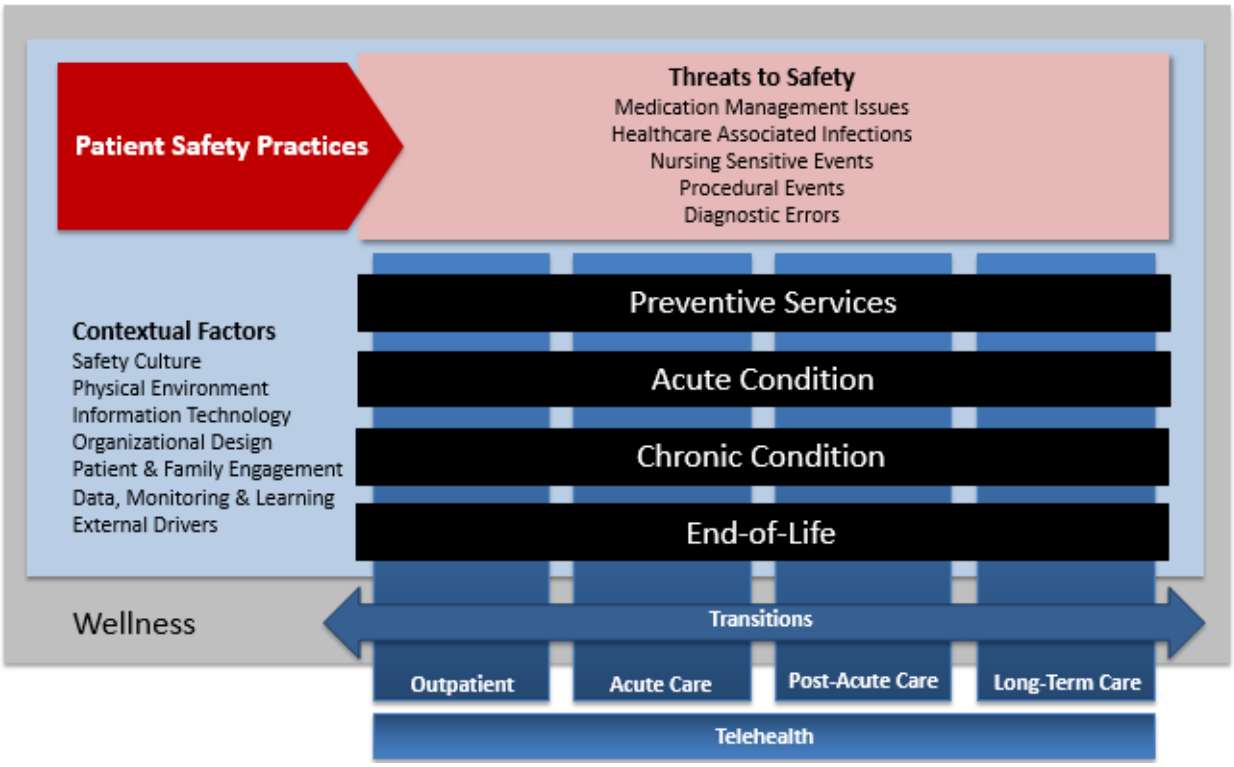
	Steps
1.	Development of Conceptual Framework
2.	Identification, Selection, and Prioritization of Harm Area Topics
3.	Identification, Selection, and Prioritization of Patient Safety Practices
4.	Literature Searches
5.	Review of the Evidence
6.	Report Development

ES.3.1 Step 1. Development of Conceptual Framework

ES.3.1.1 Description of Framework

To help guide the development and content of this report, the project team created a patient-centric framework of safety. The framework focuses on the experience of the individual as they interact with the health care system throughout various phases of health and in different settings (Figure ES.1).

Figure ES.1: Framework for Making Healthcare Safer III Report



The underlying state of the individual is wellness, in which the patient may be receiving intermittent preventive care, such as surveillance for diseases or immunizations, or receiving regular care to maintain stability of chronic conditions. As the patient moves from state to state, they interact with different providers in different settings and the resources, tools, culture, and environments specific to those settings. Threats to safety including medication management issues, healthcare-associated infections, nursing-sensitive events, procedural events, and diagnostic errors can be present during these interactions and patient safety practices (PSP), which are the focus of this report, are used during the provision of care to mitigate the effects of these threats.

ES.3.2 Step 2. Identification, Selection, and Prioritization of Harm Area Topics

The project team conducted an environmental scan of patient safety resources to identify existing and potentially new harm areas. Sources reviewed included AHRQ's PSNet website, the National Quality Strategy, the Joint Commission's National Patient Safety Goals, the National Quality Forum's 2015 Patient Safety Report, the Centers for Medicare & Medicaid Services Hospital Value-Based Purchasing Program and Partnership for Patients, ECRI Institute's 2017 and 2016 Top 10 Patient Safety Issues briefs, and Becker's Hospital Review 10 Top Patient Safety Issues for 2018.[4-12] This scan identified 8 broad categories of harm (e.g., healthcare-associated infections) and 74 specific harm area topics (e.g., *Clostridium difficile* infection).

The AG performed an initial review of the identified harm areas and topics, resulting in the exclusion of seven topics deemed outside the scope of this report. In order to determine which of the remaining 67 topics should be included, the TEP and AG prioritized the topics on a scale of 1 to 5 (1 = low priority; 5 = high priority) and provided feedback through an electronic survey. The results were presented to AHRQ and, after several iterative rounds, which included adding several topics not among the initial 67 harm area topics (shown in Table M.2 of the report's Methods section), a total of 17 harm area topics (shown in Table M.3 of the report's Methods section) were identified for inclusion in the report.

ES.3.3 Step 3. Identification, Selection, and Prioritization of Patient Safety Practices

The project used guidelines and systematic reviews to identify PSPs for the 17 harm area topics. The inclusion of a PSP in the report was based on how many TEP and AG members selected a specific PSP as a high priority for inclusion. After a comprehensive review of the results by AHRQ, a master list of 47 PSPs composed of 40 core PSPs and 7 additional AHRQ-identified PSPs was generated.

ES.3.4 Step 4. Literature Searches

The authors identified PSP-specific search terms and the team librarian ran the search terms for every PSP in the MEDLINE and CINHAL databases while also filtering for English-language publications only between the years 2008 and 2018. The individual studies for some PSPs, such as Patient and Family Engagement and Cultural Competency, were limited; therefore, the project team followed the approach outlined by Whitlock et al. (2008), which was to search for systematic reviews first and decide if the primary literature was of a determined level of adequate quality.[13] The MeaSurement Tool to Assess systematic Reviews (AMSTAR) was then applied to determine systematic review quality.[14] The studies were screened based on the exclusion criteria established using the population, interventions,

comparators, outcomes, and study designs (PICOS) criteria.[15] For example, we excluded studies with specialized populations such as armed forces and pilot study designs, particularly when the PSP was considered new or developing. Other exclusion criteria included lack of rigor, small sample size), lack of intervention or protocol description, PSP not universally applicable to most settings and populations, and study found to be out of scope.

ES.3.5 Step 5. Review of the Evidence

Across the PSPs examined there was wide variation in the rigor of studies included in the evidence reviews, and individual authors were permitted to decide the minimum threshold of quality for including specific studies given the state of the field for each PSP. Similar to the previous report (Making Health Care Safer II), we aimed to apply the criteria drawn from the AHRQ Guides on strength of evidence derived from Grading of Recommendations, Assessment, Development, and Evaluations (GRADE), a framework for developing and presenting summaries of evidence.[2,16-19] To the extent possible, authors for each review indicated the strength of evidence by practice, outcome, and/or setting.

ES.3.6 Step 6. Report Development

For this report, the project team has made an effort to synthesize the evidence through a research lens, while placing it in a format that allows for practical application for the end user. Each chapter, as written by the project team with final review from AHRQ, represents a specific threat to safety (i.e., the harm) that can occur to a patient when exposed to healthcare and includes the targeted PSPs selected for review.

Given the wide variation in study availability and quality, as well as the variation in strength of evidence sometimes by setting and specific outcomes, the project team decided against providing a single determination of strength of evidence by PSP (as was done in the previous report). Instead, the project team—with expert input from AHRQ, the TEP, and the AG—determined it was most appropriate to provide tables that summarize for each harm area, by PSP, the following: key safety outcomes: Table ES.2 summarizes these points for each PSP to provide a user-friendly overview of what stakeholders will find in each specific review.

ES.4 Results

The results of the 47 PSPs grouped according to the 17 topics are summarized in Table ES.2. Instead of including strength of evidence for each PSP, the project team decided to include key takeaways as a way to allow the user to determine if the PSP is of interest or beneficial.

Table ES.2: Patient Safety Practice Summary Table

Patient Safety Practice	Key Safety Outcomes	Studies and Systematic Reviews (#)	Settings	Key Takeaways/Points
Diagnostic Error: Clinical Decision Support (CDS)	• Diagnostic accuracy	31 studies; 3 systematic reviews; 1 meta-review; 1 meta-analysis	Inpatient and outpatient (primary care and specialty care), emergency department (ED)	• CDS has been shown to improve diagnosis in exploratory and validation studies, but the systems need to be fully implemented and tested in a clinical setting. • They are best used as adjuncts to the clinician's decision-making process and not as replacements.
Diagnostic Error: Peer Review	• Diagnostic errors • Diagnostic discrepancy rates	14 studies; 2 systematic reviews	Inpatient and outpatient (radiology and pathology)	• There is a lack of evidence to show that traditional random peer review and feedback mechanisms improve diagnostic quality over time or prevent diagnostic errors from reaching the patient. • Nonrandom peer review appears to be more effective at identifying diagnostic errors than random peer review. • When nonrandom peer review is conducted prospectively, there is an opportunity to identify and remediate the diagnostic error before it reaches the patient.
Diagnostic Error: Result Notification Systems (RNS)	• Acknowledgement of result receipt • Timeliness of result receipt • Timeliness of action taken on test result • Documented action	15 studies; 2 systematic reviews	Inpatient and outpatient (primary care and specialty care), ED	• Results varied by type of test result, setting, synchronous vs. asynchronous communication, and manual vs. automated alerting mechanisms. • For both critical and noncritical clinically significant test results of radiologic studies, lab studies and tests pending at discharge, the use of RNS showed mixed results in the timeliness of receipt and action on the test results.
Diagnostic Error: Education and Training	• Diagnostic accuracy • Diagnostic errors • Cognitive biases	19 studies; 2 systematic reviews; 1 meta-analysis	Classroom, online training, inpatient and outpatient (primary care, specialty care)	• Although there are a limited number of studies, training on metacognitive skills may improve diagnostic accuracy, particularly as clinical experience increases. • Online training, either didactic or via simulation, can be successfully used as a mode of delivery for educational interventions targeting clinical reasoning and diagnostic safety.
Failure To Rescue: Patient Monitoring Systems (PMS)	• Number of rescue events (rapid response team [RRT] or code blue calls) • Time to collect vital signs • Mortality • Hospital length of stay (LOS) • Intensive care unit (ICU) transfer • ICU length of stay (LOS)	8 studies; 3 systematic reviews	Hospital (medical/surgical units)	• There was moderate evidence for a reduction in rescue events following implementation of a PMS with continuous monitoring (CM), but studies were inconsistent. • PMS with CM showed no significant effect on mortality, while PMS with intermittent vital sign input had a moderate and inconsistent association with mortality rates. • There was moderate evidence for improvement in hospital LOS but low evidence for improvement in other outcome measures (ICU LOS, ICU transfers).

Patient Safety Practice	Key Safety Outcomes	Studies and Systematic Reviews (#)	Settings	Key Takeaways/Points
Failure To Rescue: Rapid Response Teams	• Hospital mortality • Cardiac arrest rate • ICU transfer rate	4 studies; 3 systematic reviews; 3 meta-analyses	Acute care hospitals	• There is inconclusive evidence as to whether RRT implementation is associated with decreased overall hospital mortality or ICU transfer rates. • There is moderate evidence that decreased non-ICU cardiac arrest rates are associated with implementation of RRT. • Recognition of the benefits of RRT implementation often takes a long time.
Sepsis: Screening Tools	• Time to Surviving Sepsis Campaign (SSC) bundle administration • Mortality • ICU transfer • ICU LOS	26 studies; 2 systematic reviews	Hospital, pre-hospital (emergency medical services [EMS]), and nursing homes	• Performance of screening tools varied widely, especially in the pre-hospital setting. More research is needed to determine the optimal variables and thresholds for a screening tool. • There was moderate evidence of process measure improvement in the hospital setting, including time to antibiotics. Pre-hospital evidence was sparse but showed improvement as well. • Evidence for outcome measures (e.g., mortality, ICU LOS, ICU transfer) was sparse but showed a trend toward improvement, although the improvement was not always significant.
Sepsis: Patient Monitoring Systems	• Time to SSC bundle administration • Mortality • Hospital LOS • ICU transfer • ICU LOS	15 studies; 4 systematic reviews	Hospital (ICU, ED, general unit, telemetry, multiple units)	• There was moderate evidence of process measure improvement across multiple types of hospital units, and evidence was most consistent outside of the ICU. • Evidence for outcome measures (e.g., mortality, ICU LOS, ICU transfer) was mixed, but over half of the studies showed a significant improvement, and several showed an absolute improvement that did not reach statistical significance.
***Clostridium difficile*:** Antimicrobial Stewardship	• *Clostridium difficile* infection (CDI) rates • Amount of prescribed high-risk antimicrobials	17 studies; 3 meta-analyses; 2 systematic reviews	Inpatient (hospitals, and long-term care facilities [LTCFs]/nursing homes)	• The majority of studies showed reductions in CDI following a period of antimicrobial stewardship (both statistically significant and statistically non-significant reductions). • In the reviewed studies, significant reductions in CDI were associated with higher baseline CDI rates/outbreaks, antimicrobial stewardship programs (ASPs) developed specifically to reduce CDI (as opposed to ASPs focused on other clinical and microbiological outcomes), and ASPs that included restrictions of high-risk antimicrobials and/or a pre-authorization component. • ASPs require staffing, technological resources, and provider buy-in.

Patient Safety Practice	Key Safety Outcomes	Studies and Systematic Reviews (#)	Settings	Key Takeaways/Points
***Clostridium difficile*:** Testing	• Sensitivity • Specificity • Predictive value (e.g., c-statistic) • Time it takes to get results	25 studies; 7 systematic reviews	Inpatient (hospitals), ED	• Screening and isolating asymptomatic carriers can prevent CDI transmission but are resource intensive. • Nucleic acid amplification tests (NAATs) of unformed stool have relatively accurate sensitivity and specificity. • Concerns with NAATs include that they detect toxigenic *C. difficile* genes, not the actual damaging toxins, and may capture colonized patients in addition to those infected with *C. difficile*. • Certain multi-step test algorithms that include a test for *C. difficile* and for CDI toxins perform as well or better than NAATs but take longer. • Tools that identify patient risk for CDI could be useful in preventing CDI.
***Clostridium difficile*:** Surveillance	• Prospective outbreak and cluster identification • Surveillance case definition accuracy • Speed of case identification	16 studies; 2 systematic reviews	Inpatient (hospitals and LTCFs), outpatient, and regional	• Studies showed that automated surveillance systems are generally accurate, and save time and resources compared to manual case review. • Automated laboratory alerts have been shown to help expedite contact precautions for CDI patients. • Classifying CDI cases using standard case definitions is important, although some researchers have found that the current definitions over-represent the number of nosocomial cases. • Case studies show that genotyping provides detail about differences in *C. difficile* virulence and has helped to identify transmission pathways and outbreaks.
***Clostridium difficile*:** Hand Hygiene	• CDI rates • Staff compliance • Hand contamination	11 studies; 1 systematic review	Inpatient (hospitals and LTCFs)	• In vitro evidence supports the use of gloves and hand washing with soap and water for *C. difficile* prevention; multiple experimental studies show alcohol-based hand rubs are not effective for eliminating *C. difficile* spores. • Studies that measured hand hygiene and CDI patient outcomes were quasi-experimental, and showed large and mostly statistically insignificant decreases in CDI following implementation of hand hygiene programs that targeted multiple healthcare-associated infections (HAIs) (statistical significance was impacted by small sample sizes).
Clostridium difficile: Environmental Cleaning and Decontamination	• CDI rates • Performance of cleaning staff • Environmental contamination • Time to clean and decontaminate	18 studies; 3 systematic reviews	Inpatient (hospitals and LTCFs)	• Studies supported daily and/or discharge cleaning with chlorine-based agents for CDI-occupied rooms. • In many studies, the addition of hydrogen peroxide decontamination or ultraviolet light decontamination to standard cleaning was associated with significant reductions in facility-level CDI rates.

Patient Safety Practice	Key Safety Outcomes	Studies and Systematic Reviews (#)	Settings	Key Takeaways/Points
Clostridium difficile: Multicomponent Interventions	• CDI rates • Staff compliance	8 studies; 3 systematic reviews	Inpatient (hospitals, LTCFs)	• Multicomponent interventions to prevent CDI were associated with significant decreases in CDI rates. • The most common component was environmental cleaning, followed by hand hygiene, and patient isolation practice,; antimicrobial stewardship, and contact precaution,; and CDI testing, and surveillance. • There was no single CDI prevention toolkit used across studies.
Controlling Multidrug-Resistant Organisms (MDROs) and Preventing MDRO-Related Infection: Hand Hygiene for Controlling MDROs	• MDRO acquisition (methicillin-resistant *Staphylococcus aureus* [MRSA], carbapenem-resistant Enterobacteriaceae [CRE], vancomycin-resistant Enterobacteriaceae [VRE], multidrug-resistant gram-negative bacteria [MDR-GNB]) • MDRO infection (including HAIs) • Environmental contamination • Hand hygiene compliance	13 studies; 3 systematic reviews; 1 meta-analysis	Hospitals (including intensive care transplant, dialysis, and general care units), LTCFs	• Hand hygiene is indispensable for infection control, and hand hygiene compliance reinforces compliance with other practices. • The World Health Organization's "My Five Moments for Hand Hygiene" was frequently recommended for improving hand hygiene compliance, but there are many effective campaign materials to choose from. • Existing campaigns can be made even more effective by having staff personalize the implementation through creating educational/promotional materials and supporting each other in observing hand hygiene. • The biggest barriers to hand hygiene compliance are: (1) awareness that an opportunity for hand hygiene is occurring; and (2) remembering to complete hand hygiene protocol consistently at every opportunity. Education can help with the first, and direct observation with immediate feedback helps improve the second.

Patient Safety Practice	Key Safety Outcomes	Studies and Systematic Reviews (#)	Settings	Key Takeaways/Points
Controlling Multidrug-Resistant Organisms (MDROs) and Preventing MDRO-Related Infection: Surveillance for Controlling MDROs	• MDRO acquisition (MRSA, CRE, VRE, MDR-GNB) • MDRO infection (including HAIs) • Results reporting completeness and accuracy • Compliance with other patient safety practices (PSPs) (such as contact precautions)	20 studies; 2 systematic reviews; 1 meta-analysis	Hospitals (including intensive care, neonatal intensive care, hematology/ oncology, and general care units)	• Targeted active surveillance performs as well as universal active surveillance for many MDROs and uses fewer resources. In places where universal active surveillance is already in place, screening for other MRDOs using the same sample may be cost-effective, due to shared risk factors. • Some consensus exists for screening high-risk patients (those with a history of MDROs or risk factors associated with MDRO colonization/ infection) on admission, but any screening approach will require compliance with infection prevention protocols when a positive culture result is found. • Surveillance may improve compliance with other PSPs when it is part of a multi-component intervention, but more research is needed on the mechanisms and circumstances of this association, as it can be confounded by the co-implementation of other, bundled practices.
Controlling Multidrug-Resistant Organisms (MDROs) and Preventing MDRO-Related Infection: Minimizing Exposure to Invasive Devices and Reducing Device-Associated Risks	• Incidence of infections (e.g., bloodstream infections, pneumonia) • Measures of antimicrobial resistance (e.g., minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC)	11 studies; 5 systematic reviews; 1 meta-analysis	Inpatient settings (e.g., hospitals, LTCFs), outpatient settings (e.g., dialysis), and patient homes	• Using devices minimally and appropriately, and practicing hygiene and infection control precautions when inserting them are basic steps that can be taken to reduce device-associated infections. • Antimicrobial resistance has not been eliminated as a concern when using antibiotics in antibiotic lock therapy (ABLs), impregnated catheters, or prophylactic treatment to prevent infections. • Ongoing implementation education, monitoring, feedback for medical staff, patients, and caregivers are recommended for improving adherence to recommended PSPs.
Controlling Multidrug-Resistant Organisms (MDROs) and Preventing MDRO-Related Infection: Chlorhexidine Bathing for Controlling MDROs	• MDRO acquisition (MRSA, CRE, VRE, MDR-GNB) • MDRO infection (including HAIs) • Measures of chlorhexidine resistance (e.g., MIC and MBC) • Adverse reactions to chlorhexidine application	38 studies; 4 systematic reviews	General healthcare settings, community settings, hospital settings (including intensive care, pediatric intensive care, transplant, and general care), LTCFs, and laboratory studies (for resistance)	• Chlorhexidine bathing is effective at reducing colonization, particularly by multi-drug resistant (MDR) gram-positive bacteria; evidence is mixed about its effectiveness in reducing MDR-related infections (beyond skin preparation for central line insertion). • As an intervention, chlorhexidine is low-cost to implement (especially if routine bathing is already in place) and generally well-received by staff, but compliance with bathing can wane over time. • Chlorhexidine resistance is a potential problem, and while there are no clinical impacts described in the literature to date, this should continue to be monitored.

Patient Safety Practice	Key Safety Outcomes	Studies and Systematic Reviews (#)	Settings	Key Takeaways/Points
Controlling Multidrug-Resistant Organisms (MDROs) and Preventing MDRO-Related Infection: Communication of Patient's MDRO Status	• Percent compliance with guidelines • Adverse patient outcomes associated with lack of or incorrect communication	12 studies; 1 systematic review	General healthcare settings, especially transfer of patients from one setting to another	• Communication failures have been linked to poor patient outcomes, especially in the field of organ transplantation. • Multimodal and redundant communication policies can improve communication compliance in settings with complex communication (e.g., organ donation) or with multiple care providers (i.e., transfers). Modes of communication can include checklists, brightly colored leaflets attached to medical records, and electronic or automated communication. • Revisiting policies to ensure they are meeting a facilities' needs, performing ongoing monitoring and feedback of policy compliance, and involving staff from multiple disciplines in policymaking are all important for improving patient status communication.
Controlling Multidrug-Resistant Organisms (MDROs) and Preventing MDRO-Related Infection: Environmental Cleaning and Disinfection	• Transmission rates • Proportion of deactivated microbial cultures • Reduction in environmental contamination markers (e.g., fluorescent gel, UV detectable powder, or adenosine triphosphate (ATP) markers) • Measures of antimicrobial resistance (e.g., MIC and MBC)	54 studies; 2 systematic reviews; 2 meta-analyses	General healthcare settings (e.g., hospitals and LTCFs)	• There is a need for more studies in clinical settings that examine the different cleaning and disinfecting agents individually, as opposed to as part of a multicomponent intervention. • No-touch disinfection technologies are promising additions to disinfection practices, but must be further studied to determine the most efficacious and cost-effective options. • Environmental screening is a useful tool for auditing and monitoring ongoing cleaning practices, and for identifying highly contaminated surfaces for targeted cleaning during outbreak scenarios.
Carbapenem-Resistant Enterobacteriaceae: Contact Precautions To Prevent CRE	• CRE carrier prevalence • CRE incidence • Compliance rate	18 studies; 3 systematic reviews	General healthcare settings (e.g., hospitals and LTCFs)	• Contact precautions have been shown to reduce transmission of CRE as part of infection control bundles in a variety of healthcare settings, including long-term care facilities and acute care facilities. • Active surveillance is recommended in outbreak scenarios, in highly endemic regions, and in healthcare facilities or units with ongoing transmission. • Additional research is needed to determine whether there is an appropriate time to discontinue contact precautions, based on duration of CRE carriage.

Patient Safety Practice	Key Safety Outcomes	Studies and Systematic Reviews (#)	Settings	Key Takeaways/Points
Anticoagulants: Anticoagulation Management Service	• Time to therapeutic range (TTR) • Bleeding events • Thrombotic events	5 studies; 6 systematic reviews	Ambulatory home-bound	• There are a range of models; most are pharmacist-led but some are led by nurse practitioners, physician assistants, or nurses. • Some models examined different modes of providing these services (e.g., telephone). • Overall quality of studies (individual and within reviews) is moderate to high given number randomized controlled trials (RCTs), non-RCTs with comparison groups, or pre/post designs. • Evidence of the effect of anticoagulant management services is moderately positive on time to therapeutic range (TTR), low and mixed on bleeding events and thromboembolic events.
Anticoagulants: Nomograms/Protocols for Novel Oral Anticoagulants	• Protocol adherence • Mean time to activated partial thromboplastin time (aPTT) stabilization	4 studies	Group practice, academic medical center, community hospital	• Standard and simplified dosing nomograms were successfully implemented by nurses. • Strength of evidence is low; no control groups were used in the four studies and all reported small sample sizes. • Cases of major bleeding were reported in some of the intervention protocols.
Anticoagulants: Anticoagulant Care in Transitions Between Hospital and Home	• Hemorrhagic events • Readmission • ED LOS • Death • Medication adherence • TTR	5 studies	Discharge from ED	• The strength of evidence for anticoagulant care transition from hospital to home was low to moderate, as small sample sizes and single sites were cited. • Most studies reported no statistically significant differences for outcomes (i.e., recurrent venous thromboembolism (VTE), death, and readmission).
Diabetic Agents: Diabetes Protocol for Reducing Hypoglycemia	• Incidence of hypoglycemia • Frequency of hypoglycemia • LOS • Blood glucose levels	11 studies	ED, ICU	• Although glycemic outcomes usually improved, a statistically significant difference was rare. • Implementation of study protocols were usually implemented by nurses.
Diabetic Agents: Teach-Back	• HbA1c levels • Diabetes knowledge score • Health literacy scores	4 studies	Federally Qualified Health Center (FQHC), academic medical center, outpatient clinic	• Each study used a different model to facilitate teach-back. • Interventions need to address various levels of health literacy to be successful. • Health literacy scores improved, but only for a limited time.

Patient Safety Practice	Key Safety Outcomes	Studies and Systematic Reviews (#)	Settings	Key Takeaways/Points
Reducing Adverse Drug Events in Older Adults: Deprescribing	• Drug burden index scores • Adverse drug reactions • Prescribing • Good health status rating • Healthcare utilization	13 studies	Residential care facility, community pharmacy, day center for senior citizens, skilled nursing facility, LTCF	• Intervention models were specifically designed to reduce harm in older adults. • Intervention models were primarily led by a pharmacist or physician. • Interventions led to a decrease in the number of medications prescribed and a decrease in medication-related costs.
Reducing Adverse Drug Events in Older Adults: Using the Screening Tool of Older Persons' Potentially inappropriate Prescriptions (STOPP) Criteria	• Prescribing • Potentially inappropriate medications • Potentially inappropriate prescriptions • Adverse drug reaction incidence	14 studies	Primary healthcare center, geriatric psychiatry admission unit, acute care admission, LTC, nursing homes, geriatrics outpatient clinic	• STOPP criteria specifically target older adults to reduce avoidable adverse drug events. • STOPP criteria are particularly effective when combined with another tool. • Implementation of the STOPP criteria was either led by a pharmacist or physician. • Studies showed improved prescribing appropriateness but no statistically significant differences in admission or in-patient death rates.
Opioids: Opioid Stewardship	• Opioid prescribing • Opioid dosage • Potential misuse • Overdose • Recommended risk mitigation practices (urine screen)	14 studies; 1 systematic review	Primary care, health system ED, hospital, specialty	• Majority of studies examined multicomponent interventions consisting of clinical interventions and implementation strategies. • Six studies had control groups (2 were randomized). • Post-intervention periods ranged from months to years. • The strength of evidence for opioid stewardship producing significant reduction in opioid dosages was moderate.
Opioids: Medication-Assisted Treatment (MAT) Initiation	• Opioid dependence • Illicit drug use • Treatment retention rates	25 studies; 1 systematic review	ED, community practice, clinic for the homeless, primary care clinic, outpatient substance use disorder treatment center, FQHC	• MAT can be initiated and provided safely in a variety of healthcare settings. • Initiation of MAT in the ED, primary care setting, or outpatient clinics may result in faster access to care and longer retention in or adherence to treatment. • The majority of studies were focused on one component of MAT, the initiation of medications, in a few specific settings.
Patient Identification Errors: Patient Identification Errors in the Operating Room	• Compliance audit • Incidence of wrong-site surgery	8 studies; 1 systematic review	Hospital operating room and theaters	• Drawing meaningful statistical comparisons is difficult because wrong-site surgeries are rare.
Infusion Pumps/Medication Error: Structured Process Change and Workflow Redesign	• Medication administration errors • Procedural errors • Process outcomes	6 studies	Hospitals	• Multiple studies identified standardization and streamlining of processes and workflows as main facilitators of optimal infusion pump use. • Integration and alignment of technology and workflows, and engaging multiple members of the care team were also found to be important facilitators.

Patient Safety Practice	Key Safety Outcomes	Studies and Systematic Reviews (#)	Settings	Key Takeaways/Points
Infusion Pumps/Medication Error: Staff Education and Training	• Adverse drug events • Nurse adherence	5 studies	Hospitals	• Five studies identified the type and content of education provided as facilitators. • One study noted that time and energy constraints on nurse educators can be barriers to implementing large hospital-wide education programs. • More research is needed to understand why clinicians commonly bypass smart pump safety technology and what type of training should be implemented to limit medical errors.
Alarm Fatigue: Safety Culture	• Number of alarms • Noise level	10 studies	Hospitals; ICU; progressive care unit; neonatal intensive care unit; or telemetry, step-down, transplant cardiology, surgical, or surgical orthopedic units	• Current literature on this PSP is primarily quality improvement initiatives and case studies; higher quality studies could help to better understand the impact of implementing elements of safety culture to address alarm fatigue.
Alarm Fatigue: Risk Assessment	• Number of alarms • Number of false alarms	8 studies	Hospitals; ICU; progressive care unit; neonatal intensive care unit; step-down, transplant cardiology, surgical, or surgical orthopedic units	• Studies reviewed focused on one hospital or specific unit and thus have limited generalizability. • The decision to engage a team and conduct a risk assessment was often in response to a specific adverse patient event or external influence.
Delirium: Screening and Assessment	• Recognition • Prevention • Management of delirium to prevent possible harms	13 studies; 2 systematic reviews; 2 non-systematic reviews	All settings were included	• Evidence identified for this review is markedly heterogeneous. • The tools most frequently used and evaluated were the Confusion Assessment Method (CAM) and the Confusion Assessment Method-Intensive Care Unit (CAM-ICU). • These tools have been tested singly and in comparison with other tools to determine concordance.
Delirium: Staff Education and Training	• Recognition • Prevention • Management of delirium to prevent possible harms	16 studies	All settings were included	• Studies reviewed identified a need for much more education and training in the identification of individuals at risk for developing delirium, the contributing factors to delirium in a variety of care settings, and strategies to appropriately manage delirium • Consideration should be given to implementing the Acute Care for the Elderly (ACE) Model • Education and training utilizing a variety of modalities—including partnering ACE units with non-ACE units, e-learning, combining didactic course work with either simulation or supervised clinical practice with feedback from experts—have shown promise.

Patient Safety Practice	Key Safety Outcomes	Studies and Systematic Reviews (#)	Settings	Key Takeaways/Points
Delirium: Nonpharmacological Interventions To Prevent Delirium	• Delirium incidence • Delirium duration	8 studies; 4 systematic reviews; 1 non-systematic review	ICU	• Multicomponent nonpharmacological interventions are effective for reduction of delirium among intensive care patients, although the quality of the evidence is low to moderate. • Reproducibility and scalability are hindered by a lack of evidence regarding which components of many are required to achieve the desired effect. • In addition, specific details of implementation required for replication and level of adherence to protocols are not often reported.
Care Transitions: Transition of Care Models				
BOOST: Better Outcomes for Older Adults through Safe Transitions	• Readmission rates	3 studies	Large hospitals	• Model contributes to reduction of 30-day re-hospitalization rates, and using the 8 Point assessment tool accurately predicts 90% of readmissions.
CTI: Care Transition Intervention	• Readmission rates	7 studies	Acute care hospitals	• Model contributes to reductions in hospital readmission at 30, 60, and 180 days. • Model contributes to significant reductions in healthcare costs.
TCM: Transitional Care Model	• Readmission rates	3 studies; 1 systematic review	Community/outpatient, academic health system	• Model reduces rates of readmission and costs for healthcare systems. • Measuring changes in key outcome categories is important for benchmarking evidence of the impact of the TCM.
Venous Thromboembolism: Use of aspirin for VTE prophylaxis	• Deep vein thrombosis • Pulmonary embolism • Operative site bleeding and other major bleeding	27 studies; 6 systematic reviews	Hospital, post-surgical care, tertiary care orthopedic referral centers; countries included USA, UK, China, Canada, and Korea	• Use of aspirin following major orthopedic surgery was generally found to be of similar effectiveness as other agents. • An overwhelming majority of studies concluded that aspirin has a lower bleeding risk rate than other pharmacologic agents which, combined with its lower cost, makes it an appealing option for VTE prophylaxis, particularly in low-risk patients. • More prospective RCTs are needed to directly compare the effectiveness of aspirin to other prophylactic methods across patient risk levels.
Cross-Cutting Factors: Patient and Family Engagement (PFE)	• Patient and provider perception and attitude to PFE	1 study; 2 systematic reviews	Hospital	• Studies revealed a lack of understanding about the effects of PFE on patient safety among healthcare providers, patients, and families. • PFE implemented through an educational intervention was linked to positive perceptions and attitudes about PFE among healthcare providers. • More studies are needed to measure the direct outcomes of patient and family engagement.

Patient Safety Practice	Key Safety Outcomes	Studies and Systematic Reviews (#)	Settings	Key Takeaways/Points
Cross-Cutting Factors: Safety Culture				
Leadership WalkRounds	• Adverse events • Perceptions of safety climate	4 studies; 1 systematic review	Hospital	• A previous systematic review reported that the use of WalkRounds was associated with a reduction in adverse events. • The single studies reviewed found that WalkRounds were associated with improvements in various aspects of safety climate.
Team Training	• Perceptions of safety climate	8 studies; 2 systematic reviews	Hospital, VA facilities, rehabilitation unit in long-term care facility	• The second Making Healthcare Safer report found improved care processes after team training was introduced to improve safety culture. • The single studies reviewed found that team training interventions were associated with improvements in various aspects of safety climate. • In the second Making Healthcare Safer report, team training was associated with reduced errors and safety events.
Comprehensive unit-based safety program (CUSP)	• Surgical site infection rates • Central line-associated blood stream infection (CLASBI) rates • Perceptions of safety culture	6 studies; 1 systematic review	Hospital	• CUSP interventions were associated with improved perceptions of various aspects of safety culture. • The introduction of CUSP was associated with patient outcomes such as decreased CLASBI rates and decreased surgical site infections.
Multiple Interventions	• Perceptions of safety culture	1 study	Hospital	• The bundle interventions were associated with improved perceptions of various aspects of safety culture, although some scores decreased in post-intervention period.
Cross-Cutting Factors: Clinical Decision Support (CDS)	NA	26 studies; 1 systematic review	All settings included in searches	• CDS is widely believed to have the potential to positively impact patient safety; this belief has face validity. • The most consistent impact of CDS in the literature reviewed was on improving medication safety. • While some results are promising, more evidence is needed to clearly establish the significant role CDS could play in increasing patient safety.

Patient Safety Practice	Key Safety Outcomes	Studies and Systematic Reviews (#)	Settings	Key Takeaways/Points
Cross-Cutting Factors: Cultural Competency	• Preventable hospital readmissions • Medication adherence • LOS • Advance care planning and informed consent	7 studies; 4 systematic reviews	Inpatient, outpatient, and home health	• Most of the small group of reviewed studies found language services were associated with improved patient safety. • There is a need for studies that explore associations between a range of cultural competency interventions and patient safety outcomes. • Interventions that are framed around cultural competency and aim to improve patient health and indicators of health have mostly positive outcomes.
Cross-Cutting Factors: Monitoring, Audit, and Feedback	NA	28 studies; 3 systematic reviews; 1 non-systematic review	All settings included in searches	• Audit and feedback is a somewhat common strategy for improving compliance with patient safety processes. • Audit and feedback appear to be most effective when both written and verbal feedback are used. • Studies show more significant improvements when performance was lower at baseline. • Research on audit and feedback predominantly focuses on process improvement, and more research is needed to measure the impact of audit and feedback on patient outcomes.
Cross-Cutting Factors: Teamwork and Team Training Crew Resource Management (CRM)	• Adverse outcome index • Standards of care • Participant reactions • Knowledge about teamwork	6 studies; 1 systematic review; 1 meta-analysis	Hospital	• Participants had greater knowledge about teamwork and felt more confident in their ability to use teamwork skills following CRM training. • Increases in participants' confidence, increased use of teamwork skills, and improved clinical processes were sustained for 6 to 9 months following training. • None of the individual studies collected clinical outcomes. Systematic review and meta-analysis reported improved patient outcomes. • Participants had positive reactions to CRM training.

Patient Safety Practice	Key Safety Outcomes	Studies and Systematic Reviews (#)	Settings	Key Takeaways/Points
Team Strategies and Tools to Enhance Performance and Patient Safety (TeamSTEPPS®)	• Infection rate • LOS • Participant reactions • Teamwork skills	6 studies; 1 systematic review; 1 meta-analysis	Hospital, ED, psychiatric hospital	• Participants had positive reactions to TeamSTEPPS training. • Participants had greater knowledge about teamwork and demonstrated more teamwork skills immediately following TeamSTEPPS training. • Some improvements in teamwork skills were sustained for up to 12 months following the training, and more accurate decisions about care were noted for up to 3 months following training. • Positive perceptions of safety culture, decreased infection rates, and decreased LOS (nonsignificant) were noted as outcomes associated with the training.
Veterans Health Administration Medical Team Training	• Surgical morbidity rates • Attitudes toward safety • Delays in care	2 studies; 1 systematic review; 1 meta-analysis.	VA facilities	• Positive attitudes toward teamwork were found 12 to 17 months after the training. • Fewer case delays were reported for up to 24 months following training. • Decreases in surgical morbidity were noted in one study for facilities that had participated in the training.
Team Simulation	• Adverse outcome score • Use of teamwork skills • Confidence in emergencies • Decision-making • Workload management	6 studies; 3 systematic reviews; 1 meta-analysis	Tertiary care medical center, teaching hospital, VA facility	• Participants were more confident in their ability to handle emergencies following simulation training. • Participants demonstrated greater teamwork skills following simulation training, with some longer term sustainment reported. • Improved neonatal outcomes and a reduction of postpartum hemorrhage cases were associated with the simulation interventions.
Brief/Debrief	• Survival to discharge • Survival with favorable neurological outcomes • Debrief quality	3 studies	ED, surgical department, ICU	• The use of briefings was associated with improved clinical processes. • The use of a coach to facilitate briefings was associated with increased quality of briefings, which was sustained on the job. • A debriefing intervention was associated with increased patient outcomes (i.e., survival to discharge rate, survival with favorable neurological outcomes).
Handoff	• Adverse events • Checklist compliance • Information sharing	3 studies	Hospital (surgical units, neurointerventional suite)	• Participants reported favorable reactions to the checklist introduced. • Compliance with checklist use and completion of checklist items increased in the post-intervention period and were sustained for up to 18 months. • Use of the checklist was associated with a decrease in adverse events.

Patient Safety Practice	Key Safety Outcomes	Studies and Systematic Reviews (#)	Settings	Key Takeaways/Points
Cross-Cutting Factors: Staff Education and Training Simulation-Based Medical Education for Residents and Fellows	• Complication rates • Frequency and time of successful procedures	5 studies; 3 systematic reviews; 1 meta-analysis	Teaching hospital, tertiary teaching hospital	• Simulation-based medical education curriculums were associated with decreased complication rates, fewer errors, reduced CLASBI rates, improved pain management of patients, and a lower proportion of adverse events across studies. • Cost savings were associated with reductions in central-line infections, overnight hospital days, or additional hospital days. • Improved procedural skills were reported for participants, such as increased rates of successful first attempts to intubate patients, fewer needle passes for central venous catheter insertion, and increased compliance with recommended guidelines and protocols.
Simulation as Part of Continuing Education of Nurses	• Infection rates • Medication administration errors • Compliance with guidelines and protocols	2 studies	Children's hospital, teaching hospital	• A decrease in medication administration errors was reported after nurses completed simulation exercises and participated in debriefs on their performance. • Simulation training provided to nurses on sterilization techniques was associated with decreased infection rates. • Knowledge of and adherence to recommended protocols increased following simulation training.

ES.5 Discussion

This report covers 47 PSPs chosen for the high-impact harms they address and interest in the status of their use. The harms include diagnostic errors, failure to rescue, sepsis, infections due to multi-drug resistant organisms, adverse drug events, and nursing-sensitive conditions. While going through the process of selecting PSPs to address specific harm areas, it became evident that several commonly recommended practices should also be reviewed. These cross-cutting practices are: improving safety culture, teamwork and team training, clinical decision support, patient and family engagement, cultural competency, staff education and training, and monitoring, audit, and feedback. All of the harm-specific PSPs and cross-cutting PSPs included in this report underwent focused systematic reviews to establish the current evidence base for their use.

The most significant harms patients face continue to be found in higher acuity settings, such as the ED and ICU, and the research is biased toward those settings. One "setting" that poses a unique threat to patients is the transition between one setting and another: the hospital to the outpatient setting, in particular. As we move out from the silos required in setting-specific research, the research needs to address these gaps.

Regardless of setting, several themes emerged from the report:

- More than one PSP can be used to reduce a given harm. The PSPs presented in the report are those that the project TEP and AG felt were ready for a fresh review of the literature or that were relatively new and needed to have an evidence base established. The PSPs in the report are not intended to be an inclusive list.
- Selecting a particular PSP should be based on the root cause of the harm. If a facility is experiencing an increase in sepsis mortality, the root cause may be a lack of recognition of patients with sepsis arriving to the ED. In another facility, it may be due to lack of monitoring of patients who are experiencing deterioration on a medical-surgical unit.
- When using a specific PSP, consideration must be given to potential new harms that can be introduced. For example, strategies to improve anticoagulation-related events must be balanced with strategies used to reduce venous thromboembolism.
- PSPs are not implemented in isolation and are often part of a broader safety strategy. The strategy often relies on a strong safety culture, teamwork, communication, and involvement of the patient and family. These cross-cutting practices are the foundation for success.
- The context in which a PSP is implemented determines success. Understanding the impact of context through rigorous, large-scale research studies is difficult. It is extremely difficult, and sometimes may be impossible, to design a study that takes into consideration all potential contextual factors, such as staffing, other PSPs in place, safety culture, and leadership engagement, and to control for those factors across enough sites to make the findings generalizable.

ES.6 Limitations

There are several limitations to conducting such a broad review of the literature as found in this report.

As our understanding of patient safety expands, there is an increasing amount of published research, with most showing positive effects of the intervention under question (i.e., publication bias). With the

paucity of recent randomized controlled trials (RCTs) in the literature and the reliance on pre-post studies and observational studies, it is difficult to assess the impact of the biases introduced by study design on the findings.

The low number of RCTs in the patient safety literature is also a limitation in conducting focused systematic reviews such as those found in this report. Many of the PSPs under examination have been implemented in some form. Staff are aware of the implementation of the PSPs, so being blinded to the intervention is not possible. Since PSPs are typically implemented across an entire facility rather than a single unit, finding a control group for comparison can be difficult.

Lastly, some of the PSPs addressed were introduced as part of multicomponent interventions (e.g., strategies to reduce *C. difficile* infections). When a specific PSP is part of a multicomponent intervention, it is difficult to ascertain which of the components is the driver for success.

ES.7 Conclusions

This report presents reviews of 47 different PSPs covering a wide variety of harms across multiple settings. The amount of research in patient safety has exponentially grown since the second report was published. PSPs that are more well-established are now being investigated in light of emerging harms, such as PSPs related to infection prevention to address multi-drug resistant organisms. Similarly, emerging PSPs are being investigated for use to address well-established harms, such as the use of clinical decision support to reduce diagnostic errors.

It is clear that many factors impact the success of any PSP on reducing harm. Patient safety culture, teamwork and communication, person and family engagement, providing culturally competent care, reinforcing good practice with education and training, and learning from data are all necessary to ensure success.

ES.8 Future Research Needs

It is clear from the reviews of these PSPs that the importance of context for implementation cannot be overstated. Context plays a large role in the successful uptake and use of a PSP. Setting, safety culture, staffing, and other organizational factors often contribute to harm reduction as much as a PSP itself. More implementation research needs to be conducted across all of the PSPs to understand and work within real-world constraints, rather than conducting studies that may be rigorous but are stripped of that context. We often know what to do, and in these cases, the challenge now is to implement PSPs into a specific facility or setting and have them succeed.

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Introduction

The *Making Health Care Safer (MHCS)* reports from the Agency for Healthcare Research and Quality (AHRQ)[1,2] have provided reliable information for improving the safety and quality of care for patients since 2001. The reports—providing an analysis of the evidence for various patient safety practices (PSPs)—have served as a consolidated and up-to-date source of information for multiple stakeholders, including healthcare providers, health system administrators, researchers, and government agencies. The reports have also identified contextual factors that contribute to successful PSP implementation and provided information about the unintended consequences of implementing proposed PSPs. As a result, the reports have helped to shape national and local actions regarding patient safety issues on which providers, payers, policy makers, and patients and families should focus attention.

Since the second MHCS report was published in 2013, there have been many improvements in patient safety, demonstrating that concerted efforts to improve patient safety, such as AHRQ's Comprehensive Unit-based Safety Program (CUSP), can reduce harm to patients and improve quality of care on a large scale.[3] Building on the success of PSPs in inpatient settings, AHRQ is seeking to support a culture of safety across the healthcare continuum, including in nursing homes, home care, outpatient, and ambulatory settings, and during care transitions. The field of patient safety continues to expand, with an increasing number of PSPs being developed, tested, and implemented across the healthcare spectrum at different scales—from single settings of care to large nationwide integrated delivery systems. For example, AHRQ's Safety Program for Nursing Homes: On-Time Prevention supported national testing of infection prevention and pressure ulcer prevention protocols in nursing homes.

There has been increasing recognition of the importance of understanding context in successful PSP implementation, creating another variable that must be considered when determining which PSPs are feasible for a particular care setting. The Partnership for Patients initiative of the Centers for Medicare & Medicaid Services (CMS) is an example of Federal policymaking that is directly focused on improving patient safety.[4] Financial incentives to reduce harms (e.g., the CMS Hospital-Acquired Condition [HAC] Reduction Program) are holding providers financially accountable for patient safety. Changes in healthcare reimbursement that emphasize value over volume can incentivize safety improvements, such as bundled episodes that require care in the right setting at the right time, as well as effective coordination during care transitions. Current trends in the healthcare marketplace can also be leveraged to enhance safety in all care settings, including expanding technologies to evaluate and monitor patients and share information across care settings. The availability of healthcare data has improved and increased, with great promise for continuously improving patient safety practices. Public reporting is also making quality of care increasingly transparent—for example, via CMS's Hospital Compare and Physician Compare websites.

This evolution of care delivery and the need to take steps to assure patient safety in all settings necessitated an expanded scope for the MHCS report.[5] Recent Federal reports, such as the Department of Health and Human Services (HHS) Office of the Inspector General adverse-event series beginning in 2008—for example, Adverse Events in Rehabilitation Hospitals: National Incidence Among Medicare Beneficiaries—have also spurred this expansion in scope.[6]

In Making Healthcare Safer III we have worked to transition from a review of predominantly acute care PSPs to include PSPs focusing on other settings and other aspects of care, such as transitions. The scope of this report has also expanded to match emerging themes and strategic goals championed by HHS,

including addressing the opioid crisis and emerging health risks (e.g., multidrug-resistant organisms), and overall directives to "put patients first" and to reduce provider burden and burnout—for example, CMS's Patients over Paperwork initiative.

The MHS III report project team began its work by developing a new conceptual framework that does the following: (1) puts the patient in the center; (2) acknowledges that patients are constantly exposed to harms; and (3) proposes patient safety approaches that mitigate patients' past and future vulnerabilities. We have thus taken an approach that is both holistic (considering the whole patient through the continuum of care) and targeted (focusing on what harms are relevant to a particular patient at a particular point in care). Additionally, by following the patient, this framework includes harms during movement between settings and harm risks from existing vulnerabilities and disparities. Starting from the new conceptual framework, we organized the report by "harm areas." This will make the work easier to access for all patient safety stakeholders, who will be able to quickly locate topics of interest and importance to their particular needs and circumstances.

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Methods

The methods by which the full project team—including AHRQ and the patient safety and clinical experts on the Advisory Group (AG) and the Technical Expert Panel (TEP)—completed the report are outlined in Table M.1.

Table M.1: Six-Step Process to Developing the Making Healthcare Safer III Report

	Steps
1.	Development of Conceptual Framework
2.	Identification, Selection, and Prioritization of Harm Area Topics
3.	Identification, Selection, and Prioritization of Patient Safety Practices
4.	Literature Searches
5	Review of the Evidence
6.	Report Development

Step 1. Development of Conceptual Framework

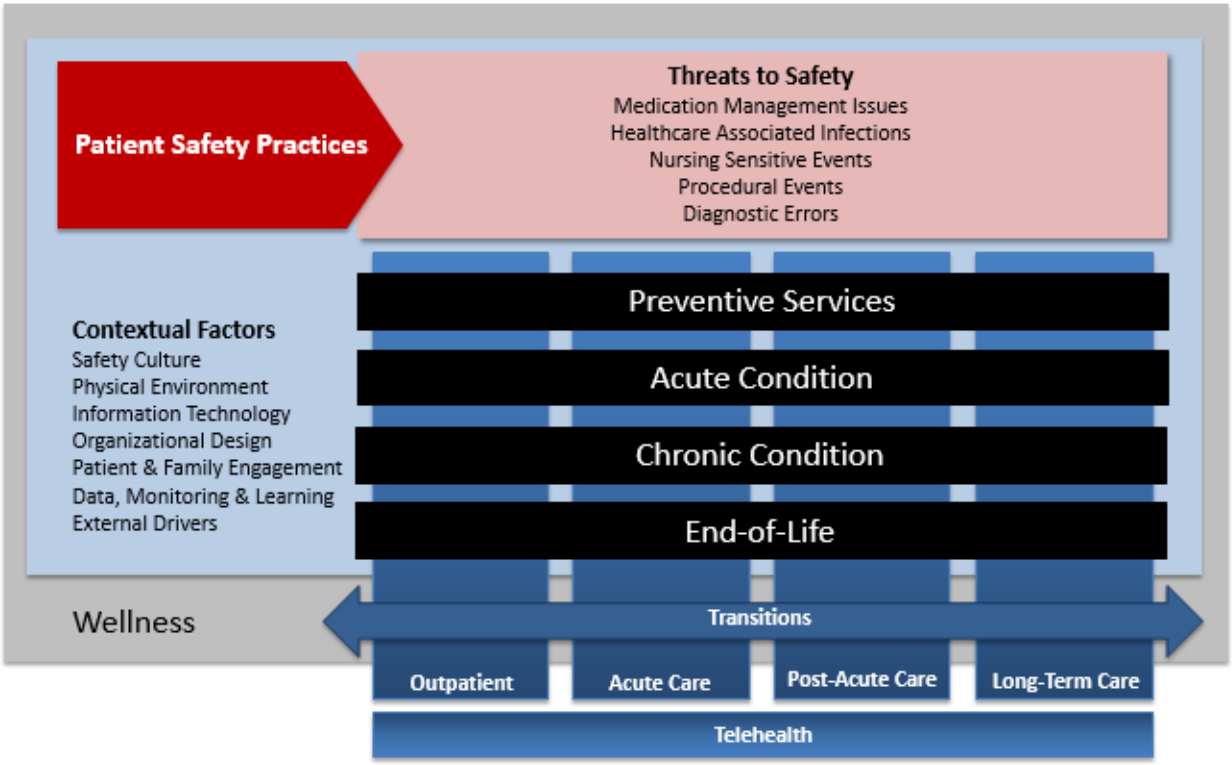
Description of Framework

To help guide the development and content of this report, the project team created a patient-centric framework of safety. The framework focuses on the experience of individuals as they interact with the healthcare system throughout various phases of health and in different settings (Figure M.1). The underlying state of the individual is wellness, in which patients may be receiving intermittent preventive care, such as surveillance for diseases or immunizations, or receiving regular care to maintain stability of chronic conditions. They may transition to and from a state of wellness to acute illness or acute exacerbations of chronic illnesses, or transition toward the end of life. As patients move from state to state, they interact with different providers in different settings, and the resources, tools, culture, and environments specific to those settings.

Throughout these interactions, the patient is exposed to various threats to safety, including medication management issues, healthcare-associated infections, nursing sensitive events (e.g., pressure injury, falls), procedural events, and diagnostic errors. Patient safety practices (PSPs), which are the focus of this report, are discrete and clearly recognizable structures and/or processes used during the provision of care that are intended to mitigate the effects of these threats.

Contextual factors are already in place before the patient interacts with the system or setting of care and remain in place after the patient's care is completed. These work-systems factors are the foundation for success in implementing and sustaining practices aimed at improving safety.[1] The patient "inherits" these elements, which tend not to change acutely but can impact the effectiveness of the practices that are intended to safeguard the patient from harm.[2,3] These factors include safety culture; physical environment; information technology; organizational design (resources and resource allocation, education); person and family engagement; data, monitoring and organizational learning; and external drivers such as Federal and State laws.

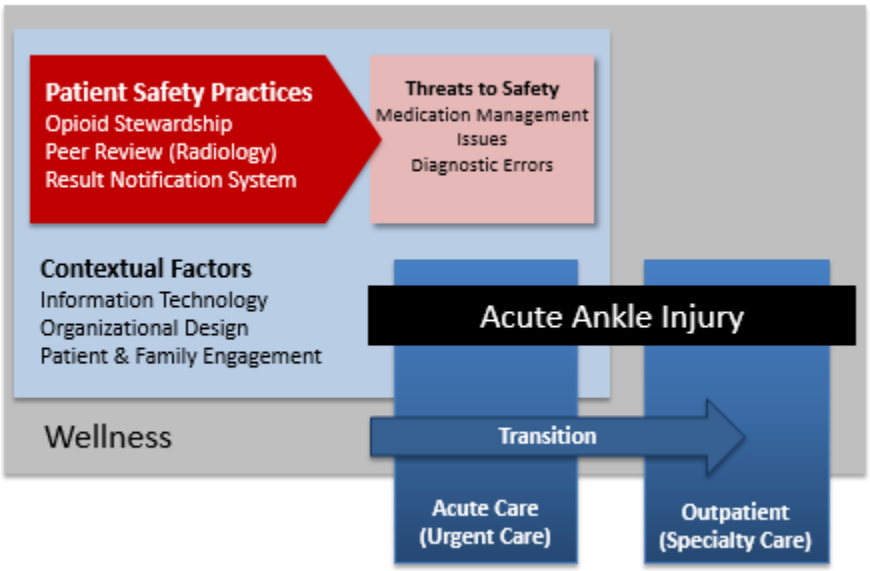
Figure M.1: Framework for the Making Healthcare Safer III Report



Application of Framework

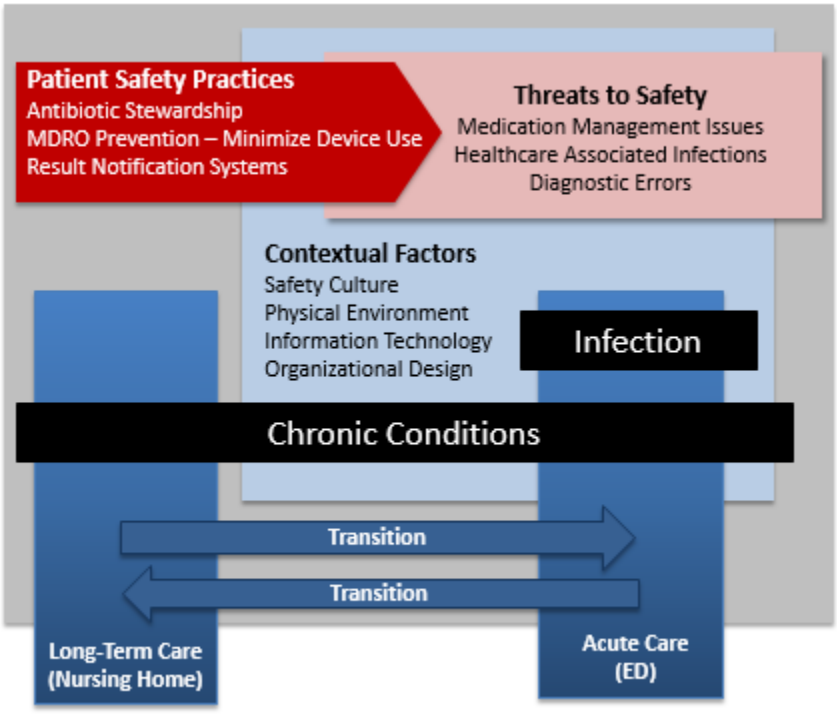
As patients experience a change in health status (e.g., moving from wellness to an acute condition or an acute exacerbation of a chronic illness), they may interact with the healthcare system and are exposed to certain threats due to their condition, where they receive treatment, and from whom. Take for example a patient who suffers an acute ankle injury and goes to an urgent care facility, receives pain medication, and is discharged home with outpatient orthopedic followup. The patient's exposure to safety threats occur during the initial visit to the urgent care facility, the transition from urgent care to the outpatient setting, and the orthopedic visit (Figure M.2). Threats could include medication management issues, particularly if the patient receives a prescription for an opioid pain medication, or diagnostic error, such as missing a fracture during the radiographic interpretation. Corresponding PSPs to mitigate these threats in the urgent care setting may include: (1) opioid stewardship to reduce unnecessary exposure to opioids; (2) peer review of radiographic studies by radiology to minimize the risk of a diagnostic error; and (3) the use of result notification systems to ensure closed-loop communication between the urgent care center and the followup care provider. The successful implementation and use of those PSPs could require contextual factors such as robust patient engagement practices, information technology that supports the result notification, and closed-loop communication with the followup provider. Across the transition to the specialty care and in the specialty care setting itself, there are different exposures to potential harm, with corresponding contextual factors for that environment.

Figure M.2: Example of Application of the Framework—Acute Ankle Injury



In another example of the framework, an elderly patient with chronic medical conditions who resides in a long-term care facility (LTCF) becomes acutely ill with a presumed infection, is sent to the emergency department (ED) for evaluation and treatment, and is then discharged back to the LTCF from the ED (Figure M.3). In this case, the patient is in a closed-loop system, where the journey begins and ends in the LTCF. Specific to the ED visit, the patient may be exposed to multidrug-resistant organisms (MDROs), diagnostic errors (e.g., if the patient has a change in mental status due to something other than infection), and harmful medication interactions. Corresponding PSPs might include screening for delirium, identifying the patient's risk for sepsis, performing antibiotic stewardship, and ensuring communication of any lab results, such as MDRO-positive cultures, back to the LTCF to ensure appropriate precautions and treatment. Contextual factors influencing safety outcomes could include the safety culture of the hospital or a physical environment designed for elder care (e.g., a geriatric ED) to prevent delirium and ensure comfort.

Figure M.3: Example of Application of the Framework—Infection



By centering the patient in the model (viewing patient safety from the patient's perspective), this approach is both holistic (considering the whole patient through the entire continuum of care) and targeted (focusing on what harms are relevant to a particular patient at a particular point in care). Additionally, by following the patient, this model includes harms during movement between settings and harm risks from existing vulnerabilities and disparities. Finally, the model also takes into account important contextual and implementation factors that broadly impact a patient's exposure to harms.

Step 2. Identification, Selection, and Prioritization of Harm Area Topics

The project team conducted an environmental scan of patient safety resources to identify existing and potentially new harm areas. Sources reviewed included AHRQ's PSNet website, the National Quality Strategy, the Joint Commission's National Patient Safety Goals, the National Quality Forum's 2015 Patient Safety Report, Centers for Medicare & Medicaid Services Hospital Value-Based Purchasing Program and Partnership for Patients, the ECRI Institute 2017 and 2016 Top 10 Patient Safety Issues briefs, and Becker's Hospital Review 10 Top Patient Safety Issues for 2018.[4-12] Also, the harm area topics from previous MHCS reports were mapped to those identified during the environmental scan. This exercise identified 8 broad categories of harm (e.g., healthcare-associated infections) and 74 specific harm area topics (e.g., Clostridioides *difficile* infection).

The AG performed an initial review of the identified harm areas and topics, resulting in the exclusion of seven topics, deemed outside the scope of this report. In order to determine which of the remaining 67 topics (shown in Table M.2) should be included, the TEP and AG prioritized the topics on a scale of 1 to 5 (1 = low priority; 5 = high priority) and provided feedback through an electronic survey. If they

selected a priority level of 3 or higher, they also selected one of the following reasons: (1) the harm has not been adequately addressed in the past, (2) this is a newer harm area, or (3) this harm should be examined in a new healthcare setting. If a respondent was unfamiliar with a topic or unsure of the priority, the option "don't know" was available. Fifteen out of 21 TEP and AG members participated, and the results were tabulated by averaging the priority level of each topic. If the topic received a score of 2.5 or lower, it was excluded. The results were presented to AHRQ and, after several iterative rounds, which included adding several topics not among the initial 67 topics, a total of 17 topics were identified for inclusion in the report (Table M.3).

Table M.2. Initial Report Topics

	Initial 67 Topics Presented to the Technical Expert Panel and Advisory Group
1.	Cognitive Errors
2.	Diagnostic Test/Radiograph Interpretation Error
3.	Failure To Rescue
4.	Failure in Diagnosis Testing, Reporting, and Followup
5.	Clinician or Cross-Cutting Communication
6.	Sepsis
7.	Clostridioides *difficile* Infection
8.	Multidrug-Resistant Organisms
9.	Surgical Site Infection
10.	Central Line-Associated Blood Stream Infection
11.	Ventilator-Associated Events
12.	Catheter-Associated Urinary Tract Infection and Hospital-Acquired Urinary Tract Infection
13.	Anticoagulants
14.	Glycemic Events
15.	Opioids
16.	Opioid Stewardship
17.	Antimicrobial/Antibiotic Stewardship
18.	Medication Management in Special Populations
19.	Ordering
20.	Medication Reconciliation
21.	Monitoring
22.	Administration: Intravenous Tubing Connections
23.	Cardiovascular Drugs
24.	Administration: Five Rights
25.	Dispensing
26.	Patient Identification Error
27.	Administration: Infusion Pump-Related Events
28.	Alarm/Alert Fatigue
29.	Delirium
30.	Venous Thromboembolism
31.	Indwelling Catheters/Intravenous Lines
32.	Pressure Injuries
33.	Patient Suicide, Attempted Suicide, and Self-Harm
34.	Elopement
35.	Restraint-Related Injury
36.	Inadequate Cleaning and Disinfection of Instrument
37.	Inappropriate Use of a Device
38.	Postpartum Hemorrhage
39.	Airway Safety
40.	Postoperative Acute Kidney Injury
41.	Postoperative Hemorrhage or Hematoma
42.	Obstetrical Trauma
43.	Radiation Safety-Related Event
44.	Postoperative Respiratory Failure
45.	Wrong Procedure

	Initial 67 Topics Presented to the Technical Expert Panel and Advisory Group
46.	Postoperative Wound Dehiscence
47.	Anesthesia Event
48.	Contrast-Related Kidney Injury
49.	Retained Object
50.	Wrong Patient
51.	Magnetic Resonance Imaging Safety
52.	Transfusion Event
53.	Implementation
54.	Safety Culture
55.	Computerized Physician Order Entry and Clinical Decision Support
56.	Telehealth
57.	Fatigue, Sleep Deprivation, and Burnout
58.	Documentation and Adhering to Patient Preferences
59.	Communication
60.	Health Literacy
61.	Shared Decision-Making and Informed Consent
62.	Teamwork in Healthcare
63.	Use of Simulation Exercises for Patient Safety
64.	Nurse-to-Patient Staffing Ratios
65.	Physical Environment
66.	Work Hour Limits
67.	Workforce Education

Table M.3. Final Report Topics

	Final 17 Topics Presented in the Report
1.	Diagnostic Error
2.	Failure To Rescue
3.	Sepsis
4.	*Clostridium difficile* Infection
5.	Infections Due to Other Multidrug-Resistant Organisms
6.	Carbapenem-Resistant Enterobacteriaceae
7.	Harms Due to Anticoagulants
8.	Harms Due to Diabetic Agents
9.	Reducing Adverse Drug Events in Older Adults
10.	Harms Due to Opioids
11.	Patient Identification Errors
12.	Infusion Pumps/Medication Errors
13.	Alarm Fatigue
14.	Delirium
15.	Care Transitions
16.	Venous Thromboembolism
17.	Cross-Cutting Patient Safety Topics/Practices

Step 3. Identification, Selection, and Prioritization of Patient Safety Practices

Using search terms identified in Step 2, the team librarian identified guidelines and systematic reviews addressing each of the 17 harm topics. The authors, who were assigned to a harm topic (i.e., chapter) based on their background and expertise, screened the results and compiled a preliminary list of PSPs for the report.

A majority of TEP and AG members completed a series of three electronic surveys to determine the final list of PSPs. The first survey was for harms related to diagnostic error and failure to rescue, the second survey was for infection-related harms, and the third survey was for transitions of care, medication

management, and nursing-related events. For each PSP under consideration, respondents were asked to select "include" or "don't include." Overall, inclusion of a PSP in the report was based on how many TEP and AG members selected a specific PSP for inclusion. After a comprehensive review of the results by AHRQ, a master list of 47 PSPs composed of 40 core PSPs and 7 additional AHRQ-identified PSPs was generated.

Step 4. Literature Searches

The authors identified PSP-specific search terms, and the team librarian ran the search terms for every PSP in the MEDLINE® and CINAHL® databases, while also filtering for English-language publications only between the years 2008 and 2018. The librarian ran searches in the Cochrane database early in the process, but found the Cochrane results similar to the MEDLINE results, so the team decided there was no value added to continue with three databases. The individual studies for some PSPs, such as Person and Family Engagement and Cultural Competency, were limited; therefore, the project team followed the approach outlined by Whitlock et al. (2008), which was to search for systematic reviews first and decide if the primary literature was of a determined level of adequate quality.[13] The MeaSurement Tool to Assess systematic Reviews (AMSTAR) was then applied to determine systematic review quality.[14]

The authors and co-authors screened the initial search results to identify titles and abstracts of relevance and if needed, the search terms were adjusted. Next, the studies were screened based on the exclusion criteria established using the population, interventions, comparators, outcomes, and study designs (PICOS) criteria.[15] For example, we excluded studies with specialized populations such as Armed Forces and excluded pilot study designs, particularly when the PSP was considered new or developing. Other exclusion criteria included lack of rigor (i.e., small sample size), lack of intervention or protocol description, PSP not universally applicable to most settings and populations, and study found to be out of scope.

Step 5. Review of the Evidence

The individual studies were identified and selected for inclusion, as seen in the individual chapter Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagrams, which is an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses (Appendix in A in each chapter topic). The studies were then assessed for risk of bias using guidance from Viswanathan et al. (2017).[16] The determination of bias is noted in the Evidence Summary tables (Appendix B in each chapter topic).

For many of the PSPs, if systematic reviews or meta-analyses were identified, they were included in the reviews. The project team also accepted the systematic reviews' assessment of the quality of the studies and overall strength of evidence.

Across the PSPs examined there was wide variation in the rigor of studies included in the evidence reviews, and individual authors were permitted to decide the minimum threshold of quality for including specific studies given the state of the field for each PSP. Similar to the previous report (Making Health Care Safer II),[17] we aimed to apply the criteria drawn from the AHRQ Methods Guide for Effectiveness and Comparative Effectiveness Reviews on strength of evidence derived from Grading of Recommendations, Assessment, Development and Evaluations (GRADE), a framework for developing and presenting summaries of evidence.[18-20] To the extent possible, authors for each review indicated the strength of evidence by practice, outcome, and/or setting.

Step 6. Report Development

The project team, AHRQ, the AG, and the TEP used the conceptual framework to guide the selection of content and organization of the report. Each chapter represents a specific threat to safety (i.e., the harm) that can occur to a patient when exposed to healthcare and includes the targeted PSPs selected for review. All settings were included in searches to understand safety across the continuum of care. When available, each PSP review includes a discussion of the implementation considerations and contextual factors that affect the successful uptake and use of that particular PSP. Each review ends with a summary of gaps and future directions for consideration.

Given the wide variation in study quality available and included in reviews, as well as the variation in strength of evidence (sometimes by setting and specific outcomes), the project team decided against providing a single determination of strength of evidence by PSP (as was done in the previous report). Instead, the project team, with expert input from AHRQ, the TEP and the AG, determined it was most appropriate to provide tables for each harm area that summarize the following by PSP: key safety outcomes; number of studies, systematic reviews, and meta-analyses; settings; and several bullets of key takeaways or points. Table M.2 summarizes these points for each PSP to provide a user-friendly overview of what stakeholders will find in each specific review.

Many existing PSP resources and references are described in a way that is reflective of work conducted through a research or academic lens and in settings that may be more favorable for implementation (e.g., academic medical centers). For this report, the project team has made an effort to synthesize the evidence through a research lens, while placing it in a format that allows for practical application for the end user. The report is directed toward those who work in healthcare and are interested in reducing a particular harm or group of harms that occur during the patient's exposure to the healthcare system.

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1. Diagnostic Errors

Introduction

Background

Diagnostic error, as defined by the National Academy of Medicine in 2015, is "the failure to (a) establish an accurate and timely explanation of the patient's health problem(s) or (b) communicate that explanation to the patient."[1] This definition focuses on the outcomes of the diagnostic process, recognizing that diagnosis is an iterative process that solidifies as more information becomes available. The diagnosis needs to be timely and accurate so that appropriate treatment is initiated to optimize the patient's outcome. Any gaps that arise in the diagnostic process can lead to error. In this chapter we discuss four patient safety practices (PSPs) that have the potential to decrease diagnostic errors: the use of clinical decision support (CDS); result notification systems (RNS); education and training; and peer review.

Importance of Harm Area

Diagnostic error is an increasingly recognized threat to public health, with estimates of 5 percent of adults being affected in the outpatient environment.[2] In the hospital setting, diagnostic error is responsible for 6 to 17 percent of adverse events.[1,3] Diagnostic error has also been shown to be responsible for more closed malpractice claims than other causes.[1,4,5] The Institute of Medicine (now the National Academy of Sciences), in their seminal report on diagnostic safety, concluded that "most people will experience at least one diagnostic error in their lifetime."[1]

PSP Selection

Using systematic reviews and reports, the Technical Expert Panel, Advisory Group, and Agency for Healthcare Research and Quality developed and reviewed an initial list of 23 PSPs that target diagnostic errors. Studies have uncovered two broad categories of underlying root causes: cognitive-based factors, such as failed heuristics, and systems-based factors, such as lack of provider-to-provider communication and coordination.[2,6,7] Therefore, the PSPs selected by consensus for inclusion in this report addressed one or both of these fundamental high-leverage areas.

- **CDS** offers solutions integrated into the workflow to address diagnostic errors by providing stakeholders with knowledge and person-specific information, intelligently filtered or presented at appropriate times, to improve decision making and communication.[8]
- **RNSs** aim to address lapses in communication, a contributing factor to delayed diagnosis and treatment of patients in both ambulatory and inpatient settings.[9,10]
- **Education and training** on the diagnostic process enhance clinical reasoning and decrease biases.[6]
- **Peer review** identifies potential diagnostic errors before they reach the patient and provides feedback with the intent of improving clinical practice and quality.[1,11]

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1.1 Patient Safety Practice: Clinical Decision Support

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Reviewer: Katharine Witgert, M.P.H.

1.1.1 Practice Description

Diagnostic error is a complex and multifaceted problem that requires systems solutions to achieve the necessary changes. Advancements in health information technology (IT) represent thoughtful and sophisticated ways to reduce delayed, missed, or incorrect diagnoses.[1] Contributions of health IT include more meaningful incorporation of evidence-based diagnostic protocols with clinical workflow, and better usability and interfaces in the electronic health record (EHR).

Key Findings:

- CDS has been shown to improve diagnosis in exploratory and validation studies, but the tools need to be fully implemented and tested in clinical settings.
- CDS is best used as an adjunct to the clinician's decision-making process and not as a replacement.
- The diagnoses generated by CDS tools are only as good as the information that is put into the system; if the initial assessment of the patient (e.g., physical exam finding) is incorrect, the output is likely to be incorrect.
- Despite their potential, diagnosis generators have had limited use, owing in large part to challenges integrating them into busy clinicians' workflows.

The Office of the National Coordinator for Health Information Technology defines CDS as providing "clinicians, staff, patients or other individuals with knowledge and person-specific information, intelligently filtered or presented at appropriate times, to enhance health and healthcare. CDS encompasses a variety of tools to enhance decision making in the clinical workflow. These tools include computerized alerts and reminders to care providers and patients; clinical guidelines; condition-specific order sets; focused patient data reports and summaries; documentation templates; diagnostic support, and contextually relevant reference information, among other tools."[2]

CDS represents a range of different interventions, from documentation templates to interruptive popup alerts. The knowledge bases triggering CDS differ as well. Rules-based or logic-based CDS often takes the form of IF-THEN rules. More advanced CDS leveraging artificial intelligence (AI) and machine learning taps awareness of past experiences and patterns in clinical data. These techniques have generated interest and excitement in their potential to better augment clinician intelligence and support decision making.

Several patient safety researchers have suggested that health IT, including CDS, can be leveraged to improve diagnosis, although the data have been mixed.[1,3-7] Therefore, the question of interest for this review is, "Does CDS lead to improved diagnostic performance?" This review's key findings are located in the box above.

1.1.2 Methods

We searched four databases (CINAHL®, MEDLINE®, PsycINFO®, and Cochrane) for articles published from 2008 through 2018 using the terms "diagnostic errors," "delayed diagnosis," "missed diagnosis," and their synonyms. Terms specific to this PSP include "clinical decision support," "medical informatics applications," "artificial intelligence," "computer-aided decision making," "computer-assisted diagnosis," and related terms. The initial search yielded 2,208 results. Once duplicates had been removed and additional relevant referenced articles added, a total of 2,202 articles were screened for inclusion, and

87 full-text articles were retrieved. Of those, 37 studies were selected for inclusion in this review. Articles were excluded if they were not focused on use of CDS specifically for diagnosis (e.g., focus on use of CDS for medication ordering), the outcome was not relevant to this review, the article was out of scope, or the study was of significantly limited rigor.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

1.1.3 Evidence Summary

1.1.3.1 CDS To Generate Diagnoses

1.1.3.1.1 Differential Diagnosis Generators

Differential diagnoses (DDX) are a list of diagnostic hypotheses generated by the clinician during the course of the patient interaction, and are based on information such as the history and physical exam. Often several different diagnostic possibilities are initially present, and as the clinician gathers additional information to support or refute the hypotheses, the list can be narrowed until arriving at the correct diagnosis.

DDX generators are "programs which assist healthcare professionals in clinical decision making by generating a DDX based on a minimum of two items of patient data."[8] DDX generators provide a list of potential diagnoses for consideration, sometimes in order of likelihood based on available information, as a means to improve diagnosis.

The first study discussed is a systematic review and meta-analysis conducted by Riches et al. (2016), which included 36 articles investigating the effects of 11 different DDX generators to retrieve accurate diagnoses (i.e., the correct diagnosis appeared in the list of possible diagnoses). Of note, only five of the tools are still in existence. Using different computational approaches, such as pattern matching and Bayesian probabilities, these diagnostic aids generate lists of DDX for consideration based on clinical data that the user inputs. With respect to the effectiveness of the DDX generators at retrieving accurate diagnoses, the authors concluded that the pooled accurate diagnosis retrieval rate was high, although with considerable heterogeneity (pooled rate=0.70, 95% confidence interval [CI], 0.63 to 0.77; I^2 = 97%, p<0.0001). In the subgroup analyses examining the accuracy of individual DDX generators, ISABEL, one of the tools under evaluation, outperformed all of the other tools, but again, the heterogeneity was considerable (pooled rate = 0.89, 95% CI, 0.83 to 0.94; I^2 = 82%, p<0.0001). When comparing the performance of the DDX tools to that of clinicians, the authors found that the DDX tools were associated with a small, nonsignificant increase in accurate diagnosis retrieval.[8]

In a study by David et al. (2011), the primary objective was to determine the misdiagnosis rate of cellulitis, an infection of the skin and tissue underneath, but the authors also determined whether or not a visually based, computerized diagnostic decision support system (VCDDSS) could generate an improved DDX based on the presenting signs and symptoms for the misdiagnosed patients. The system requires the user to input relevant patient findings (e.g., clinical information, physical examination findings) to generate a ranked list of potential diagnoses. Using a cellulitis-specific module of the VCDDSS, the authors found that the system included the correct diagnosis in the DDX 64 percent of the time. This was significantly greater than the diagnostic accuracy of the admitting residents, who

included the correct diagnosis in their DDX only 14 percent of the time without the use of the VCDDSS (p=0.0003).[9] Gegundez-Fernandez et al. (2017) evaluated the diagnostic performance of Uvemaster, a mobile DDX generator that provides a ranked list of syndromes that cause uveitis, a form of eye inflammation, based on clinical findings. The percentage of cases for which a diagnosis included in the DDX by the app matched the original clinician diagnosis was 96.6 percent (95% CI, 84.1 to 96.6). When the diagnoses were ordered by sensitivity, the original diagnosis was listed within the top three diagnoses generated by the app in 90.9% of cases (95% CI, 84.1 to 96.6) and was listed as the first diagnosis in 73.9% of cases (95% CI, 63.6 to 83.0).[10]

Using real-case vignettes, Segal et al. (2014) and Segal et al. (2016) both evaluated the use of a DDX generator, SimulConsult, on diagnostic performance.[11,12] In the first study, pediatric neurologists were asked to read case vignettes and generate a ranked list of DDX and baseline workups (e.g., diagnostic studies). The clinicians then used the tool, and again provided a list of DDX and workups. The authors found the use of the tool significantly reduced the number of missing diagnoses in the DDX (36% to 15%; P<0.0001) across all clinicians and increased the relevance of the diagnoses listed.[11] In their second paper, Segal and colleagues evaluated the use of SimulConsult by nonspecialists to diagnose pediatric rheumatologic diseases via case vignettes. Similar to the earlier study, when using the DDX generator, the nonspecialists demonstrated a significant reduction in missed diagnoses in the DDX, which fell from 28 percent unaided to 15 percent using the tool (p<0.0001).[12]

Three papers provide evidence that DDX generators modestly improve the diagnostic accuracy of clinicians.[13-15] Using test patient cases in an exam format, Martinez-Franco et al. (2018) compared the diagnostic accuracy of first-year family medicine residents randomized to the control group with those in the intervention group, which used a DDX generator, DXplain. This tool requires the user to enter patients' signs, symptoms, and laboratory tests. Using these data, the tool generates a list of possible diagnoses ranked from highest to lowest probability. The mean percent-correct score and standard deviation was 74.1 ± 9.4 for the control group and 82.4 ± 8.5 for the intervention group (p<0.001).[13] Kostopoulou et al. (2017) developed a prototype DDX generator integrated with a commercial EHR system for use in general practice and tested it using high-fidelity simulation. As soon as the clinician enters the reason for encounter (RfE), the system generates a list of diagnostic suggestions based on the patient's RfE, age, and sex, and groups them according to published incidence rates (i.e., common, uncommon, and rare diagnoses). At the time of the study, the prototype supported three RfEs: chest pain, abdominal pain, and shortness of breath. Using standardized patients simulating 12 cases (4 cases per RfE), 34 general practitioners established their baseline performance with half of the cases and then used the DDX tool with the other half. Diagnostic accuracy improved significantly when using the tool, going from 49.5 percent to 58.3 percent accuracy (p<0.003).[14] Chou et al. (2017) tested the effect of a VCDDSS on the diagnostic accuracy of medical students and dermatology residents in a dermatology clinic. In this pilot study, the students' diagnostic accuracy increased significantly, from 62.5 percent without the VCDDSS to 81.25 percent using the VCDDSS (p<0.01).[15]

1.1.3.1.2 Specific Diagnoses

In addition to the differential diagnosis generators, the search identified papers that describe the development and evaluation of CDS models that determine whether a specific disease is present.

Several papers described rule-based or logic-based CDS for diagnosis where the tool had been integrated into a real clinical setting. Niemi et al. (2009) developed an automated CDS tool to identify

patients admitted to the hospital with pneumonia or heart failure (HF) in real time to aid in timely administration of treatment. The system continually monitors data from existing information systems such as the pharmacy information system, laboratory management system, and radiology management system, and applies rules for pneumonia and HF. When the patient accumulates enough points to be diagnosed with either HF or pneumonia, the system looks to see whether appropriate treatment has been provided (e.g., in the case of pneumonia, an antibiotic) within set time limits, and if it has not, the system generates an alert to the clinician and nursing unit. In the emergency department (ED), the sensitivity and specificity of the system to identify pneumonia was 89 percent and 86 percent, respectively, and in the inpatient setting it was 92 percent and 90 percent, respectively. For HF, the sensitivity was 94 percent and the specificity 90 percent. In addition, the system allowed the hospital to increase compliance with national quality indicators for both of these conditions.[16]

Deleger et al. (2013) developed and tested an automated appendicitis—inflammation of the appendix—risk categorization algorithm for pediatric patients with abdominal pain, based on content from the EHR, and found this system to be comparable to use of physician experts. Using retrospective data, the CDS tool had an average F-measure of 0.867, with a sensitivity (recall) of 0.869 and a positive predictive value (precision) of 0.863.[17] Kharbanda et al. (2016) developed and implemented an electronic CDS tool for pediatric patients with abdominal pain that included a standardized abdominal pain order set, a web-based risk stratification tool, and an ordering alert. Compared with in the pre-implementation period, the trend of computed tomography (CT) scan use during the implementation period decreased significantly each month (p=0.007), and showed a 54-percent relative decrease in CT use in the post-implementation period. The authors found that the decrease in CT use was not associated with the potential unintended consequences of decreased use of CT: significant changes to the rates of appendectomies or missed appendicitis cases.[18]

Chamberlain et al. (2016) developed a mobile smart phone application for screening patients for pulmonary disease and conducted preliminary testing of the algorithms in a clinic setting. The application uses an electronic stethoscope, a method of digitizing peak flow meter readings, and patient questionnaire to identify patients with asthma and chronic obstructive pulmonary disease. The classification algorithms were successful in identifying patients with asthma and chronic obstructive pulmonary disease from the general patient population, with an area under the receiver operating characteristic curve of 0.97. Of note, during the study, patient breath sounds were auscultated using the electronic stethoscope but were evaluated by a pulmonologist. The authors note that they have since been able to develop algorithms to automatically identify abnormal lung sounds, making this technology possible for use by non-pulmonologists and potentially even non-clinicians to assist with diagnosis.[19]

One study focused on a CDS tool patients could use to aid in the screening of skin lesions. Wolf et al. (2013) investigated the use of four readily available smart phone applications designed to evaluate photographs of skin lesions and provide feedback on the risk of malignancy. Clinical images of previously diagnosed skin lesions were submitted for evaluation through the applications. The application with the highest sensitivity (98.1%) sent images directly to a board-certified dermatologist for analysis—essentially tele-dermatology. The sensitivity of the other three applications ranged from 6.8 percent to 70.0 percent, and they relied on automated algorithms to analyze the images.[20]

More-advanced CDS tools leveraging AI and machine learning have generated excitement over the potential to better augment clinician intelligence and support decision making. A cohort of the papers in

our review describe models based on AI techniques to screen for and diagnose specific disorders and diseases. A systematic review by Wagholikar et al. (2011) includes 220 reports of new decision models or evaluations of existing models. The authors generalized their findings and concluded that these techniques have growing popularity for simple classifications but have yet to achieve an acceptable degree of accuracy, particularly for complex medical problems.[21] Other studies of AI identified beyond this systematic review all show promise in identifying disease, although the research continues to be investigational in nature, with a lack of implementation and testing in real clinical settings.[17,22-28]

1.1.3.2 CDS To Assist With Diagnostic Study Interpretation

Several papers included in this review described investigational studies of CDS tools to assist with diagnostic study interpretation, including imaging studies, electrocardiograms (ECGs), and pathology. Although these CDS tools are proof-of-concept in nature, they demonstrate the potential to augment clinician diagnostic performance but not completely replace it.

1.1.3.2.1 Use in Imaging

Three papers identified through the search focused on techniques to assist with interpretation of imaging studies. All were investigational in nature, describing the development and validation of the models.[27,29,30] Herweh et al. (2016) compared the diagnostic performance of an automated machine-learning algorithm to detect acute stroke on CT scans using a standardized scoring method to the performance of stroke experts and novices using the algorithm. Although this study had a small sample size, the automated tool showed similar scoring results to that of experts and better performance than the novices.[29] Bien et al. (2018) used deep learning, a subset of machine learning, to model the complex relationships between images and their interpretations. The model was designed to detect general abnormalities and two specific diagnoses (anterior cruciate ligament [ACL] tears and meniscal tears) on knee magnetic resonance imaging (MRI). For general abnormalities, there was no difference between the performance of the model and the general radiologists. For ACL tear detection, the model was highly specific but not significantly different from the specificity achieved by the radiologists. Radiologists achieved a significantly higher sensitivity (p=0.002) in detecting ACL tears. For meniscal tears, the radiologists achieved significantly higher specificity compared with the model (p=0.003). The authors also found that providing the radiologists with the predictions from the model improved their quality of interpretation of the MRI studies.[27] Li et al. (2018) developed an AI tool to detect nasopharyngeal malignancies under endoscopic evaluation by oncologists. Results indicate that the tool was significantly better in its performance compared with oncological experts; the overall accuracy was 88.0 percent (95% CI, 86.1 to 89.6) versus 80.5 percent (95% CI, 77 to 84).[30]

1.1.3.2.2 ECG Interpretation

In the evaluation of cardiac health, 12-lead ECGs are accompanied by computer interpretations to assist the clinician with diagnoses. These interpretations have been shown to often be inaccurate, primarily because of noisy background signals that interfere with automated pattern recognition by the machine algorithms. However, four studies in this review evaluated ECG interpretations by automated systems, and all found that the systems were no better or worse than human performance alone.[31-34]

Hughes et al. (2017) sought to improve ED workflow and reduce physician interruptions generated by the need to rapidly read triage ECGs for patients with chest pain. The authors examined the accuracy of ECGs identified as normal by the computer with the hypothesis that these normal ECGs would not have

clinically significant findings. The negative predictive value of the normal computer interpretations was 99 percent (95% CI, 97 to 99), indicating that there may be a group of ECGs for which rapid physician re-interpretation is not necessary, thereby reducing interruptions.[31]

Two studies tested the accuracy of the diagnoses generated by the automated systems compared with human interpretation. Given that nonexpert ECG readers are more likely to rely on automated system interpretation for diagnosis, Hakacova et al. (2012) compared the accuracy of two different rhythm analysis software products with the accuracy of nonexpert readers and found no significant difference in performance. The authors also looked at the accuracy of the software for ECGs for which the diagnosis by the nonexpert was incorrect, and found that only 28 percent+/-10 percent (system A) and 25 percent+/-10 percent (system B) of the automated diagnoses were correct.[33] Mawri et al. (2016) examined whether the use of automated ECG interpretation would affect time to treatment for patients with ST-elevation myocardial infarction. The authors found that the computer-interpreted ECGs failed to identify 30 percent of patients with ST-elevation myocardial infarction and found significant differences in two quality-of-care measures: immediate emergency physician interpretation led to faster catheterization laboratory activation time ($p<0.029$) and faster median door-to-balloon time ($p<0.001$).[34] A study by Cairns et al. (2017) tested a semi-automated system that attempts to overcome the accuracy issues of automated systems by leveraging the strengths of human performance (i.e., the ability to recognize patterns through noisy signals). The system integrates a rule-based computer algorithm with interactive questions and prompts for the clinician to generate multiple diagnostic possibilities. The use of this semi-automated system increased the number of correct interpretations, but the increase was not statistically significant.[32]

1.1.3.2.3 Use in Pathology

Two studies evaluated the use of AI to aid in the diagnostic work of pathologists.[35,36] Vandenberghe et al. (2017) developed and evaluated the use of deep learning, an AI method, to identify specific cancer cell types. For 71 breast tumor samples, they found that the use of this computer-aided diagnosis tool had a concordance rate of 83 percent with pathologist review. The pathologist re-reviewed the 12 samples that had discordance between the diagnoses of the pathologist and the computer-aided diagnosis tool, prompting modifications to 8 of the original diagnoses.[35] Xiong et al. (2018), also using deep learning, developed and tested an AI-assisted method for the automatic detection of mycobacterium tuberculosis. Results showed high sensitivity (97.9%) and moderate specificity (83.6%), with 2 false negatives and 17 false positive cases due to contaminants.[36]

1.1.3.3 CDS To Identify Patients at Risk for Diagnostic Errors

Three studies examined the use of CDS tools to identify patients who are at risk of having a diagnostic error.[35,37,38] The systems were all effective at identifying at-risk patients and allowed potential diagnostic errors, including missed or delayed diagnoses, to be prevented, while saving the clinicians time by reducing manual workloads and cognitive burden. As previously discussed, the study by Vandenberghe et al. (2017) used discordance between the diagnoses generated by the AI tool and the diagnoses by the pathologist to flag cases where there may be a high risk of diagnostic error.[35]

Koopman et al. (2015) developed a system to compare final radiology reports with final ED diagnoses to ensure that the ED identified and appropriately treated an abnormality on radiologic examination. A text analysis system first screens radiology reports to identify limb abnormalities, including fractures, dislocations, and foreign bodies. If the system identifies an abnormality, the diagnosis is reconciled with

the ED diagnosis, as defined by International Classification of Diseases, 10th Revision (ICD-10) codes. If there is a discrepancy, the chart is flagged as a possible misdiagnosis, allowing immediate review and followup. Across the three settings in which the study took place, 274 of 2,018 patients (13.6%) with radiologic abnormalities were flagged for potentially missed diagnoses, and the chart was reviewed manually. Nine of the cases were identified as truly missed diagnoses, and the other instances were due to the ED ICD-10 discharge diagnoses being ambiguous, and not indicative of a diagnostic error. The value in this method is that clinicians need to review only a small subset of the radiology reports, in this case 11 percent of the total number or radiology studies, to determine whether there were potentially missed diagnoses.[37]

Murphy et al. (2015) applied electronic triggers to EHR data to identify the presences of "red flags," exclude records for which further evaluation is not warranted (e.g., patients in hospice), and identify the presence of a delay in diagnostic evaluation for three conditions: colon cancer, lung cancer, and prostate cancer. Examples of red flags include positive fecal occult blood testing for colon cancer, concerning imaging studies for lung cancer, and elevated prostate-specific antigen for prostate cancer. Delayed diagnostic evaluation was defined by the absence of documented followup action. The trigger flagged 1,256 patients out of 10,673 patients with abnormal findings (11.8%) as being high risk for delayed diagnostic evaluation. Of these, 749 were true positives, a positive predictive value of 59.6 percent. Times to diagnostic evaluation were significantly lower in intervention patients compared with control patients flagged by the colorectal trigger and prostate trigger. There was no significant difference for the lung trigger.[38]

1.1.3.4 Unintended Consequences

In general, the CDS tools have an added benefit of improving access to specialized care by providing the clinician with assistance in diagnosing conditions that would typically fall in the realm of a specialist.[12,19,27]

Several of the CDS tools identified in this review, in addition to improving diagnostic accuracy, would also allow prioritization of work, creating greater efficiencies and improving workflow once implemented in clinical settings.[27,31,38] These systems flagged studies or diagnoses that required followup, allowing the clinicians to prioritize their work.

For the CDS tools that generate DDX, Graber and Mathew (2008) raised the concern that presenting the clinician with a long list of diagnostic possibilities could be distracting or lead to unnecessary testing and procedures.[3] Elkin et al. (2010) suggested that these tools actually reduce the cost of care by assisting the clinician with a broader differential diagnosis list, which is more likely to contain the correct diagnosis. In the case of the DXplain tool, providing the list of diagnoses in order of likelihood can lead to the clinicians evaluating the more likely diagnoses earlier.[39]

1.1.4 Implementation

1.1.4.1 Facilitators

Since many of the studies were conducted to validate algorithms or were exploratory in nature (e.g., testing AI algorithms to determine their ability to predict correct diagnosis), few described experiences with implementation in real clinical settings.

In the meta-review of systematic reviews by Nurek et al. (2015), the authors determined the features and effectiveness of computerized diagnostic decision support systems for medical diagnosis in primary care. The authors identified conditions that need to be met if a fully integrated CDS tool for diagnoses is to be successfully implemented and used: the tool can readily be integrated into EHRs; is based on standard terminologies, such as diagnosis codes (e.g., ICD-10); has the ability to be easily updated; is thoughtfully integrated into the clinicians' cognitive workflow; and interfaces with the clinicians at appropriate action points.[40]

1.1.4.2 Barriers

The information generated by CDS for use in diagnosis is only as good as the information that is put into the system. For example, if the clinician interprets the physical exam incorrectly (e.g., saying that a physical sign is absent when it is present) and inputs that incorrect information into the tool, that error may negatively affect any diagnosis that is partially based on the presence of that sign.[10,11,25,37] In the study by Koopman et al. (2015), discharge diagnoses, as indicated by ICD-10 codes, are reconciled with the diagnosis from radiology reports. If the ICD-10 code is incorrect, the system may not recognize a potential missed diagnosis.[37] Gegundez-Fernandez et al. (2017) commented that accurate diagnosis can be achieved only if the clinician's assessment of the patients' signs and symptoms is correct, because the automated system will process only data that humans introduce.[10]

In the case of ECG interpretation, accurate ECG recording depends on many variables, including lead placement, weight, movement, coexisting electrolyte abnormalities, and symptoms. If the placement is wrong (e.g., leads are placed in wrong location), the interpretation may be wrong.[33,34]

1.1.5 Resources

Additional information can be found at the HealthIT.gov site, which offers information on how the use of EHRs can improve diagnosis (https://www.healthit.gov/topic/health-it-and-health-information-exchange-basics/improved-diagnostics-patient-outcomes) and through the National Academies report Improving Diagnosis in Health Care (http://www.nationalacademies.org/hmd/Reports/2015/Improving-Diagnosis-in-Healthcare).

1.1.6 Gaps and Future Directions

Although research in the use of CDS for diagnosis has been conducted for many years, there has been a failure to implement these tools widely, and published work continues to be predominantly that of exploratory studies in educational settings, testing of algorithms using retrospective data, or evaluation through simulation.[8] Wagholikar et al. (2012), in their systematic review of modeling techniques for diagnostic decision support, provided several suggestions for research and future work in this area, including evaluation of these applications in clinical settings.[21]

1.1.6.1 Leveraging the "CDS Five Rights" Approach

A useful framework for achieving success in CDS design, development, and implementation is the "CDS Five Rights" approach.[41] The CDS Five Rights model states that CDS-supported improvements in desired healthcare outcomes can be achieved if we communicate: (1) the right information: evidence-based, suitable to guide action, pertinent to the circumstance; (2) to the right person: considering all members of the care team, including clinicians, patients, and their caretakers; (3) in the right CDS intervention format, such as an alert, order set, or reference information to answer a clinical question; (4) through

the right channel: for example, a clinical information system such as the EHR, a personal health record, or a more general channel such as the Internet or a mobile device; (5) at the right time in workflow, for example, at the time of decision/action/need. CDS has not reached its full potential in driving care transformation, in part because opportunities to optimize each of the five rights have not been fully explored and cultivated.[42]

Providing the Right Information to the End User: The process of integrating real-time analytics into clinical workflow represents a shift towards more agile and collaborative infrastructure building, expected to be a key feature of future health information technology strategies. As interoperability and big data analytics capabilities become increasingly central to crafting the healthcare information systems of the future, the need to address issues that ease the flow of health information and communication becomes even more important. Without tools that select, aggregate, and visualize relevant information among the vast display of information competing for visual processing, clinicians must rely on cues by "hunting and gathering" in the EHR. Alerts that embody "right information" should provide just enough data to drive end user action, but not so much as to cause overload.[43] Overload can create alert fatigue and lead to desensitization to the alerts, resulting in the failure to respond to warnings, both important and less important. Experience from the use of CDS in the medication ordering process has demonstrated this paradoxical increase in risk of harm due to alerts that were intended to improve safety.[44,45]

Providing Information in the Right Format: Lack of knowledge regarding how to present CDS to providers has impeded alert optimization, specifically the most effective ways to differentiate alerts, highlighting important pieces of information without adding noise, to create a universal standard. The potential solution that CDS represents is limited by problems associated with improper design, implementation, and local customization. In the absence of evidence-based guidelines specific to EHR alerting, effective alert design can be informed by several guidelines for design, implementation, and reengineering that help providers take the correct action at the correct time in response to recognition of the patient's condition.[46]

Right Workflow: A well-thought-out user-centered design or equivalent process during the implementation phase includes critical elements of leadership buy-in, dissemination plans, and outcome measurements. Knowledge needs to be gained about how to implement the CDS and how to create an interface between the system and the clinician that takes into consideration the cognitive and clinical workflow.[27,47] The optimal approach to CDS should not be focused primarily—or even secondarily—on technology. Implementation is about people, processes, and technology. Systems engineering approaches, including consideration of user experience and improvements in user interface, can greatly improve the ability of CDS tools to reach their potential to improve quality of care and patient outcomes. The application of human factors engineering in determining the right workflow includes but is not limited to ethnographic research including workflow analysis and usability testing.

1.1.6.2 Trust in Automation

CDS is meant to augment clinician performance, not replace it, making it an imperative to carry existing work forward into actual clinical settings.[1] CDS has advanced to the point of becoming a "type of automation that supplements the human powers of observation and decision." Technologies related to big data bring both exciting opportunities and worrying prospects for misinformation, disinformation,

and falsified information. Further work is required to demonstrate clinical and economic evidence using data from a population representative of the health system in a way that clinicians find trustworthy.

1.1.6.3 Measurement

Successful CDS deployment requires evaluating not only whether the intended clinicians are using the tool at the point of care, but also whether CDS use translates into improvements in clinical outcomes, workflows, and provider and patient satisfaction. However, success measures are often not clearly enunciated at the outset when developing or implementing CDS tools. As a result, it is often difficult to quantify the extent to which CDS has been effectively deployed, as well as whether it is effective at managing the original diagnostic problem it was designed to address.

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1.2 Patient Safety Practice: Result Notification Systems

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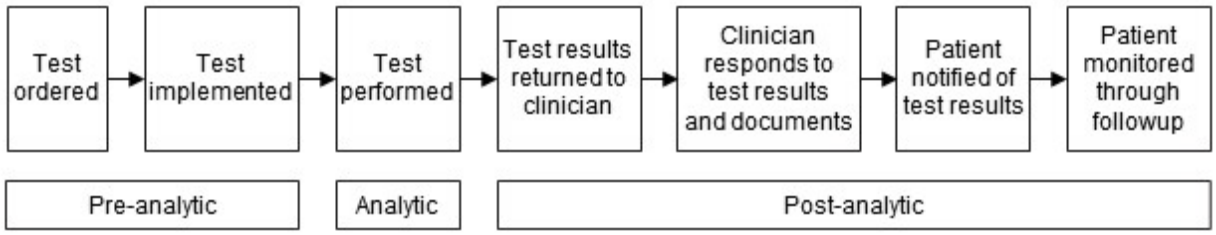
1.2.1 Practice Description

Failure to communicate test results has been repeatedly noted as a contributing factor to delayed diagnosis and treatment of patients in both ambulatory and inpatient settings.[1,2] Due to the negative impact on patients of missed communication of results, The Joint Commission made timely reporting of critical results of tests and diagnostic procedures a National Patient Safety Goal (NPSG.02.03.01) for their Critical Access Hospital and Hospital Programs.[3]

The laboratory and radiographic testing process has three distinct phases: the pre-analytic phase, during which the test is ordered and that order is implemented; the analytic phase, when the test is performed; and the post-analytic phase, in which results are relayed to the ordering clinician, who acts upon the results, and notifies and follows up with the patient (Figure 1.1).[4]

Figure 1.1: Conceptual Framework of the Testing Process[4]



The post-analytic phase, specifically the step where results, clinically significant test results (CSTR) in particular, are relayed back to the ordering clinician, is a source of diagnostic error.[4,5] To reduce errors that occur during this step, experts have advocated for the use of automated alert notification systems to ensure timely communication of CSTR.[5-7] RNSs, which are the focus of this review, vary. They can be completely automated, where an abnormal result generates an alert to the ordering clinician; or the RNS may require manual activation by the clinician. There are also a variety of modalities that can be used to alert the practitioner of actionable test results, including short messages relayed via mobile phones; emails; and results (with or without accompanying alerts) in the EHR.[8]

1.2.2 Methods

The question of interest for this review is, "Do RNSs for radiologic and laboratory tests improve timeliness and reliability of receipt of results and action on the results?" To answer this question, we searched two databases (CINAHL® and MEDLINE®) for articles published from 2008 to 2018 using the terms "diagnostic errors," "delayed diagnosis," "missed diagnosis," and synonyms. Additional terms included "alerts," "automated systems," "communication systems," "critical test results," "alert notification," and other similar terms. The initial search yielded 1,965 results. Once duplicates had been removed and additional relevant articles from selected other sources added, a total of 1,981 articles were screened for inclusion, and 46 full-text articles were retrieved. Of those, 17 were selected for inclusion in this review, including 2 systematic reviews. Articles were excluded if the outcomes were not

relevant to this review, the article was out of scope (including not quantitative), the study was of limited rigor, or if the study design or results were insufficiently described.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

1.2.3 Evidence Summary

The papers selected use RNS for CSTR, both life-threatening and nonurgent, for laboratory or radiological studies in inpatient and ambulatory settings. The RNS varied across studies and included both manual and automated mechanisms to generate the alert, and a variety of asynchronous and synchronous modalities to receive the alert. Outcomes included alerts being received (and acknowledged) by a clinician, and alerts being received and/or acted upon by the clinician (Table 1.1).

We reviewed one meta-analysis and one systematic review, both focusing on automated RNSs for laboratory results.[8,9] There were also several single studies of high-quality design, with two randomized controlled trials[10,11] and three cluster-randomized controlled trials.[12-14] Most of the single studies were quasi-experimental, with either pre/post or post-only designs.

Key Findings:

- Performance of result notification systems varied by type of test result, setting, synchronous versus asynchronous communication, and manual versus automated alerting mechanisms.
- For both critical and non-critical CSTR of radiologic studies, lab studies and tests pending at discharge, the use of RNS showed some positive but often mixed results in the timeliness and reliability of receipt, action acknowledgment, and action on the test results.
- Policies and procedures that aligned with the system, mindful integration of the RNS into the workflow and the EHR, and appropriate staffing were identified as factors supporting successful RNS.
- Significant barriers to successful implementation include poor system design, the lack of connectivity between hospitals and non-network physicians, challenges associated with changing schedules and providing critical alerts to physicians who may not be available, and variations in clinician response to alerted results.

1.2.3.1 Use of RNS for Radiologic Studies

Five studies focused on the impact of RNS on the communication of CSTR in radiology. The CSTR ranged from results requiring treatment but not immediately life-threatening to immediately life-threatening results. The impact of the RNS on the communication of results, and action taken on the results, was mixed.

Two studies, both by Lacson and colleagues, evaluated the use of an Alert Notification of Critical Results (ANCR) system to facilitate communication of critical imaging test results to ordering clinicians at a large academic medical center. The ANCR system, integrated into the clinical workflow, allows both synchronous communication (e.g., pagers) for results related to life-threatening conditions, and asynchronous communications (e.g., email). The system relies on radiologists who read and interpret the radiographic images to initiate an alert to the ordering clinician, rather than using a completely automated system. In the first study, the authors evaluated the ANCR system on adherence to a hospital policy for timeliness of notifications that is based on criticality of the imaging result.[15] Using a pre/post study design, the authors found a significant improvement in adherence to the timeliness policy, with adherence increasing from 91.3 percent before the ANCR intervention to 95.0 percent after ($p<0.0001$).

In the second study, also using a pre/post study design, the authors evaluated the impact of implementing both the ANCR system and the policy of communication of the critical imaging test result in reducing critical results that lacked documented communication (date, time, and name of ordering clinician contacted). After the implementation of the critical imaging test result policy and the ANCR, critical results lacking documented communication decreased nearly fourfold between 2009 and 2014 (0.19 to 0.05, p<0.0001).[16]

Table 1.1: Overview of Single Studies

Author, Year	Clinically Significant Test Result Type & Severity	Result Notification System	Setting
Chen et al., 2011[21]	Laboratory—critical	Automated phone alert using short message service (SMS)	Inpatient/academic medical center
Dalal et al., 2014[12]	Test pending at discharge (TPAD)	Automated email system	Inpatient and outpatient/academic medical center
Dalal et al., 2018[13]	TPAD	Automated email system	Inpatient and outpatient/academic medical center
Eisenberg et al., 2010[10]	Radiologic—nonurgent	Manual, Web-based electronic messaging system	Academic medical center/inpatient and outpatient
El-Kareh et al., 2012[27]	TPAD	Automated email system	Inpatient and outpatient/academic medical center
Etchells et al., 2010[10]	Laboratory—critical	Automated paging system	Inpatient/academic medical center
Etchells et al., 2011[11]	Laboratory—critical	Automated alerts via mobile phone or pager and link to clinical decision support for alert	Inpatient/academic medical center
Lacson et al., 2014[15]	Radiology—critical	Manually triggered alert via pager or email	Inpatient/academic medical center
Lacson et al., 2016[16]	Radiology—critical	Manually triggered alert via pager or email	Inpatient/academic medical center
Lin et al., 2014[23]	Laboratory—critical	Automated phone text-message alert	Outpatient/academic medical center
O'Connor et al., 2016[17]	Radiology—nonurgent	Manually triggered alert via pager or email/alert in electronic medical record (EMR)	Outpatient/academic medical center
O'Connor et al., 2018[24]	Laboratory—nonurgent	Manually triggered alert via pager or email	Outpatient/academic medical center-affiliated community hospital
Park et al., 2008[20]	Laboratory—critical	Automated phone alert using SMS and callback	Inpatient/academic medical center
Singh et al., 2009[18]	Radiology—critical	Automated EMR alert notification system	Outpatient/U.S. Veterans Affairs (VA) medical center
Singh et al., 2010[5]	Laboratory—noncritical	Automated EMR alert notification system	Outpatient/VA medical center

In a study linked to the work of Lacson and colleagues, O'Connor et al. (2015) integrated an ANCR with an EHR-based results management application and evaluated its adoption and impact on followup of actionable results by primary care providers (PCPs) in the outpatient setting. Prior to integration, PCPs used the EHR application to track and acknowledge results from laboratory studies. The integration of the two systems allowed the PCPs to receive and acknowledge the ANCR-generated non-urgent CSTR alerts in the EHR or through the ANCR system. During the 2 years after implementation, 15.5 percent of the ANCR alerts were acknowledged in the EHR (15.6% year 1, 15.4% year 2). In the post-intervention period, there was a significant difference (p=.03) between the proportion of alerts acted upon that were

acknowledged in the EHR application (79%; 95% CI, 52 to 92) compared with the alerts acknowledged in the ANCR system (97%; 95% CI, 90 to 99).[17]

Singh et al. (2009) evaluated the impact of an EHR-based system to alert clinicians to critical imaging results in a multidisciplinary ambulatory clinic at a large Veterans Administration (VA) medical center and its five satellite clinics. The VA EHR has an embedded notification system for alerting clinicians to CSTR in a "View Alert" window. The system requires that the radiologist reading an image flag abnormal imaging results, and these alerts are then transmitted to the "View Alert" window. During the study period there were 1,196 abnormal imaging alerts generated (0.97% of all imaging studies), and 217 (18.1%) of these alerts remained unacknowledged (i.e., the ordering clinician did not click on and open the alert) after 2 weeks. Using logistic regression, variables associated with a lack of acknowledgement included physician assistants compared with attending physicians (odds ratio [OR]: 0.46; 95% CI, 0.22 to 0.98); resident physicians compared with attending physicians (OR: 5.58; 95% CI, 2.86 to 10.89); and dual communication (i.e., communication with two clinicians) compared with communication with a single clinician (OR: 2.02; 95% CI, 1.22 to 3.36). Notably, 92 alerts, both acknowledged (n=71) and unacknowledged (n=21), lacked followup at 4 weeks.[18]

Eisenberg et al. (2010) evaluated the use of a Web-based electronic messaging system to communicate non-urgent CSTRs and recommend followup to ordering clinicians. As in the system used in the studies by Lacson and colleagues, the alerts were initiated by radiologists responsible for interpreting images through a web-based application. The request is received by a facilitator, who is then responsible for conveying the results to the ordering clinician. Once the results have been conveyed, the facilitator sends a confirmation back to the radiologist to close the loop. The authors recognized that the study design was weak (post-only with a satisfaction survey). They authors found that 82.2 percent of the alerts were communicated to the ordering clinicians within a 48-hour window, as defined by the time the radiologist submits a communication request to the time the facilitator conveys the communication to the ordering physician. The authors also found that the day of week affected the outcome, with more alerts submitted by the radiologists Monday–Thursday before 3 p.m. communicated within 48 hours (93.7% +/- 2.4), compared with alerts generated on Thursday afternoon through Sunday (73.0% +/- 9.2). The authors incidentally noted that for one-third of communications in which additional imaging or followup had been recommended, the electronic medical record had no documentation that these services were actually performed.[19]

1.2.3.2 Use of RNS for Laboratory Studies

Nine of the included studies focused on the use of RNS for laboratory studies, including one meta-analysis and one systematic review. As was the case for the RNS for radiologic studies, the evaluated interventions varied across studies and included paging, email, text messages, and EHR alerts. Results of the RNS were mixed.

The meta-analysis and the systematic review examined the effectiveness of automated electronic RNS to alert ordering clinicians to CSTR, and found insufficient/inconclusive evidence for the use of these systems.[8,9] The systematic review by Liebow et al. included four studies, two of which were used to calculate a standardized effect size (ES).[10,20] Etchells et al. reported results of a randomized controlled trial evaluating an automated RNS that sends critical laboratory values directly from the laboratory information system to a pager carried by the ordering physician. The objective was to evaluate the effect of the system on physician response time, defined as the time from when the critical result is

entered into the lab system to the time an order is written in response to the critical value, or the documented time of treatment (whichever is relevant). They found a 23-minute reduction in median response time, 16 minutes (interquartile range [IQR] 2–141) for the automated paging group, and 39.5 minutes (IQR 7–104.5) for the usual care group, but this difference was not statistically significant.[10] Park et al. used a pre/post design to test the impact of a short message service and callbacks for action on critical hyperkalemia results. Across all patients in both intensive care units and general wards, the median and interquartile ranges for the clinical response times, defined as the frequency of clinical responses divided by the number of critical value alerts during a given time period, were significantly reduced, going from 213.0 minutes in the intensive care unit and 476.0 minutes in the general wards to 74.5 minutes and 241 minutes, respectively ($p<.001$).[20] Using Cohen's d, Liebow and colleagues calculated a grand mean reduction of time to communicate critical results for these two studies (d=.42; 95% CI, 0.23 to 0.62), indicating that the time to report a randomly selected CSTR using the automated system will be shorter than with a randomly selected manually reported value 61.8 percent of the time. Liebow et al. gave an overall strength of evidence rating of "suggestive" for automated RNS.[8]

Liebow et al. also conducted a systematic review of five studies evaluating the use of centralized call centers that communicate critical CSTRs to the ordering clinician.[8] Four of the five studies whose primary outcome was percent of calls completed within a specified interval after results were available from the laboratory (either <30 min or <60 min) contained sufficient data to calculate a standardized ES. The results of a random-effects meta-analysis support the implementation of call centers (mean OR=22.2; 95% CI, 17.1 to 28.7). This translates to critical lab values being reported faster with the call system than results reported via usual means (e.g., call to unit by laboratory technologist) approximately 88.6 percent of the time. Liebow et al. consider the overall strength of evidence for call center systems to be "moderate."

A systematic review by Slovis et al. included 34 articles published through 2016, representing 40 years of research related to asynchronous automated electronic laboratory RNS.[9] Although a wide variety of systems were represented and the study designs and outcomes differed, the authors summarized that these systems can be successfully implemented and improve timeliness of result notification and action. On closer examination of the five most recent studies that were included in the review and also identified through our search, the findings neither fully supported nor opposed use of these systems.[10,11,20-22]

In the first of two randomized controlled trials by Etchells et al. (2010) and included in the systematic review by Slovis et al., an automated paging system to convey critical laboratory results was evaluated in an urban academic medical center.[10] As described above, although there was a 23-minute reduction in the median response time, this was not statistically significant. In their second study, Etchells et al. (2011) combined an automated RNS with CDS.[11] The alerts, sent via text to a smart phone or to a pager, contained information about the specific patient and the abnormal result, and offered a URL to a webpage with decision support for the specific alert. The primary outcome was the proportion of pre-defined potential actions that were completed in response to the alert. A secondary outcome was the number of adverse events, defined as worsening of the patient's condition or complications related to the treatment of the condition. The median proportion of potential clinical actions that were completed was 50 percent (IQR 33–75%) with the alerting RNS with CDS and 50 percent (IQR 33–100%) without it, a difference that was not statistically significant, Without the system, there were 111 adverse events (33%) within 48 hours following an alert and with the alerting system on, there were 67 adverse events

(42%); a 9 percent increase when using the alerting system that bordered on statistical significance (p=0.06).

In addition to the five studies included in Slovis et al, two additional studies about laboratory RNS were reviewed for this report. In the outpatient department of a large (2,500-bed) tertiary teaching hospital in Taiwan, Lin et al. studied the impact of a phone-based RNS on clinical outcomes of patients taking the anticoagulant warfarin.[23] Their RNS automatically generates and delivers text messages about critical lab CSTRs to providers' mobile phones 24 hours a day, 7 days a week. Using a pre/post study design, the investigators found no significant differences in warfarin-associated adverse events. The rate of major venous thromboembolism events was 1.6 percent for both the manual alert period and the test RNS period. The rate of major hemorrhage requiring an ED visit or hospital admission was 3.1 percent in the manual alert period and 4.2 percent in the RNS alert period (p=0.198). As with the findings in Etchells et al. (2010), the secondary outcome of timeliness of physician followup actions after receipt of an automated critical alert was not significantly improved (11.13 ± 7.65 days for manual alert period vs. 11.32 ± 8.17 days for phone-based RNS period; p=0.814).

Expanding on the work previously described by Lacson and O'Connor, O'Connor et al. (2018) examined the use of the ANCR for communication of non-urgent clinically significant pathology reports indicating new malignancies.[24] After a pathologist identifies the CSTR, the ordering physician is contacted via pager about critical or urgent results, and via pager or secure email for non-urgent results, and the CSTR is entered into the ANCR system. For results that the ordering physician does not acknowledge, the system sends reminders to the pathologist and the ordering physician. Acknowledgment of the CTSR within 15 days, the institutional policy for non-urgent CSTR, was documented for 98 of 107 cases (91.6%) before the RNS had been implemented, and for 89 of 103 (86.4%) after the RNS had been implemented, a difference that was not statistically significant. There was also no significant difference in median time to acknowledgment for new malignancies when comparing the pre-RNS period (7 days; IQR 3–11) and post-intervention period (6 days; IQR 2–10). In the post-RNS period, for CTSR using the ANCR, median time to acknowledgment was significantly shorter than when an ANCR alert was not generated (2 vs. 7 days, p=0.0351).

1.2.3.3 Use of RNS for Tests Pending at Discharge

Tests pending at discharge (TPADs) involve transitions, span more than one setting (e.g., the hospital setting to the ambulatory setting), and often involve more than one clinician (e.g., inpatient attending physician and outpatient primary care physician). The risk of missed communication and potential harm to patients is greater during these transitions between settings and clinicians.[25,26] Three cluster-randomized controlled studies from a single institution investigated the use of an automated email CSTR notification system for TPAD.[12-14] Awareness and confirmed acknowledgement of the test result after discharge were statistically higher in the intervention group, but there was no difference between the intervention and control groups in documented actions taken in response to the test results (i.e., receiving/confirming receipt of a test result did not improve timeliness of acting upon that information).

Two cluster-randomized controlled studies by Dalal et al. (2014 and 2018) included inpatient attending physicians and PCPs whose patients were discharged from inpatient cardiology and medicine units in a large academic medical center, and who had TPAD for both radiology and laboratory studies.[12,13] In these studies, a patient's discharge triggers a series of electronic events that updates the status of any remaining TPADs on a daily basis. As results for these pending tests are finalized, the responsible in-

patient attending and outpatient PCP receive an automatic email containing the test result. The primary outcome of the first study was self-reported awareness of the TPAD result by the patient's inpatient attending physician.[12] There was a statistically significant increase in the awareness of TPAD results by attending physicians for patients assigned to the intervention compared with those assigned to usual care (76% vs. 38%, adjusted/clustered OR 6.30, 95% CI, 3.02 to 13.16, p<0.001). The second study was larger, and the primary outcome was the proportion of actionable TPADs with documented action in the EHR.[13] For the primary outcome of documentation of action, there was no significant difference between the intervention and usual care groups (60.7% vs. 56.3%). For those that had an action documented, the median days between result notification and documented action was significantly lower in the intervention group (9 days, CI, 6.2 to 11.8) compared with the usual care group (14 days, 95% CI, 10.2 to 17.8) (p=0.04).

In the third study, by El-Kareh et al., the automated RNS described previously was used to alert inpatient and outpatient physicians about positive cultures when the final lab result was returned after patient discharge and the patient was not adequately treated with antibiotics. The alerts included patient identifiers, names and contact information for the physicians involved in their care, the culture results, the discharge medication list, and patient allergy information. Twenty-eight percent of results in the intervention group and 13 percent in the control group met the primary outcome of documented followup (in outpatient chart) within 3 days of receipt of the post-discharge lab result, a statistically significant difference [adjusted OR 3.2, 95% CI, 1.3 to 8.4; p=0.01].[27]

1.2.3.4 Unintended Consequences

Study authors raised a hypothetical concern about alert fatigue, a potential unintended consequence of implementing alerting RNSs, but only one study measured a related outcome: overuse of the alerting system. Lacson et al. (2016) found that the proportion of reports without critical CSTR and using the ANCR was significantly less than when the ANCR was not used (0.09 vs. 0.20, p<0.002, $\chi 2$ test).[16] Etchells et al. (2010) noted that critical results, such as those from repeated troponin tests, were viewed as nuisances by receiving clinicians during a pilot of the system.[10] They also noted that because physician schedules were not fully automated, it was not possible to consistently route critical results to a responsible *and available* physician to take action. To compensate for this, physicians handed off "critical value pagers" so that the physician-on-call carried several pagers. Although this could reduce the number of missed alerts, it also created confusion when the on-call physician often could not discern which pager was alerting.

Unexpectedly, Singh et al. (2009) found that dual communication, a duplication intended to ensure that at least one physician received the alert, was associated with delayed followup. This finding was attributed to the lack of clarity about who was responsible for handling the alert.[18]

1.2.4 Implementation

The studies included in this review demonstrated the critical importance of the local environment and technologies, and circumstances surrounding the success of RNS. Facilitators and barriers to implementation of RNSs are described below.

1.2.4.1 Facilitators

1.2.4.1.1 Integration of RNS Into Workflow

Dalal et al. (2014) attributed the successful implementation of their TPAD email-generating RNS to the existing institutional culture that supports the use of email as a routine part of clinical care. The RNS was integrated into their current practice, which facilitated uptake.[12] Two additional studies mention that alignment of the RNS with existing workflows minimized the need to actively seek results, and policies and procedures of the institution supported success.[17,27]

1.2.4.1.2 Clear Policies and Procedures for RNS Use

Several authors mentioned the need for clear policies and procedures for the RNS. Singh et al. (2009) indicated that institutions need to have clear policies about who is responsible for acknowledging an alert and taking action, so that there is no ambiguity.[18] One institution, after much deliberation, established the policy that the responsibility for following up a test rested on the "ordering" clinician, and that this responsibility could be discharged only after a handoff where the "new owner" recipient acknowledged receipt and agreed to take over the followup.[6] Other studies mentioned the need for policies establishing which types of alerts warrant use of the RNS and the timeliness of responding to those alerts, based on the criticality of the CSTR.[10,15-17,19]

1.2.4.1.3 Adequate Staffing To Support the RNS

Two studies mentioned the need for adequate staffing to support the implementation of RNS.[19, 21] Chen et al. implemented a two-pronged approach to improved communication times, involving increasing the number of staff in the laboratory to improve lab performance and quality, and implementing an RNS with secure messaging.[21] Eisenberg et al. noted that their RNS required the hiring of two full-time staff to manage the electronic messaging system.[19]

1.2.4.2 Barriers

1.2.4.2.1 Unaligned Policies and Procedures

Etchells et al. (2011) found that during weekends and nights there were differences in process between the study sites that involved the receipt of the alerts.[11] At one site, the smart phone on which alerts were received was handed from the attending daytime physician to the physician-on-call, so critical alerts could be received after hours. At the other site, the smart phone was not handed off, and the physician-on-call relied on telephone calls from the lab. O'Connor et al. (2018) documented that there were conflicting policies about what could trigger an alert: per local departmental policy, only unexpected malignancies should trigger an alert; but per enterprise policy, any new malignancy should trigger an alert.[24]

1.2.4.2.2 Lack of Connectivity Between Hospitals and PCPs Outside of Network

The three studies of using RNS to facilitate communication of TPADs during care transitions at hospital discharge all showed challenges in communicating with PCPs outside their hospital system.[12,13,27] If RNSs are relied on for TPAD result communication, they must be able to notify non-network and network PCPs.

1.2.4.2.3 Physician Handoffs and Scheduling

Automated physician scheduling is important for optimal performance of automated critical value alerting systems. This barrier to successful implementation was identified by Etchells et al. (2010), who found that when physician schedules are not fully automated, it is impossible to route alerts to the responsible (e.g., on-call) physician who can take action.[10,11]

1.2.4.2.4 Availability of Resources and Technology Limitations

Lin et al. (2014) indicated that the full implementation of their alert system was challenged by the unavailability of phones for adjunct physician staff, rendering them unable to receive critical alerts sent via the RNS.[23] Park et al. (2008) identified that their secure messaging phone reception had inconsistent signal strength in the hospital, but this had a minimal effect, since they had continued to manually call results to the unit in addition to the smartphone alerts.[20]

1.2.4.2.5 Financial Costs

There is an implied financial burden to implementing these systems, including costs of the systems themselves, and as mentioned previously, the potential need for increased staffing for successful implementation and use.[8,19,21]

1.2.5 Resources

The book "Getting Results: Reliably Communicating and Acting on Critical Test Results," (Schiff GD, ed., Joint Commission Resources, 2006) is "a collection of articles and case studies on how healthcare organizations are improving communication of critical test results," as described in the AHRQ Patient Safety Network.[28]

Pennsylvania passed the Patient Test Result Information Act (2018 Act 112) to ensure that patients with significant abnormalities on imaging exams are notified of the need for medical followup. Information on the law is available through the Pennsylvania General Assembly website: https://www.legis.state.pa.us/cfdocs/legis/li/uconsCheck.cfm?yr=2018&sessInd=0&act=112.]

1.2.6 Gaps and Future Directions

Over half of the studies in this review address the experiences of a small group of researchers from a single large academic institution and its affiliated medical centers. Although these studies are of high quality and some findings are significant, studies in other settings are needed to test and demonstrate generalizability, as well as to engage research in this field more widely. Diagnostic errors due to lapses in communication occur during care transitions, but only three studies (again, all in the same healthcare system) evaluated RNS to improve delivery of results finalized after the transition from the inpatient to the outpatient setting.

As mentioned above, it is challenging when many providers are taking care of a patient, as the RNS needs to discern who is responsible for which patient at any given time. Institutions are establishing policies aimed at addressing this challenge, but how the policies perform needs to be investigated.[6]

Another area for future study is the development and testing of RNS that are "smart" and use CDS to recognize the difference between critical results that require notification for emergent intervention versus those that do not. Future studies that track the number and types of alerts generated, including

synchronous communication for only those CSTR that require urgent action, could include outcomes related to reducing alert fatigue.

References for Section 1.2

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1.3 Patient Safety Practice: Education and Training

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1.3.1 Practice Description

In the 2015 National Academies of Sciences, Engineering, and Medicine (NASEM) report Improving Diagnosis in Health Care, one of the recommended strategies for improving diagnosis is to enhance healthcare professional education and training in the diagnostic process.[1] The content of this education can be guided by an understanding of the root causes of diagnostic errors. Studies have uncovered two broad categories of underlying root causes: cognitive-based factors, such as failed heuristics; and systems-based factors, such as lack of provider-to-provider communication and coordination.[2-4] In the realm of cognitive-based errors, there are also two main streams of thought about causes: heuristics failures and shortcomings in disease-specific knowledge and experience. These sets of broad conceptual factors are by no means mutually exclusive, and ideally system redesign and educational efforts can leverage overlaps and synergies. How to best provide education and training to change these underlying factors and thereby improve diagnostic accuracy and reduce diagnostic errors leads to a more fundamental question that this review attempts to address, "Do education and training lead to improved diagnostic performance?"

1.3.2 Methods

We searched four databases (CINAHL®, MEDLINE Cochrane, and PsycINFO®) for articles published from 2008 to 2018 using the terms "diagnostic errors," "delayed diagnosis," "missed diagnosis," and synonyms. Terms specific to this PSP include "education, professional," "training," "simulation training," "structured practice," and related terms. The initial search yielded 211 results. Once duplicates had been removed and additional relevant referenced articles added, 187 articles were screened for inclusion and 29 full-text articles were retrieved. Of those, 22 studies were selected for inclusion in this review. Articles were included if the intervention being tested was training and an outcome was diagnostic accuracy. Articles were excluded if the article was out of scope, or the study provided limited detail or was of limited rigor.

Key Findings:

- Although there are a limited number of studies, the literature suggests that training on metacognitive skills may improve diagnostic accuracy, particularly as clinical experience increases.
- Online training, either didactic or via simulation, can be successfully used as a mode of delivery for educational interventions targeting clinical reasoning and diagnostic safety.
- There are several promising training interventions to improve visual perception for radiology practice.
- Limitations include a dearth of studies that examine the transfer of learning from the educational setting into the clinical setting and actual patient care.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

1.3.3 Evidence Summary

A majority of the selected studies focused on training directed at the cognitive aspects of diagnostic errors, such as clinical reasoning and biases. Other studies focused on training in visual perception skills

for radiologists and specific diagnostic skills. Few studies involved experienced clinicians, with medical students and residents being the predominant types of learners.

Overall, the quality of evidence was moderate, with some strong study designs, such as randomized controlled trials, but with low numbers of subjects, making generalization of findings challenging. The educational interventions varied in both their content and the mode by which the content was delivered, and in several cases the distinction between the testing of the content versus the testing of the mode of delivery was difficult to ascertain.

1.3.3.1 General Training in Clinical Reasoning

Clinical reasoning is the process by which clinicians collect data, process the information, and develop a problem representation, leading to the generation and testing of a hypothesis to eventually arrive at a diagnosis.[5,6]

Cook et al. (2010) conducted a meta-analysis and systematic review of the effects on training outcomes of using virtual patients, including the effects on clinical reasoning. The learners interact with a computer program that simulates real-life clinical scenarios to obtain a history, conduct a physical exam, and make diagnostic and treatment decisions. In comparing virtual patients to no intervention, the pooled ES for the five studies with an outcome of clinical reasoning was 0.80 (95% CI, 0.52 to 1.08). Pooled ESs for the outcomes of knowledge (N=11 studies) and other skills (N=9 studies) were also large. When comparing the use of virtual patients to noncomputer instruction (e.g., didactic instruction, standardize patients, routine clinical activities), the pooled ES for the outcome of clinical reasoning was -0.004 (95% CI, -0.30 to 0.29, N=10 studies), and it was also low for satisfaction, knowledge, and other skills. The main takeaway from this meta-analysis and review was that the use of virtual patients is associated with large positive effects on clinical reasoning and other learning outcomes when compared with no intervention and is associated with small effects in comparison with noncomputer instruction.[7]

Graber et al. (2012) in their systematic review identified papers that reported testing interventions aimed at reducing cognitive errors.[8] Three broad categories of interventions emerged: interventions to improve knowledge and experience, interventions to improve clinical reasoning, and interventions that provide cognitive support. Several papers examined the use of training in metacognitive skills to improve clinical reasoning, which is below. Wolpaw et al. (2009) studied the use of a learner-centered technique by third-year medical students to present clinical cases in a structured manner (SNAPPS: Summarize, Narrow, Analyze, Probe, Plan, Select). Although the authors did not assess whether the DDX were accurate, they found that students using the SNAPPS technique performed better on all outcomes, including analyzing possibilities of the DDX, expressing uncertainties, and obtaining clarification.[9]

1.3.3.2 Training in Metacognitive Skills To Reduce Biases

Cognitive biases can affect clinical reasoning and influence the diagnostic process, contributing to a large proportion of misdiagnoses.[6,8,10,11] Metacognition, the understanding, control, and monitoring of one's cognitive processes, can be used to gain better insight and counteract these biases.[12,13] Nine studies focused on techniques to enhance metacognitive skills, specifically training on the use of cognitive forcing strategies (CFS) and the use of reflection during the diagnostic process. The results of the studies are mixed, but overall suggest the use of training metacognitive strategies to improve diagnostic performance.

The use of CFS, a metacognitive strategy, is a technique to bring about self-monitoring of decision making and to force the consideration of alterative diagnoses.[13] Three studies (Sherbino et al., 2011, Sherbino et al., 2014, Smith and Slack, 2015) provided medical students and residents with training on the use of CFS and measured its impact on diagnosis.[14-16] The results did not show any appreciable improvement in diagnostic accuracy. In a preliminary and followup study, Sherbino et al. employed a 90-minute, standardized, interactive, case-based teaching seminar on CFS for medical students during their emergency medicine rotation.[14,15] Neither study showed any improvement in diagnostic errors. In the first study, they found that fewer than half of the students could use the CFS to debias themselves, and that 2 weeks post-training the students' knowledge of debiasing was no longer present. In the second study, there was no difference in the diagnostic accuracy between the control and intervention groups. In the study by Smith and Slack (2015), family medicine residents participated in a debiasing workshop that included training on CFS. They found that the residents' ability to formulate an acceptable plan to mitigate the effect of cognitive biases significantly improved after the training (p=0.02), although the residents were not able to translate the plan into practice, as evidenced by no change in the outcomes of preceptor concurrence with the residents' diagnoses, residents' ability to recognize their risk of bias, and the preceptors' perception of an unrecognized bias in the residents' presentations. This study was limited in that CFS targets biases related to nonanalytic reasoning (so-called pattern recognition). Novice diagnosticians, such as medical students, may lack sufficient experience to employ nonanalytic reasoning, rendering these methods increasingly more useful as experience increases.[16]

In a frequently cited study, Mamede et al. (2010) investigated whether recent diagnostic experiences elicit availability bias (i.e., judging a diagnosis that comes to mind more readily as being correct), and then tested a simple instructional procedure to reduce that bias. The training consisted of a five-step procedure to induce structured reflection and improve diagnostic accuracy in first- and second-year internal medicine residents. The use of reflection did reduce availability bias and improved diagnostic accuracy.[17] Two additional studies by this group of investigators (Mamede 2012, Mamede 2014), furthered this work on the use of structured reflection as a tool to facilitate diagnosis. The first of these studies found that the use of structured reflection after providing an immediate diagnosis when practicing with clinical cases fostered the learning of clinical knowledge more effectively than providing an immediate diagnosis only, or generating an immediate diagnosis followed by a differential diagnosis.[18] In the second study, the use of this technique enhanced learning of the diagnosis practiced as well as its alternative diagnoses.[19]

Coderre et al. (2010) tested the effectiveness of questioning a medical student's initial hypothesis as a means to induce cognitive reflection. The authors found that the questioning of an initial correct diagnosis did not change the final diagnosis; the students tended to retain the initial diagnosis. If the student's initial diagnosis was incorrect, the questioning provided an opportunity for the students to recognize and react to their error, and correct their diagnosis.[20]

In a randomized controlled study, Nendaz et al. (2011) studied the impact of weekly in-person case-based clinical reasoning seminars incorporating diagnostic reflection, during which the students were prompted to reflect on their reasoning process and were provided feedback on each step of that process. They found no difference in the accuracy of the medical students' final diagnoses between intervention and control groups (74% vs. 63%), although the students in the intervention group were more likely to have mentioned the correct diagnosis somewhere on their working list of DDX under consideration (75% vs. 97%, p=0.02).[21]

Reilly et al. (2013) incorporated the promotion of reflection on past experiences where a cognitive bias led to a diagnostic error, as part of a longitudinal curriculum on cognitive bias and diagnostic errors for residents. Residents who completed the curriculum significantly improved their ability to recognize cognitive biases when compared with their baseline performance ($p=0.002$) and when compared with the control group ($p<0.0001$). The study was limited in that it did not evaluate the impact of the intervention on diagnostic accuracy.[22]

1.3.3.3 Training on the Use of Heuristics

Heuristics are decision strategies, or mental shortcuts, that allow fast processing of information to arrive at a decision or judgment. One type of heuristic is representativeness; the use of the degree to which an event is representative of other, similar events to assess the probability of an event occurring.[23,24] Although the literature around the use of heuristics in medicine tends to focus on the biases they introduce, there is a recognized potential for training with heuristics to achieve better diagnostic accuracy.[25,26]

Mohan et al. (2018) conducted a randomized controlled trial comparing two training interventions designed to improve the use of the representativeness heuristic to improve trauma triage by emergency physicians. The authors developed two serious video games to train in the use of the heuristic. The first was an adventure game, based on the theory of narrative engagement, and the second was a puzzle-based game, based on the theory of analogical reasoning, using comparisons to help train the learners on applying decision principles. Both games incorporated feedback on diagnostic errors and how they could be corrected. Results showed that both games had positive effects on trauma triage, whereas traditional medical education had none.[26]

1.3.3.4 Training To Improve Visual Perception Skills

In radiology, diagnostic errors fall into two broad categories: perceptual errors, in which an abnormality on an image is not seen or identified, and interpretive errors, in which an abnormality is seen but the meaning or the importance of the finding is not correctly understood.[27,28] Perceptual errors account for a majority of misdiagnoses in radiology,[27,29,30] and can be rooted in faulty visual processing or, to a lesser extent, cognitive biases.[31]

Improving visual perception skills, which predominate the diagnostic process in radiology, requires methods of training different from those to improve clinical reasoning.[28] Four studies were identified through our search that evaluated the impact of educational interventions on perceptive skills, with three showing improvement in perceptive performance.[32-34] The studies involved subjects early in their medical training, and each tested a different intervention to improve perceptive performance, making aggregation of findings challenging.

A novel study by Goodman and Kelleher (2017) took 15 first-year radiology residents to an art gallery, where experts with experience in teaching fine art perception trained the residents on how to thoroughly analyze a painting. The trainees were instructed to write down everything they could see in the painting, after which the art instructor showed the trainees how to identify additional items in the painting that they had not perceived. To test this intervention, the residents were given 15 radiographs pre-intervention and another 15 post-intervention and asked to identify the abnormalities. At baseline, the residents scored an average of 2.3 out of a maximum score of 15 (standard deviation [SD] 1.4, range 0–4). After the art training, the residents' scores significantly improved, with an average score of 6.3 (SD

of 1.8, range 3–9, p<.0001), indicating that perception training may improve radiology residents' abilities to identify abnormalities in radiographs.[32]

In a small randomized crossover study by van der Gijp et al. (2017), 19 first- and second-year radiology residents received training on two different visual search strategies to determine their effect on accuracy of detecting lung nodules on CT scans. The first search strategy was "scanning," in which the resident views all the visible lung tissue on a single image and slowly scrolls down, image by image, through the entire study. The second search strategy, "drilling," has the resident mentally divide each lung into three regions and scroll through each region individually while keeping the eyes fixed on that region. Perceptual performance for both scanning and drilling strategies and a pre-test using a free search strategy was determined by the mean numbers of true positives and false positives. There was a significant effect of year of residency on the true positive score ($p<0.01$) but not for false positives. Drilling ($p<0.001$) and free search ($p<0.001$) both resulted in significantly higher true positive scores (i.e., lung nodules identified appropriately) than did scanning. There was no difference between the drilling or free search strategies. The free search strategy resulted in higher false positive scores than drilling ($p<0.001$) and scanning ($p<0.001$). The authors concluded that drilling outperforms scanning for detecting lung-nodules and should be the preferred strategy when teaching perceptive skills.[33]

In a randomized controlled trial, Soh et al. (2013) used an online e-learning tutorial to train 14 first-year medical radiation sciences students (i.e., radiology technologists) in Australia to improve their ability to detect breast lesions on mammographic images. The 1-hour tutorial focused on anatomy, image positioning, mammogram viewing and analysis, and the appearance of normal breast tissue and asymmetric densities and masses. The students were randomized to the intervention (tutorial) or control group, with their performance evaluated by their viewing normal and abnormal mammograms. The study used eye-tracking technology to determine when and how often the student fixated on a lesion. The intervention group demonstrated improvement in the mean number of fixations per case ($p=.047$), and decreased time to first fixation on a lesion by 49 percent ($p=.016$). The intervention increased students' ability to identify lesions (i.e., sensitivity) by 30 percent ($p=.022$).[34]

The fourth study evaluated different proportions of normal and abnormal radiographs in image training sets to determine the best case-mix for achieving higher perceptive performance.[35] For the intervention, Pusic et al. (2012) used three different 50-case training sets, which varied in their proportions of abnormal cases (30%, 50%, 70%). One hundred emergency medicine residents, pediatric residents, and pediatric emergency medicine fellows were randomized to use one of the training sets. After the intervention, all participants completed the same post-test. All three groups showed improvement after the intervention, but with varying sensitivity-specificity trade-offs. The group that received the lowest proportion (30%) of abnormal radiographs had a higher specificity and was more accurate with negative radiographs. The group that trained on the set with the highest proportion of abnormal radiographs (70%) detected more abnormalities when abnormalities were present, achieving higher sensitivity. These findings have significant implications for medical education, as it may be that case mix should be adjusted based on the desired sensitivity or specificity for a given examination type (e.g., screening exams vs. diagnostic test).[35]

1.3.3.5 Other Education and Training Interventions

In the systematic review of patient safety strategies targeted at diagnostic errors, McDonald et al. (2013) identified 11 studies, ranging in dates from 1981 to 2011, that involved a variety of interventions.

Two randomized trials targeted patients and families, and found that the interventions improved performance: the first found that parent education improved parents' ability to identify serious symptoms requiring a physician office visit, and the second showed that patient education, in addition to reminders, improved breast cancer screening rates.[36]

Medical teaching typically involves error avoidance training (EAT), in which the focus is on how to perform a task correctly rather than on how to manage errors. However, evidence suggests that in the early stages of learning a skill, errors are necessary in order to avoid them in the future.[37] In their randomized trial with 56 medical students, Dyre et al. (2017) compared the use of error management training (EMT), in which students were given "permission" to make errors while conducting simulation-based ultrasound examinations, with EAT. Two outcomes were measured: the objective structured assessment of ultrasound scale, a measure of ultrasound performance; and diagnostic accuracy. The scale scores showed a significant improvement by the EMT group compared with the EAT group ($p<0.001$). Although diagnostic accuracy showed some improvement, this was not statistically significant. The study is limited in that the authors cannot determine whether the outcomes were a result of EMT, the positive framing of errors, or the combination of these two components.[38]

In a quasi-randomized controlled trial, Schwartz et al. (2010) tested the use of in-person didactic sessions to teach fourth-year medical students skills in contextualizing patient care. The authors based this work on the premise that there are both biomedical and contextual data that must be ascertained during the diagnostic process and incorporated into the treatment plan. Students who participated in the didactic sessions were significantly more likely to probe for contextual issues and significantly more likely to develop appropriate treatment plans for the standardized patients with contextual issues.[39]

Two studies investigated the use of online training to improve specific diagnostic skills, both resulting in significant improvements in diagnostic accuracy.[40,41] Smith et al. (2009) conducted a 4-month online didactic continuing education program to improve the ability of radiographers in rural areas to interpret plain musculoskeletal radiographs. The results showed a significant improvement in image interpretation accuracy for more complex cases ($p<0.05$), although there was no change in accuracy for less complex cases.[40] McFadden et al. (2016), using convenience sampling, compared a traditional in-person training with an on-line simulation-based training, both designed to improve the diagnosis by primary care practitioners of the etiology of joint pain. The online training included interactive practice opportunities and feedback delivered by an AI-driven tutor. The intervention group's diagnostic performance was significantly improved from baseline ($p<0.02$) compared with the group that received the traditional training.[41]

1.3.4 Implementation

Many of the studies were conducted in training and simulated environments. As such, there were limited discussions regarding facilitators and barriers to implementation in the clinical practice environment.

1.3.4.1 Facilitators

Several of the studies used interventions that brought the education to the learner, such as those using information technology–based platforms.[34,35,40,41] Although there are costs in both time and money associated with the set-up of these online learning systems, once implemented, the training is more easily administered to more learners and is more flexible to being customized.[42]

1.3.4.2 Barriers

The use of cognitive training interventions, such as reflective practice, may yield the greatest improvements for only the most complex diagnostic cases.[17,21] This makes application of appropriate strategies in actual clinical settings difficult, as whether a case is complex is often not determined until after the diagnostic process has begun.

In addition, some of these teaching techniques, such as those using standardized patients or requiring development of simulations, are labor intensive and may not be generalizable.

1.3.5 Resources

The Society to Improve Diagnosis in Medicine offers a clinical reasoning toolkit that contains resources to help clinicians and educators. The toolkit can be accessed at the Society's website: https://www.improvediagnosis.org/clinicalreasoning/.

1.3.6 Gaps and Future Directions

Graber et al. (2012) noted that the research directed at improving cognition as a means to reduce diagnostic errors was immature, and recommended more research to study different approaches and interventions, including training strategies.[8] Since the publication of that paper, as evidenced in this review, there has been a modest increase in research focused on education and training to improve diagnostic accuracy, but gaps persist and many questions remain unanswered and untested. There is a particularly strong need to be able to take the educational work out of the realm of the classroom and into the real and complex world that busy diagnosticians work in to reliably make accurate and timely diagnoses.

It should be noted that interventions, such as education and training, that address human error directly are considered to be weaker at driving effective and sustained improvement compared with stronger actions that remove dependence on the human.[43] There is an opportunity to identify and investigate the use of system supports (e.g., process changes) to complement and solidify these educational efforts. The supports should prevent the need for clinicians to rely solely on their human, hence fallible, memory to recall what they learned both about diseases and about heuristics pitfalls.

Many of the studies engaged medical students or first-year residents, who were relatively new in their careers and lacked clinical experience. Improving clinical reasoning through the use of metacognitive strategies, particularly CFS, is targeted at reducing biases associated with the use of nonanalytic reasoning. Expanding training on these strategies to more experienced clinicians, as opposed to trainees, may yield stronger results.[14,15] In contrast, visual perceptive skills develop earlier and faster than interpretive skills.[28,44] Therefore, educational interventions directed at improving perception would more likely benefit medical students and residents early in their training. Understanding the best timing for different educational strategies to maximize their effectiveness in the continuum of medical education, from student through experienced clinician, would be beneficial.

A variety of methodological aspects of the studies could have been improved to strengthen the evidence base. Several of the studies occurred outside of clinical settings (e.g., online training and testing), and did not involve transferring the skills to diagnostic accuracy outcomes in actual clinical practice. Some of the studies were limited due to the inability to untangle the effect of the mode of the training (e.g., online didactic training) from the content that was being delivered.

Finally, although research indicates that the root causes of diagnostic errors include both cognitive factors and systems-based factors,[2-4] nearly all the identified studies targeted cognitive-based training strategies. The 2015 NASEM report on improving diagnosis in healthcare included a call for training in systems-based factors. This is an opportunity to conduct studies on the impact of team-training and communication on diagnostic errors, which is lacking, and training to support patient integration into the diagnostic process.

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1.4 Patient Safety Practice: Peer Review

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1.4.1 Practice Description

Key Findings:

- Second reviews of radiology or pathology interpretations by peers consistently uncover small but significant numbers of misread tests.
- The existence of any positive outcomes from increasing awareness of this general vulnerability and its effects on personal accountability—knowing that readings are being scrutinized—cannot be determined from the published studies.
- There is a lack of evidence to show that traditional random peer review and feedback mechanisms, which are used to maintain compliance with accreditation requirements, improve diagnostic quality over time or prevent diagnostic errors from reaching the patient.
- When nonrandom peer review is conducted prospectively, there is an opportunity to identify and remediate the diagnostic error before it reaches the patient.
- Limiting peer review to specific case types where it was most impactful was identified as a factor supporting implementation.
- Significant barriers to successful implementation include the increased staffing needs, workload, associated costs, concern over fairness, and maintenance of confidentiality of clinician performance.

Peer review is the systematic and critical evaluation of performance by colleagues with similar competencies using structured procedures.[1] Peer review in clinical settings has two recognized objectives: data collection and analysis to identify errors; and feedback with the intention of improving clinical performance and practice quality.[2,3] It also serves to fulfill accreditation requirements, such as The Joint Commission requirement that all physicians who have been granted privileges at an organization undergo evaluation of and collect data relating to their performance, or the American College of Radiology physician peer review requirements for accreditation.[4-6] When done systematically and fairly, peer review contributes to and derives from a culture of safety and learning.[7]

For this PSP, we are focusing the use of peer review as a tool to help identify, analyze, and discuss failures in establishing timely and accurate diagnoses, as well as a method to reduce diagnostic errors in the future.

Peer review, when designed appropriately, has the potential to achieve patient safety goals by having an impact on care either directly at the time of testing (e.g., identifying and resolving the error before it affects the patient) or indirectly by improving physician practice through continual learning and feedback. Thus, the question of interest for this review is, "Do peer review and feedback lead to improved diagnostic performance, i.e., fewer diagnostic errors?"

1.4.2 Methods

We searched three databases (CINAHL®, MEDLINE, and PsycINFO®) for articles published from 2008 to 2018 using the terms "diagnostic errors," "delayed diagnosis," "missed diagnosis," and synonyms. Terms specific to this PSP include "peer review," "performance review," "performance feedback," "feedback," "quality assurance," and related terms. The initial search yielded 426 results. Once duplicates had been removed and additional relevant referenced articles added, 334 articles were screened for inclusion and 42 full-text articles were retrieved. Of those, 16 studies were selected for inclusion in this review. Articles were excluded if the focus was on the use of peer review in medical student or resident

education, the outcome was not relevant to this review, the article was out of scope, or the study was of significantly limited rigor.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

1.4.3 Evidence Summary

A summary of key findings related to the use of peer review and feedback to reduce diagnostic error is located in the text box above. After the inclusion and exclusion criteria are applied, the preponderance of published literature about peer review related to diagnosis is from the specialties of radiology and pathology, likely due to findings that are "fixed" in images or specimens, leaving an artifact of the error that the review process can identify. It is also likely a testament to the leadership in these specialties, who have engaged their practitioners in responsibly reviewing their peers and caring for their patients.

Overall, the quality of evidence was moderate, with many descriptive study designs characterizing the rate and types of missed diagnoses using peer review. Studies also noted that scoring of radiological discrepancies is subjective and has significant variations in interrater reliability.[8]

The selected studies were categorized into two types of peer review, random and nonrandom, based on the methods of case selection.[5] Random peer review is characterized by the random selection of cases for review. There are several types of nonrandom review, including double reading of selected cases, review of diagnostically complex cases, and review of cases where potential diagnostic errors have been identified.

1.4.3.1 Traditional Peer Review: Random Versus Nonrandom Selection

Evaluation of professional practice, which can be accomplished through peer review, is a requirement for accreditation by organizations such as the American College of Radiology (ACR) and The Joint Commission, and recommended by professional associations such as the College of American Pathologists. The best-known example is that used in radiology, the ACR's RADPEER™ program, which is a standardized process with a set number of cases targeted for review (typically 5%) and a uniform scoring system.[9] The cases, which are originally interpreted images being used for comparison during a subsequent imaging exam by the reviewing "peer" radiologist, are randomly selected and scored.[5,6] Scores are assigned based on the clinical significance of the discrepancy between the initial radiologist's interpretation and the review radiologist's interpretation: (1) concur with interpretation; (2) discrepancy in interpretation, correct interpretation is not ordinarily expected to be made (i.e., an understandable miss); and (3) discrepancy in interpretation and the correct interpretation should be made most of the time. Scores of 2 and 3 can be modified with an additional designation of (a) unlikely to be clinically significant or (b) likely to be clinically significant. Scores of 2b, 3a, or 3b are reviewed by a third party, typically a department chair, medical director, or quality assurance committee.[9] Discrepancy rates can then be calculated for individual radiologists and used for comparison against peer groups or national benchmarks, and for improving practice.

Six studies involved the use of random peer review strategies similar to that of RADPEER. Each of these studies calculated discrepancy rates of case interpretation between the initial physician's diagnosis and

the peer reviewer's diagnosis, with some studies using a third party to adjudicate the presence and severity of a diagnostic error.[10-13] Four of the studies compared random versus nonrandom approaches.[11-14] Table 1.2 lists the studies by case type, case selection, and discrepancy (i.e., diagnostic error) rates. The definition of discrepancy varied slightly across studies, but typically ranged from minor disagreements between reviewers that would necessitate a change to a report but are incidental to treatment, to major disagreements that may directly affect a patient's outcome.

Table 1.2: Discrepancy Rates for Peer Review in Pathology and Radiology

Author, Year	Case Type	Case Selection	Discrepancy Rates
Harvey et al., 2016[10]	Radiology	Random—consensus-oriented group review of random cases	2.7% (306/10,852)
Itri et al., 2016[11]	Radiology	Random—each radiologist reviews 20 random cases/month	2.6% (44/1,646)
		Nonrandom—submitted cases of potential diagnostic errors	100% (190/190)*
Kamat, et al., 2011[15]	Pathology	Random—8% review	2.6% (35/1,339)
Layfield and Frazier, 2016[14]	Pathology	Random—10% targeted review	0.8% (17/2147)
		Nonrandom—solicited external opinion	7.1% (5/70)
		Nonrandom—unsolicited review by external institution	1.6% (3/190)
		Nonrandom—specific pathology study type	8.5% (5/59)
Raab et al., 2008[12]	Pathology	Random—5% targeted review	2.6% (195/7444)
		Nonrandom—focused review of specific pathology study type	13.2% (50/380)
Swanson et al., 2012[13]	Radiology	Random—mandatory 4 prior comparison studies per shift	3.8% (186/4,892)
		Nonrandom—voluntary review of cases of interest	12% (46/386)

*All cases were selected for review due to the presence of a potential diagnostic error.

Cases selected for review by a random process consistently had lower discrepancy rates between the initial interpretation and the peer review interpretation (0.8%–3.8%) than the cases selected nonrandomly (1.6%–13.2%). The more focused the case selection criteria, the higher the yield of identified diagnostic errors.

In their study of the effectiveness of random and focused reviews in anatomic pathology, Raab et al. found that the 5 percent targeted random selection method identified significantly fewer cases with diagnostic errors than the focused review of case types known to be diagnostically challenging or where there is a lack of standardization (2.6% vs. 13.2%, $p<.001$).[12] In practical terms, the focused review detected approximately 4 times the number of errors compared with the random reviews, which involved 20 times the number of specimens. Layfield and Frazier compared four different methods of anatomic pathology case selection and found that randomly targeted cases had the lowest rate of identified diagnostic errors (0.8%) compared with the three non-random methods. The focused review, in which all cases of a specific type are reviewed (all dermatopathology cases), identified the greatest percentage of diagnostic errors (8.5%).[14] In a study by Itri et al., at an institution where radiologists are required to review 20 randomly selected cases per month, the discrepancy rate was found to be 2.6 percent, with all identified errors being considered minor discrepancies.[11] The authors also found that, among 190 additional cases selected for review because of concern about potential errors, 130 (68.4%) had significant discrepancies: 94 were significant discrepancies that may affect treatment but not outcomes, and 36 were major discrepancies that may affect outcomes. In a study conducted at a large, urban, multidisciplinary children's hospital, Swanson et al. (2012) describe discrepancy rates of 3.6 percent using their mandatory random peer review process, where each radiologist reviews four cases per shift. Radiologists could also conduct nonrandom reviews on cases of interest or concern, or if they

were referenced in a clinical consultation or part of a review conference. There was a 12-percent discrepancy rate using this method.[13]

One study combined the use of random case selection with a prospective review approach, where the peer review occurred prior to report finalization.[15] The rate of discrepancies using this method was 2.6 percent, aligning with the findings of the other studies using random case review. There was one discrepancy considered to be of major significance identified, which was resolved prior to patient care decisions being made.

1.4.3.2 Double Reading

A common form of nonrandom peer review, particularly in radiology practice, is the use of double reading, in which a second clinician reviews a recently completed case.[5] With this method the review is integrated into the diagnostic process rather than conduced retrospectively, allowing errors to be identified and resolved prior to a report being transmitted to the ordering provider or the patient.

Geijer and Geijer (2018) reviewed 46 studies to identify the value of double reading in radiology. The studies fell into two categories: those that used two radiologists of similar degree of subspecialization (e.g., both neuroradiologists) and those that used a subspecialized radiologist only for the second review (e.g., general radiologist followed by hepatobiliary radiologist). Across both types of studies included in the review, double reading increased sensitivity at the expense of reduced specificity. In other words, double reading tended to identify more disease, while also identifying disease in cases that were actually negative (i.e., false positives). With discrepancy rates in studies between 26 and 37 percent, the authors suggest that double reading might be most impactful for trauma CT scans, for which there are a large number of images generated that need to be read quickly under stressful circumstances. The authors also suggest that it may be more efficient to use a single subspecialized radiologist rather than implement double reading, as using a subspecialist as a second reviewer introduced discrepancy rates up to 50 percent. This was thought to be a result of the subspecialist changing the initial reports and the bias introduced by having the subspecialist being the reference standard for the study.[16]

Pow et al. (2016) reviewed 41 studies to assess the use of double reading on diagnostic efficacy for screening and diagnostic imaging studies. As with the previously described systematic review, the use of double reading was found to increase sensitivity and reduce specificity, making it more desirable for tests, such as cancer screening, where high sensitivity is desired.[17] Also consistent with Geijer and Geijer (2018), the authors recommended the use of double reading in trauma due to the large number of images generated and emergent need for results. They also found that the level of expertise of the reviewers influences the error rate, with those review processes using a subspecialist for the second review having higher rates of error detection than those using two radiologists with similar training.

Four studies evaluated the use of double reading, in which the second reading occurred either concurrently with or in immediate proximity to the first reading.[18-21] In each of these studies, significant numbers of discrepancies were determined to be clinically significant by RADPEER scoring criteria. In Agrawal et al, dual reporting identified 145 errors (3.8%; 95% CI, 3.2 to 4.4) that led to report modification, with 69 determined to be clinically significant.[18] Lauritzen et al. identified 146/1,071 (14%, 95% CI, 11.6% to 15.8%) of changes to abdominal CT exam reports that were clinically significant.[19] In a similar study of dual reading for thoracic CT, 91/1,023 (9%) of the report changes were clinically significant, including 3 that were critical and required immediate action and 15 that were major and

required a change in treatment.[20] In both studies, the authors found that double reading uncovered errors with less delay and during the time when patient treatment was still able to be affected. Murphy et al. (2010), unlike the other prospective double-reading studies, evaluated blinded double reporting for patients undergoing colon CT scans. They found that, of the 24 significant findings, 7 were identified by only one of the two observers. Although this is counter-intuitive, the probability that a patient with a finding on CT examination had colon cancer was 69 percent for single reporting (11 true positives, 5 false positives) and 54.5 percent for double reporting (12 true positives, 10 false positives). For double reporting, one extra true-positive colon cancer was detected at the expense of five unnecessary colonoscopies (false positives), reducing the positive predictive value.[21]

Lian et al. (2011) compared the diagnostic error rates in a study in which CT angiograms of the head and neck were initially read by a staff neuroradiologist alone (n=144), double-read by staff and a diagnostic radiology resident (n=209), or double-read by staff and a neuroradiology fellow (n=150). Retrospectively, the CT angiograms were then blindly reviewed by two neuroradiologists to detect errors; 503 cases were included, with 26 significant discrepancies discovered in 20/503 studies (4.0%), and all errors were missed diagnoses. Ten of the 26 discrepancies were originally missed by staff alone (6.9% of studies read), 9 by staff and a resident (4.3%), and 7 by staff and a fellow (4.7%). The authors concluded that double reading with a resident or fellow reduces error.[22]

1.4.3.2.1 Economic Outcomes

In their systematic review, Pow et al. (2016) identified six studies from different countries that evaluated cost-effectiveness of double reading for screening mammography. The authors concluded that double reading is a cost-effective strategy. The increased early cancer detection rates outweigh the costs incurred by the double reading, such as infrastructure and additional clinician resources necessary to carry out double reading.[17]

Natarajan et al. (2017) quantified the hospital charges associated with the dual reading by an orthopedist and a radiologist for radiographs at a hospital-based orthopedic clinic. The authors calculated that the total charges for the radiology interpretations for the 2,264 radiographs was $87,362, or $39/study. There were 23 cases where the radiology report provided additional clinically relevant diagnoses not noted by the orthopedist, at the average cost of $3,798 in hospital charges per occurrence.[23]

1.4.3.3 Reinterpretation of Studies Conducted at Outside Institutions

Two studies examined the effect of reinterpretations of radiology studies done at outside institutions. Onwubiko and Mooney (2016) found that out of 98 reinterpreted CT scans of the abdomen and pelvis done in the context of pediatric blunt trauma, 12 significant new injuries were identified, 3 patients had their solid organ injuries upgraded, and 4 patients were downgraded to no injury. The benefit of reinterpreting scans extends beyond identifying potential diagnostic errors to limiting radiation exposure and unnecessary testing in the pediatric population.[24] Lindgren et al. (2014) determined the clinical impact and value of having outside abdominal imaging exams reinterpreted by subspecialized radiologists. Twenty of the 398 report comparison discrepancies (5.0%) had high clinical significance and 30 (7.5%) medium clinical significance. Over half of these discrepancies were due to overcalls, where the outside institution placed more importance on the significance of a finding than was warranted by the second review.[25]

1.4.3.4 Unintended Consequences

1.4.3.4.1 Negative

In the case of dual reading, Natarajan et al. (2017) found that the addition of the radiologist interpretation to the orthopedic interpretation of musculoskeletal films in pediatric orthopedic practice added clinically relevant information in 1.0 percent of the cases, yet misinterpreted 1.7 percent of the cases, potentially adding diagnostic errors into the process.[23] Murphy et al. (2010) found that double reading of colon CT scans increased the number of individuals falsely diagnosed with colon pathology. The protocol found one extra-colonic cancer, but at the expense of five unnecessary endoscopic procedures.[21]

1.4.3.4.2 Positive

Harvey et al. (2016) identified that their group-oriented consensus review method had a secondary effect of fostering a culture of safety in their department, where radiologists feel comfortable identifying and openly discussing diagnostic errors.[10] This finding was supported by Itri et al. (2018), who recognized that peer learning conferences, during which diagnostic errors were reviewed, supported a culture of safety where clinicians learned from their mistakes.[11]

1.4.4 Implementation

1.4.4.1 Facilitators

1.4.4.1.1 Limiting Peer Review to Specific Case Types

Several studies found that certain more complex radiology cases, such as trauma scans or MRIs, benefited more from double reading when compared with examinations such as plain musculoskeletal radiographs.[16,17] Recommendations include the use of subspecialty reinterpretation of high-risk cases, such as in patients with history of cancer or trauma, or using data from peer review to identify areas where there are more likely to be missed diagnoses and focusing peer review on those areas. Raab et al. (2008) recommended a similar approach in pathology, using focused peer review for specific subspecialty cases.[12]

1.4.4.2 Barriers

1.4.4.2.1 Concern Over Maintenance of Confidentiality and Medical Malpractice

Concerns over maintenance of confidentiality by the physicians and fears about the impact of peer review findings on medical malpractice litigation have been identified as a barrier to participation in peer review.[1,26] Several of the studies identified these concerns as barriers to implementing their peer review systems.[10,19] As a way to overcome this challenge, Harvey et al. (2016) described deliberately designing their program to ensure that all information disclosed through the process of peer review is protected under their State's statutory peer review privilege, preventing the information from being used against a clinician in malpractice claims.[10,27] At this time, all 50 States and the District of Columbia have privilege statutes that protect peer review records of medical staff members, although how the privilege is applied may vary by State.

1.4.4.2.2 Increased Staffing Needs, Workload, and Associated Costs

Several studies mentioned the need for increased staffing for peer review activities, requiring additional funds and departmental leadership support and engagement.[10,14-16,21,23,24] One study posited that error

rates will depend on the workload of the clinician, with greater workloads leading to greater error rates.[22]

1.4.5 Resources

There are limited resources related to conducting peer review to prevent diagnostic error. As mentioned previously, the ACR offers information regarding RADPEER, their peer review system, on their association's website.[28]

1.4.6 Gaps and Future Directions

Based on the literature identified in this review, traditional random peer review mechanisms employed to maintain compliance with accreditation requirements have not consistently been demonstrated to improve diagnostic accuracy. The studies focus on the rates of discrepancies as detected by the peer review process, but lack follow-through to examine the direct effects on patient harm and clinician performance over time. In addition to uncovering discrepancy rates, there is also a need to identify the root causes of the discrepancies so that they can be understood and prevented. Discrepancies that are generated because of poor image or specimen quality will be addressed very differently from those that are a result of a lack of time or knowledge by the clinician.

The studies did not address the impact of peer feedback, a critical component of peer review.[2,29] There is a missed opportunity to learn from errors, both at the individual and practice levels.[2] It would be beneficial to understand how to best deliver performance feedback and how the feedback is then used to change clinical practice.

There is also a need to design and test different types of peer review systems to maximize their value for improving care while maximizing limited resources. From the literature reviewed, it appears that there is benefit, at least in the field of radiology, to using both random and nonrandom case selection, subspecialist involvement, and prospective and retrospective reviews. Finding the right balance between the different modes of review in terms of clinical effectiveness and cost-effectiveness would be of use.

The available literature on peer review and its impact on diagnosis is focused on the fields of pathology and radiology, areas where peer review has been used the longest as part of quality assurance programs. It would be valuable to expand the breadth of studies to include other forms of peer review, including group consensus or conferences that could potentially be used to improve diagnostic accuracy in other fields, such as primary care, as these methods might be suitable for diagnostic dilemmas encountered in a variety of settings.

Lastly, even with the use of peer review in any of its forms, patients continue to experience errors in diagnostics, some significant and with a real potential for harm. In the Improving Diagnosis in Health Care report, the Committee on Diagnostic Error in Health Care, after reviewing the evidence, concluded that "most people will experience at least one diagnostic error in their lifetime, sometimes with devastating consequences."[3] This is disconcerting and speaks to the need for considering "upstream" measures as well—not just relying on the inspection mode at the point of care but also looking at re-engineering the entire process for more- accurate diagnosis.[30] In order to start this process, efforts should be directed to elucidate the root causes of diagnostic errors. This knowledge can then be used to guide the development of strategies aimed at improving the underlying system of care.

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Conclusion and Comment

The PSPs reviewed in this chapter aim to reduce diagnostic errors by targeting cognitive-based factors and systems-based factors. The evidence in support of these practices varied in depth and consistency.

CDS offers solutions to address diagnostic errors through incorporation of evidence-based diagnostic protocols, and improve communication and integration with clinical workflow. This review found that CDS may improve diagnosis, although the studies tend to be exploratory in nature, validating the decision algorithms. The use of AI and machine learning has generated excitement over its potential, but they are also exploratory and lack testing during the care of actual patients. These systems need to be reassessed once fully implemented and iteratively improved in real clinical settings on patients actively undergoing diagnosis. Studies included in the review also support the notion that CDS tools are best used as adjuncts to the clinician's decision making process and not as replacements. This was particularly true for CDS tools that assist with diagnostic study interpretation, such as ECG interpretation. The literature also identified that the diagnoses generated by CDS tools are only as good as the information that is put into the system; if the initial assessment of the patient (e.g., physical exam finding) is incorrect, it is likely that the output will be incorrect.

RNSs aim to address lapses in communication, a contributing factor to delayed diagnosis and treatment of patients in both ambulatory and inpatient settings. There was considerable variability in the findings of the included studies, with the results being dependent on many factors, including the type of the test, the type of communication (i.e., synchronous or asynchronous), and whether the alert was manual or automated. Studies were conducted in a surprisingly limited number of institutions. For both critical and non-critical CSTR of radiologic studies, lab studies, and tests pending at discharge, the use of RNS showed mixed results in the timeliness of receipt and in action on the test results. Policies and procedures that aligned with the system, mindful integration of the RNS into the existing workflow, and appropriate staffing were identified as factors supporting successful implementation of the systems. Barriers to successful implementation, particularly when results are conveyed across transitions from inpatient to outpatient settings, include the lack of connectivity between hospitals and non-network physicians. Additionally, there were operational challenges associated with providing critical alerts to physicians who may not be available at the time the result is available (e.g., not on call). Ultimately, they have a central role to play in closed-loop systems to ensure reliability and tracking of critical test results.

Evidence to support education and training on the diagnostic process to enhance clinical reasoning and decrease biases showed generally positive results, with study designs being strong (e.g., randomized controlled trials), although there was some lack of generalizability, as many of the studies had low numbers of subjects. Training on metacognitive skills as a way to reduce biases may improve diagnostic accuracy, particularly as clinical experience increases. Online training, either didactic or simulation based, was shown to be successful at improving clinical reasoning skills. Of note, there was a dearth of studies that examined the transfer of learning from classroom or simulated settings into the clinical setting and actual patient care, where there is a critical need for future research.

For the PSP of peer review, studies show significant numbers of missed or misread test interpretations. However, there is a lack of evidence to show that traditional random peer review and feedback mechanisms used in radiology or pathology to maintain compliance with accreditation requirements improve diagnostic quality over time or prevent diagnostic errors from reaching the patient. For both radiology and pathology, nonrandom peer review appears to be more effective at identifying diagnostic

errors than random peer review; and when peer review is conducted prospectively, there is an opportunity to identify diagnostic errors before they reach or harm the patient.

Since the previous Making Health Care Safer Report was published, studies examining the use of these four PSPs are increasing in both number and quality. Overall, there is still a relative dearth of studies focused on diagnostic error prevention and methods to improve diagnostic accuracy compared with other patient safety topics. General considerations for future research in diagnostic safety include the use of consistent measures and definitions of diagnostic error to allow comparisons of studies and aggregation of data across smaller studies (i.e., meta-analyses), moving from exploratory studies to studies conducted in real clinical settings in real time, and understanding how to best integrate technology with the current workflow to support diagnosis-related activities. There is also a need to design and test innovative and more refined versions of the past interventions using more advanced educational, quality improvement, and health information technology tools in the future.

2. Failure To Rescue

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Reviewer: Katharine Witgert, M.P.H.

Introduction

Background

Failure to rescue (FTR) is failure or delay in recognizing and responding to a hospitalized patient experiencing complications from a disease process or medical intervention. As a patient safety and healthcare quality metric, FTR is typically defined as mortality following a complication, although there is no universally agreed upon definition and slight variations exist between institutions.[1,2] In this chapter, we discuss two patient safety practices (PSPs) that have been widely implemented to address FTR: patient monitoring systems (PMS) and rapid response teams (RRTs).

Importance of Harm Area

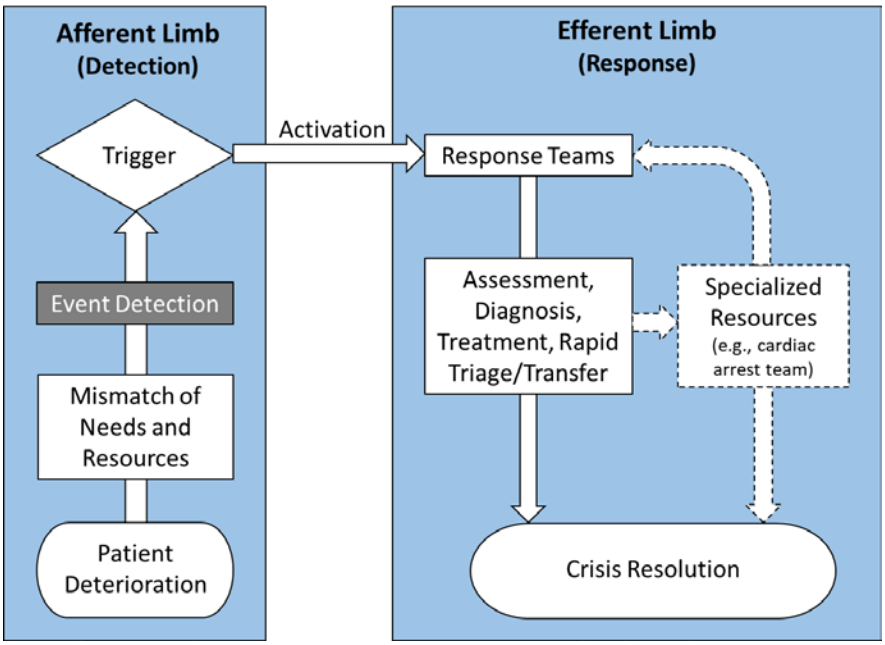
Failure to rescue is a well-established issue in patient safety and healthcare quality. Over the past two decades, there have been numerous studies identifying clinical antecedents to in-hospital mortality as well as strategies to respond to these events.[3-5] Silber and colleagues were the first to use the term as a metric for safety and quality in their 1992 study hypothesizing that FTR might be associated more with hospital characteristics than with patient illness severity.[6] Since then, many studies have investigated the variations in patient outcomes following in-hospital complications and in 2005, the Institute of Healthcare Improvement's 100,000 Lives campaign identified FTR as one of six key safety initiatives, estimating that implementation of rapid response systems could save 66,000 lives.[7] Because in-hospital complication can occur to any patient regardless of their diagnosis or disease process, FTR represents a ubiquitously significant problem and is therefore an important indicator of care quality.

PSP Selection

Using a review of guidelines and systematic reviews, an initial list of seven PSPs was developed: staff education and training, risk scoring systems, RRTs, clinical decision support, collaboration and teamwork, patient monitoring systems, and person and family engagement. Some identified PSPs (e.g., clinical decision support, patient and family engagement, and education and training) spanned multiple harm areas and appear in cross-cutting chapters. Through engagement of a Technical Expert Panel, two PSPs that are specific to FTR and have enough evidence to support a review were selected for review in this chapter: patient monitoring systems and RRTs.

Rapid response systems (RRSs) are hospital-based systems to detect and treat deteriorating patients before adverse events occur. They have emerged as an intuitive approach to address the two core contributors to FTR: failure in adequately monitoring and identifying and failure in responding to hospitalized patients who are at high risk for rapid clinical deterioration. A conceptual model for RRSs, adapted from DeVita et al,[8] depicts the relationship between the afferent limb, in which the event is detected and a trigger is activated, and the efferent limb, in which a systematic response is carried out and the crisis resolved (Figure 2.1). In this chapter we will be discussing patient monitoring systems as part of the afferent limb, and RRTs as part of the efferent limb of the RRS.

Figure 2.1: Conceptual Model for Rapid Response System[8]



Patient monitoring involves assessment of various vital signs and physiological changes. Monitoring criteria are then used to help guide activation of the RRT. Although there is no universal standard, most rapid response call criteria include abnormalities in physiologic measures such as respiratory rate, heart rate, systolic blood pressure, oxygen saturation, and urine output. Additional criteria may include staff member or family member concern about the patient's condition, mental status changes, or uncontrolled pain.[9]

Once activated by the monitoring staff, the RRT then responds to the patient to prevent avoidable morbidity and mortality. Other models exist, including medical emergency teams and critical care outreach. In this chapter we will use "RRT" as an umbrella term, as all models are conceptually united by the goal of early intervention for patients who are at high risk for clinical deterioration. The RRT team is typically multidisciplinary and can consist of a nurse, physician, and respiratory therapist, although team composition may vary depending on institutional policy and guidelines. They are able to assess the patient, diagnose, provide initial treatment, and rapidly triage the patient. Patients can then transfer to a higher level of care (i.e., intensive care unit), have their care returned care back to the primary medical team, or have their treatment plan revised. Specialized resources such as cardiac arrest teams or stroke teams are considered separate from the RRT and may be involved in the care of the patient, if warranted.

Driven by quality and safety requirements as well as recommendations, a swift uptake in RRTs has been noted in the United States and Australia, and is increasingly being seen in other developed countries. Because use of RRT is now so widespread, it has become difficult to produce high-quality, randomized controlled trials, and that causes apprehension in those who advocate for a more rigorously studied and evidence-based intervention.

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2.1 PSP 1: Patient Monitoring Systems

Reviewers: Bruce Spurlock, M.D., Kristen Miller, Dr. P.H., C.P.P.S., and Katharine Witgert, M.P.H.

2.1.1 Practice Description

Key Findings:

- There was moderate evidence of a reduction in rescue events following implementation of a patient monitoring system (PMS) with continuous monitoring (CM), but study results were inconsistent.
- PMSs with CM showed no significant effect on mortality, while PMSs with intermittent vital sign input had a moderate and inconsistent effect on mortality.
- There was moderate evidence for improvement in hospital length of stay (LOS) with a PMS, but low evidence for improvement in other outcome measures (intensive care unit [ICU] LOS, ICU transfers).
- More high-quality studies (e.g., robust prospective, randomized, quasi-experimental) are needed to test the effects of PMSs on patient outcomes.

Early clinician recognition of signs of patient deterioration is critical to reducing the risk of preventable death and other adverse events.[1] While RRTs have been widely implemented, their success depends on recognizing a deteriorating patient before serious harm has occurred.[2] Patient monitoring system (PMS) is an umbrella term for electronic systems that scan patient data (e.g. vital signs and other variables) for signs of deterioration and alert a clinician if certain criteria are met.[3] These systems can decrease the time from the onset of deterioration to the initiation of treatment, increasing the potential for better patient outcomes. While the training and clinical reasoning of staff cannot be discounted, PMSs can provide a valuable counterpart and backstop to ensure that no deteriorating patients are missed. Patients who are at a high risk of deterioration are usually admitted to a critical care setting or a telemetry unit, where patient vital signs are continuously monitored (CM) and there is a low patient-to-nurse ratio. However, most hospital beds are outside of these intensive settings, and most patients are boarded in general medical and surgical wards. These units typically do not have continuous PMS, and rely on intermittent collection of patient vital signs on a predetermined schedule (e.g., every 4–6 hours) and on nursing activation of the RRT. A delay of several hours in recognizing a patient's deterioration can lead to avoidable morbidity, ICU transfers, and mortality.[2] This section will review patient monitoring systems that use CM devices (e.g., pulse oximetry monitors), as well as electronic monitoring of intermittent manually collected vital signs.

2.1.2 Methods

To answer the question, "Does patient monitoring for deterioration improve patient outcomes?" we searched three databases (CINAHL®, MEDLINE®, and Cochrane) for articles published from 2008 to 2018 using the terms "patient deterioration," "failure to rescue," and related synonyms, as well as "hemodynamic monitoring," "patient monitoring," and other similar terms. The initial search yielded 35 results. Once duplicates had been removed and additional relevant articles from selected other sources added, a total of 29 articles were screened for inclusion, and 20 full-text articles were retrieved. Of those, eight were selected for inclusion in this review. Articles were excluded if the outcomes were not relevant to this review, the article was out of scope (including not quantitative), or study design was insufficiently described.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in report appendixes A through C.

2.1.3 Evidence Summary

A summary of key findings related to FTR and PMS appears above. This section reviews applicable studies in more depth, organized by measure type (process and outcome). Please note that sensitivities and specificities of PMSs are not examined, because PMS algorithms that scan for signs of deterioration can be constantly adjusted to fit the needs of the setting and to optimize performance. Upon designing and implementing a PMS, the clinicians/administrators typically test the system performance and adjust variable thresholds to best balance speed, sensitivity, and specificity for their setting.

All included studies took place in the hospital setting, and all in general medical/surgical units. Five of the studies used continuous vital sign monitoring systems (i.e., CM), and three used intermittent monitoring (IM) of electronically collected vital sign data.

2.1.3.1 Effect on Process Measures

While testing a PMS for its effect on outcome measures (e.g., mortality) is the ultimate goal of this PSP, it is also important to test whether the PMS improves processes of care for deteriorating patients. Seven of the eight studies reported one or more process measures for PMSs, all of which took place in general medical/surgical units. Articles assessing an effect on process measures had a variety of study designs, with one randomized trial and six experimental studies of varying type. In addition, one systematic review addressed this topic.

The most commonly reported process measure in the reviewed articles was the number of rescue events, including RRT calls or Code Blue calls (i.e., calls activated by healthcare professionals in the hospital when there is a patient in cardiac or respiratory arrest). It is unclear how to interpret this measure in relation to the PMS. A decrease in rescue events likely indicates that more deteriorating patients are discovered early and are stabilized by staff without needing to call the RRT. It could also indicate that patients in decline are being missed. Ultimately, this process measure needs to be combined with outcome measures to understand its true effect. Other reported process measures were related to vital sign collection times.

Of the six studies that reported the number of rescue events, three quasi-experimental studies found a significant difference between treatment and comparison groups after PMS implementation.[4,5,6] All three of these used CM systems. For example, Taenzer and colleagues reported that rescue events decreased from 3.4 to 1.2 per 1,000 patient discharges after implementing pulse oximetry monitoring in a 36-bed orthopedic unit within a 395-bed hospital (p=0.01).[4] They projected that this would lead to a decrease in annual rescue events in the unit from 37 to 11.[4] Similarly, Weller et al. found that RRT calls dropped from 189 to 158 per 1,000 discharges (p=<0.05) after a 26-bed neurological unit in an academic medical center implemented multi-parameter monitoring.[6] Although the quasi-experimental study by Fletcher and colleagues found no significant effect on the volume of total rescue events, they found a significant 20-percent increase in first RRT calls (as opposed to second or third calls for the same patient) after implementing a dashboard with color-coded risk levels by patient using IM (incidence rate ratio [IRR]: 1.20, p=0.04), while subsequent calls decreased nonsignificantly. They interpret this as a beneficial outcome, because after an initial RRT call, the providers will monitor the patient more vigilantly for deterioration.[7] These studies did not find a significant effect on outcome measures (mortality, ICU transfers, etc.), except for one study that found a decrease in the average hospital length of stay (LOS).[8]

Accurate vital sign documentation is critical for a PMS to detect patient deterioration, and CM devices that display the collected vital signs to nurses decrease the time needed to obtain and document a full set of vital signs. Two studies (McGrath et al. and Bellomo et al.) report this outcome.[9,10] As an example, Bellomo and colleagues found a significant decrease in the average time required for a nurse to obtain and record vital signs, from 4.1 minutes per patient to 2.5 minutes (p=<0.0001), which they estimate would save 1,750 nursing hours/year/ward.[10]

Seven studies, all in general hospital wards, reported outcome measures for PMS. Outcomes in these studies included mortality, ICU transfer rate, and hospital and ICU LOS. Three of these studies were also covered in a systematic review/meta-analysis. Study designs included two randomized controlled trials and five quasi-experimental studies of varying type.

It is important to note that attributing improvement in these outcomes to a PMS is difficult because patients who deteriorate are generally older, have multiple co-morbidities, and may have advance directives for end-of-life care.[11] In addition, reasons for ICU transfer and ICU length of stay are multi-factorial and not necessarily correlated with the use of a PMS.

A systematic review and meta-analysis by Cardona-Morrell and colleagues reported that implementing a PMS with CM was not associated with a reduction in mortality (odds ratio [OR]=0.87, 95% CI 0.57–1.33), while PMS with IM was associated with a statistically significant but modest reduction in mortality (OR=0.78, 95% CI 0.61–0.99).[12] This may seem counterintuitive, but the authors note that studies included in the meta-analysis were heterogeneous and most were observational. They conclude that more studies are needed of both CM and IM systems before drawing a definitive conclusion. Four other studies not included in that systematic review (3 CM and 1 IM) found no impact on mortality.[6-8,13] Several studies noted that a generally low mortality rate before and during their studies made it unlikely that they could detect a significant change without a large increase in the sample size.

2.1.3.1.1 ICU Transfers

Of the seven studies that reported ICU transfer rate, only one CM study (Taenzer et al.) found a significant reduction in the ICU transfer rate after implementing a PMS.[4] This quasi-experimental study was implemented in a 36-bed orthopedic unit in a 395-bed hospital; it found that following the implementation of a PMS there was an observed reduction in ICU transfers from 5.6 per 1,000 patient days to 2.9 (p=0.02). The authors reported that this would lower overall hospital ICU transfers from 54 to 28 annually.[4]

Four studies (3 CM and 1 IM) reported average hospital LOS, and three of these found a significant effect of a PMS (2 CM studies and 1 IM study). Study designs included one randomized study and two quasi-experimental studies. Kollef and colleagues implemented IM in eight medical units randomized to intervention versus control, and reported that average LOS was 9.4 patient days in the control units and 8.4 in the intervention units (p=0.038).[8] Interestingly, Bellomo and colleagues found a significant decrease in average LOS in the five U.S. hospitals studied (3.4 days vs. 3.0 days, p=<0.0001), but not in five non-U.S. hospitals implementing the same type of intervention, implying that other factors may affect the impact of a PMS.[10]

Two studies reported on ICU LOS, one of which found a significant effect of a CM system. Brown and colleagues implemented CM of vital signs in a 33-bed medical/surgical unit in a 316-bed community hospital, and found that ICU days per 1,000 admissions were lower in the intervention unit post-

implementation when compared with ICU days in the intervention unit pre-implementation and in the control unit post-implementation (63.5 versus 120.1 and 85.36 days, respectively; P=.04).[5] Taenzer and colleagues, as described above, reported a decrease in ICU transfers after PMS implementation, but did not find a significant reduction in ICU LOS.[4]

2.1.3.2 Unintended Consequences

2.1.3.2.1 Negative

Study authors did not indicate many unintended negative consequences as a result of implementing a PMS to detect patient deterioration. Some expressed hypothetical concern raised of over-testing and over-treating patients, but no studies measured outcomes to test these. If the PMS has a low predictive value, patients who are not deteriorating could receive unnecessary treatment or be transferred to a higher level of care as a result. However, this risk can be mitigated by ensuring the use of a highly predictive system.

2.1.3.2.2 Positive

Positive unintended consequences were mentioned by several authors. The tracking and display of patient vitals gave nurses and other clinicians a sense of increased knowledge about their patients. It also allowed the RRT and other primary team members to take a proactive approach to patient care, rather than relying solely on nursing staff activating an RRT call.[7,9] Authors also noted that when nurses did call for an RRT, the system allowed them to communicate their concerns about a patient with objective, quantifiable data. Other potential benefits included nurses spending more time on patient-centered tasks and less time on vital sign collection, and reduced reliance on RRTs. The latter is supported by several studies that found a decrease in rescue events after PMS implementation.

2.1.3.3 Implementation

Implementing a PMS can be difficult technologically, financially, and in terms of workflow changes for staff. The studies we reviewed identified factors that facilitate PMS implementation, as well as barriers to successful PMS implementation.

2.1.3.3.1 Facilitators

A PMS will be effective only if it is both sensitive and specific, to engender clinician trust and reduce false-positive alerts. To achieve this, several prospective studies used an iterative method of setting the PMS variable thresholds with input from clinicians.

When a PMS identifies a deteriorating patient, clinicians who can respond need to be quickly notified. Study authors disagreed on the best method for communicating this need to clinicians. Some favored auditory and visual alerts, and others preferred a noninterruptive dashboard at both the bedside and a central station to reduce potential alert fatigue.[3,7]

Good communication between the bedside clinicians and the RRT was also cited as a facilitator, as well as staff who are well trained and have strong clinical reasoning. Finally, in relation to cost, several PMS systems are now available as electronic health record add-on modules or as standalone systems, sparing hospitals the cost of designing, building, and testing a system.

2.1.3.3.2 Barriers

The nonspecific nature of patient deterioration makes achieving a highly predictive system difficult. Therefore, it is important for clinicians/administrators to test system performance and adjust variable thresholds to best balance speed, sensitivity, and specificity for their setting. For example, some settings may be willing to accept a lower sensitivity to reduce alarm fatigue.

A poorly designed system that is difficult to use can be a barrier. However, even in a well-designed system, staff need to understand the potential value of the PMS, be trained to use it correctly, understand the alerts/indicators it generates, and know how to respond quickly (calling the RRT or activating a Code Blue). A PMS will improve outcomes only if accompanied by comprehensive procedures for escalation, RRT activation, and audit and feedback to staff.

Some PMSs that require manual input of vital signs into the electronic health record can actually delay vital sign recording and recognition of patient deterioration. Insufficient computers to input data and the practice of busy staff taking vital signs but delaying entry of the data were cited as barriers.[7] Finally, the cost of designing, implementing, and storing data for a PMS can be prohibitive for smaller facilities.

2.1.4 Resources

The nonprofit Patient Safety Movement Foundation offers a toolkit on early sepsis detection that includes a technology plan for an automated PMS.

2.1.5 Gaps and Future Directions

More high-quality studies (e.g., robust prospective, randomized, quasi-experimental) could help to understand the effects of CM and IM patient monitoring systems on process and outcome measures in medical/surgical units as well as other hospital units. As pointed out above, the main process measure in these studies (rescue events) is somewhat ambiguous in terms of its effect on outcomes. In addition, traditional outcome measures (mortality, LOS) may be insufficient to evaluate the impact of a PMS. Therefore, clarifying the validity of existing measures with additional studies and/or using other process and outcome measures (e.g., unanticipated cardiac arrests) would be a beneficial future direction. Finally, more studies on effectiveness of different escalation systems would aid the implementation of PMS.

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2.2 PSP 2: Rapid Response Teams

Reviewers: Kristen Miller, Dr.P.H., C.P.P.S., and Katharine Witgert, M.P.H.

2.2.1 Practice Description

Brought to widespread attention by the 2005 Institute for Healthcare Improvement's 100,000 Lives Campaign, the RRT was developed in response to a growing body of evidence that revealed deficiencies in responding to rapid clinical decline in the inpatient setting.[1] A key principle underlying RRTs is that early intervention can prevent avoidable morbidity and mortality in the non-intensive care hospital setting. RRTs have since been widely implemented across the globe.

RRTs act as the efferent limb of the RRS and include the clinical care team that responds to the afferent limb's calls. This team is typically multidisciplinary, ad consists of a nurse, a physician, and a respiratory therapist, although team composition may vary slightly depending on institution policy and guidelines. The RRT assesses patient disposition, which can result in transfer of the patient to the ICU, return of care back to the primary medical team, or revision of the treatment plan.

2.2.2 Methods

To answer the question, "Do RRTs improve patient outcomes?" four databases (CINAHL®, MEDLINE®, PsycINFO®, and Cochrane) were searched for articles published from 2008 to 2018 using the terms "patient deterioration," "failure to rescue," and related synonyms, in addition to "rapid response system," "rapid response teams," "medical emergency teams," and other similar terms. The initial search yielded 121 results. Once duplicates were removed and additional relevant articles from selected other sources were added, a total of 97 articles were screened for inclusion and 37 full-text articles were retrieved. Of those, 10 were selected for inclusion in this review. Articles were excluded if the outcomes were not relevant to this review, the article was out of scope (including not quantitative), or study design was insufficiently described.

Key Findings:

- There is inconclusive evidence as to whether RRT implementation is associated with decreased overall hospital mortality or ICU transfer rates.
- There is moderate evidence that decreased non-ICU cardiac arrest rates are associated with implementation of RRT.
- Recognition of the benefits of RRT implementation often takes a long time.
- Poor safety culture and hierarchies inherent in healthcare are barriers to successful implementation.
- Future studies should focus on developing and adopting common terminology and definitions for RRT mechanisms, outcome measures, and activation mechanisms, as well as on investigating the costs associated with RRT implementation.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

2.2.3 Evidence Summary

A summary of key findings related to FTR and RRT appears above. This section reviews selected studies in greater depth, organized by process and outcome measures.

The 14 studies included in this review include three meta-analyses and two systematic reviews and took place in the non-ICU general medical/surgical units of acute care hospitals. Thirteen of the 14 studies focused on evaluating the impact of RRTs on patient outcomes. One study investigates outcome differences between ICU physician-led and senior-resident-led RRTs.

2.2.3.1 Clinical Outcomes

The included studies reported a range of outcome measures, including cardiac arrest rate, ICU admission, overall hospital mortality, cardiac arrest rate-related mortality, 1-year post-discharge mortality rate for survivors of cardiac arrest, and length of stay. While each study discussed multiple outcome measures, this review focuses on overall hospital mortality rates, cardiac arrest rates, and ICU admission rates, as these were the outcomes most relevant to our review topic as well as most frequently investigated among the included studies.

2.2.3.1.1 Overall Hospital Mortality

Of the three meta-analyses that reported the impact of RRS implementation on overall hospital mortality, two found significant decreases in mortality rates.[2,3] Chan et al.,[4] using 15 adult and pediatric studies with considerable heterogeneity (I^2=90.3%, P<0.001), found no difference in overall hospital mortality. A subgroup analysis of the four pediatric studies did show significant decrease in hospital mortality (RR, 0.79; 95% CI, 0.63-0.98), but significant heterogeneity was observed (I^2=66.0%, P=0.03). Without a control group in most studies, it is difficult to draw conclusions about causality. This is especially true for the overall hospital mortality rate, which Solomon et al. note has been falling since 2000.[3] This trend may confound the results of studies that observed decreases in hospital mortality rate following RRT implementation.

Indeed, Chen et al., in a 2016 study assessing the impact of RRT implementation across New South Wales, Australia, found that overall hospital mortality rates and cardiac arrest rates had decreased in the 2 years prior to RRT implementation.[5] There were no significant changes in these trends once an RRT had been implemented. However, there was a significant decrease in mortality among patients with low mortality risk. This decreased mortality rate was attributed to RRT prevention of cardiac arrests, suggesting that the low-risk population is where future RRT implementation may have the most impact.

2.2.3.1.2 Cardiac Arrest Rate

In their meta-analysis in 2010, Chan et al.[4] determined the pooled relative risk (RR) using 16 studies and found an overall decrease in non-ICU cardiac arrests (CA) after RRT implementation, although with substantial heterogeneity among the included studies (RR= 0.65, 95% CI 0.55-0.77; I^2=73.9%, P<0.001). In subgroup analyses, RRT was associated with a 33.8% reduction (RR, 0.66; 95% CI, 0.54-0.80) in the adult population and a 37.7% reduction (RR, 0.62; 95% CI, 0.46-0.84) in the pediatric population. Similar results were described in the meta-analysis by Maharaj et al.,[2] who found a significant reduction in CA in the adult (RR, 0.65; 95 % CI, 0.61–0.70) and pediatric (RR, 0.64; 95% CI, 0.55–0.74) populations. In the 2016 meta-analysis by Solomon et al.,[3] implementation of an RRT was found to be associated with significantly decreased rates of non-ICU CA (RR, 0.62; 95% CI, 0.55-0.69), with substantial heterogeneity among the included studies. The systematic reviews conducted by Winters et al.,[6] and McNeill et al.,[7] are in alignment with these findings, concluding that RRT significantly reduces in-hospital CA rates.

Two of the single studies reached similar conclusions [8,9] and one study[5] showed a continuing significant trend of decreasing CA that was present before the implementation of the RRT, but unchanged by its introduction.

2.2.3.1.3 ICU Transfers

Three studies reported ICU transfer/admission rates, with varying results. Blotsky et al. found a decrease in ICU admissions from 4.8 to 3.3 per 1,000 patient days (p=0.04), suggesting that the intervention of a

senior-resident-led RRT decreased ICU transfers by intervening prior to patient deterioration.[8] Conversely, Moriarty et al. found an increase in ICU transfers from 13.7 to 15.2 transfers per 1,000 floor days ($p<0.001$), hypothesizing that this could be due to a larger number of deteriorating patients being seen and transferred to the ICU appropriately by the RRT.[10] Meanwhile, Maharaj et al. found no association between RRT and ICU admissions, based on their meta-analysis of 10 studies.[2]

2.2.3.2 Process Outcomes

While all included studies were primarily interested in clinical outcomes, one study used the rate at which the monitoring team called the response team (known as the rapid response call [RRC] rate) as a measure for assessing uptake and use of RRT.

Pain et al. (2017) found that RRT implementation was associated with a 27.3-percent increased RRC rate ($p<0.05$) between initial implementation and after 3 years of RRT use, compared with a 108.6-percent increased RRC rate ($p<0.05$) between 3 and 5 years of RRT use, suggesting that there is a delay between initial implementation of an RRT and staff adaptation to the process.[9]

2.2.4 Unintended Consequences

2.2.4.1 Negative

Study authors did not raise many concerns about unintended negative consequences as a result of RRT implementation. Winters et al. mentioned the potential for a loss of skill and diversion of staff due to dependence on the RRT, staff conflict, and miscommunication.[6] Maharaj et al. suggested that "very sensitive RRC criteria may over-activate the response team, causing fatigue with no tangible benefit."[4] Despite noting potential negative consequences, none of the reviewed studies reported any data related to these hypotheses.[2]

2.2.4.2 Positive

Two studies mentioned RRT implementation impacting do-not-resuscitate (DNR) status of patients.[4,8] In these studies, RRT implementation was found to increase DNR orders, suggesting that RRTs may enhance end-of-life care by allowing earlier opportunities for discussion of patients' DNR status. This may, in turn, further reduce unnecessary ICU admissions, patient suffering, cost, and use of resources.

2.2.5 Implementation

Successful implementation of an RRT requires adoption by both monitoring and response teams, which may be influenced by cost, team composition, and staff perception. Facilitators and barriers to implementation of the RRT are described below.

2.2.5.1 Facilitators

As mentioned above, benefits from RRT implementation may become apparent only after the RRT has been in place for some time. Moriarty et al. saw significant findings beginning in the second year following response team implementation.[10] However, these changes coincided with the institution's efforts to educate nursing staff as well as to increase positive perception of the RRT, suggesting that educational efforts, rather than time, drive lasting culture and process changes. In a systematic review by Daniele et al., eight of nine studies that found significantly decreased rates of cardiac arrests were of institutions that had an RRT in place for at least 1 year.[11] In contrast, a meta-analysis by Maharaj et al.

was unable to find any dose-response relationship between duration of RRT implementation and hospital mortality.[2]

It remains unclear whether RRT composition is an important factor in successful implementation. One systematic review and two meta-analyses found that RRT composition had no impact on cardiac arrest or ICU transfer rates.[2,3,11]

In their systematic review, McNeill et al.,[7] concluded that physician-led medical emergency teams might improve survival, and reduce CA rates and unplanned ICU admissions, whereas the evidence to support nurse-led teams is equivocal. Blotsky et al. [8] studied the use of a single person, the senior resident, as the responder to the afferent limb activation. They were still able to demonstrate significantly decreased cardiac arrest and ICU transfer rates. However, because all of these single studies included a physician as part of the RRT, we cannot draw conclusions regarding optimal team composition.

2.2.5.2 Barriers

Cultural barriers and traditional hierarchical models of patient monitoring and rapid response may prevent successful implementation of RRTs. For example, Moriarty et al. suggest that the monitoring team may hesitate to activate the response team in fear of the call being viewed "as an acknowledgment of inadequacy on their part."[10] Just as a culture of clear communication and teamwork can help to facilitate successful RRT implementation, one that discourages speaking up and instead supports a hierarchical structure can impede both perceptions and use of an RRT.[6]

The RRT is dependent on the monitoring team's engagement, perception, and activation of the RRT. While all included studies detail criteria for activation of the RRT, the actual mechanism of the activation process is often left undefined, without clear descriptions of who participates, what the process involves, or whether activation is mandatory versus voluntary. One study included in Daniele et al.'s systematic review found that changing the activation mechanism from a voluntary to a mandatory call based on physiologic criteria resulted in a statistically significant decrease in cardiopulmonary arrest rates.[11] This suggests that voluntary activation may present a barrier to successful RRT use, while mandatory activation may act as a facilitator. Further research on this topic is needed.

2.2.6 Resources

The Institute for Healthcare Improvement, Agency for Healthcare Research and Quality, and other organizations offer toolkits to help facilitate implementation of an RRT.

2.2.7 Gaps and Future Directions

Despite widespread implementation of RRTs, and perhaps due to such a rapid uptake of RRTs in recent years, several gaps in the research grow increasingly difficult to address. There have been several high-quality systematic reviews and meta-analyses to date, but the methodological quality of each study included in these reviews is generally moderate. Studies to date have been mostly single center, before-after observational, and retrospective, without control groups or accounting for confounding factors. Conventional randomized controlled trials may no longer be possible due to widespread uptake, which eliminates the pool of control groups.[12] Furthermore, even if control groups can be identified, the possibility for contamination of knowledge and cultural changes around RRT is difficult to control for.

Another way to improve the quality of future studies would be for institutions and healthcare systems to develop and adopt common terminology and definitions for RRTs, including mechanisms for activation and outcome measures. This might help to better identify processes or patient groups that are most vulnerable to unnoticed deterioration and therefore stand to benefit the most from intervention, as suggested by Chen et al.[5] The mechanism of RRT activation is one such process that requires further research. Winters et al. hypothesized that RRT utilization rates may be low in some studies due to inadequate RRT activation, despite activation criteria having been met.[6] However, very few studies define the activation process and address the association between the mechanism for activation (e.g., family activation) and patient outcomes.

Finally, no studies to date have investigated the costs associated with RRT implementation.

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Conclusion and Comment

The PSPs reviewed in this chapter aim to reduce FTR by addressing two of its core components: failure to identify and failure to respond to hospital patients who are at risk for rapid clinical deterioration. This review of the evidence finds that implementation of continuous patient monitoring may decrease rescue events and hospital length of stay but not mortality, while IM shows a moderate but inconsistent effect on mortality. It remains unclear whether RRT reduces mortality or ICU transfer rates. Together, these findings suggest that both the afferent and efferent arms of the rapid response system decrease in-hospital adverse events but not overall mortality. Many studies were observational and had an increased risk for bias, indicating a need for more rigorous, high-quality studies.

Findings in both PSPs suggest that an RRS is most successful when there is effective and efficient communication. The electronic monitoring system, bedside staff, and rapid response staff are all susceptible to communication breakdown, and all points along the RRS pathway warrant careful consideration when deciding to implement an RRS. This requires not only education and training but also technical care so as not to create alert fatigue, as well as a cultural shift to support rather than discourage speaking up. Finally, very few studies comment on RRT activation, which is an important bridge connecting the RRS's identification of deterioration and the response to prevent harm. A better understanding of the mechanism and components of this process may elucidate further interventions for minimizing FTR.

3. Sepsis Recognition

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Introduction

Sepsis has been a leading cause of hospitalization and death in U.S. healthcare settings for many years, and accounts for more hospital admissions and spending than any other condition.[1] As a result, preventing, diagnosing, and treating sepsis effectively has been a focus of patient safety and public health in recent years. In this chapter, we discuss two patient safety practices that aim to identify signs of sepsis and septic shock as quickly as possible so that treatment can be started: manual screening tools and electronic patient monitoring systems (PMSs).

Screening tools are manually administered paper or electronic forms that guide clinicians through a set of criteria as they are assessing a patient. The screening process is administered either at a care transition (e.g., presentation at the emergency department [ED] or to emergency medical services [EMS]) or at regular intervals (e.g., the start of every nursing shift). Current evidence indicates that performance (sensitivity/specificity) of the tools varies, especially in the prehospital setting. Evidence for process measure improvement (i.e., time to initiation of treatment) was of moderate strength in both the hospital and prehospital setting. Evidence for outcome measure improvement (mortality, hospital length of stay [LOS], intensive care unit [ICU] transfer, and ICU LOS) was sparse but showed a trend toward improvement. More high-quality studies are needed in diverse settings to test the effects of sepsis screening tools.

Automated systems continuously monitor patient status, such as vital signs, and alert a clinician if criteria for possible sepsis are met. These systems are becoming more widespread, especially in hospitals, which have sophisticated technology infrastructures. While the studies were inconsistent, there appears to be evidence of moderate strength in the current literature for improvement in both process and outcome measures for PMSs. More high-quality studies are needed to confirm these findings, and to identify implementation best practices and lessons learned.

Importance of Harm Area

Sepsis is a syndrome of life-threatening organ dysfunction due to a person's systemic dysregulated response to infection.[2] Sepsis can be caused by many types of infection (bacterial, fungal, and viral) and can affect any age group, from neonatal to geriatric. It is a common reason for hospital admission and readmission, with an estimated incidence of 6 percent of all hospital admissions, or more than 1 million admissions in the United States every year.[3,4] Sepsis also has one of the highest mortality rates of any hospital condition, estimated at 15–30 percent.[4,5] Tracking incidence and mortality over time is challenging due to shifting definitions and an increasing awareness of sepsis. Some studies show an increase in incidence and a decrease in mortality in recent years, but some show no significant change in either.[4,6] Among subgroups, older adults and nursing home residents are much more likely to develop and die from sepsis compared with younger adults and non-nursing home residents.[7] In 2013, $24 billion was spent treating sepsis, more than any other condition treated in U.S. hospitals.[1]

The symptoms of sepsis (e.g., high temperature, high blood pressure) are shared by many other conditions, making sepsis difficult to diagnose, especially in the early stages.[8] In addition, sepsis can start

suddenly and quickly lead to organ dysfunction and death.[8] In response to this, international organizations such as the Society for Critical Care Medicine have focused on addressing the two problems that sepsis presents: delay in recognition and diagnosis of sepsis, and delay in start of treatment, which combined contribute to the high mortality rate for sepsis.[9]

The need for early recognition and rapid treatment have led to guidelines about how to treat septic patients, with aggressive interventions and timeframes. The most commonly adopted of these is the Surviving Sepsis Campaign (SSC) bundle, which has gone through many iterations, and includes starting broad-spectrum antibiotics and intravenous (IV) fluids, and obtaining blood culture and lactate measurements within a 1- to 6-hour timeframe.[10] Many government agencies across the world have proposed measuring and evaluating hospital compliance with the bundle elements to strongly encourage its use. Most notably, since October 2015, the Centers for Medicare & Medicaid Services requires U.S. hospitals to report their performance on a composite process-of-care measure for severe sepsis and septic shock, and ties reimbursement to the measure results. There is occasionally tension between the goals of antibiotic stewardship and sepsis guidelines, with the former focused on reducing inappropriate use of broad-spectrum antibiotics, and the latter requiring rapid and barrier-free initiation of broad-spectrum antibiotics.[11] Clinicians sometimes perceive antibiotic stewardship goals as being purely restrictive, thereby creating tension in decisions about antibiotics; however, good antibiotic stewardship encompasses appropriate administration of antibiotics, including when there is clinical suspicion for severe sepsis or septic shock. In addition, many clinicians have apprehension about the IV fluid level due to the risk of fluid overload.[12]

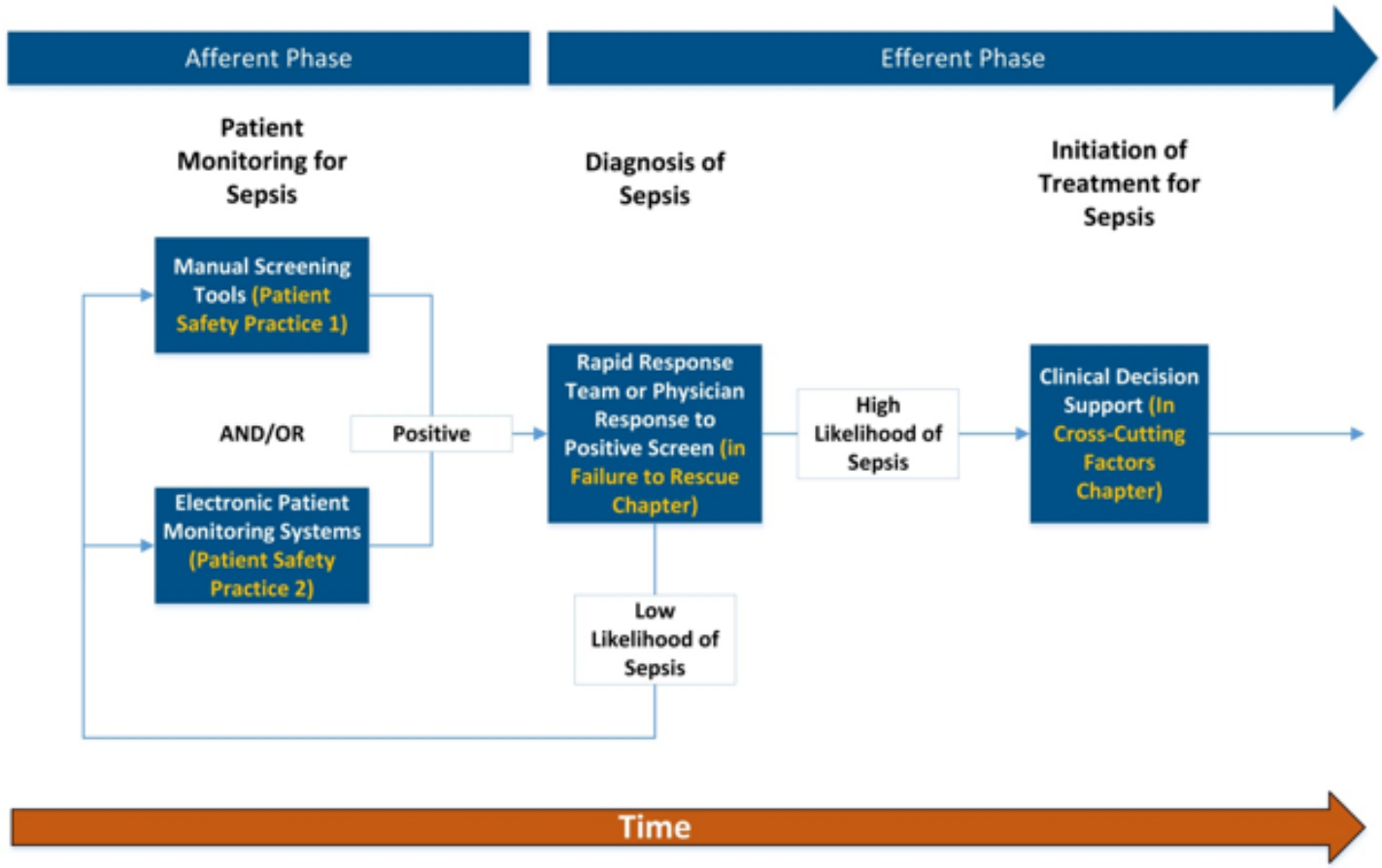
The need to diagnose sepsis unambiguously and quickly has led to development of various diagnostic criteria. The signs and thresholds used in these criteria vary but always include at least one vital sign with abnormal thresholds (heart rate [HR], respiratory rate [RR], blood pressure [BP], temperature, etc.), and sometimes include clinical assessments (mental status, suspicion of infection) and laboratory results (lactate, creatinine). The most commonly used criteria are the qSOFA (quick Sequential Organ Failure Assessment), the NEWS (National Early Warning Score), and the increasingly abandoned SIRS (systemic inflammatory response syndrome) criteria.[13]

Patient Safety Practice (PSP) Selection

A literature search was conducted on six sepsis PSPs in three databases (CINAHL®, MEDLINE®, and Cochrane), and resulting abstracts were reviewed for relevance. Some identified sepsis PSPs (e.g., clinical decision support) spanned multiple harm areas and appear in cross-cutting chapters. One sepsis PSP about readily available antibiotics did not have enough information to warrant a review. The two remaining PSPs (screening tools and patient monitoring systems) are specific to sepsis and have enough evidence to support a review.

Borrowing from the "failure to rescue" literature, diagnostic and treatment processes for sepsis can be grouped into two phases, afferent and efferent, each containing its own related practices.[14] Figure 3.1 below is a conceptual model related to sepsis. The focus of the PSPs contained in this chapter is the afferent phase: how clinicians and hospitals use diagnostic criteria to recognize sepsis quickly, using either manual screening or continuous electronic monitoring. Because of the changing criteria for sepsis, the PSPs do not compare the accuracy of the various diagnostic criteria but rather the effect of these strategies in clinical practice settings. The efferent phase, including treatment for sepsis, occurs after screening/surveillance and is outside the scope of this chapter.

Figure 3.1: Conceptual Model for Sepsis



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3.1 Patient Safety Practice 1: Sepsis Screening Tools

3.1.1 Practice Description

Identifying signs of sepsis as early as possible is critical to averting organ failure and risk of death.[1] However, sepsis does not have a simple diagnostic test or specific symptoms that unambiguously indicate onset. International organizations have developed diagnostic criteria and have recommended screening patients at risk of sepsis using these criteria.[2] Manual paper or electronic tools guide clinicians through the criteria as they assess a patient. The screening process generally takes place either during a care transition (e.g., presentation at the ED or to EMS) or at regular intervals (e.g., the start of every nursing shift). A tool's embedded logic determines if the patient is suspected of having sepsis. If so, the clinician must start treatment as quickly as possible, which has been shown to increase survival.[3,4]

3.1.2 Methods

To answer the question, "Do sepsis screening tools improve patient outcomes?" three databases (CINAHL®, MEDLINE®, and Cochrane) were searched for "sepsis" and related synonyms, as well as "screening," "algorithm," "triage tool," "Early Warning Score," "early alert," and other similar terms from 2008 to 2018. The initial search yielded 998 results; after duplicates were removed, 923 were screened for inclusion and 53 full-text articles were retrieved. Of those, 26 were selected for inclusion in this review. Articles were excluded if the outcomes were not relevant, the article was out of scope (including no quantitative results), or the study design was insufficiently described. Studies in which screening tool implementation was accompanied by other significant sepsis interventions (e.g., changes in antibiotic delivery) are considered in Section 3.3.

General methods for this report are described in the Methods section of the full report.

Key Findings:

- Performance of screening tools varied widely, especially in the prehospital setting. More research is needed to determine the optimal variables and thresholds for a sepsis screening tool.
- There was moderate evidence of process measure improvement in the hospital setting with screening, including time to antibiotics. Prehospital evidence was sparse but showed improvement as well.
- Evidence for outcome measures (e.g., mortality, ICU LOS, ICU transfer) was sparse but showed a trend toward improvement, although the improvement was not always significant.
- Higher quality studies in diverse settings are needed to test the effects of sepsis screening tools.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

3.1.3 Evidence Summary

A summary of key findings related to sepsis screening tools is located in the Key Findings box. The following section reviews the applicable studies in more depth, by measure type and setting.

Fifteen of the 26 studies examining the use of sepsis screening tools took place in a hospital setting, 10 took place in a prehospital setting, and 1 took place in a nursing home. Over 20 different screening tools that incorporate somewhat different diagnostic criteria were used in the 26 studies. The indicators and thresholds used to determine if a patient screens positive for sepsis also differed across tools. Vital signs (HR, RR, BP, temperature, etc.) were present in all tools; clinical assessments (mental status, suspicion of infection) were also common, while laboratory results (lactate, creatinine) were used in only a few tools due to the time it takes to run lab tests and receive results back. Many studies used diagnostic criteria

developed by consensus-based professional organizations, such as the qSOFA, MEWS (Modified Early Warning Score), and the SIRS criteria, but some studies tested other indicators and thresholds.

3.1.3.1 Sensitivities/Specificities of Screening Tools

Diagnostic performance of various screening tools for sepsis was reported in 20 of the 26 studies. None reported process measures or outcomes other than diagnostic performance. Twelve studies were retrospective cohort analyses that assessed whether the screening tool would have identified or ruled out sepsis correctly. Such studies support validity testing of the tools but have a lower strength of evidence than prospective studies because they were not implemented in a clinical setting. Despite these limitations, it is important to have a high-performing tool that reliably identifies and rules out sepsis before testing its effect on processes or outcomes of care. The hospital was the setting in 11 studies, while 8 were focused on the prehospital setting, and 1 focused on the nursing home setting.

The studies each report some or all of the following performance metrics for screening tools: sensitivity, specificity, positive predictive value, negative predictive value, and area under the receiver operating curve. The most widely reported were sensitivity and specificity. When deciding on an acceptable level of sensitivity and specificity for a tool, it is important to consider where the tool is implemented and the processes surrounding its use. For example, in a prehospital setting (EMS) or nursing home, high sensitivity is usually valued over specificity because patients will be reevaluated at the hospital before treatment is started. In a hospital setting, high specificity is also important to reduce alert fatigue and unnecessary treatment.[5]

3.1.3.1.1 Prehospital and Nursing Home

The sensitivity and specificity of the prehospital and nursing home screening tools varied widely. Seven of the eight prehospital studies were retrospective and they were addressed in a 2016 systematic review by Smyth and colleagues that found low to very-low quality evidence for the accuracy of prehospital sepsis screening tools. The authors attributed this to lack of EMS personnel training about sepsis and the inaccuracy of using SIRS criteria alone.[a] They conclude that more validation studies are needed to determine the efficacy of prehospital sepsis screening tools.[6] Hunter et al. (2016) was the only prospective study, and it produced the highest sensitivity of any prehospital screening tool (0.90). That tool was implemented with EMS personnel and was based on SIRS criteria and end tidal carbon dioxide ($ETCO_2$) measurement. Specificity of the tool was 0.54.[7] The only study in a nursing home setting was a retrospective analysis of five different sepsis screening tools, which had sensitivity ranging from 0.27 to 0.79 and specificity ranging from 0.69 to 0.93.[5] The performance of the prehospital tools is summarized in Table 3.1.

[a]SIRS criteria include: temperature higher than 100.4°F or lower than 96.8°F, HR higher than 90 beats/min, RR higher than 20 breaths/min or arterial carbon dioxide tension lower than 32 mm Hg, and white blood cell count higher than 12,000/µL or lower than 4000/µL or with 10 percent immature (band) forms.

Table 3.1: Sensitivities and Specificities of Prehospital Studies

Author, Year	Variables	Sensitivity	Specificity
Bayer et al., 2015[20] (PRESEP)	Temperature (temp), oxygen saturation (SaO2), respiratory rate (RR,) and Glasgow Coma Sclae (GCS)	0.85	0.86
Hunter et al. 2016[7]	Systemic inflammatory response syndrome (SIRS) (temp, heart rate [HR], RR) and end tidal carbon dioxide (ETCO2)	0.90	0.58
Hunter et al., 2018[13]	ETCO2 Quick sequential organ failure assessment (qSOFA) (GCS, blood pressure [BP], RR)	ETCO2: 0.80 qSOFA: 0.68	ETCO2: 0.42 qSOFA: 0.40
McClelland et al., 2015[24] (SST)	SIRS: HR, temp, white blood cells (WBC), RR, arterial carbon dioxide pressure (PaCO2)	0.43	0.14
Polito et al., 2015[25] (PRESS)	HR, RR, BP	0.86	0.47
Seymour et al., 2017[3]	BP, HR, RR, GCS,pulse oximetry (POx)	0.22	0.98
Shiuh et al., 2012[26]	SIRS: HR, RR, temp, plus suspicious of infection and lactate measurement	NR	NR
Sloane et al., 2018[5] (Nursing Home)	Temp, qSOFA (GCS, BP, RR), SIRS (temp, HR, RR), 100-100-100 (temp, HR, BP)	Temp>100.2F: 0.40 qSOFA: 0.27 SIRS: 0.36 100-100-100: 0.79 Temp >99.0F: 0.51	Temp >100.2F: 0.93 qSOFA: 0.88 SIRS: 0.86 100-100-100: 0.69 Temp >99.0F: 0.85
Wallgren et al., 2014[7]	Robson: temp, HR, RR, alert, verbal, pain, unresponsive (AVPU) (glucose, infection possible BAS 90-30-30 Sacle: BP, RR, SaO2	Robson: 0.75 BAS 90-30-90: 0.43	NR

3.1.3.1.2 Hospital

Performance of screening tools in the hospital setting was tested in 11 studies: 7 in the ED, 3 in medical and/or surgical wards, and 1 in a surgical ICU. In the ED setting, Goerlich and colleagues' triage screening tool had the most balanced performance, with sensitivity of 0.85 and specificity of 0.78. The tool was prospectively implemented in the ED of a tertiary hospital and used standard vital signs and muscle oxygen saturation (StO2) to generate a cumulative screening score.[8] The other prospective screening tool, used in the ED setting by Singer and colleagues, achieved a high specificity (0.82) but a low sensitivity (0.34). This tool was implemented in a suburban academic medical center ED and used SIRS criteria and lactate measurement.[9] In medical and/or surgical wards, Gyang et al. reported on a highly sensitive (0.95) and specific (0.92) tool that was prospectively implemented in a 26-bed medical/surgical intermediate care unit based on SIRS criteria and suspicion of infection.[10] MacQueen et al. also reported on a highly sensitive (1.00) and specific tool (0.88) implemented in a general surgical unit that used routinely collected vital signs.[11] In the one surgical ICU study, Wawrose and colleagues found that a screening tool based on vital signs outperformed a more complex tool on sensitivity (0.75 vs. 0.45) while maintaining a high specificity (0.85).[12] The performance of the hospital tools is summarized in Table 3.2.

Table 3.2: Sensitivities and Specificities of Hospital Studies

Author	Variables	Sensitivity	Specificity	Unit
Berger et al., 2013[28]	Hear rate (HR), blood pressure (BP)	0.71	0.41	Emergency Department (ED)
Filbin et al., 2018[22]	Quick sequential organ failure assessment (qSOFA): respiratory rate (RR), Glasgow Coma Sclae (GCS), SBP Sepsis Prediction and Optimization Therapy (SPoT): HR, BP	qSOFA: 0.28 SPoT: 0.56	qSOFA: 0.97 SPoT: 0.95	ED
Goerlich et al., 2014[8]	oxygen saturation StO2, HR, RR, temp	0.86	0.78	ED
Gyang et al., 2015[10]	Systemic Inflammatory Response Syndrome (SIRS): HR, temperature, white blood cells (WBC), RR, arterial carbon dioxide pressure (PaCO2)	0.95	0.92	Medical/Surgery
MacQueen et al., 2015[11]	Temp, HR, RR, spontaneous bacterial peritonitis (SBP), mean arterial pressure (MAP)	1.00	0.88	Surgical
Scott et al., 2014[29]	Cytokine release syndrome (CRS): mental status, capillary refill, peripheral pulse quality, cold/mottled extremities	0.08-0.54	0.84-0.98	Children's ED
Shapiro et al., 2008[30]	Temp, BP, HR, RR, blood culture results	0.97-0.98	0.29	ED
Shetty et al., 2016[35]	SIRS (temp, HR, RR), Muscle oxygen saturation/ Fraction of inspired oxygen (SpO2/FiO2), creatine, bilirubin, platelet count	0.20-0.82	0.57-0.95	ED
Singer et al., 2014[9]	SIRS (temp, HR, RR) and lactate measurement	0.34	0.82	ED
Tirotta et al., 2017[31]	Modified Early Warning Score (MEWS) [temp, HR, RR, BP, and alert, verbal, pain, unresponsive (AVPU)	0.35	0.83	Medical wards
Wawrose et al., 2016[12]	Sepsis Severity Score (SSS): temp, RR, WBC, mental status St. John's Sepsis Agent (SJSA): temp, HR, RR, glucose level, urinalysis results, and blood culture results	SJSA: 0.45 SSS: 0.75	SJSA: 0.85 SSS: 0.86	Surgical Intensive Care Unit

3.1.3.2 Effect on Process Measures

Process measures for a sepsis screening tool were reported in five studies, two in a prehospital setting and three in a hospital setting. The tools used in the studies were not independently validated, but the studies target important process goals, including timely administration of antibiotics and fluids, that have been shown to improve outcomes in patients with sepsis.[3,4] Time to antibiotic administration was reported in all five studies, while time to lactate measurement was reported in four, time to fluid administration in three, and blood culture draw was reported in one study.

3.1.3.2.1 Prehospital

Both prehospital studies showed that use of a sepsis screening tool affected process timeliness measures, although only one effect reached significance; these studies had sample sizes of less than 300 and a moderate risk of bias. Hunter et al. (2019) showed that EMS personnel using a sepsis screening tool decreased time to IV fluid administration, blood culture draw, lactate level draw, and administration of antibiotics compared with septic patients who were not screened. They attribute this

effect to hospitals preparing staff and supplies for a septic patient arrival, and EMS staff gaining IV access and/or starting IV fluids before hospital arrival.[13] Guerra and colleagues found a non-significant decrease in time to antibiotics (p=0.07) for septic patients who were identified by EMS personnel using a screening tool, compared with those not identified by EMS and did not find a significant effect on any other process measures of timeliness.[14]

3.1.3.2.2 Hospital

Among the hospital screening tools that were evaluated for their effect on care processes, one was implemented in the ED and two in the ICU. While the study designs varied, all three studies showed a significant decrease in time to antibiotic administration or an increase in compliance with the SSC time guideline for antibiotic administration. For example, Patocka and colleagues showed that mean time to antibiotics decreased by 21 percent (p= 0.0074) after the implementation of an ED triage screening tool in a 637-bed urban tertiary hospital.[15] Rincon et al. used a tele-health approach for ICU sepsis screening across 10 hospitals and found that it increased compliance with the SSC antibiotic administration guideline from 55 percent to 74 percent (p= 0.001), as well as increasing compliance with the guideline for IV fluids from 23 percent to 70 percent (p = 0.001).[16] A significant improvement in time to lactate measurement was also found in all three studies, in both the ED and the ICU. [15-17]

3.1.3.3 Effect on Outcome Measures

The ultimate goal of a patient safety practice is to improve the patient outcomes. Three sepsis screening tools were studied prospectively and measured patient outcomes: one in the prehospital setting and two in the hospital setting. All three studies were observational in design and had low to moderately sized samples. The outcomes studied were mortality, ICU admissions rate, and ICU LOS. Attributing improvement in these outcomes to sepsis screening tools is difficult, however, because patients with sepsis are generally older, have multiple comorbidities, and may have advance directives for end-of-life care. In addition, reasons for ICU transfer and ICU LOS are multifactorial and not necessarily correlated with sepsis or the use of a screening tool.[13]

3.1.3.3.1 Prehospital

Hunter et al. (2018 was the only prehospital study that measured patient outcomes. This study involved an EMS screening tool with a subsequent alert to the hospital; it found a significant reduction in ICU admissions rate (33% with screening vs. 52% without screening, p=0.003), and a non-significant reduction in mortality (11% with screening, 14% without screening, p=0.565).[13]

3.1.3.3.2 Hospital

In the hospital setting, one study focused on the ICU and one on the ED. Tedesco and colleagues found that a nurse-administered screening tool in the ED of a 320-bed community hospital led to a significant reduction in mortality (18.4% vs. 13.2% days; P = 0.015).[18] Larosa and colleagues implemented an ICU sepsis screening tool in a 673-bed urban teaching hospital and found a significant reduction in mortality after controlling for factors such as mortality in emergency department sepsis (MEDS) score, leucopenia, and age (p=0.01). However, the sample size for this study was quite small (n=58).[17]

3.1.4 Implementation

Despite the lack of conclusive evidence of effectiveness, use of tools to screen patients for signs of sepsis is widespread due to the urgency for identifying sepsis, and based on guidelines and hospital

quality performance measures. However, implementing these tools can prove challenging in terms of resource use and workflow change for staff.

3.1.4.1 Facilitators

Two common facilitators mentioned across studies were education of the clinical staff who will be responsible for administering the screening, and a tool that is easy to learn and use. First, educating nurses and EMS staff about sepsis pathophysiology helps them to better understand and interpret screening parameters, just as these staff are trained to recognize signs of stroke or cardiac arrest. [19] This education may have the additional effect of increasing sepsis care quality, independent of the screening tool itself. Authors stressed that screening tools cannot substitute for the clinical acumen of staff.[10] Second, a tool should be as easy as possible to fit into a clinician's workflow, such as a checklist using a selected number of readily available or routinely collected variables.[20] As a result, lab test results were generally excluded from screening tools. However, it is important to balance the simplicity of a tool and its ease of use with strong sensitivity and specificity. Other facilitators mentioned in these studies included consistent and complete documentation of vital signs on which screening algorithms are based, and standardized use of the tool across hospital units to reduce confusion and communication breakdowns when patients or staff move between units.[5,21]

3.1.4.2 Barriers

Screening every patient for signs of sepsis on a regular basis is labor and time intensive, regardless of the setting. The yield in terms of identifying emerging sepsis may also be low, depending on the prevalence of sepsis in the setting in question. Additionally, the frequency of screening (for example, once per hospital shift) can delay diagnosis of sepsis, defeating the purpose of the screening tool. As a result, transitions of care such as EMS ambulance transport and ED admission are often targeted as optimal times for screening.[22,23] Other potential barriers include alert fatigue if the tool used is not specific enough, and a possible increase in drug resistance from more and longer use of antibiotics. However, there is no reported evidence about these effects. Finally, without proper training and an easy-to-use tool, adherence by clinical staff may be suboptimal, as reported by O'Shaughnessy et al., diminishing potential benefits.[19]

3.1.5 Resources

- The SSC website offers numerous paper screening tools for different settings: http://www.survivingsepsis.org/Resources/Pages/Protocols-and-Checklists.aspx.
- The Minnesota Hospital Association published their sepsis toolkit for the ED and long-term care settings, including the screening tool, posters, and sepsis order set: https://www.mnhospitals.org/quality-patient-safety/quality-patient-safety-initiatives/sepsis-and-septic-shock#/videos/list
- The New Jersey Hospital Association published a sepsis toolkit for post-acute care settings that includes a screening tool, educational materials and quizzes, and a communication tool: http://www.njha.com/media/328416/NJSepsisLACToolkitPost-AcuteCareSettings.pdf
- The Hospital Improvement Innovation Network (HIIN) held a webinar on sepsis screening in 2017 that includes some examples of tools and lessons learned: http://www.hret-hiin.org/Resources/sepsis/17/Sepsis%20020917_508.pdf

- Finally, the U.S. Centers for Disease Control and Prevention (CDC) published a toolkit on sepsis surveillance in 2018 that includes processes for tracking sepsis incidence in a hospital: https://www.cdc.gov/sepsis/pdfs/Sepsis-Surveillance-Toolkit-Aug-2018_508.pdf

3.1.6 Gaps and Future Directions

It is clear from the available literature that higher quality studies (e.g., robust prospective, randomized, quasi-experimental) with larger sample sizes and diverse settings would quantify the effects of sepsis screening tools on process and outcome measures. In addition, the optimal set of variables and thresholds for rapidly identifying a septic patient is not completely settled.

With the emergence of automated electronic screening (see Section 3.2), the use of paper screening tools may be less common in the hospital setting, and more appropriate for prehospital settings such as EMS, nursing home, and home health. Robust studies on the effects of screening tools in these settings would be beneficial.

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3.2 Patient Safety Practice 2: Sepsis Patient Monitoring Systems

3.2.1 Practice Description

Identifying signs of sepsis in a patient as early as possible is critical to averting organ failure and risk of death.[1] However, sepsis does not have a simple diagnostic test or specific symptoms that unambiguously indicates onset. International organizations have developed diagnostic criteria and recommend screening patients at risk of sepsis using these criteria.[2] Automated electronic patient monitoring (i.e., surveillance) for signs of emerging sepsis is becoming more widespread, especially in hospitals, which have sophisticated technology infrastructures. Such systems automatically and continuously monitor data from telemetry devices and/or electronic health record (EHR) entries, and alert a clinician if set criteria for sepsis are met. If, after evaluation, a clinician determines that the patient has sepsis, the clinician must start treatment immediately to reduce mortality and improve patient outcomes.[2] The goal is to decrease the time to treatment initiation for sepsis, which has been shown to increase survival.[3,4]

3.2.2 Methods

To answer the question, "Does continuous patient monitoring for sepsis improve patient outcomes?" three databases (CINAHL®, MEDLINE®, and Cochrane) were searched for "sepsis" and related synonyms, as well "monitoring," "surveillance," and other similar terms, from 2008 to 2018. Additional relevant articles from other sources were added as they were found. The initial search yielded 345 results; after duplicates were removed and additional articles added, 350 were screened for inclusion and 55 full-text articles were retrieved. Of those, 15 were selected for inclusion in this review. Articles were excluded if the outcomes were not relevant, the article was out of scope (including not quantitative), or study design was insufficiently described. Studies about PMS implementation that also included significant sepsis interventions (e.g., changes in antibiotic delivery) are considered in Section 3.3.

Key Findings:

- There was moderate evidence of process measure improvement across multiple types of hospital units, and evidence was most consistent outside of the ICU.
- Evidence for outcome measures (e.g., mortality, ICU LOS, ICU transfer) was mixed, but over half of the studies showed a significant improvement, and several showed an absolute improvement that did not reach statistical significance.
- Higher quality studies are needed to test the effects of sepsis monitoring systems on process and outcome measures.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

3.2.3 Evidence Summary

A summary of key findings related to sepsis PMS is located in the Key Findings box. This section reviews applicable studies in more depth, by measure type (process and outcome) and setting. Please note that sensitivities and specificities of PMSs are not examined because the algorithms within PMSs that scan for sepsis can be constantly adjusted to fit the needs of the setting and optimize performance, as opposed to a static manual screening tool. Upon designing and implementing a sepsis PMS, the

clinicians/administrators typically test the system performance and adjust variable thresholds to best balance speed, sensitivity, and specificity for their setting.

All included studies took place in the hospital setting: five in the ICU, five in the ED, three in general units, one in a telemetry unit, and one in multiple hospital units (ICU, pediatric ICU, and medical/surgical units).

3.2.3.1 Effect on Process Measures

While assessing PMSs for effects on outcome measures (e.g., mortality) is the ultimate goal of this PSP, it is also important to evaluate whether a PMS improves sepsis care processes. Process measures are typically based on evidence-based clinical recommendations, and an improvement in process measures would indicate that patients are receiving care that has been shown to lead to better outcomes. Processes that are commonly targeted for improvement are the timely administration of antibiotics, lactate measurement, blood culture draw, and fluid administration. One or more process measures for sepsis PMSs were reported in nine studies: four in the ED, three in the ICU, and two in noncritical care units. Studies had various designs, including two randomized controlled trials (RCTs), one quasi-experimental study, and six observational pre/post studies. In addition, four systematic reviews covered this topic to some degree. The most commonly reported process measure was time to antibiotic administration (n=8), followed by time to lactate measurement and blood culture draw (n=5 each), and time to fluid administration (n=3).

A systematic review by Warttig and colleagues, which included RCTs conducted in the ICU through September 2017, determined that there is very low-quality evidence for any improvement in time to antibiotic administration after implementation of a PMS, and none of the studies they reviewed showed a significant improvement.[5] None of these studies reported on any other process measures. Three other systematic reviews (Despins, Makam et al., and Alberto et al.) included both non-RCT and non-ICU studies, and found mixed results on improvement in sepsis process measures. Despins searched for automated sepsis detection in the hospital setting from 2005 to 2015;[6] Makam and colleagues searched for electronic sepsis systems through June 2014;[7] and Alberto and colleagues searched for both continuous monitoring and intermittent monitoring through June 2016.[1] Several studies these authors reviewed (all observational and all outside of the ICU) reported that PMSs significantly improved time to administration of antibiotics, lactate draw, blood culture draw, and/or fluid administration. For example, Narayanan and colleagues, after implementing a PMS monitoring vital signs in the ED of an academic medical center, found that average time to antibiotic administration decreased from 61.5 minutes to 29.0 minutes ($p=<0.001$).[8] The authors of one systematic review hypothesized that PMSs in the ICU may not be as effective as those outside of the ICU because clinicians in the ICU are already vigilant for signs of patient deterioration, so a sepsis alert may be redundant, among other reasons. [7]

Of the six studies we reviewed that were published after the systematic reviews were conducted, five found a significant effect of a PMS on at least one process measure. Of these five, one was an RCT and the others were observational studies. An RCT in two ICU units with a total of 32 beds at an urban medical center (Shimabukuro et al.) found that patients with automated sepsis monitoring received antibiotics an average of 2.76 hours earlier than patients in the control group and had blood cultures drawn an average of 2.79 hours earlier than patients in the control group.[9] Austrian et al. was the only new study that found no effect of a PMS on time to first lactate measurement or antibiotic administration prior to blood cultures. This study was conducted in the ED and urgent care units of an

urban academic medical center;[10] it was a pre/post observational study with control of possible cofounders, and the authors suggested that alert fatigue from a tool with low positive predictive value contributed to the lack of impact on process measures.

3.2.3.2 Effect on Outcome Measures

The patient outcomes in the studies of automated PMSs included mortality, ICU transfer rate, hospital LOS, and ICU LOS. Outcome measures for sepsis PMSs were reported in 12 studies: 3 in the ED, 5 in the ICU, 2 in general units, 1 in a telemetry unit, and 1 in multiple hospital units (ICU, PCU, and medical/surgical units). It is difficult to attribute effects on any of these measures, or lack thereof, to a PMS intervention, because many patients who develop sepsis are older, have multiple comorbidities, and may have advance directives for end-of-life care, all of which also affect the outcomes of interest. In addition, reasons for ICU transfer and ICU LOS are multifactorial and not necessarily correlated with sepsis or the PMS.[11]

Eight of the 12 studies found a significant effect of a sepsis PMS in improving at least one outcome measure, and others showed absolute, but not statistically significant, improvements. The studies that showed a significant improvement included two RCTs, one quasi-experimental study, and five observational studies. Six of the 12 studies that reported mortality showed a statistically significant decrease after implementing a PMS. For example, Manaktala and Claypool found a 41–53 percent drop in sepsis mortality ($p = 0.03$-0.06) after implementing a PMS in the three general units of a 941-bed tertiary teaching hospital.[12] A study in nine neonatal ICUs across the United States showed a significant reduction in mortality (8.1% vs. 10.2%, $p = 0.04$) after implementing a neonatal sepsis PMS.[13] Several studies showed an absolute reduction in mortality that was not statistically significant. For example, Hooper and colleagues conducted an RCT of a "listening application" that monitored patient vital signs in the 35-bed medical ICU of a large academic tertiary medical center, and found 14 percent mortality in the control group and 10 percent in the intervention group ($p = 0.29$).[14]

Nine studies reported on hospital LOS, and four found a significant effect of the sepsis PMS. For example, McCoy and Das found a 9.55-percent decrease in hospital LOS after the implementation of a machine learning-based PMS in multiple hospital units (ICU, PCU, and medical/surgical units) in a 242-bed regional community hospital.[15] In contrast, Manaktala and Claypool, described above, showed a significant decrease in mortality but did not find a significant decrease in hospital LOS.[12]

Only one of the four studies (Jung et al.) that reported on ICU LOS found a significant effect from a PMS. This was an observational study of a PMS implemented in a 34-bed surgical ICU in a large academic medical center.[16] The studies that found no effect on ICU LOS varied in setting, with one implemented in the ED, one in a medical ICU, and one in all noncritical care units.[b] One study attributed lack of impact on ICU LOS to a PMS with poor predictive value,[10] and one credited the already vigilant ICU staff;[14] the third was underpowered to detect modest changes in ICU LOS. Two studies reported on ICU transfer rate, and neither found a significant effect on this or any other outcome measure.[10,17] Several studies that showed significant effects on process measures showed no significant effects on outcome measures; for example Umschied and colleagues.[17]

[b]Studies conducted outside of the ICU measured subsequent ICU LOS in patients who were transferred to the ICU from their unit.

3.2.4 Implementation

An automated surveillance system is less time consuming for staff than manual screening for sepsis and alerts clinicians in near real time to a patient's deteriorating condition, more quickly than most manual screening strategies. However, implementing an automated PMS for sepsis can be difficult technologically, financially, and in terms of workflow changes for staff. The studies we reviewed identified supporting factors that facilitate PMS implementation, as well as barriers to successful PMS implementation.

3.2.4.1 Facilitators

As with manual screening tools, implementing a PMS will be effective only if the system has a high level of sensitivity and specificity, to engender clinician trust and reduce false-positive alerts. To achieve this, some prospective studies iteratively revised thresholds for key values, with input from the clinicians, to optimize tool performance.[15,18] Some more recent studies used machine learning to optimize system performance. [9,18] To improve system usability, input from clinicians was solicited in some studies, followed by adaptations. These included allowing a nurse to "snooze" an alert for 6 hours if the patient is already under assessment for sepsis, or implementing a "traffic light" system on a dashboard to visually show clinicians which patients are in a warning zone (yellow) or need urgent attention (red).[15,19] Other facilitators mentioned in the studies included: consistent and complete input of vital signs on which the PMS relies, having a specific staff member assigned to receive all alerts and determine if a physician needs to be called, and designing the PMS to work reliably even if data are incomplete.[15,20,21] Building an automated PMS from scratch is costly, but several PMS systems are now available as an add-on EHR or telemedicine module, which is more efficient for a hospital than designing and testing a de novo system.

3.2.4.2 Barriers

The nonspecific nature of sepsis makes achieving a highly predictive system difficult, whether on paper or in an automated PMS. This is particularly difficult in pediatric settings because the "normal" ranges for vital signs are age dependent and more difficult to fine tune.[22] In addition, if the electronic monitoring and alerting system is poorly designed or difficult to use, it can lead to clinician confusion, frustration, and possibly to worse patient care. [23] For example, if the alert physicians receive contains too little information (or too much), or if the action required is not clear, physicians may find the system too difficult or burdensome to use. [23,24] Lack of adequate staff training on using the system is also a potential barrier, even if a system has high sensitivity and specificity. Additionally, the cost of designing and implementing a PMS can be prohibitive for smaller hospitals, and while an EHR add-on can reduce cost, it may result in less customizable functionality. Finally, after a system is implemented, refining the algorithm and updating it based on changing sepsis criteria require close work with the facility's IT department, which can be resource and time intensive.

3.2.5 Resources

The nonprofit Patient Safety Movement Foundation offers a toolkit on early sepsis detection that includes a technology plan for an automated PMS: http://patientsafetymovement.org/wp-content/uploads/2016/02/10-Sepsis-April-2016.pdf.

3.2.6 Gaps and Future Directions

Due to the mixed results, more high-quality studies could help to understand the effects of sepsis PMSs on important process and outcome measures in different hospital units.

The emergence of machine learning technology has the potential to improve the accuracy, consistency, and customizability of PMSs. Rather than rules-based patient monitoring with predetermined thresholds, machine learning can continually learn from sepsis and nonsepsis cases, and be able to better and more quickly predict when a patient is at risk of sepsis.[15] More studies testing the effect of these systems on processes and outcomes are needed. In addition, the design and usability of systems could benefit from additional studies to determine the optimal display of alerts, dashboards, and other clinical decision support.

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3.3 Multicomponent Sepsis Interventions

3.3.1 Overview

Identifying sepsis as quickly as possible is of critical importance to improving outcomes, but there are other areas of sepsis care and management that can improve outcomes, such as test ordering and results delivery, and initiation of treatment following a sepsis diagnosis. In response to this complexity, some institutions have implemented multicomponent quality improvement (QI) programs aimed at improving the full spectrum of sepsis recognition and care. Several studies found in the search results for the PSPs Patient Monitoring Systems and Screening Tools concern such multifaceted QI initiatives. We did not include these studies in the PSPs above, because it is impossible to know which elements of an initiative are responsible for any process or outcome effects. However, five such studies are briefly discussed here.

All five studies were in the hospital setting, three of them in the ED.[1-5] All five included a manual screening tool or a PMS accompanied by an education program for clinicians and other components that varied by study. Four of the five included a sepsis-specific EHR order set so that clinicians could efficiently order the initial workup and goal-directed therapy (i.e., broad-spectrum antibiotics, IV fluid) specified in the SSC bundle. Several programs aimed to improve time from antibiotic ordering to initiation of treatment and used strategies such as ensuring that antibiotics are well stocked on the unit. One study increased the number of nurses in the ED and provided more space for triage. All studies were observational in design and therefore more prone to bias than randomized or quasi-experimental studies.

3.3.2 Evidence Summary

All five multicomponent studies reported an improvement in at least one process measure, including time to antibiotic administration or compliance with the SSC bundle. For example, Judd and colleagues found that time to antibiotic administration fell from 154 minutes to 57 minutes (p=<0.001) after implementing a screening and fast antibiotics program in all units of a 433-bed tertiary care medical center.[3] Gatewood and colleagues implemented a manual screening tool, EHR alerts, and an order set in the ED of a 450-bed academic hospital, and found that SSC bundle compliance increased from 28 percent to 71 percent (p=<0.001).[2]

Despite these process improvements, only two of the five studies found a significant effect on outcome measures. Judd et al., described above, reported a significant reduction in ICU LOS (5.85 vs. 4.21 days, p=0.003).[3] MacRedmond and colleagues reported a decrease in hospital mortality rate (51.4% vs. 27.0%, p=0.02) after implementation of a screening and order set QI program in the ED of a 500-bed tertiary care teaching hospital.[4] Three studies reported absolute improvements in mortality or hospital LOS that did not reach statistical significance. One study reported an improvement in a sepsis-related mortality index, but did not report a p score or confidence interval to assess significance.[1]

3.3.3 Implementation

Many of the barriers and facilitators to the implementation of a multicomponent intervention are similar to those for implementing a screening tool or PMS, including the importance of clinician education to identify signs of sepsis onset and consistent protocols across hospital units. Additional facilitators mentioned in these five studies included strong teamwork among providers, pharmacy staff, and nursing personnel, and empowering the pharmacy staff to take a more active role in prescribing and

ensuring initiation of antibiotics. One study found that additional nursing staff and space for triage were needed to overcome delays in diagnosis and treatment of sepsis.[5]

3.3.4 Gaps and Future Directions

While implementing complex QI for sepsis care is difficult to study in an evidence-based systematic review, the complexity of sepsis detection and treatment may require a multicomponent approach to reduce mortality and improve other process and outcome measures. More studies with consistent sepsis QI components and rigorous designs (randomized, quasi-experimental, etc.) would be needed to be able to review the consistent effects across studies.

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Conclusion and Comment

The two PSPs reviewed in this chapter aim to reduce the time to recognition of sepsis so that treatment can be initiated quickly, with improvement in important patient outcomes. The review of evidence shows that manual screening tools can improve time to treatment, but the effect on mortality and other outcome measures is uncertain. Such tools may be most useful in non-hospital settings such as EMS and nursing homes, but many more studies are needed to test their effects in these settings. Evidence for PMSs in the hospital setting showed some improvement in both process and outcome measures, especially in non-ICU units. However, many studies were observational in design, limiting their strength and increasing the risk of bias. More rigorous studies are needed to test the effects of these systems.

Implementing a screening tool or PMS for sepsis requires dedicated resources and effective staff training, and it can be costly. Either type of tool can be effective if it demonstrates acceptable and sustained sensitivity and specificity, which requires pre-validation and regular monitoring. A manual screening tool is more time intensive for clinicians, but an electronic PMS may be more costly to implement and more difficult for staff to use. The customizability of a PMS's features (e.g., "snooze" button) can add flexibility to the complexities of sepsis care, but this comes with a higher cost to implement than a manual screening tool. The decision to implement a sepsis recognition PSP, and whether it should be manual or automated, should be based on the needs and constraints of the particular setting rather than a "one-size-fits-all" approach.

4. *Clostridioides difficile*[c] Infection

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Introduction

Preventing *Clostridioides difficile* infection (CDI) in healthcare settings is an important U.S. public health priority and has led to new research, guidelines, and reporting requirements that have emerged since the last version of this report, *Making Health Care Safer II* (MCHS II). While many of the patient safety practices (PSPs) that help prevent a range of healthcare-associated infections (HAIs) also help to prevent the transmission of CDI (e.g., contact precautions), several CDI-specific practices address the unique risk factors, pathology, and transmission of CDI.

After discussions with the Agency for Healthcare Research and Quality (AHRQ) and the Technical Expert Panel, as well as an indepth review of published guidelines and PSP research, the following CDI-specific PSPs were selected for review in the CDI chapter of this report:

- Antimicrobial Stewardship
- Hand Hygiene
- Environmental Cleaning
- Surveillance
- Testing

We retrieved and screened studies that evaluated these PSPs and were published in English from 2008 onward. Many studies were quasi-experimental with a pre-post design, and most were in hospital settings (although some research was in long-term care facilities [LTCFs]).

The search revealed multiple studies that evaluated outcomes following combined implementation of more than one enhanced prevention strategy. After reviewing the results of our search for the five above PSPs, we decided to include a section on:

- Multicomponent CDI prevention Interventions.

Multicomponent studies show outcomes associated with different combinations of CDI PSPs. They also offer insight into implementation methods, as well as challenges and facilitators of CDI prevention interventions.

Other CDI PSPs such as contact precautions and patient isolation continue to be recommended by experts[1] and were addressed briefly in the last MHCS report. Communication and staff education were also identified in the CDI PSP guidelines and are often important components of the reviewed PSPs (e.g., clinician *education* about revised antimicrobial prescribing guidelines and *communication* of CDI status

[c]During the writing of this report, the Clinical and Laboratory Standards Institute (CLSI) and the CDC transitioned from use of the name *Clostridium difficile* to *Clostridioides difficile*. For the purposes of this report, the names are synonymous.

after testing). Since these are cross-cutting practices and little research focused on these practices and this harm area specifically, they are discussed separately in the cross-cutting chapter of the report.

Background

C. difficile is a contagious bacterium that can cause diarrhea, fever, colitis (an inflammation of the colon), toxic megacolon (a dilated colon that may be accompanied by septic shock), and, in some cases, death. The *C. difficile* bacterium colonizes in the large intestine. In infected patients, toxins produced by the organism cause CDI symptoms, primarily diarrhea and colitis. The most common risk factors for *CDI* are antimicrobial use, advanced age, hospitalization, and a weakened immune system. *C. difficile* is transmitted through the fecal-oral route and acquisition is most frequently attributed to the healthcare setting.[2,3]

Complications are common in patients age 65 and older and an estimated 1 in 11 patients 65 and older with healthcare-associated *CDI* dies within 30 days of CDI diagnosis.[4] Patients with a healthy immune response to the organism can be carriers of *C. difficile* (and contagious) but asymptomatic. These patients are considered "colonized" and are at higher risk of developing CDI.[5]

Research on CDI prevention practices has evolved and expanded over the last decade. Therefore, to address *C. difficile* prevention, this report dedicates an entire chapter to CDI PSPs; in the last report, much of the information on HAI PSPs was grouped together, in a more "horizontal" approach to prevention. In addition, the previous report noted the emergence of hypervirulent *C. difficile* strains and briefly discussed research on CDI risk prediction tools. That report noted that CDI PSPs with good supporting evidence were wearing gloves and antimicrobial stewardship. Alternatively, the current review found strong evidence that supports not just contact precautions and antimicrobial stewardship, but also environmental cleaning practices, surveillance, and testing as effective PSPs for preventing CDI.

The research reviewed in this report reflects not only new knowledge, but also new technologies and policies now in widespread use. For example, electronic health records (EHRs) are now commonly used and are valuable for antimicrobial stewardship efforts and CDI surveillance. Research on no-touch decontamination technology has grown in the last 10 years, as has understanding of CDI transmission pathways. Testing methods have also evolved, with Food and Drug Administration (FDA) approval of nucleic acid amplification tests (NAATs) in 2009. There are increased mandates for surveillance of CDI and the standard interim CDI case definitions that the CDC published in 2007 have been revised in recent years.[1,6] Facilities have implemented new automated surveillance systems, and CDI data collection at the national level is now standardized, with the advent of the National Healthcare Safety Network's (NHSN's) LabID Event reporting in 2013.

Importance of Harm Area

CDI is among the most common HAIs, representing roughly 12 percent of all HAIs.[7] According to a recent estimate, approximately half a million incident clinical infections occur (with more than 100,000 in U.S. nursing homes) per year in the United States, with around 30,000 deaths per year as a result of the pathogen.[3,4] The financial cost of CDI is also high; in recent years, CDI has resulted in about $5 billion a year in healthcare costs.[8,9] Costs attributable to primary and recurrent CDI are $24,205 and $10,580 per case, respectively.[10] CDI colonization is also a concern, and two U.S. studies found that around 10 percent of admitted hospital patients were colonized with *C. difficile*.[11,12]

CDI incidence nearly tripled in the first decade of the 21st century,[13] and data from 2010 to 2016 showed CDI rates plateauing. However, after falling short of 2013 reduction goals, the Department of Health and Human Services set a target reduction of 30 percent in hospital-onset CDI from 2015 to 2020.[14] Healthcare-associated CDI has been decreasing slightly, while community-associated (CA) CDI is stable or increasing slightly; according to CDC estimates, in 2015, almost half of CDI cases were CA.[15]

The clinical severity of the infection has also evolved since the last report. Increasingly virulent strains were a concern roughly 10 years ago.[1] However, a 10-year study of a sample of inpatient data found CDI-related mortality rates declined from 2005 to 2014.[16] Other CDI incidence outcomes, including rates of recurrent CDI, have increased.[17] It is notable that healthcare-associated CDI incidence trends differ based on setting, with a greater decline seen in nursing homes versus hospitals and other healthcare facilities.[18]

Reimbursement policies have increasingly mandated and reinforced the reduction of CDI. CDI LabID Event reporting began in January 2013 for all acute care hospitals facilitywide using the NHSN. The Centers for Medicare & Medicaid Services (CMS) Inpatient Quality Reporting program's CDI reporting requirements became mandatory as of January 1, 2013. Since 2017, CDI rates are among the hospital-acquired complications CMS uses to penalize the lowest performing hospitals. Many States also now mandate CDI data submission by hospitals to NHSN as part of State HAI public reporting programs.[19] In the future, participation in surveillance reporting will increase and include a broader spectrum of settings. For example, data from a larger group of LTCFs will be used to establish national benchmarks and track achievement of prevention goals.[20]

PSP Selection

To identify the PSPs for inclusion in this report, we started by reviewing the consensus guidelines for CDI prevention published by government agencies and reputable organizations. From this review, we developed an initial list that was reviewed by AHRQ and the Technical Expert Panel. The focus of this review was to identify practices that combat a prevalent harm in the U.S. healthcare system or a harm that has a high impact (e.g., high mortality). After this review and a narrowing of practices, we conducted a literature search in two databases (CINAHL and MEDLINE) and reviewed resulting abstracts for relevance. As noted, some CDI PSPs (e.g., staff training) spanned multiple harm areas, so they were moved to cross-cutting chapters (and some CDI PSP searches yielded too few articles to warrant a review [e.g., communication, contact precautions]).

Five PSPs had sufficient research in the last 10 years to conduct a review. While screening articles, we found several studies of interventions that included more than one CDI PSP (i.e., multicomponent prevention interventions). Due to the number of studies on multicomponent interventions that included patient outcomes, we decided to include an addendum on this topic.

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4.1 PSP 1: Antimicrobial Stewardship

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This review includes a summary of evidence published from 2008 to 2018 for antimicrobial stewardship[d] as a practice to prevent CDI. After a brief overview of the foundational elements of antimicrobial stewardship programs (ASPs) as recommended by the CDC, this review explains how antimicrobial stewardship is believed to work as a safety practice for preventing CDI and discusses implications of recent policy changes. We examine the evidence for the estimated effect of ASPs on CDI incidence rates, starting with meta-analyses and followed by individual studies in hospitals and LTCFs. We then provide a summary of common ASP components and explores additional implementation and contextual factors, including settings, resources, and provider buy-in. Finally, we discuss research gaps and future directions for ASPs and CDI prevention.

Key Findings

- Most studies showed statistically significant or statistically nonsignificant decreases in facility or ward-level CDI after a period of antimicrobial stewardship.
- The most common ASP interventions are formulary restrictions, audit and feedback, and education.
- In the reviewed studies, significant reductions in CDI were associated with higher baseline CDI rates/outbreaks, ASPs developed specifically to reduce CDI (as opposed to ASPs focused on other clinical and microbiological outcomes), and ASPs that included restrictions of high-risk antimicrobials and/or a preauthorization component.
- Research is needed on the impact of different ASP components, financial costs/savings of ASPs, and ASPs in a variety of healthcare settings.
- ASPs require staffing, technological resources, and provider buy-in.
- In the future, ASPs and ASP research will benefit from improved study design and a regional perspective on CDI prevention.

4.1.1 Practice Description

ASPs are intended to limit and optimize antimicrobial prescribing, reduce the evolution of antibiotic-resistant bacteria, and improve patient outcomes. To meet these goals, the CDC provides the "Summary of Core Elements of Hospital Antibiotic Stewardship Programs." The elements outlined below provide a basic framework of recommendations for hospital settings. (The CDC also provides core elements for nursing homes, outpatient settings, and small and critical access hospitals, and resource-limited settings).[1]

- Leadership Commitment: Dedicating necessary human, financial, and information technology resources.
- Accountability: Appointing a single leader responsible for program outcomes. Experience with successful programs shows that a physician leader is effective.
- Drug Expertise: Appointing a single pharmacist leader responsible for working to improve antibiotic use.
- Action: Implementing at least one recommended action, such as systemic evaluation of ongoing treatment needs after a set period of initial treatment (e.g., "antibiotic time out" after 48 hours).
- Tracking: Monitoring antibiotic prescribing and resistance patterns.
- Reporting: Regularly reporting information on antibiotic use and resistance to doctors, nurses, and relevant staff.

[d]The term "antibiotic stewardship" is also used in the research; however, increasingly, "antimicrobial stewardship" is the preferred term, as it includes medicines used to treat a broader scope of organisms. In this review, we use the terms synonymously.

- Education: Educating clinicians about resistance and optimal prescribing.

These elements are foundational and meant to complement additional ASP guidelines. The CDC notes that no template exists for an ASP, and ASPs can be effective in a variety of settings and under a diverse set of conditions. While the ASPs studied in the papers selected for this report included these foundational elements to varying degrees, they take many different forms based primarily on a particular facility's resources and needs. Frequently, the ASPs were developed and executed by a multidisciplinary team with medical, pharmaceutical, and/or microbiological expertise.

The studied ASPs required tracking and reporting of data (at minimum quantifying antimicrobial use and CDI rates), as well as staff education and outreach. The "Action" element was operationalized through different strategies, the most common of which were patient case reviews, audits of antimicrobial use, restrictions on high-risk antimicrobials, and provider education. The Infectious Diseases Society of America and Society for Healthcare Epidemiology of America (IDSA/SHEA) guidelines[2] recommend minimizing the frequency and duration of high-risk antimicrobials and using local epidemiology to determine which antimicrobials to address in an ASP. The guidelines further state that ASPs should consider reducing/restricting the use of drugs including fluoroquinolones, clindamycin, and cephalosporins.

4.1.2 Antimicrobial Stewardship as a PSP

Antimicrobial exposure is widely considered one of the most significant and modifiable risk factors for CDI. In the last two decades, at the population level, increasing rates of CDI have been linked to increases in antimicrobial prescribing, particularly in older patients.[3] Patients receiving, or having recently received, antimicrobial therapy are more susceptible to colonization or infection with pathogenic bacteria such as *C. difficile* because antimicrobials alter gastrointestinal tract flora, destroying the bacteria that help to protect against *C. difficile.*

The length and type of regimen also impacts CDI risk. Several broad-spectrum antimicrobials have been most strongly linked to CDI,[4] and certain outbreaks appear to be associated with heavy prescribing of particular antimicrobials.[5] Therefore, many CDI ASPs are designed to reduce the use of particular "high-risk" antimicrobials. The CDC found that people receiving high-risk antimicrobials had a three times higher risk of CDI than did people with low-risk or no antibiotic use.[6]

There is increasing urgency about reducing overreliance on antimicrobials).[7] The CDC estimates that between 30 and 50 percent of antimicrobial prescriptions are clinically inappropriate.[8] In 2015, the White House released a National Action Plan that included goals to implement antimicrobial stewardship in healthcare facilities. In 2016, CMS implemented a rule requiring nursing homes and LTCFs to have ASPs to monitor the use of antimicrobial drugs; and in 2017, The Joint Commission began assessing ASPs as part of their accreditation standards. Other countries have similar efforts,[9] and a number of resources are designed to help facilities implement ASPs. We highlight some of these resources later in this section.

4.1.3 Methods

This section describes literature search and review methods specific to the CDI PSPs; general methods will be described in a Methods chapter for the whole report.

The question of interest for this review is: Do ASPs reduce the risk of CDI?

To answer this question, we searched two English language databases (CINAHL, MEDLINE) for papers published from 2008 through 2019 for "*Clostridium difficile*" and other related Medical Subject Heading (MeSH) terms and synonyms, as well as "Antimicrobial Stewardship" or "Antibiotic Stewardship" or "Antibiotic Prescribing Practices." The search string also included all healthcare settings, including "hospitals," "inpatient," "ambulatory care," "long-term care," "nursing homes," "transitional care," and "home health." The search included both "prevention" and "treatment."

The initial search of databases yielded 134 results and 16 papers from other sources. After duplicates were removed, 126 papers were screened for inclusion. From these papers, 43 full-text articles were retrieved. Of those, 17 studies, 3 meta-analyses, and 2 systematic reviews were selected for this review. Reference lists of included articles were also screened to ensure thoroughness. Articles were excluded at each stage if they were not primary studies, systematic reviews, or meta-analyses; treatment variables or outcomes were not relevant; or study design was insufficient. Studies in which antimicrobial stewardship implementation was accompanied by other significant infection control practices (e.g., changes in environmental cleaning) were ruled out for this section and are considered in Section 4.6, Multicomponent CDI Prevention Interventions.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

4.1.4 Review of the Evidence

We reviewed the evidence from 3 meta-analyses and 17 individual studies that examined ASPs and CDI. Three meta-analyses found significant decreases in CDI following implementation of ASPs. Six individual studies on CDI outcomes showed statistically significant decreases in CDI following ASP implementation[5, 10-14], 1 showed borderline significance, and 9 showed statistically nonsignificant decreases in CDI following ASP implementation. One additional study reviewed local strategies for determining high-risk antimicrobials.[15] Study designs were generally quasi-experimental (pre-post analyses).

4.1.4.1 Meta-Analyses

Three meta-analyses of ASP studies in hospital settings found that studies collectively show that antimicrobial stewardship is effective in reducing CDI rates.[16-18] Feazel et al. (2014) analyzed studies published between 1997 and 2012 on ASPs in hospitals during non-outbreak situations. When the results of all studies were pooled in a random effects model, ASPs conferred a significant 52 percent risk reduction (pooled risk ratio 0.48; 95% confidence interval [CI], 0.38 to 0.62; $p<0.00001$) on CDI incidence. Of note, geriatric patients had the largest risk reduction for CDI following implementation of an ASP.[16]

Similarly, in their meta-analysis of hospital ASPs in 11 articles going back several decades, Baur et al. (2017) determined that following ASP implementation periods, the incidence of CDI decreased 32 percent (incidence rate 0.68, 95% CI, 0.53 to 0.88; p=0.0029).[17] Davey et al. (2017) reviewed seven studies published up to January 2015 on hospital antimicrobial stewardship and CDI. They found a range of CDI rate reductions related to antimicrobial stewardship (median 48.6%, interquartile range 19.2% to 80.7%). They note that across all antimicrobial stewardship studies (including those that measured

impact on other infections), antimicrobial stewardship generally reduced hospital stay and did not appear to impact patient mortality.[18]

4.1.4.2 Studies: Overview

Studies reviewed for this report show that ASPs are usually effective in reducing the use of targeted antibiotics and are often, but not always, associated with decreased CDI rates. In addition, studies that measured clinical outcomes, such as mortality or length of hospital stay, following the implementation of an ASP found that ASPs did not appear to influence the efficacy of a patient's treatment.[5,19] Factors found to be most associated with significant CDI decreases were:

- ASPs in smaller facilities,
- Higher pre-ASP baseline CDI rates (more room to improve),
- ASPs developed specifically to reduce CDI (as opposed to ASPs focused on other clinical and microbiological outcomes), and
- ASPs that included a formulary restriction component.

The majority of the studies on CDI outcomes (13/16) examined ASPs in hospitals or hospital units. The duration of the ASP period ranged from 6 months to a little over 6 years (mean 19.3 months; standard deviation [SD] 16.7). Most studies were quasi-experimental (interrupted time series or before and after design) and lacked a control or comparison group. All included studies measured the amount of prescribed antimicrobials (e.g., defined daily dose, or DDD, as defined by the World Health Organization [WHO], per 1,000 patient days) and CDI rates pre- and post-ASP implementation.

While many of the studies controlled for other contemporaneous prevention initiatives, the study designs may not account for potential covariates and confounders such as previous infection prevention efforts (e.g., hand hygiene, environmental cleaning), patient risk factors, changes in testing method, or seasonal, regional CDI fluctuations. This finding is consistent with the findings of two systematic reviews by Louh and colleagues (2017) and Pitiriga et al. (2017), which both indicated that the diversity in ASPs and weaknesses in study design undermine the strength of the evidence.[20,21]

4.1.4.3 Studies: ASPs With Significant CDI Reductions

Six of the 16 studies on CDI outcomes and ASPs found statistically significant reductions in CDI, using $p<0.05$ as the basis for statistical significance.[5, 10-14] For example, Libertin et al. (2017) studied a new ASP in a rural community hospital with fewer than 100 beds. This ASP included an educational lecture series and the dissemination of clinical guidelines and algorithms on advised antibiotic use for specific infectious disease syndromes. When a provider ordered antimicrobial therapy that used one of 12 targeted antimicrobials, they were allowed to order an initial 72-hour course. Ordering of one of the targeted antimicrobials triggered review by a clinical pharmacist and infectious disease physician, and microbiologic data were given to the provider to aid in antimicrobial selection and de-escalation. The rate of CDIs went from 3.35 cases per 1,000 occupied bed days in 2013 (the year prior to the ASP) to 1.35 cases per 1,000 1 year later ($p<0.001$). Overall antimicrobial use (in DDDs per 1,000 occupied bed days) decreased 10 percent from before the ASP initiative to 1 year after, and annualized antimicrobial savings was $280,000.[10]

Another example of significant reductions in CDI after a period of ASP was at an acute general hospital with over 500 beds in the United Kingdom.[5] This ASP consisted of removal of "high-risk" antibiotics such as fluoroquinolones, cephalosporins, clindamycin, and broad-spectrum penicillins such as amoxicillin/clavulanate, from ward stocks in order to reduce their availability. These antimicrobials were targeted because they were associated with antimicrobial resistance and CDI. New prescribing guidelines with low-risk alternatives were featured in educational sessions and hospital posters and distributed to clinicians as laminated pocket-sized guides. In addition, an antibiotic management team performed regular ward rounds five times a week (compared with irregular rounds 3x/week) to optimize adherence to revised antibiotic guidelines and control the use of high-risk antibiotics. These changes corresponded to a 58.5 percent drop in fluoroquinolone use and a 45.8 percent drop in cephalosporin use. A negative binomial regression showed a significant decrease in CDI associated with the ASP (incidence rate ratio [IRR] 0.34; 95% CI, 0.20 to 0.58, p<0.0001). The researchers found no significant differences in clinical outcomes (as measured by length of stay and readmission rate for elderly patients treated for urinary tract and lower respiratory tract infections) associated with the change in prescribing practices.[5]

4.1.4.4 Studies: ASPs With Borderline Significant CDI Reductions

One study at a 48-bed orthopedic ward in Mexico showed borderline significant reductions in CDI[22] after restricting clindamycin (i.e., only patients with a previous infectious disease consult could receive clindamycin). After a 7-month baseline period, there was a 16-month ASP period in which clindamycin use, measured in mean DDDs per 1,000 patient days, decreased by 92.61 percent (p=0.0002). CDI rates went from 1.07 per 1,000 patient days during the baseline period to 0.12 per 1,000 patient days during the ASP period, constituting a decrease of 88.78 percent (p=0.056).[22]

The reductions in CDI were generally greater in studies with higher pre-ASP (i.e., baseline) CDI rates. This finding could be because those hospitals had more room to improve than hospitals where rates were already low. Another possibility is that studies that report ASPs in the context of an outbreak could find reductions that reflect a natural regression to the mean as the outbreak wanes, rather than a result of the intervention.[23]

4.1.4.5 Studies: ASPs With Nonsignificant Decreases in CDI Rates

Nine studies in hospital settings showed statistically nonsignificant changes or no decrease in CDI associated with ASP implementation.[19,24-31] In one example, antimicrobial stewardship practices were enhanced at a 525-bed public safety-net hospital, where CDI and antimicrobial prescribing rates were declining and already low, relative to other hospitals in the region.[24] New ASP practices included a preauthorization requirement for select broad-spectrum, toxic, or costly antibiotics, retrospective audit and feedback, and revised prescribing guidelines. After the changes, Jenkins et al. (2015) found total antimicrobial and high-risk antimicrobial use declined, and antimicrobial expenditures decreased, but CDI rates did not change.[24] While there are confounding factors, such as a switch to more sensitive testing methods, the authors point out that in the context of relatively low CDI rates and low antimicrobial prescribing, there may have been little room for additional decreases, since a minimal level of antimicrobial use is necessary to maintain optimal clinical outcomes.

Hospital ASPs in which CDI was not the primary clinical/microbiological target also showed nonsignificant changes or no decrease in CDI rates.[25-29] For example, Taggart et al. (2015) examined an ASP in two intensive care units (ICUs) in a 465-bed teaching hospital in Toronto, Canada. The ICUs

included a trauma and neurosurgery ICU and a medical/surgical ICU. In both units, following a 12-month audit and feedback ASP, there were no significant changes in the CDI rate. Mean total monthly antimicrobial use declined in the trauma/neuro ICU but increased in the medical/surgical ICU. The authors speculate that the baseline prescribing practices in the medical/surgical unit were more appropriate (with more room to improve in the trauma/neuro ICU).[25]

4.1.4.6 Studies: ASPs in LTCFs

While most of the studies included in this review examined ASPs in hospitals, three studies evaluated ASPs in LTCFs.[11,14,31] LTCFs are important sites for antimicrobial stewardship due to the number of patient infections, frequent overuse of antimicrobials, and numerous transfers to and from the hospital.[31] ASPs that centered on outside infectious disease consultation showed promising results in LTCFs.[11,14] For example, Jump et al. (2012) measured antimicrobial use and CDIs 36 months before and 18 months after bringing in a Long-Term Care Infectious Disease consult team to a 160-bed Veterans Affairs (VA) LTCF. The team was composed of an infectious disease physician and a nurse practitioner who examined residents at the facility once each week and provided case review, feedback, and antimicrobial prescribing recommendations. In contrast to the pre-ASP period, total systemic antibiotic administration decreased by 30 percent ($p<0.001$), with steeper decreases in use of certain broad-spectrum antimicrobials.

The rate of change of positive *C. difficile* tests in the pre-ASP period showed a trend toward increasing ($p=0.09$), whereas in the post-ASP period the trend was reversed ($p=0.21$). The difference between the slopes in pre- versus post-ASP period is significant ($p=0.04$). While the rate of change in positive *C. difficile* tests did not change significantly over time for the two individual time periods, the difference in the rates of change between the two time periods was significantly different.[14]

4.1.4.6.1 Interventions

Several common ASP interventions were studied in this review. To implement changes in prescribing practices, the ASPs use various strategies or interventions, which, as shown in Table 4.1, are typically grouped into the following categories: formulary restrictions, audit and feedback, and provider education. There is some research about outcomes associated with each individual strategy, but usually ASPs use more than one of the above interventions, making it difficult to assess each approach individually. Feazel et al. (2014) state that approaches that are "restrictive," (i.e., restrict high-risk antimicrobials) are more effective than the "persuasive" strategies (i.e., audit and feedback, education, guidelines).[16] Pitiriga et al. (2017) made no such overarching distinction about the efficacy of different strategies.[21] There is no consensus on which interventions are most effective, and it is likely that the most effective approach may differ in different settings; effective programs are dynamic and can be adapted to facility needs.[32]

Table 4.1: Studies on Antimicrobial Stewardship and *Clostridioides difficile* Infection Outcomes Published 2008 to 2018

Article	ASP Intervention: Formulary Restrictions	ASP Intervention: Audit and Feedback	ASP Intervention: Education	*Clostridioides dfficile* Infection (CDI) Outcomes
Carbo et al., 2016[26]		✓	✓	The incidence of CDI did not differ between pre-antimicrobial stewardship program (ASP) and ASP groups (p=0.81).
Chung et al., 2015[15]	✓			Although the relationship between piperacillin and tazobactam and CDI remained, third- and fourth-generation cephalosporins and fluoroquinolones were no longer significantly associated with CDI.
Cruz-Rodriguez et al., 2014[22]	✓			Borderline statistically nonsignificant reduction of 88% in CDI (1.07 to 0.12 per 1,000 patient days, p=0.056)
Dancer et al., 2013[29]			✓	Adjusting for a decreasing trend, the ASP policy was associated with a 45.22% reduction (95% confidence interval [CI], -4.79% to 72.05%; p=0.09) in the rate of CDIs.
Jenkins et al., 2015[24]	✓	✓	✓	Few apparent changes in CDI and other patient-centered outcomes (p-values not provided).
Jump et al., 2012[14]		✓	✓	The rate of change of positive *C. difficile* tests in the pre-ASP period showed a trend toward increasing (p=0.09), whereas in the post-ASP period, the trend reversed (p=0.21). The difference between the slopes in pre- versus post-intervention period was significant (p=0.04).
Libertin et al., 2017[10]		✓	✓	Decrease from 3.35 cases per 1,000 occupied bed days in 2013 to 1.35 cases per 1,000 occupied bed days in 2015 (p<0.001).
Lowe et al., 2017[27]		✓		No statistically significant difference in CDIs pre-/post-ASP (p=0.24).
Ostrowsky et al., 2014[28]	✓	✓	✓	On average, intervention hospitals reported slightly fewer hospital-onset CDI cases (2.8 fewer CDI cases per 10,000 patient days), as well as slightly fewer hospital-onset CDI combined with community-onset (CO)-healthcare facility-associated (HCFA) CDI cases (3.9 fewer CDI cases per 10,000 patient days). Both of these rate differences were not statistically significant.
Patton et al., 2018[19]			✓	Statistically nonsignificant reduction in CDI of 7.0 cases/1,000 admissions (relative change -24% [95% CI, -55 to 6]) in Medicine, but no change in Surgery (estimated 0.1 fewer cases/1,000 admissions [-2% {95% CI, -116 to 112}]).
Rahme, et al, 2016[31]			✓	CDI rate per 1,000 resident days pre- and post-intervention showed statistically nonsignificant decrease of 19.47% from 0.094 to 0.076 (p=0.58).
Shea et al., 2017[12]	✓		✓	CDI rates decreased significantly (p=0.044) from pre-intervention using education (3.43 cases/10,000 patient days) and restriction (2.2 cases/ 10,000 patient days). In addition, mean and SD monthly CDI cases/10,000 patient days decreased by roughly 50% from 4.0 (SD=2.1) pre-intervention to 2.2 (SD=1.35) post-restriction.
Taggart et al., 2015[25]		✓		Nonsignificant decreases in CDI in two intensive care units (ICUs) (e.g., the rate of CDI in the trauma/neuro ICU decreased from 0.66 cases per 1,000 patient days pre-intervention to 0.48 cases per 1,000 patient days post-intervention; p=0.69).
Talpaert et al., 2011[5]		✓	✓	Significant decrease in CDI following the intervention (IRR 0.34 [0.20 to 0.58], p<0.0001).
Tedeschi et al., 2017[11]		✓	✓	The incidence of CDI decreased from 3.6 to 1.2 cases per 10,000 patient days (p=0.001).

Article	ASP Intervention: Formulary Restrictions	ASP Intervention: Audit and Feedback	ASP Intervention: Education	*Clostridioides dfficile* Infection (CDI) Outcomes
Wenisch et al., 2014[13]	✓	✓	✓	The mean (+/- standard error of the mean) numbers of CDI cases in the baseline period were 59 +/-3 per month and in period 2 were 32 +/-3 per month (46% reduction; p=0.0044)
Yam et al., 2012[30]		✓	✓	Nosocomial CDI decreased from an average of 5.5 cases per 10,000 patient days to an average of 1.6 cases per 10,000 patient days (no p-value provided).

4.1.4.7 Target Antimicrobials, Antimicrobial Formulary Restrictions, and Preauthorization Requirements

An important first step in formulary restriction is determining which antimicrobials to target for restriction. In addition to reducing the high-risk antimicrobials outlined in current guidelines, facilities may use data on regional and facility associations between CDI and antimicrobials. In one example, an ASP team examined temporal associations between antimicrobial use and CDI cases in their facility to determine which antimicrobials to target for restriction.[19]

Several studies examined the role of different CDI ribotypes (more common in certain regions) and certain antimicrobials.[5,13] Using case-control studies to identify antibiotics that should be restricted is one way to assess local associations between antimicrobial classes and CDI. In a multicenter study in New York, each hospital performed its own case-control study to determine CDI-associated antimicrobials.[28] The hospitals used odds ratios to compare case (CDIs) and control groups. Chung et al. (2014) describe this process in more detail and found that, while more complex matching strategies are preferable, using criteria such as admission date (to correct for variation in hospital CDI prevalence) and length of stay (as a surrogate for cumulative risk of developing CDI) may be sufficient to identify high-risk antibiotics associated with CDI. For more accurate associations between antimicrobials and CDI, the researchers included additional matching variables, such as age and comorbidities.[15]

Once target antimicrobials have been identified, ASPs may use strategies such as preauthorization requirements and removing access to the target antimicrobials. In their review, Feazel et al. (2014) reported that interventions that included restricting high-risk antimicrobials (e.g., preauthorization requirements, restrictions on certain antibiotics except in unusual circumstances) were associated with the greatest reductions in CDI rates.[16]

To assess the CDI associations with a formulary restriction, Dancer and colleagues (2013) measured the associations of an ASP education program and restriction policy separately. They attributed decreases in CDI (a decline of 6.59% per month [95% CI,-2.52% to 15.02%; p=0.169) to the educational component of the ASP, while the restriction policy was associated with a 45.22 percent reduction (95% CI, -4.79% to 72.05%; p=0.09) in the rate of CDIs (although neither intervention had a statistically significant effect at the 0.05 level.) This study was one of the few to measure the unique contributions of individual ASP interventions.[29]

4.1.4.8 Audit and Feedback

Audit and feedback include case reviews of patients receiving antimicrobial therapy, often involving a multidisciplinary team (e.g., prescribers, pharmacists, infectious disease experts, administrators) and feedback to providers, as well as audits of targeted antibiotics and other clinical measures both before and/or after treating the patient. Feedback to prescribers may include advice about switching to alternative antimicrobial agents (e.g., broad to narrow spectrum), discontinuation of antimicrobial treatment, shortened duration of microbial dose, higher or lower dose, and switch from intravenous to oral antibiotics. The latter recommendation is based on the idea that an earlier switch to oral therapy allows faster discharge from the hospital, thereby reducing exposure to CDI and drug-resistant organisms.[23]

ASPs with an audit and feedback component were common in the studies we reviewed, and these are widely recommended antimicrobial stewardship practices;[17,21] however, ASPs based solely on an audit and feedback program showed no statistically significant reductions in CDI.[25,27] One benefit of audit and feedback is that the practice itself educates prescribers and other healthcare staff.[11,14] In most studies, audit and feedback are accompanied by a staff education component, making it difficult to find associations between audit and feedback alone and CDI rates.

4.1.4.9 Staff Education

Researchers suggest that education is important to provide context and convince physicians and other staff to participate in antimicrobial stewardship activities.[11,29] Jump et al. (2012) note that some rehabilitation physicians may be aware of the problem of antimicrobial resistance but unaware of local resistance patterns. The education programs described in the reviewed studies included information about antimicrobial resistance, local and facility antibiogram data, treatment guidelines, and/or CDI-specific education. Educational methods included the use of emails, pocket cards, presentations, and trainings.[14]

In an attempt to isolate the CDI associations of an educational program (as part of a multicomponent strategy), Shea et al. (2017) assessed results associated with a 3-month education campaign, then, separately, the results following a subsequent 12 months of a fluoroquinolone restriction policy. The shorter education component appeared to have a significant impact, which was enhanced by the restriction policy. Compared with pre-ASP, the four hospitals experienced 48 percent and 88 percent average reductions in fluoroquinolone utilization (days of therapy per 1,000 patient days) after education and restriction, respectively. CDI rates decreased significantly ($p=0.044$) from 4.0 cases/10,000 patient days pre-ASP to 3.43 cases/10,000 patient days following staff education, and to 2.2 cases/10,000 patient days following restriction.[12]

4.1.5 Unanticipated Outcomes of ASPs

One potential consideration with ASPs is that they may encourage the use of (untargeted) broad-spectrum agents and/or alternative "lower-risk" antimicrobials, which, in turn, may lead to increased resistance to the unrestricted drugs. Pitiriga and colleagues (2017) promoted the restriction of quinolones but also warn against the so-called "squeezing the balloon" phenomenon, wherein restriction policies for use of one set of drugs leads to increased use of unrestricted alternatives, which leads to resistance. This practice runs counter to the goal of decreasing antimicrobial selection pressure.[21]

While many of the reviewed studies found overall reductions in antibiotic use up to 30 percent ($p<0.001$),[14] or no significant change in overall antimicrobial use,[13,22] some researchers reported increases in nontargeted antimicrobials.[5] For example, Dancer and colleagues (2013) found that while targeted antimicrobials decreased during the ASP period, use of empiric amoxicillin and gentamicin increased, and resistance to these antimicrobials increased.[29]

One of the positive outcomes of a CDI-targeted ASP can be lower rates of MRSA (methicillin-resistant *Staphylococcus aureus*), ESBL (extended-spectrum beta-lactamases)-producing coliform infections, and other MDROs (multidrug-resistant organisms). For example, while the primary reason for the antimicrobial restrictions and revised prescribing guidelines in the ASP studied by Dancer et al. (2013) was to decrease CDI rates at the hospital, the researchers also found decreases in ESBL-producing coliforms following the ASP an 8.21 percent reduction [95% CI, -0.39% to 16.15%]). During the following 3 years, both ESBL-producing coliform infections and MRSA declined.[29]

Similarly, from the baseline to the end of the intervention period, Tedeschi et al. (2017) reported the prevalence of extensively drug-resistant strains decreased from 55 percent to 12 percent for *P. aeruginosa* ($p<0.001$) and from 96 percent to 73 percent for *A. baumannii* ($p=0.03$). In addition, the prevalence of ESBL-producing strains decreased from 42 percent to 17 percent for *K. pneumoniae*; the prevalence of carbapenem-resistant strains decreased significantly from 42 percent to 17 percent ($p=0.005$); and MRSA strains decreased significantly from 77 percent to 40 percent ($p<0.0008$).[11]

One additional benefit (or perhaps less identified outcome of an ASP) was an increase in the accuracy of patient diagnoses following audit and feedback interventions. Talpaert et al. (2011) found that, out of 386 interventions by the ASP team, on 75 occasions the clinicians changed the patient's diagnosis.[5] Similarly, Lowe et al. (2017) describe how virology results tied to ASP consults helped facilitate appropriate antimicrobial treatment. Many patients in that study (17/19) who were on empiric oseltamivir were found not to have proven influenza, and following proper diagnosis, oseltamivir was promptly discontinued.[27]

4.1.6 Implementation Barriers and Facilitators

ASPs require resources, and sometimes creative mechanisms to address resource gaps. Researchers noted challenges with staffing limitations (when additional staff were not hired for the ASP) and a need for technical resources to track antimicrobial use.[28] In addition, the lack of EHRs in many LTCFs can make it hard to track the exact indication for antimicrobial use.[30,31] However, even with limited means, antimicrobial stewardship can produce meaningful benefits.[26] For example, Yam et al. (2012) described the challenges of resource constraints in a small rural hospital. The ASP team decided to use scheduled and as-needed consultations with a remote infectious disease specialist physician. After the ASP worked with the remote specialist for 13 months, the researchers found nosocomial CDI decreased from an average of 5.5 cases per 10,000 patient days to an average of 1.6 cases per 10,000 patient days, and antibiotic purchase costs decreased nearly 50 percent.[30]

The CDC provides recommendations for resource-limited settings,[33] which include:

- Using nontraditional staff types to lead the ASP (e.g., infection control nurses, clinical microbiologists, or pharmacists without infectious disease training);
- Using telehealth for advising on prescribing decisions;

- Identifying a single priority hospital unit (e.g., ICU) in which to implement an ASP; or
- Choosing and implementing a single prescribing practice (e.g., reviewing the need for antibiotics after 48 hours, or improving adherence to guidelines for empiric treatment for CA pneumonia or sepsis).

There are several examples of ASP collaborations that overcame resource and expertise gaps. Lowe et al. (2017) described an efficient collaboration between the ASP physician or pharmacist and the virology laboratory for polymerase chain reaction (PCR) testing on respiratory tract infection, in order to optimize antiviral and antimicrobial use.[27] LTCFs often lack appropriate personnel, funding, and electronic resources, and face a paucity of well-validated strategies for their sector.[14]

To implement an ASP in an LTCF, Rahme et al. (2016) document a hospital that collaborated with an LTCF for antimicrobial stewardship in part because the facilities shared patients and there was concern about interfacility HAI transmission.[31] The hospital ASP team provided microbiology data, provider education and treatment guidelines, and a 24-hour hotline for LTCF prescribers. Some LTCFs collaborated with outside consultants to implement audit and feedback ASPs.[11,14,30]

Resistance on the part of providers is a major barrier to ASP implementation that is described in the literature; conversely, a facilitator to implementation is a good relationship between the ASP team and prescribers.[17] Educating physicians and providing proof of ASP safety and efficacy are essential to garnering support.[19] Dancer et al. (2013) found that gaining support for their ASP was challenging at the outset, especially when ASP recommendations for prescribing conflicted with previously published guidelines for a specific infection. For example, gastroenterologists initially refused to curtail ciprofloxacin prescribing for spontaneous bacterial peritonitis.[29] After being educated about the microbiological etiology of the infection, the gastroenterologists were persuaded to change prescribing practices. This observation aligns with the findings of Libertin and colleagues (2017), who noted that development of a "collegial environment for a health care provider's growth in ASP knowledge was important in achieving acceptance of the program" (p. 981).[10]

4.1.6.1 Resources To Assist With Implementation

The following are resources for implementing an ASP, starting with a CDI-specific resource and followed by ASP resources in general:

AHRQ: Toolkit for Reduction of Clostridium difficile Infections Through Antimicrobial Stewardship: https://www.ahrq.gov/professionals/quality-patient-safety/patient-safety-resources/resources/cdifftoolkit/index.html

CDC Antibiotic Stewardship Implementation Resources: https://www.cdc.gov/antibiotic-use/healthcare/implementation.html

IDSA/SHEA Guidelines on implementing antimicrobial stewardship: https://www.idsociety.org/globalassets/idsa/practice-guidelines/implementing-an-antibiotic-stewardship-program-guidelines-by-the-infectious-diseases-society-of-america-and-the-society-for-healthcare-epidemiology-of-america.pdf

National Quality Forum stewardship in acute care: a practical playbook: https://www.qualityforum.org/Publications/2016/05/National_Quality_Partners_Playbook__Antibiotic_Stewardship_in_Acute_Care.aspx

SHEA Antimicrobial Stewardship: Implementation Tools & Resources: https://www.shea-online.org/index.php/practice-resources/priority-topics/antimicrobial-stewardship/implementation-tools-resources

4.1.7 Gaps

There is a notable absence of research on the implementation of ASPs in settings other than hospitals. Of the 16 studies included in this review, we only found 3 ASP studies in LTCFs.[11,14,31] In these three studies, facilities worked with outside consultants to provide expertise and feedback. Researchers commented on the challenges of ASP implementation in LTCF settings due to high rates of infection[25] and a "treat-first" culture.[34] At the same time, ASPs in these settings could potentially have a large impact as they serve high-risk patients and share patients with other facilities. In addition, ASPs in outpatient settings warrant attention, since according to 2016 data reported to the NHSN, CA CDI is on the rise.[8] Our search found no studies on CDI and ASPs in outpatient settings. This is an important gap in the literature and an area for further exploration, especially given the links between antimicrobial prescribing in the outpatient setting and CA CDI.[35]

The reviewed articles had little information on financial outcomes and antimicrobial stewardship. While Jenkins et al. (2015), Libertin et al., (2017) and Taggart et al. (2015) show total reductions in the cost of antibiotics, particularly from reductions in use of costly broad-spectrum antibiotics,[10,24,25] other financial outcomes are not examined in these or other ASP studies. It has been speculated that the financial savings of ASPs measured in cost of antimicrobials and expenses associated with CDI management outweigh the costs of investing in infectious disease expertise to support an ASP.[11]

On a national level, it is believed that antimicrobial stewardship is extremely cost effective in terms of prevention of healthcare costs.[36] However, there is a need for more economic information for healthcare systems and facilities to determine costs and savings.[37] More robust and nuanced cost-effectiveness analyses would help staff in various settings, particularly those with resource limitations, to consider how to best invest in support for an ASP.

Despite the methodological, technological, and resource challenges of research on ASPs, many researchers noted a need for more rigorous study design, including randomized controlled trials (in addition to pre-post) study design.[16] There is also a need for studies that consider the costs and benefits of antimicrobial stewardship over the course of multiple years, to measure longer term associations that may not be evident in shorter study periods.[17]

Researchers have pointed out that reducing antimicrobial use is not always equivalent to improved prescribing and antibiotic appropriateness is as important as counts of prescriptions.[38] One of the issues that comes up in systematic reviews and studies of ASPs is the heterogeneity in process measures, which, in addition to study design, makes comparison and generalization difficult.[38] As noted by Ostrowsky et al. (2014), the prescribed daily doses relative to WHO DDDs may vary between hospitals.[28] DDDs are based on standard dosing and therefore may not accurately capture administered doses that are lower than the routine dose. Point prevalence (accurate surveys taken at particular points in time that can compared) has been suggested as a low-cost way to understand antimicrobial consumption.[39]

Finally, there are different measures of clinical and microbiological outcomes,[38] as evidenced in the studies in this review.

4.1.8 Future Directions

Some future directions for ASPs to reduce CDI include patient and family education on antimicrobial stewardship. The ASP described by Rahme et al. (2016) included an education component to address the pressure on prescribers from patients' families in an LTCF. It was theorized that including a focus on family education would lessen the pressure on prescribers to treat symptoms unnecessarily with antibiotics.[31] Findings of qualitative provider surveys confirm that family pressure can be a challenge. For example, Cole (2014) found that 55 percent of doctors felt under pressure—mainly from patients—to prescribe antibiotics.[40] Similarly, Sanchez et al. (2014) reported a major reason for nonadherence to prescribing guidelines is a concern for patient or family satisfaction.[41]

In LTCFs, doctors report being influenced by family pressure to prescribe antimicrobials, especially in situations when they are undecided about whether to prescribe an antimicrobial.[42] Greater public awareness could help patients and families to better understand why judicious use of antimicrobials is important, thereby lessening pressure on prescribers and promoting better prescribing practices.

The use of technology for more accurate and rapid diagnosis of viral versus bacterial infections is another area for future ASP improvement. Lowe et al. (2017) point out how rapid diagnostics can help decrease antimicrobial use, as in the case of PCR testing to help determine if antibiotic treatment is required.[27] Pitiriga et al. (2017) also endorse "diagnostic stewardship programs" incorporating rapid molecular diagnostics, genomic pathogen profiling, and estimation of patient–pathogen–treatment interactions to help individualize prescribing practices.[21] A more detailed review of the use of improved diagnostics can be found in the Section 4.5, Testing.

Finally, regionally and ecologically informed antimicrobial stewardship is another direction for the future. CDI is transferred across settings in a region, and regional resistance patterns and CDI strains are important prescribing considerations.[14] Regional, multifacility, and collective ASP efforts could be especially effective strategies. As ASPs become more common due to increasing regulations, more LTCFs will be involved, intervening with a population at high risk of CDI and providing an opportunity for an increased understanding of ASPs.

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4.2 PSP 2: Hand Hygiene

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This review includes a summary of evidence published from 2008 to 2018 on hand hygiene as a prevention practice for CDI. After a brief practice description of hand hygiene, as recommended by IDSA, the review explains how hand hygiene is believed to work as a safety practice for preventing the transmission of *C. difficile*. Next, we examine evidence for the estimated effect of healthcare worker (HCW) and patient hand hygiene interventions on CDI incidence rates, and we provide a brief look at research on specific hand hygiene methods for *C. difficile*. The review then explores hand hygiene intervention implementation and contextual factors, including compliance strategies, sink location, and tailoring to staff needs. Finally, we explore research gaps and future directions for hand hygiene and CDI prevention. The review's key findings are located in the box on the right.

Key Findings

- Gloves and handwashing with soap and water are the recommended hand hygiene practices for *C. difficile* prevention.
- Multiple experimental studies show ABHRs are not effective in eliminating *C. difficile* spores.
- Studies were quasi-experimental and showed large and mostly statistically nonsignificant decreases in CDI following implementation of hand hygiene programs that targeted multiple HAIs (statistical significance was impacted by small sample sizes).
- Studies are needed that measure *C. difficile*-targeted hand hygiene initiatives, as well as financial outcomes, and hand hygiene programs in nonhospital settings.
- Important contextual factors for CDI/hand hygiene include sink location, visibility, and accessibility.
- Future directions for hand hygiene programs include patient hand hygiene, studies on glove compliance, electronic monitoring, and sustainable interventions.

4.2.1 Practice Description

In the 2017 clinical practice guidelines for preventing *C. difficile*, IDSA states that HCWs "must" use gloves while caring for CDI patients, including when entering a room with a CDI patient. In CDI outbreaks or hyperendemic settings (periods of persistently high levels of CDI), the guidelines include performing hand hygiene with soap and water before and after caring for a patient with CDI and after removing gloves. When working with CDI patients in routine or endemic situations, the guidelines recommend washing hands with soap and water or using alcohol-based hand rubs (ABHRs) for hand hygiene after removing gloves.[1] While ABHRs are the preferred means of disinfecting hands for most pathogens, alcohol is not active against *C. difficile* spores, and it is believed that the most efficacious way to eliminate *C. difficile* is via the mechanical action of handwashing.[2,3] Washing hands with soap and water is recommended after any contact with feces.[1]

The 2002 CDC and 2009 WHO recommendations for HCW hand hygiene are the most commonly cited guidelines in the literature reviewed for this report. The 2002 CDC guidelines do not include a recommendation to wash hands for CDI prevention, but it is promoted on other CDC sites online and the agency's current "Clean Hands Count" campaign.[4] Both sets of recommendations have been incorporated into campaigns to promote HCW hand hygiene. The WHO campaign, "My Five Moments for Hand Hygiene," promotes hand hygiene at the following times:

- Before touching a patient
- Before clean/aseptic procedures
- After body fluid exposure/risk

- After touching a patient
- After touching patient surroundings

Use of proper handwashing technique is important for *C. difficile* spore removal.[5] When handwashing is indicated, both the CDC and WHO recommend vigorous and thorough washing of all surfaces for at least 15 seconds.[6] The entire process from start to finish should take between 40 and 60 seconds.[7] This technique has been tested against unstructured and alternative techniques and found to be most effective at removing *C. difficile* spores.[5]

Concerning the type of soap to use during handwashing, the general CDC recommendations (for all HAIs) call for antibacterial soap over plain soap. However, in experimental studies, some researchers have found that plain soap is more effective for removing C. difficile spores.[2,8] This is one of several unresolved issues in hand hygiene for *C. difficile* that is explored in the research included in this review.

The CDC defines hand hygiene as "a general term that applies to either handwashing, antiseptic hand wash, antiseptic hand rub, or surgical hand antisepsis" (pp. 12-40).[e] As such, glove use was not included in most of the reviewed studies. However, *C. difficile* hand hygiene recommendations strongly recommend the use of gloves.[1,9] One study found that universal glove use (with emollients for skin care) at 78 percent compliance was more effective than standard contact precautions (use of gowns and gloves; 67% compliance) to avoid *C. difficile* transmission.[10]

According to the WHO (2009), HCWs should conduct hand hygiene before and after wearing gloves. Appropriate technique helps prevent potential hand contamination when removing gloves.[11,12] Gloves should not be reused on more than one patient.[7] The 2009 WHO guidelines also provide guidance on proper skin and nail care.[7]

4.2.2 Hand Hygiene as a PSP

Multiple studies have found *C. difficile* contamination on HCWs' hands and several studies have linked cases of CDI and CDI outbreaks to HCW transmission.[11] Similarly, inadequate hand hygiene has been linked to higher incidence of CDI.[13] A study that looked specifically at HCW hand contamination after contact with CDI patients found that 24 percent of HCW hands ($p<0.001$) were contaminated with CDI (even when gloves were used in 356/386 of patient contacts). In addition, contact without the use of gloves was independently associated with hand contamination (adjusted OR, 6.26; 95% CI, 1.27 to 30.78; $p=0.02$).[14]

Tomas et al. (2016) found that HCWs may spread *C. difficile* directly from one patient to another or by touching contaminated surfaces in the environment.[15] Each hand-to-surface exposure can result in the hand transmission of microorganisms.[16] Cross-contamination of *C. difficile* originates in the feces of people who are infected, including in the form of spores (a resilient form of the bacterium), which, if not properly cleaned, can survive in the patient's surroundings on any surface (e.g., toilet areas, clothing, sheets, furniture[7]) for over 4 days.[17] *C. difficile* is transmitted when the spores found in feces are ingested via the fecal-oral route or into the colon directly through shared equipment.[18]

[e]See National Healthcare Safety Network (NHSN) Patient Safety Component Manual, Chapter 12, Multidrug-Resistant Organism & *Clostridioides difficile* Infection (MDRO/CDI) Module for more information on hand hygiene.

Recent studies provide additional evidence supporting handwashing with soap and water over ABHRs for *C. difficile* prevention.[3,8,19,20] For example, Kundrapu et al. (2014) tested hands contaminated with *C. difficile* after several methods of hand hygiene. Before conducting hand hygiene, roughly half of the subjects were found to have *C. difficile* spores on their hands. Handwashing significantly reduced the percentage of positive cultures (from ~48% to 10%, n=62; p=0.0005), as well as the number of spores recovered from contaminated hands; conversely, ABHR did not significantly reduce positive cultures or spores (from ~51% to ~49% positive cultures, n=59; p=0.85).[19] While the in vitro evidence for handwashing is consistent across multiple studies, evidence is limited on the impact of handwashing on CDI rates in healthcare settings.

Due to concern about HAI rates and poor HCW hand hygiene compliance, hand hygiene (including use of ABHRs) has been heavily promoted over the last two decades. One systematic review found median hand hygiene compliance across 96 studies in a variety of healthcare settings was 40 percent,[21] and hand hygiene rates are potentially even lower at LTCFs.[22] Single-facility studies on compliance with CDI-specific guidelines also show the need for improved practice. Deyneko et al. (2016) found that, at a 637-bed tertiary care hospital in Canada, glove use compliance was 85.4 percent (211/247), but handwashing compliance after care of CDI patients was only 14.2 percent (35/247) and hand rubbing with ABHR was performed instead of handwashing in 33.2 percent of opportunities (82/247).[23] Similarly, in a study in a single surgical transplant unit, Zellmer et al. (2015) found that the baseline percentage of visitors and staff seeing CDI patients that did not practice hand hygiene was 72.5 percent (58/80) before entering the room and 54.6 percent (42/77) after exiting the room (11.7% of which was ABHR hygiene only).[24]

Regulatory agencies have implemented hand hygiene and reporting requirements in an effort to improve compliance. In 2004, The Joint Commission required healthcare facilities to implement hand hygiene programs, and starting in 2018, observation by surveyors of *individual staff* failure to perform hand hygiene in the process of direct patient care began to be cited as a deficiency. CMS also identifies deficiencies in LTCFs that do not meet hand hygiene standards, and requirements for Medicare and Medicaid participation were revised in 2016 to reflect advances in the theory and practice of patient safety.

4.2.3 Methods

The question of interest for this review is: Is hand hygiene effective at preventing CDI?

To answer this question, we searched the databases CINAHL and MEDLINE from 2008 to 2018 for "*Clostridium difficile*" and related MeSH terms and synonyms, as well as "Hand Hygiene," "Hand Disinfection," or "anti-infective agents." The initial search yielded 168 results, and, after duplicates were removed, 165 were screened for inclusion and 20 full-text articles were retrieved. Of those, 11 studies and one systematic review were selected for inclusion in this review. Reference lists of included articles were also screened to ensure thoroughness and four additional studies were retrieved via this method. Articles were excluded if the outcomes were not relevant or precisely reported or study design was insufficient. Studies in which hand hygiene was accompanied by other significant infection control practices (e.g., changes in environmental cleaning) were ruled out for this section and are considered in Section 4.6, Multicomponent CDI Prevention Interventions.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report A through C appendixes.

4.2.4 Review of the Evidence

We reviewed five quasi-experimental studies on HCW hand hygiene initiatives and CDI rates in real-world clinical settings. Most of the studies (4/5) showed statistically nonsignificant improvements in CDI rates after implementation of a hand hygiene intervention. In all the studies, the hand hygiene initiatives targeted multiple HAIs and not CDI specifically. In this review of the evidence, we first present important methodological considerations, followed by more detailed study outcomes. We then highlight one study on patient hand hygiene. Then we discuss an additional five in vitro studies that focus on methods for hand hygiene (e.g., type of cleaning agent, handwashing technique, glove removal) to reduce *C. difficile* hand contamination.

4.2.4.1 Evidence Limitations

Consistent with the findings of others (e.g., Louh et al., 2017), the studies on hand hygiene and CDI were generally of low quality and did not address multiple confounding factors.[25] In some studies, the researchers failed to control for important variables, such as antimicrobial prescribing.[26] In addition, there were issues with internal validity when measuring hand hygiene compliance, such as observer reliability and the potential of workers to temporarily alter their behavior while being observed (i.e., Hawthorne effect). The studied hand hygiene interventions were intended to reduce transfer of multiple infectious agents; while the researchers state that the interventions followed established guidelines, it was not always clear how "compliance" was defined and measured and whether CDI-specific hand hygiene guidelines were included.

More specifically, the studied hand hygiene initiatives aimed to reduce multiple HAIs, and study authors reported that the interventions included the promotion of ABHRs (either through additional dispensers or by encouraging ABHR use). It is therefore important to consider the potential impact of ABHRs as a strategy on the incidence of CDI. While ABHRs work to eliminate many other pathogens that cause infection, ABHRs are shown to have limited effectiveness for CDI eradication.[2,3] However, several hospital studies that measured CDI rates after ABHR hand hygiene campaigns found that CDI rates decreased or remained stable.

For example, Knight et al. (2010) conducted a retrospective chart analysis following 5 years of a hospital ABHR policy (which included education and installation of ABHR dispensers) and found a significant decrease in CDI (3.98 per 10,000 patient days after implementation of the ABHR policy, compared with 4.96 per 10,000 patient days before implementation (p=0.0036).[27] Conversely, Silva et al. (2013) found that hospital CDI rates remained stable despite several years of increased use of ABHRs.[28] Researchers speculate that these findings may be attributable to improved compliance with CDI prevention strategies, increased awareness of the importance of hand hygiene in reducing infection, and the effect of hand rubbing in reducing the bacterial load on hands. It is because promotion of ABHRs has not been linked to increases in CDI that the CDC guidance promotes handwashing (not ABHRs) in cases of high endemic CDI or CDI outbreaks.[9]

4.2.4.2 HCW Hand Hygiene Interventions and CDI Outcomes

As noted, the studied hand hygiene initiatives were intended to reduce several HAIs and included some or all of the following components: staff education, compliance monitoring and feedback, incentives,

promotion of guidelines, and, in some studies, new ABHR dispensers. Using p<0.05 as the standard, four studies found decreases in CDI that were not statistically significant.[29-31] One study did not provide a p-value.[26] The duration of the studied hand hygiene interventions ranged from 1 to 4 years. Measures were based on pre-/post-hand hygiene compliance data and CDI incidence data. Results are presented in Table 4.2.

Table 4.2: Studies on HCW Hand Hygiene Initiatives and CDI Rates (Published 2008-2018)

Article	Setting	Intervention	CDI Outcome
Al-Tawfiq et al., 2017[30]	Oncology unit at 350-bed hospital	Root cause evaluation tool, targeted staff education, monitoring	Decrease in CDIs from 7.95 (CI, 0.8937 to 28.72) to 1.84 (CI, 0.02411 to 10.26) per 10,000 patient days (p=0.23)
Kirkland et al., 2012[29]	383-bed hospital	Staff education, promotions, measurement and feedback	Decline in CDIs from 0.9 to 0.6 per 1,000 patient days (p=0.1).
Schweon et al., 2013[31]	174-bed skilled nursing facility	Increased ABHR dispensers, staff education, monitoring, monthly staff hand hygiene champion, patient education	Decrease in CDI rate per 1,000 resident days from 0.08 to 0.04 (p=0.36)
Sickbert-Bennett et al., 2016[28]	853-bed hospital	Staff education, promotion/communications, data collection and feedback	14% reduction in healthcare-acquired CDI (p=0.070)
Stone et al., 2012[26]	187 acute hospitals	Regional program, increased ABHR dispensers, staff education, communications/ promotion, hand hygiene audits	Decrease in CDI from 16.75 to 9.49 cases per 10,000 bed days (no p-value given).

Sickbert-Bennett et al. (2016) evaluated HCW hand hygiene compliance and HAIs following the implementation of "Clean In, Clean Out" in an 853-bed hospital in North Carolina. The hospital hand hygiene program included focus on cleaning hands before and after working with patients, covert observation of compliance, staff data collection, and feedback. After 17 months, the researchers found a 10 percent improvement in appropriate hand hygiene compliance and a 14 percent reduction in healthcare-acquired CDI (p=0.070), as well as decreases in other HAIs. The published article did not clarify what constituted hand hygiene compliance, and whether ABHR use or handwashing was considered compliant, making it difficult to determine which practice may have contributed to the CDI reduction.[32]

Following a 3-year hand hygiene initiative in a 383-bed teaching hospital in rural New Hampshire, Kirkland et al. (2012) evaluated hand hygiene compliance and HAI rates. This study described promotion of published hand hygiene guidelines but did not specify whether handwashing for CDI was emphasized. The initiative included leadership endorsement, measurement and feedback on hand hygiene compliance, and education. Over the study period, observed hand hygiene compliance increased significantly from 41 percent to 87 percent (p<0.01), and the overall HAI rate declined significantly (from 4.8 to 3.3 per 1,000 inpatient days; p<0.01). The decline in CDI was not statistically significant (0.9 to 0.6 per 1,000 patient days, p=0.1); like other smaller studies, statistical significance was potentially due to small sample size.[29] This was one of three studies that found statistically nonsignificant decreases in CDI following staff hand hygiene initiatives.[29-31]

Several studies explored initiatives in which ABHR protocols were described as a key component. For example, in the only study in a nonhospital setting, Schweon et al. (2013) studied a hand hygiene program in a 174-bed skilled nursing facility. The program included installation of a number of new ABHR dispensers, staff education on handwashing guidelines, staff monitoring, and patient education on *when* to conduct hand hygiene. A monthly hand hygiene champion was recognized, and hand hygiene

posters were placed around the facility. Following the year-long program, most HAIs decreased but only lower respiratory tract infections showed statistically significant decreases. CDI rate per 1,000 resident days decreased but was not significant (from 0.08 to 0.04; p=0.36). Again, it is not clear the degree to which the use of ABHRs was deemed an appropriate practice for hand hygiene.[31]

Like the hand hygiene program studied by Schweon and colleagues (2013),[31] the regional initiative described by Stone et al. (2012) measured HAI rates following a hygiene initiative at acute care hospitals in England and Wales, which included ABHR promotion in addition to other strategies (although in year 4 of the study, the 2009 WHO protocols for hand hygiene were adopted). The initiative titled "Cleanyourhands" was informed by Habit-Forming Theory[33,34] and included installation of ABHR dispensers, materials promoting hand hygiene, and regular hand hygiene audits. After 4 years, the CDI rate decreased from 16.75 to 9.49 cases per 10,000 bed days, but the report did not mention statistical significance. Researchers found that increases in the amount of soap purchased by facilities was independently associated with reduced CDI throughout the study. The researchers also noted potential confounders that they did not study (e.g., antimicrobial prescribing rates).[26]

4.2.4.3 Patient Hand Hygiene

In the past decade, patient hand hygiene has received increasing attention as a potential major source of *C. difficile* transmission in healthcare settings. Patients colonized with *C. difficile* often go undetected and may transmit *C. difficile* to HCWs' hands directly, or indirectly through contaminated surfaces in the healthcare environment. Patient mobility, dexterity, and cognitive limitations can be barriers to patient hand hygiene.[20,35] One study found patient hand hygiene compliance rates as low as 10 percent.[36]

Pokrywka et al. (2017) conducted a study in a 495-bed university-affiliated medical center on a patient handwashing program focused specifically on CDI reduction. In this intervention, hospital staff were educated about specific times when they should encourage and assist patients with handwashing and hand hygiene (i.e., practicing hand hygiene prior to meals, after using the toilet or bedpan, prior to touching dressings and incisions, after returning from testing or a procedure, before and after having visitors). After a trial conducted on four units in the hospital, the initiative was implemented hospitalwide.

Post-implementation patient survey results showed some improvement in staff assistance with patient hand hygiene, and the CDI standardized infection ratio (SIR) decreased in the first two quarters after implementation, from 0.834 to 0.572 and 0.497 ($p \leq 0.05$). (The NHSN uses SIRs to track HAIs over time; the SIR compares the actual number of HAIs at each hospital with the predicted number). Infection rates increased in the third and final quarters of the measurement period, which potentially shows the need for sustained staff education and reminders to consistently educate new patients.[35]

4.2.4.4 Studies on Hand Hygiene Methods for *C. difficile* Decontamination

It is believed that the mechanical action and friction from handwashing helps to remove C. difficile spores from hands. To explore this theory, Isaacson et al. (2015) experimented with the use of sand to remove *C. difficile* spores from hands and compared these results with washing with soap and water. In this study, 14 subjects each used five different hand hygiene methods following contamination with *C. difficile* (4×10^5 colony forming units). The hand hygiene methods were water rinse, water rub and rinse, water and antibacterial soap, oil/baking soda/dish detergent/water, and sand rub and water rinse.

The use of sand and water resulted in the greatest reduction in spores, but results were not significant. Compared with antibacterial soap and water, which resulted in an average 1.84 log reduction (SD 0.46) or 98.5 percent, sand and water resulted in an average 2.34 log reduction (SD 0.33) or 99.5 percent. Compared with soap and water, the sand and water method removed a statistically significant greater average amount of *C. difficile* spores (-0.50; p=0.003).[37]

Other studies examined the efficacy of handwashing with soap and water. To compare five practical strategies for hand hygiene, Oughton et al. (2009) conducted an experiment with 10 volunteers to measure the efficacy for *C. difficile* spore removal from the whole hand or just the surface of the palm. The researchers found that, using both whole hand and palmar surface protocols, washing with warm water with plain soap left the lowest amount of *C. difficile* spores, followed by cold water with plain soap, warm water with antibacterial soap, antiseptic hand wipe, ABHR, and no hand hygiene.

Perhaps the most interesting finding from this study was that plain soap performed better than antimicrobial soap in the whole-hand protocol.[2] Washing with non-antimicrobial soap and water was more effective for removing *C. difficile* than 4% chlorhexidine gluconate hand wash. The researchers speculate that this finding may be because a higher amount of organic matter is present on the whole hand than on the palm, and high levels of organic matter interfere with the activity of chlorhexidine. Edmonds et al. (2013) found similar results and noted that the most effective antibacterial products were too harsh to be used on human skin (e.g., peracetic acid surfactant prototype [Triton-X], commercial ink and stain remover, sodium tetraborate decahydrate powder [Borax]).[8]

Tomas et al. (2015) explored preventing HCW hand contamination from the removal of gloves and other personal protective equipment. The study found that, after CDI patient care, 16 percent of HCWs had CDI spores on their hands after removing gloves and personal protective equipment (n=25). The frequency of contamination was reduced to 7 percent after an educational intervention on proper glove/gown removal (p=0.4) and further reduced to 0 percent after disinfection of gloves with bleach wipes (p=0.04).[12]

Due to complaints of irritation from the bleach wipes, Tomas et al. (2016) conducted a second study in which HCWs used a sporicidal formula (of acidic ethanol) instead of bleach for glove decontamination (to use before glove removal). The findings suggest that the sporicidal properties of certain solutions could be useful for glove disinfection before removal, when caring for CDI patients. The reduction achieved by the sporicidal ethanol solution (70% ethanol pH 1.3) was equivalent to the 1:100 dilution of bleach on artificially contaminated gloves. Researchers tested glove contamination of HCWs following 159 CDI patient care episodes and found that the sporicidal ethanol resulted in significantly reduced glove contamination, whereas 70% ethanol did not. Despite the promise of glove decontamination as a prevention strategy, the authors stipulate that decontaminating gloves would not replace HCWs washing their hands after glove removal.[15]

4.2.4.5 Economic Outcomes

In general, the literature regarding hand hygiene indicates that the costs associated with preventing HAIs far outweigh the costs to improve hand hygiene compliance.[29,32] Sickbert-Bennett et al. (2016) reported that the cumulative prevention of HAIs saved approximately $5 million at their institution.[32] Although some cost-effectiveness analyses are available for hand hygiene programs in general, we could not find financial outcomes related to hand hygiene and CDI specifically. To better understand and

encourage the implementation of hand hygiene initiatives, it would be beneficial to take into account the cost of a hand hygiene initiative (staffing, staff time, supplies, installation of sinks, etc.), as well as the costs of sustaining a program, and compare these totals with estimated savings in terms of medical costs from CDI prevention.

4.2.5 Implementation

A systematic review by Neo et al. (2016) of 73 studies published from 2002 to 2015 on interventions to increase hand hygiene compliance in healthcare settings found five general intervention types:

- Education
- Facility design (installation of sinks and ABHRs)
- Unit-level protocols and procedures
- Hospitalwide programs
- Multimodal interventions

Among the review's conclusions were recommendations that hand hygiene education be interactive and engaging and that interventions be tailored to the institution's unique needs.[38] Researchers have assessed barriers to hand hygiene and report that hand hygiene interventions should be tailored to the particular classification/role of staff and that context and staff needs should be taken into account when designing hand hygiene interventions. For example, Kirkland et al. (2012) noted that regular review of data linking hand hygiene performance to HAIs was persuasive for physicians, but they were less likely to engage in educational programs geared toward staff with less medical knowledge.[29]

In an example of addressing a facility's unique needs, Al-Tawfiq et al. (2018) described positive experience using The Joint Commission Center for Transforming Healthcare's web-based Targeted Solutions Tool® (TST®) to improve hand hygiene and reduce HAIs in a 30-bed oncology/hematology inpatient unit in Saudi Arabia. The tool is designed to identify root causes of nonadherence to hand hygiene and improve process outcomes. Researchers found that housekeepers needed more help than other staff help with improving hand hygiene, but these workers were not fluent in either English or Arabic (the dominant languages) and their educational levels varied substantially. To address this issue, an extensive training program was developed for housekeeping staff using in-action learning tools and translators. After 1 year, the hand hygiene compliance rate increased from 75.4 percent at baseline to 88.6 percent ($p<0.0001$). Researchers found a decrease in CDIs from 7.95 (CI, 0.8937 to 28.72) to 1.84 (CI, 0.02411 to 10.26) infections per 10,000 patient days that was not significant ($p=0.23$) and cited sample size as a barrier to statistical significance.[30]

An interactive strategy to assist HCWs in improving glove and gown removal technique includes the use of fluorescent lotion. In the training described by Tomas et al. (2015), fluorescent lotions were used to help HCWs learn proper glove and gown removal to minimize hand contamination. The fluorescent lotion provides immediate visual feedback on contaminated sites.[12] A similar strategy includes the use of nonpathogenic RNA beads that fluoresce under ultraviolet (UV) light to help track contamination during removal of personal protective equipment. This practice can help HCWs see that glove use does not preclude the need for hand hygiene.[39]

4.2.6 Additional Contextual Factors

The design of the healthcare environment can affect hand hygiene compliance. Some researchers suggest a human factors engineering approach that calls for abundant, convenient, and available sinks, handwashing products, and ABHRs to improve compliance.[40] Several researchers found that longer distances to sinks, and sink visibility, were related to HCW handwashing compliance. For example, Zellmer et al. (2015) reviewed the practices of HCWs and visitors for CDI-positive patients on a transplant medical-surgical unit at a large academic medical center. While there were sinks in the patients' rooms, these were not used due to the placement of furniture, patients' personal items blocking access, and lack of foot pedals. Before the study began, the only two easily accessible sinks were at the end of a hallway. After the installment of two highly visible sinks in the unit, completion of proper hand hygiene on exiting the CDI patient room improved by 18 percent ($p=0.03$).[24]

In another example, Deyneko et al. (2016) investigated the relationship between sink location and HCW compliance with handwashing; their multivariate analysis found that increased distance between the patient zone and the nearest sink was inversely associated with handwashing compliance. The median distance to the nearest sink was 7.6 meters when hand hygiene was correctly performed, but 14.9 meters when it was omitted ($p<0.001$). There was also a strong association between the number of 90° turns required to reach the sink and handwashing compliance.[23]

4.2.7 Resources To Assist with Implementation

AHRQ Safety Program for Long-Term Care: HAIs/CAUTI—The How-To's of Hand Hygiene: https://www.ahrq.gov/professionals/quality-patient-safety/quality-resources/tools/cauti-ltc/modules/implementaion/education-bundles/infection-prevention/hand-hygiene/hand-hygiene-slides.html

CDC Clean Hands Count Campaign: https://www.cdc.gov/handhygiene/campaign/index.html

Sequence for putting on and removing personal protective equipment: https://www.cdc.gov/hai/pdfs/ppe/PPE-Sequence.pdf

The Joint Commission Center for Transforming Healthcare Hand Hygiene Targeted Solutions Tool: https://www.centerfortransforminghealthcare.org/what-we-offer/targeted-solutions-tool/hand-hygiene-tst

Veterans Health Administration: Infection: Don't Pass It On education and communication materials: https://www.publichealth.va.gov/infectiondontpassiton/index.asp

WHO Hand Hygiene Tools and Resources: https://www.who.int/infection-prevention/tools/hand-hygiene/en/

4.2.8 Gaps and Future Directions

As already noted, there is a need for more real-world randomized and crossover hand hygiene studies in which CDI prevention is a primary focus. One of the most important omissions of the reviewed clinical/quasi-experimental studies was that compliance with hand hygiene practices specific to CDI was not distinctly measured and reported. In several of the reviewed studies, hand hygiene processes (end points) were clinician hand hygiene at the appropriate moments, not whether a CDI-appropriate

method (e.g., use of gloves and washing hands in outbreak/hyperendemic settings) was used.[30,32] CDI-specific research would help improve understanding about the impact of using ABHRs versus handwashing when working with CDI patients. In addition, the strength of the research on hand hygiene in clinical settings and hand hygiene methods was limited by small sample sizes.

Research on hand hygiene interventions in a wide variety of setting types (and in multiple settings) is needed given that hand hygiene behaviors and challenges differ across settings. Neo et al. (2016) found in their review that most studies of hand hygiene interventions were in hospitals or ICUs.[38] As CDI disproportionately impacts elderly and immunocompromised patients, more research is needed on CDI and hand hygiene in LTCFs that serve these specific patient populations. In addition, LTCFs have unique staffing and environmental factors and require different types of patient contacts than hospitals do. Many nursing home facilities are designed to encourage social contact between patients, and patients move throughout the facility coming into contact with spaces outside their rooms (e.g., dining room, physical therapy room). In such settings, hand hygiene programs aimed at patients could be particularly impactful. Additional studies in the outpatient setting would also be useful.

Patient hand hygiene is a promising area of prevention and research. As the role of colonized patients is increasingly understood, patient hand hygiene analyses will likely account for patients with asymptomatic colonization in addition to those with CDI. As found by Kundrapu et al. (2014), the numbers of CDI colonies recovered from patients' hands were similar for those diagnosed with CDI and asymptomatic carriers.[19] Due to some of the barriers for patient hand hygiene, including mobility, some have suggested more research into the potential of using skin-safe cleaning wipes with *C. difficile* eliminating agents (e.g., sporicidal electrochemically generated hypochlorous acid solution) for patients who cannot ambulate or be brought to sinks for routine handwashing.[19,41] Patient education about *C. difficile* is potentially important. Kundrapu et al. (2014) found that 73 percent of colonized and infected patients in their study were not aware that ABHR does not kill *C. difficile* spores.[19]

Some research has been conducted to identify new ways to decontaminate HCWs' hands. Researchers may continue to explore potential noncorrosive hand rubs that provide the convenience of a hand rub and are more effective at killing all pathogens, including *C. difficile* spores.[35] For example, an experimental study by Nerandzic et al. (2013) found that sporicidal electrochemically generated hypochlorous acid solution (Vashe), used to soak or as a wipe, is effective in reducing spores. Wiping with Vashe-soaked cloths significantly enhanced reduction of *C. difficile* spores by approximately 68 percent (0.5 $\log_{10}$ CFU [colony-forming unit]; $p<0.01$).[41] Vashe is FDA approved for use on wounds, and more research is needed to determine safety for other uses. In addition, more real-world research is needed to determine efficacy for HCW exposure to *C. difficile.*

Direct and persistent observation is both a study technique and an intervention to encourage hand hygiene. There are some limits to in-person monitoring, including cost, feasibility of achieving sufficient sample size, sustainability, potential for HCWs to temporarily alter behavior while being observed, and lack of consistency (within and across studies) for measuring compliance. Monitoring by video is another observation strategy that eliminates the physical presence of the observer but has some of the same drawbacks as in-person monitoring.[41]

Staats et al. (2017) studied the use of electronic monitoring, using radio frequency identification, in 71 hospital units. HCWs were given badges that communicated with a network of sensors throughout the hospital and at hand hygiene stations. Monitoring measured whether the HCWs used hand hygiene

stations at the appropriate place and time. The researchers found that electronically monitoring individual compliance resulted in a large, positive increase in compliance that was not sustained.[43]

One drawback of electronic monitoring and censors is cost, and more research is needed. Other strategies include use of electronic counters on ABHRs and measuring handwashing product use. The drawbacks of these strategies is they do not account for appropriate hand hygiene technique, hand hygiene moments, and person using the product (patients and visitors may also use these products).[42]

The use of gloves for preventing transmission of CDI is strongly recommended in the guidelines yet not well studied in the healthcare setting. More research could be done on promoting HCW compliance with glove use, barriers and facilitators, and best practices for glove use when working with CDI patients.

Finally, interventions for hand hygiene will need to address issues of sustainability, as multiple studies reported declines in compliance after the hand hygiene intervention period.[35,43] For example, Pokrywka et al. (2017) report that sustainability requires ongoing leadership, continued staff reminders, education for new staff, and ongoing resources, without which hand hygiene compliance rates will fall.[35] Kirkland et al. (2012) report that understanding the hospital context, based on responses to the initiative across units and HCW types, helped sustain improved hand hygiene compliance rates for a year following a 3-year hand hygiene initiative.[29] Additional research concerning the sustainability of hand hygiene programs would be helpful to improve understanding.

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4.3 CDI PSP 3: Environmental Cleaning and Decontamination

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This review includes a summary of evidence published from 2008 to 2018 on environmental cleaning and decontamination as a prevention practice for CDI. We start with a definition of terms by the CDC and a brief practice description for environmental cleaning and decontamination for *C. difficile* from the 2017 guidelines by the IDSA and SHEA. The review then provides an overview of how environmental cleaning and decontamination work as a safety practice for preventing the transmission of *C. difficile*.

Next, we summarize the evidence for the impact of environmental cleaning and decontamination interventions on CDI rates and highlight some experimental research on cleaning agents for *C. difficile*. We then explore implementation factors, including monitoring and improving the performance of environmental service workers and challenges with the use of decontamination equipment. Finally, we explore gaps and future directions for environmental cleaning and decontamination for *C. difficile*. The review's key findings are located in the box on the right.

Key Findings

- The most recommended cleaning and decontamination agents for manual use are chlorine-based solutions.
- In many of the reviewed studies, the addition of hydrogen peroxide decontamination (HPD) or ultraviolet light decontamination (UVD) to standard cleaning was associated with significant reductions in facility-level CDI rates.
- HPD and UVD have drawbacks, including expense and the time it takes to decontaminate a room. However, the process for UVD is shorter than for HPD.
- The performance of environmental cleaning services staff is important and can be improved through the use of training, checklists, and audit and feedback.
- There is a need for higher quality studies, multifacility studies, and studies that compare cleaning and decontamination methods.
- Future directions include research and development of nontoxic decontamination agents, new technologies, and research on patient outcomes and environmental cleaning in diverse healthcare settings.

4.3.1 Practice Description

The CDC (2008) in their guideline for sterilization and disinfection of healthcare facilities define the practice of cleaning in the healthcare environment as "the removal of visible soil (e.g., organic and inorganic material) from objects and surfaces" (page 9).[1] The CDC defines disinfection as the elimination of many or all pathogenic microorganisms from the environment, while sterilization refers to the elimination of all forms of microbial life.

Decontamination is the process to remove pathogenic microorganisms from objects for the purposes of safe handling and use. The CDC states that cleaning (i.e., removing visible material from surfaces) is a first step in the decontamination process so that organic or inorganic material does not interfere with decontamination. As outlined in this report, the use of sporicidal agents to manually clean healthcare environments is a form of both cleaning and decontamination. Use of touchless automated methods are solely for the purpose of environmental decontamination.

Recommended environmental cleaning and decontamination practices are outlined in the IDSA/SHEA 2017 revised guidelines for *C. difficile*.[2] These recommendations include IDSA/SHEA statements about

the strength of the recommendation and quality of evidence. Recommendations applicable to environmental cleaning and decontamination include:

- Terminal room cleaning (cleaning after a patient is discharged or transferred from a room) with a sporicidal agent should be considered in conjunction with other measures to prevent CDI during endemic high rates or outbreaks, or if there is evidence of repeated cases of CDI in the same room *(weak recommendation, low quality of evidence)*.
- Daily cleaning with a sporicidal agent should be considered in conjunction with other measures to prevent CDI during outbreaks or in hyperendemic (sustained high rates) settings, or if there is evidence of repeated cases of CDI in the same room *(weak recommendation, low quality of evidence)*.
- Measures of cleaning effectiveness should be incorporated to ensure quality of environmental cleaning (*good practice recommendation*).
- Disposable patient equipment should be used when possible and reusable equipment should be thoroughly cleaned and disinfected, preferably with a sporicidal disinfectant that is equipment compatible *(strong recommendation, moderate quality of evidence).*

The IDSA/SHEA state in the guidelines that they have no recommendation for the use of automated touchless terminal (i.e., upon discharge) disinfection CDI prevention due to data limitations. The CDC guidelines for environmental cleaning and decontamination for *C. difficile* include the creation of daily and terminal cleaning protocols and checklists for patient-care areas and equipment.[3] Other guidelines from an earlier SHEA/IDSA report for acute care facilities recommend frequent education for environmental service personnel in the primary language of the cleaning team and the use of various techniques to help improve cleaning and decontamination practice as outlined by the CDC[4] (e.g., observation, fluorescent markers, and bioluminescence).[4,5]

Safety practices for laundry, bedding, and other environmental services are included in the CDC's "Guidelines for Environmental Infection Control in Health Care Facilities."[6] Guidelines for specific facility types, including hospitals, nursing homes, long-term acute care facilities, and outpatient facilities, are available from the CDC and other healthcare agencies. We include some of these resources later in this chapter.

4.3.2 Environmental Cleaning as a Safety Practice

The healthcare environment is recognized as a primary source of *C. difficile* transmission.[7] *C. difficile* is spread through the feces of infected and colonized patients. Patients with contaminated hands may spread *C. difficile* by touching surfaces in the healthcare environment. Some evidence suggests *C. difficile* may be dispersed to surfaces near the patient through droplets in the air.[8,9] Transmission can occur when other patients, healthcare staff, or visitors touch contaminated surfaces and orally ingest *C. difficile* (e.g., while eating).[7] Those who take antimicrobials, are advanced in age, or have compromised immune systems are at high risk of getting CDI from exposure to the pathogen. Others may become asymptomatic carriers of *C. difficile*.[2]

Both symptomatic and asymptomatic carriers have the potential to contaminate the environment. In one hospital, *C. difficile* was recovered from 59 percent of samples in rooms of asymptomatic carriers[10]

and 75 percent of samples of rooms with patients with CDI.[11] Patients may continue to contaminate the environment after treatment.[12] The most contaminated areas, or "high-touch surfaces," include the bed rails, bed surface, supply cart, over-bed table, and intravenous pumps.[13]

In one study, CHWs' hands were just as likely to be contaminated with *C. difficile* after touching high-touch surfaces as they were by touching a CDI patient.[14] *C. difficile* produces spores that are especially robust and may remain viable in the environment for over 4 days.[15] Shaughnessy et al. (2011) examined the potential role of environmental transmission of *C. difficile* through a prior room occupant and found that the prior occupant's CDI status was a significant risk factor for acquiring CDI (p=0.01; hazard ratio, 2.35), after controlling for other risk factors (e.g., antimicrobial use, age, proton pump inhibitors).[16]

Eliminating *C. difficile* in the healthcare environment requires specialized practices. Evidence shows that *C. difficile* spores are resistant to alcohol and many hospital disinfectants.[17] In one study, exposure of the bacteria to low levels of certain cleaning agents resulted in higher CDI sporulation capacity (the ability for vegetative cells to forms spores during unfavorable environmental conditions).[18]

Among cleaning and decontamination agents for washing surfaces by hand, chlorine-releasing solutions (e.g., bleach), at sufficient concentration and with appropriate exposure time (at least 10 minutes), demonstrate the best evidence for killing *C. difficile*.[17] The CDC-recommended cleaning/decontamination agents for *C. difficile* can be found on EPA List K: Registered Antimicrobial Products Effective Against *Clostridium difficile* Spores.[19]

Decontamination by hand is challenging and not always effective in reaching all contaminated surfaces in the healthcare environment.[12,20] Automated touchless methods have been developed and implemented to supplement cleaning by hand and prevent the spread of CDI and other HAIs. The two most commonly studied touchless methods for *C. difficile* decontamination are hydrogen peroxide decontamination (HPD)—including vaporized, aerosolized, atomized, and dry mist systems—and ultraviolet disinfection (UVD), which includes UV radiation and pulsed xenon UV light systems. In laboratory studies, both methods have shown effectiveness in almost entirely eliminating *C. difficile* contamination from targeted surfaces.[21,22]

Although subject to some debate, it is generally recommended that surfaces be precleaned by hand prior to use of UVD or HPD, as organic matter is thought to reduce the efficacy of the UVD and HPD methods.[23] In their review, Doll et al. (2015) found that studies were mixed as to which no-touch method (UVD or HPD) was most effective at killing *C. difficile.* The UVD methods generally take less time than HPD to decontaminate a room.[23]

There is increasing incentive for facilities to implement an effective environmental cleaning and decontamination program as facility rankings and CMS reimbursement rates are tied to reported rates of healthcare facility-acquired onset (HO CDI). The 2016 revised requirements for participation in Medicare and Medicaid outlined the specific components of an effective infection control program, including environmental cleaning and decontamination procedures. One review found that, among several PSPs, environmental cleaning and decontamination practices were the most cost effective for reducing facility-level CDI rates.[24]

4.3.3 Methods

The question of interest for this review is: What are the most effective and feasible environmental cleaning and decontamination practices to prevent CDI?

To answer this question, we searched the databases CINAHL and MEDLINE from 2008 to 2018 for "*Clostridium difficile*" and related MeSH terms and synonyms, in combination with terms such as "Disinfection," "Decontamination," and "No-touch decontamination." The search string also included a variety of healthcare settings, including "hospitals," "inpatient," "ambulatory care," "long-term care," and "transitional care." After duplicates were removed, the initial search yielded 121 results that were screened for inclusion. Of these, 45 full-text articles were retrieved. Of those, 18 studies and 3 systematic reviews were selected for this review.

Reference lists of retrieved articles were also screened to ensure thoroughness, and five studies were retrieved that way. Articles from the searches were excluded if the outcomes were not relevant or precisely reported or study design was insufficient (e.g., opinion pieces, nonsystematic reviews). Due to the number of experimental studies on this topic, a select group are included in the evidence tables and cited in the review. Studies in which environmental cleaning and decontamination were accompanied by other significant infection control practices (e.g., changes in hand hygiene practices) were ruled out for this section and are considered in Section 4.6, Multicomponent CDI Prevention Interventions.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

4.3.4 Review of the Evidence

In this evidence summary, we review 12 articles and 2 reviews on environmental cleaning and CDI patient outcomes. These studies were primarily (10/12) based in hospitals and examined CDI rates after a period of enhanced cleaning and decontamination. In our search of the literature, we also found numerous experimental studies published from 2008 to 2018 on environmental cleaning and disinfection methods and CDI. Among these were three studies that compared UVD or HPD with bleach cleaning. We also found two studies on alternatives to chlorine-based solutions for the manual elimination of *C. difficile* from healthcare surfaces. We include a review of these experimental studies and information from one qualitative study on concerns about the effects of bleach on HCWs. Two systematic reviews included studies on environmental cleaning and CDI rates, and a third examined research on cleaning agents used to eliminate the *C. difficile* organism.

4.3.4.1 Environmental Cleaning and Patient Outcomes: Studies and Reviews

As shown in Table 4.3, the evidence for environmental cleaning and decontamination and CDI patient outcomes includes 12 studies published from 2008 to 2018. Most studies showed statistically significant reductions in CDI rates after a period of an environmental cleaning intervention; however, study quality was low. These findings align with the review conducted by Louh et al. (2017) in their examination of studies on CDI prevention practices in acute care hospitals from 2009 to 2015.[24] We review five of the same studies here.[25-29]

Louh et al. (2017) reported that environmental cleaning was the most cost effective of the multiple strategies they studied.[24] Khanafer et al. (2015) found nine studies on environmental cleaning and CDI published from 1982 to December 2013.[30] They concluded that environmental cleaning with a 10:1 bleach solution was both practical and effective. Of the nine studies, four are included here;[26,27,29,31] we excluded the remaining studies because they were published before 2008 or measured the combined effect of several PSPs.

The environmental decontamination strategies in this review fall into one of four categories: use of a chlorine-based agent, use of a chlorine-based agent plus the use of HPD, a chlorine-based agent plus the use of UVD, and one study about washable bed covers. Within these categories, certain variables differed, such as the frequency of cleaning (e.g., daily or at discharge) and the area of cleaning (e.g., CDI patient rooms, all patient rooms, communal spaces).

The studies reviewed here were primarily quasi-experimental with a before-after approach. The study by Anderson et al. (2017) was the only randomized trial in the group of studies.[32] The cleaning intervention period ranged roughly from 8 months[31] to 2 years.[26] Two of the studies on HPD no-touch decontamination methods received some financial support from the makers of the products, in the form of free use of equipment[33] and reduced cost to use the products.[31] Two UVD studies had more than one author who was an employees of Xenex, the company that sells the machines that were studied in the intervention.[34,35]

Table 4.3: Studies From 2008 to 2018 on Environmental Cleaning/Decontamination and CDI Patients

Article	Setting	Intervention	CDI Outcome
Anderson et al., 2017[32]	9 hospitals	Rooms from which a patient with infection or colonization with *C. difficile* was discharged were terminally disinfected with one of two strategies: (1) bleach, and (2) UVD and bleach.	CDI incidence among exposed patients was not changed after adding UV to cleaning with bleach (n=38 vs. 36; 30,4 cases vs. 31,6 cases per 10,000 exposure days (relative risk [RR] 1.0, 95% CI, 0.57 to 1.75; p=0.997).
Best et al., 2014[33]	30-bed stroke rehabilitation unit	The unit performed one-time deep cleaning (1,000 parts per million [ppm] chlorine-based disinfectant) and atomized HPD, following a high incidence of CDI in the unit.	There were 20 CDI cases in the 10 months before the intervention and 7 CDI cases in the following 10 months.
Boyce et al., 2008[31]	500-bed university hospital	Highest incidence wards received wardwide HPD cleaning. The hospital also added terminal disinfection of rooms occupied by CDI patients using HPD (in addition to cleaning with 5,000 ppm dilution of household bleach).	On five high-incidence wards, the incidence of nosocomial *Clostridium difficile*-associated disease (CDAD) was significantly lower during the intervention period than during the pre-intervention period (1.28 vs 2.28 cases per 1,000 patient days, p=0.047).
Hacek et al., 2010[26]	3 hospitals with total ~850 beds	Quaternary ammonium compound was replaced as a room cleaning agent with diluted bleach (5,000 ppm sodium hypochlorite) for terminal cleaning of rooms occupied by patients with CDI. Cleaning walls was added to checklist.	There was a 48% reduction in the prevalence density of CDI after the bleaching intervention [95% CI, 36% to 58%, p<0.0001].
Haas et al., 2014[25]	643-bed tertiary care academic medical center	UVD followed discharge cleaning of contact precautions rooms (with 5,550 ppm bleach solution) and other high-risk areas.	Significant decrease in all measured HAIs. Healthcare associated CDI decreased from 0.79 per 1,000 patient days to 0.65 per 1,000 patient days (p=0.02).

Article	Setting	Intervention	CDI Outcome
Hooker et al., 2015[37]	Two long-term acute care hospitals, one with 74 beds and the other with 30 beds	A washable cover was used for the mattress and bed deck. The cover was removed at discharge and laundered with hot water, chlorine, and detergent.	At Hospital A, the use of bedcovers reduced the rate of HO CDI by 47.8% (95% CI, 47.1 to 48.6), controlling for the rate of handwashing compliance and length of stay in days. At Hospital B, the use of bedcovers reduced the rate of HO CDI by 50% (95% CI, 47.5 to 52.7), controlling for the rate of handwashing compliance and length of stay in days (no p-value provided).
Levin et al., 2013[28]	140-bed acute care community hospital	UVD followed terminal cleaning with chlorine-based wipes (5,250 ppm) in CDI rooms. UVD was used in CDI and contact precautions rooms.	In 2010, the hospital-associated CDI rate was 9.46 per 10,000 patient days; in 2011, (1 year post-intervention), the CDI rate was 4.45 per 10,000 patient days (53% reduction, p=0.01).
Manian et al., 2013[29]	900-bed community hospital	Terminal "enhanced cleaning" consisted of use of bleach (5,000 ppm) followed by HPD using a priority scale based on the pathogen and room location.	The nosocomial CDAD rate dropped significantly from 0.88 cases/1,000 patient days to 0.55 cases/1,000 patient days (rate ratio, 0.63; 95% CI, 0.50 to 0.79, p<0.0001).
Miller et al., 2015[35]	Long-term acute care facility (bed count not provided)	UVD disinfection system was used for patient rooms (at discharge) and common areas (weekly).	Healthcare-associated CDI rates decreased over a 15-month period from 19.3 per 1,000 patient days to 8.3 per 1,000 patient days, a 56.9% reduction (p=0.02).
Nagaraja et al., 2015[36]	180-bed ICU	Terminal cleaning with UVD was used in addition to standard cleaning for all contact precautions rooms.	Compared with pre-UVD, during UVD, CDI was 22% less (p=0.06) (borderline statistical significance).
Orenstein et al., 2011[27]	2 medical units at 1,249-bed hospital	Daily and terminal cleaning with germicidal bleach wipes (0.55% bleach, i.e., 5,500 ppm) took place in all patient rooms. (Replaced quaternary ammonium compound.)	Hospital-acquired CDI incidence decreased by 85%, from 24.2 to 3.6 cases per 10,000 patient days (p<0.001).
Vianna et al., 2016[34]	206-bed community hospital	In the ICU, the goal was for all room discharges and transfers to be treated with UVD disinfection after standard cleaning and prior to the next patient occupying the room. For all non-ICU discharges and transfers, the UVD was only used for *C. difficile* discharges.	CDIs decreased by 41% (p=0.01). Greater reductions were seen in ICU versus hospital (61% vs. 29%).

4.3.4.2 Studies: Cleaning With Bleach

Two of the reviewed studies examined patient outcomes after a period in which patient rooms were cleaned with bleach either daily or at patient discharge. Hacek et al. (2010) evaluated a cleaning intervention at three hospitals with a total of approximately 850 beds in which terminal cleaning of the rooms occupied by CDI patients was conducted with a bleach solution (5,000 ppm) as a replacement for quaternary ammonium compound. In addition to the switch to bleach, walls were added to a checklist of surfaces to clean after patient discharge. The change in cleaning practices was a response to increases in CDI at the hospitals. The cleaning initiative included periodic unannounced cleaning assessments by supervisory staff.

Following 2 years of the new cleaning procedures, the average number of CDI patients per 1,000 patient days decreased from 0.85 before the use of bleach to 0.45 during bleach cleaning. There was a 48 percent reduction in the prevalence density of CDI (95% CI, 36% to 58%, p<0.0001) compared with the

10 prior months. The researchers report that there were no other significant infection prevention practice changes during the cleaning intervention implementation period.[26]

Orenstein et al. (2011) measured CDI outcomes following a cleaning intervention on two hospital wards with high baseline incidences of CDI. The cleaning program included switching from the use of quaternary ammonium compound to that of germicidal bleach wipes (5,500 ppm active chlorine) for daily and terminal cleaning of patient rooms. To evaluate progress and cleaning performance, certain rooms were randomly assessed for cleanliness with the use of adenosine triphosphate bioluminescence, which detects organic matter on surfaces.

Following a year of the new cleaning procedures, the researchers found a reduction in hospital-acquired CDI incidence of 85 percent, from 24.2 to 3.6 cases per 10,000 patient days ($p<0.001$). The researchers cite evidence about the role of asymptomatic carriers in contaminating the environment with *C. difficile* and conclude that *daily* bleach cleaning of *all* rooms on the wards with high incidence of CDI may be more effective than only terminal cleaning of the CDI rooms. They theorize that cleaning with bleach helps to reduce the chance of transmission of *C. difficile* via the environment and onto the hands of HCWs. Orenstein et al. (2011) examined the potential influence of confounding factors and report that they controlled for other infection prevention practices prior to the intervention.[27]

4.3.4.3 Studies: Hydrogen Peroxide Decontamination

Three reviewed studies examined the use of HPD for patient room decontamination and found reductions in CDI rates.[29,31,33] The three cleaning and decontamination interventions all added the use of HPD to cleaning with bleach and were using bleach for terminal cleaning of CDI rooms prior to the intervention. The frequency of HPD varied across the studies, ranging from a one-time HPD deep clean of a ward,[33] to priority-based HPD terminal cleaning of rooms,[29] to a one-time deep HPD cleaning of five high-incidence wards followed by terminal HPD cleaning of CDI patient rooms.[31]

Boyce et al. (2008) found that, following a deep cleaning of five wards with HPD, then 8 months of terminal cleaning of CDI-occupied rooms with bleach and HPD, the incidence of nosocomial CDI decreased from 2.28 to 1.28 cases per 1,000 patient days ($p=0.047$).[31] Manian et al. (2013) evaluated an intervention at a 900-bed community hospital, in which HPD was added to terminal cleaning of all rooms. When HPD decontamination was not possible, CDI rooms were cleaned with four rounds of bleach cleaning. After approximately 7 months, the rate of nosocomial CDAD dropped significantly, from 0.88 cases/1,000 patient days to 0.55 cases/1,000 patient days (rate ratio, 0.63; 95% CI, 0.50 to 0.79, $p<0.0001$). These results are somewhat difficult to interpret as approximately half of the CDI rooms were cleaned with HPD and half were cleaned with four rounds of bleach cleaning.[29]

4.3.4.4 Studies: Ultraviolet Environmental Disinfection

Six studies selected for this review examined the use of UVD and CDI patient outcomes. Of these, four studies showed statistically significant decreases in CDI following a period of UVD added to standard terminal cleaning with bleach of CDI patient rooms[25,28,34,35] and one found borderline significant reductions in CDI.[36] In one example, Vianna et al. (2016) report on the addition of UVD to terminal cleaning with bleach in a 206-bed hospital. The terminal UVD procedure was implemented for all room discharges in the ICU and for rooms occupied by patients with *C. difficile* in the rest of the hospital.

Following 21 months of the UVD intervention, the researchers reported a 41 percent decrease in CDI ($p=0.01$). CDI reductions were greater in the ICU than in the rest of the hospital (61% vs. 29%). The

results indicate that UVD is effective when deployed to higher risk/higher acuity settings (e.g., the ICU) and/or when used in all room discharges (not just for patients with *C. difficile*). One potential confounder was an ASP, implemented 11 months prior to adoption of UVD. However, this change was not statistically linked to the reduction in CDI rates during the UVD period.[34]

Long-term acute care facilities have different environmental cleaning/decontamination needs than hospitals. For example, patient stays are longer than in the hospital, so patient rooms turn over less frequently. In a study of CDI patient outcomes and environmental cleaning in a long-term acute care facility, Miller et al. (2015) looked at the addition of UVD to standard procedures for cleaning patient rooms at discharge and for cleaning common areas on an approximately weekly basis. For rooms occupied by *C. difficile* patients, standard procedures also included cleaning with a bleach solution.

During a 15-month period of added UVD, CDI rates decreased from 19.3 per 1,000 patient days to 8.3 per 1,000 patient days, a 56.9 percent reduction (p=0.02). It is important to note that in the prior year, the facility had implemented additional infection prevention measures consisting of education for staff around hand hygiene for CDI, disposable equipment, additional handwashing sinks, reminders about equipment decontamination, and a checklist for terminal cleaning. It is possible that the reductions in CDI rates reflect the longer term impact of these measures.[35]

In the most robust study, less favorable results were found in a broad cluster-randomized study of nine hospitals, in which terminal cleaning with bleach of all rooms occupied by CDI patients was compared with terminal cleaning with bleach plus UVD. In this crossover trial, Anderson et al. (2017) found that, comparing the strategies for 7 months each, the incidence of CDI infection among patients exposed to rooms previously occupied by patients with CDI was unchanged (n=38 vs 36; 30.4 cases vs 31.6 cases per 10,000 exposure days; relative risk 1.0, 95% CI 0.57 to 1.75, p=0.997).[32]

4.3.4.5 Study: Launderable Bed Covers

Hooker et al. (2015) examined CDI rates associated with the introduction of launderable bed covers at two long-term acute care hospitals. The researchers note that prior studies had shown that HAIs could be spread through contaminated mattresses (which are difficult to clean without damaging) and bedframes (i.e., bed decks). To prevent this source of transmission, the cleaning intervention consisted of the use of washable bed covers that covered both the mattress and bed deck. (The covers consisted of the same material used in high-end mattresses and allow moisture transmission.) The washable covers were used on all patient beds, removed after every patient discharge, and replaced with a clean cover.

After 14 months of use of the bed covers, the rate of CDIs at one hospital decreased 47.8 percent (95% CI, 47.1 to 48.6), controlling for the rate of handwashing compliance and length of stay in days. At the second hospital, the rate of CDIs decreased by 50 percent (95% CI, 47.5 to 52.7), controlling for the rate of handwashing compliance and length of stay in days. Data were not available on antimicrobial use, so this variable was not factored into the analyses. Hooker and colleagues (2015) theorized that, in addition to reducing the spread of *C. difficile*, the use of bed covers could help to reduce room turnover time between patients as the bed surfaces did not require thorough cleaning.[37]

4.3.4.6 Laboratory and Quasi-Experimental Studies

A number of studies and one review compare the performance of different cleaning agents and methods in removal/eradication of the *C. difficile* organism. We provide a sample of studies in the next two segments.

4.3.4.6.1 Experimental Studies: HPD and UVD Versus Bleach

Several experimental studies compared the touchless methods with bleach cleaning with mixed results. Ghantoji et al. (2015) examined whether, after cleaning with standard detergents, terminal cleaning with bleach solution or UVD was more effective at removing *C. difficile*. High-touch surfaces in rooms previously occupied by CDI patients were sampled after discharge and before and after the use of both methods. The researchers found that the difference in final contamination levels between the two cleaning protocols was not significant (p=0.98).[38] Similarly, Mosci et al. (2017) looked at hydrogen peroxide and silver ion solution compared with cleaning with bleach following standard cleaning for removing *C. difficile* on different surfaces in a hospital. After disinfection, 0 percent (p<0.001) of samples were contaminated with *C. difficile* after HPD, and 3 percent (p<0.001) of samples were contaminated after bleach cleaning. The differences between groups was not statistically significant and the time for each cleaning intervention was roughly the same.[39]

Barbut et al. (2009) found that an *in situ* hydrogen peroxide dry mist system was more effective than 0.5% sodium hypochlorite solution at eradicating *C. difficile* spores; samples taken from hydrogen peroxide-treated rooms showed a 91 percent decrease in *C. difficile,* whereas samples taken after hypochlorite decontamination showed a 50 percent decrease in *C. difficile* (p<0.005).[40]

4.3.4.6.2 Experimental Studies: Alternatives to Bleach

While cleaning with bleach and chlorine-based solutions has been shown to be highly effective in eliminating *C. difficile* from surfaces, these agents can be corrosive to metals and irritating to skin and mucus membranes.[17] Housekeepers have reported respiratory irritation when using bleach and other chlorine-based disinfectants.[41] One reason for terminal cleaning rather than daily cleaning of CDI patient rooms is for environmental services staff to avoid excessive exposure to bleach.[26] Concerns for patients and employees include the appearance of bleach residue left on surfaces, odors, and respiratory tract irritation.[41] Due to the toxicity of bleach, the Occupational Safety and Health Administration recommends using gloves and eye protection, ventilating the room properly, preparing the bleach solution daily, and allowing the solution to stand at least 30 minutes after preparation before use.

Several studies have examined potential alternatives to bleach. For example, Alfa et al. (2008) looked at different formulations of hydrogen peroxide for cleaning toilets contaminated with *C. difficile.* The researchers found that one of the tested hydrogen peroxide alternatives was equivalent to bleach 1,000 ppm after 1 minute but was not as efficient as that achieved for bleach at 5,000 ppm (1:10 bleach to water).[42]

Peracetic acid has performed similarly to bleach.[43] Kundrapu et al. (2012) studied the potential use of a peracetic acid-based disinfectant because preliminary studies indicated that it was as effective as bleach solution but less corrosive and irritating. The peracetic acid was associated with a significant reduction in the frequency of acquisition of pathogens on investigators' hands after contact with the surfaces and in the mean number of colony-forming units acquired. Patients in the rooms reported no adverse effects during use of the product, and there were no complaints from the nursing staff.[44]

4.3.4.7 Economic Outcomes

In the reviewed studies, there was limited financial information on the studied cleaning and disinfection interventions. The article by Orenstein et al. (2011) was an exception, reporting that the cost of the bleach wipes used for the daily and terminal cleaning of two medical units was $12,684 per year. They estimated that 27 cases of healthcare-associated CDI were prevented in this study, resulting in healthcare savings of between $135,000 and $216,000. While additional staffing time for daily and terminal bleach cleaning was not factored into the analyses, the researchers say that "it added little extra time to the housekeepers' daily routine" (page 1138), indicating that there were minor increases in room turnover time.[27]

Other reviewed studies provided some information about the costs of UVD and HPD. These findings are summarized in Table 4.4. Specifically, Miller et al. (2015) and Vianna et al. (2016) reported that UVD was cost effective in terms of CDIs avoided.[34,35] Levin et al. (2013) reported that the cost to lease two UVD machines was less than $5,000 per month[28] and Doan et al. (2012) estimated the cost of HPD equipment was $1,154.98 per month.[43]

Ghantoji et al. (2015) reported that UVD was more cost effective than HPD, primarily because of the time needed to use each device—HPD takes longer than UVD per room. Both methods require that rooms be vacant and items be placed in a manner that allows adequate contact with the hydrogen peroxide mist or UV light. Before the HPD process starts, all heating, ventilation, and air-conditioning ducts in the area need to be sealed.[38]

Boyce et al. (2008) reported that the HPD process took approximately 3 to 4 hours per patient room and approximately 12 hours for an entire ward. Doll et al. (2015) stated the time per room for UVD depended on the type of UVD; pulsed xenon UV takes 15 to 20 minutes and UVC radiation takes 20 to 40 minutes.[31] Haas et al. (2014) reported that the time for UVD light exposure in their study was around 6 minutes, but it took close to a half hour for setup (including setting up blackout curtains), depending on the room. Haas et al. (2014) also reported that cleaning can be more efficient by using UVD first in the bathroom, while finishing cleaning the larger room by hand.[25]

While UVD may be more time efficient than HPD, it has some limitations; the process has decreased effectiveness at higher distances (over 1.22 m) and cannot decontaminate items in shadow.[36] Finally, in their review of multiple cleaning methods, Doan et al. (2012) report that decontamination with bleach was cheaper than and as effective as touchless methods.[43]

Table 4.4: Cost, Decontamination Time, and Setup for HPD and UVD

	Equipment Costs	Time for Cleaning	Room Setup for Cleaning
HPD	$1,155/mo. for 1 unit (Doan et al., 2012)	3–4 hours per patient room 12 hours per ward	Must be vacant Must have HVAC ducts sealed
UVD	<$5,000/mo. for 2 units (Levin et al., 2013)	15–40 minutes per patient room	Must be vacant Requires blackout curtains (for windows and to cordon off areas of rooms) Requires items be moved out of shadows

4.3.5 Implementation: Challenges and Facilitators

One of the challenges reported across several of the studies on HPD and UVD was being able to use the touchless machines in all intended cases.[28,29] For example, Levin et al. (2013) reported that the goal was

to conduct terminal UVD on all contact precautions rooms but only 56 percent of discharged contact precautions rooms received the UVD treatment. This discrepancy was due to limited device availability or the presence of a second room occupant.[28]

Similarly, Haas et al. (2014) reported 76 percent of contact precautions rooms received the UVD treatment, rather than the intended 100 percent. Reasons for not conducting the UVD included a second room occupant who could not be moved, an urgent need for the room, and labor constraints.[25] Manian et al. (2013) report that using a system that prioritized use of the HPD machine based on the HAI of the discharging patient (with CDI as the top priority) allowed the machine to be used for rooms not inhabited by CDI patients when possible. When the HPD machine was not available for a CDI room, the room was cleaned multiple times with bleach.[29]

Compliance with cleaning procedures is essential for eliminating active *C. difficile* from the environment. Research shows that touchless methods require appropriate operation. For example, the UVD machine may require repositioning in order to be most effective.[23,36] Ways to assist with manual cleaning compliance include cleaning checklists and audit and monitoring. Khanafer et al. (2015) recommend the use of checklists to guide housekeepers on the cleaning sequence and provision of education and direct and immediate feedback to environmental services staff.[30]

Denton et al. (2016) discussed survey results from cleaning staff and others following a period of use of an audit and monitoring tool. They reported positive responses about the tool, saying that education of—and investment by—the housekeeping staff, in addition to positive, approachable, and supportive leaders, helped make the tool effective.[45] The use of adenosine triphosphate bioluminescence[27] or fluorescent markers can be effective in auditing/monitoring the thoroughness of cleaning and a basis from which to provide feedback.[46]

4.3.6 Resources To Assist With Implementation

C. difficile **Collaborative Non-ICU Environmental Cleaning Checklist:**
http://www.rochesterpatientsafety.com/Images_Content/Site1/Files/Pages/Hospitals/Non-ICU%20Cleaning%20Checklist.pdf

CDC Guide to Infection Prevention for Outpatient Settings**:**
https://www.cdc.gov/infectioncontrol/pdf/outpatient/guide.pdf

CDC Options for Evaluating Environmental Cleaning:
https://www.cdc.gov/HAI/toolkits/Evaluating-Environmental-Cleaning.html

List K: **EPA's Registered Antimicrobial Products Effective Against** *Clostridium difficile* **Spores:**
https://www.epa.gov/pesticide-registration/list-k-epas-registered-antimicrobial-products-effective-against-clostridium

Not Just a Maid Service:
https://www.youtube.com/watch?v=nfZftqBELsA

SHEA/IDSA Clinical Practice Guidelines for *C. difficile*: 2017 Update:
https://www.idsociety.org/globalassets/idsa/practice-guidelines/clinical-practice-guidelines-for-clostridium-difficile.pdf

SHEA/APIC Guideline: Infection Prevention and Control in the Long-Term Care Facility: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3319407/

4.3.7 Gaps

There are several gaps in the studies on environmental cleaning for CDI prevention. While much of the evidence is promising for the environmental cleaning interventions included in this review, there is a need for more high-quality (e.g., randomized, robust) studies in diverse healthcare environments and larger multifacility studies to better understand this PSP. The only randomized/crossover study, by Anderson et al. (2017), found no significant change in CDI incidence following the addition of UVD to bleach cleaning for room discharges at nine hospitals.[32] More randomized studies are needed to compare the evidence. In addition, more robust financial evaluations that investigate the various methods and combinations of methods and incorporate staff time, room turnover time, and cost of no-touch devices and other cleaning machines and supplies would be beneficial.

There is also a gap in the literature with regard to cleaning and CDI patient outcomes outside of the patient rooms in the larger facility environment. Only Miller et al. (2015) describe decontamination of common areas,[35] while Best et al. (2014) and Boyce et al. (2008) describe one-time "deep" cleaning of entire wards using HPD.[31,33] While patient rooms are the primary focus of most of the reviewed studies, *C. difficile* contamination has been found in nonisolation rooms, in physician and nurse work areas, and on portable equipment.[47]

Finally, there is a shortage of studies on environmental cleaning/decontamination in long-term facilities, outpatient, and other nonhospital settings. We identified only two studies of sufficient sample size on environmental cleaning and CDI outcomes in long-term acute care settings.[35,37] Nursing home residents are at high risk for CDI due to frequent antimicrobial exposure and the relatively high number of colonized patients in LTCFs. A systematic review found that 14.8 percent (95% CI, 7.6% to 24.0%) of LTCF residents are asymptomatic carriers of toxigenic *C. difficile*.[48]

CDI recurrence is also high in LTCFs due to new infection or recurrence of the original infection. Given longer patient stays and the presence of more patient belongings (creating additional possible transmission pathways), and that LTCFs are intended to promote social interaction, LTCFs have unique environmental decontamination needs that require further study.[49]

4.3.8 Future Directions

Future directions for environmental cleaning practices to prevent *C. difficile* transmission include advances in hospital equipment and standard hospital items.[50] For example, research has explored the use of copper for hospital surfaces (e.g., cabinets, tables). Copper has been shown to provide a significant (>70 percent) reduction in survival of *C. difficile* vegetative cells and spores on copper alloys compared with stainless steel.[15] Sporicidal properties in common hospital items such as curtains has also been explored.[51] Installation of items such as toilet lids can help prevent the spread of CDI droplets when a contaminated toilet is flushed.[8] Some studies show that microfiber cloths (made of a combination of polyamide and polyester) perform better than standard cotton materials at removing *C. difficile*.[52]

Future research could build on and enhance existing cleaning and decontamination technologies. One example is hand-held wands that can be used on items such as keyboards and portable medical devices to kill pathogens with UV radiation.[53] Another example involves rendering *C. difficile* spores more susceptible

to UVD and increasing the efficacy of UVD by initiation of *C. difficile* germination. (The initiation of germination has been shown to make spores more susceptible to heat and radiation.) Application of germination solution to a contaminated surface prior to UVD was shown to increase the number of spores killed by UVD compared with UVD alone.[54] Finally, continued research on environmental services systems and efficacy of methods, as well as improved support and training of environmental services workers, will help to advance cleaning and decontamination practices in the future.

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4.4 PSP 4: Surveillance

Reviewers: Arjun Srinivasan, M.D., and Luba Katz, Ph.D.

This review includes a summary of evidence published from 2008 to 2018 on surveillance practices for CDI. After a brief practice description from CDC, IDSA/SHEA, and others, the review explains how regional and facility-level surveillance work as safety practices for preventing the transmission of *C. difficile*. Next, we provide a review of studies on CDI surveillance methods and explore surveillance contextual factors, such as setting and CDI testing method. Finally, we discuss research gaps and future directions for CDI surveillance. The review's key findings are listed in the box below.

4.4.1 Practice Description

The CDC defines public health surveillance as "the ongoing, systematic collection, analysis, and interpretation of health data, essential to the planning, implementation and evaluation of public health practice, closely integrated with the dissemination of these data to those who need to know and linked to prevention and control."[1,2] Experts emphasize the importance of using standard surveillance criteria to make accurate comparisons over time, report data to the public, and compare data across facilities.[3,4] According to the IDSA/SHEA *C. difficile* clinical practice guidelines,[4] facilities should implement the following surveillance activities for adult patients (the strength of recommendation is from the IDSA/SHEA guidelines):

Key Findings

- Research has shown that automated surveillance systems are generally accurate and save time and resources, compared with manual case review.
- Automated laboratory alerts have been shown to help expedite contact precautions for CDI patients.
- Classifying CDI cases using standard case definitions is important although some researchers have found that the current definitions over represent the number of nosocomial cases.
- There is a need for research that evaluates and compares different facility-level CDI surveillance strategies and implementation barriers and facilitators.
- Genotyping provides detail about differences in *C. difficile* virulence and has helped to identify transmission pathways and outbreaks.
- Promising technologies include rapid molecular typing, integrated systems that can track CDIs across health systems and facilities, and facility-access to regional real-time surveillance data.

- Use available standardized case definitions for surveillance of (1) healthcare facility-onset (HO) CDI; (2) community-onset, healthcare facility–associated (CO-HCFA) CDI; and (3) community-associated (CA) CDI (*good practice recommendation*).
- At a minimum, conduct surveillance for HO CDI in all inpatient healthcare facilities to detect elevated rates or outbreaks (*weak recommendation, low quality of evidence*).
- Express the rate of HO CDI as the number of cases per 10,000 patient days. Express the CO-HCFA prevalence rate as the number of cases per 1,000 patient admissions *(good practice recommendation*).
- In settings of high endemic rates or outbreaks, stratify data by patient location to target control measures when CDI incidence is above national or facility reduction goals, or if an outbreak is noted (*weak recommendation, low quality of evidence*).

Facility *C. difficile* surveillance practices include conducting internal surveillance data collection and analyses and reporting to State and Federal agencies via CDC's NHSN. The NHSN assists facilities in collecting data to help determine local, regional, and national infection prevention priorities. The NHSN also helps facilities meet quality benchmarks, identify areas for improvement, and comply with CMS infection reporting requirements. To track national CDI incidence and establish reduction targets, the NHSN calculates standardized infection ratios. The standardized infection ratio is a risk-adjusted summary measure used to track HAIs at a national, statewide, or local level over time and by facility type. The NHSN also collects information on certain infection safety practices and antimicrobial resistance.[5]

Another national surveillance program is the CDC Emerging Infections Program, a network of 10 State health departments, academic institutions, Federal agencies, and other public health stakeholders that collect data and support research and training to inform policy and public health practice. The national Healthcare Cost and Utilization Project is a database resource sponsored by AHRQ that has been used to track and report *C. difficile* hospitalizations.[6] *C. difficile* is also among the conditions tracked in the AHRQ National Scorecard on Hospital-Acquired Conditions.[7]

At the State level, CDI reporting requirements vary; some States require facilities to report on *C. difficile* (via the NHSN) either by adopting CMS's quality reporting requirements as State law, or through State mandates.[8] Many States implemented reporting requirements in 2013, the year in which hospitals were first required to report HAIs via NHSN for the CMS Hospital Inpatient Quality Reporting program.[9]

Internal facility surveillance practices vary depending on facility resources and local requirements. Facilities may use the NHSN system to conduct internal CDI surveillance using the MDRO/CDI Module.[10] The LabID option, introduced in 2013, uses admission date, laboratory test results, and patient care location to automatically estimate measures of CDIs. An incident case is defined as any CDI LabID event from a specimen obtained more than 56 days after the most recent CDI LabID Event. A recurrent case is any CDI LabID event from a specimen obtained >14 days and ≤56 days after the most recent CDI LabID event for that patient. The day of the first specimen collection is considered day 1. HO-CDI cases are those LabID events collected more than 3 days after admission to an inpatient facility (i.e., on or after day 4). The Infection Surveillance Reporting option for CDI is based on clinical case reviews to identify and report CDIs. Facilities may report at the facility level or by different units within the facility.

Facilities may also report on adherence to hand hygiene and contact precautions for *C. difficile* patients. The NHSN system allows facilities to use their data to:

- Calculate CDI measures (e.g., prevalence at admission, CO prevalence, facility or unit incidence),
- Create charts,
- Filter data,
- Track incidence in different facility locations,
- Identify trends,
- Recognize deviations from the norm, and
- Compare rates with other facilities.

The NHSN also collects data on antimicrobial use and resistance in a separate module. CDC's Targeted Assessment for Prevention (TAP) provides infection prevention resources and guidance on how to interpret surveillance data and report feedback to stakeholders such as facility leaders and administrators.[11] Links to this and other resources are available later in this section of the CDI chapter.

Facility surveillance practices include using alerts for positive CDI cultures and tracking the movement of CDI patients within a facility or health system.[12,13] It is recommended that facilities have procedures for investigating outbreaks, protocols to guide referrals for strain typing, and processes to communicate with associated healthcare facilities and relevant jurisdictional bodies, as required.[14]

4.4.2 Surveillance as a PSP

The epidemiology of CDI has been evolving, with particular increases in CO CDI and hypervirulent strains.[15] Regional and national surveillance provide information on CDI epidemiology and help to identify clusters, outbreaks, and emerging ribotypes. Analyses of these data inform policy and public health programs.[16]

At the facility level, CDI surveillance is used to identify transmission pathways and CDI clusters, evaluate safety improvement initiatives, and signal when facilities must enhance measures to prevent further transmission.[13,16] Monitoring HO-CDI incidence is a first step in identifying and controlling outbreaks at facilities. In one example, an outbreak on a vascular surgery unit was identified by an increase in the number of cases within 30 days and a change in the pattern of new cases. Samples were sent to a regional lab for PCR testing and results revealed that outbreak cases were caused by *C. difficile* ribotype 106, a clindamycin-resistant strain. Based on these findings, the facility implemented restrictions on the prescribing of clindamycin. Controlling the outbreak was attributed to this measure.[17] Root cause analysis of HO-CDI cases, another surveillance practice, helps facilities understand the reasons for hospital transmission and make workflow improvements, such as reducing testing delays.[18]

In 2007, the CDC adopted standardized case definitions to track disease trends, detect outbreaks, facilitate comparison of CDI rates among similar institutions, and incorporate previous healthcare facility exposure information.[19] These definitions have been updated. For example, the 2007 case definition for healthcare facility onset was defined as a patient with CDAD symptom onset more than 48 hours after admission to a healthcare facility. Now, the definition for healthcare facility onset is defined as LabID events collected >3 days after admission to an inpatient facility.[4]

CDI case identification and classification were traditionally conducted by individual case review; however, manual data abstraction is labor intensive, burdensome, and costly.[20] As technology evolves and reporting mandates increase, more facilities are using commercial infection control systems that process electronic health data to identify and classify cases.[12,20] Swift and automated identification of patients with *C. difficile* helps expedite contact precautions and reduce the potential for additional healthcare transmissions.[12] Research using genotyping technology (described below) supports rapid identification of CDI isolates and helps track transmission and identify virulent strains both within a facility and regionally.[21] Ribotyping (described below) during periods of increased CDI incidence can help identify CDI clusters and outbreaks.[22]

Currently, there are a lack of studies that compare or evaluate facility-level CDI surveillance strategies.

4.4.3 Methods

The question of interest for this review is: What are the most recommended and promising institutional surveillance practices for *C. difficile*?

To answer this question, we searched the databases CINAHL and MEDLINE from 2008 to 2018 for "*Clostridium difficile*" and related MeSH terms and synonyms, as well as "Surveillance" OR "monitoring and surveillance" OR "epidemiologic surveillance" OR "infectious diseases surveillance" and synonyms. The search string also included a variety of healthcare settings, such as "hospitals," "inpatient," "long-term care," "transitional care," and "home health." After duplicates were removed, the initial search yielded 503 results, all of which were screened for inclusion, and 42 full-text articles were retrieved.

Reference lists of included articles were also screened to ensure thoroughness and 14 additional studies were identified and retrieved. Articles were excluded if the intervention or outcomes were not relevant or precisely reported or if the study design was insufficient (e.g., opinion pieces, nonsystematic reviews). Studies in which surveillance was followed by other significant infection control practices (e.g., changes in environmental cleaning) were ruled out for this section and are considered in Section 4.6, Multicomponent CDI Prevention Interventions. Of the total retrieved articles, 16 studies and 2 systematic reviews were selected for inclusion in this review.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report A through C appendixes.

4.4.4 Review of the Evidence

We found 16 studies and 2 systematic reviews that examined facility *C. difficil*e surveillance practices. These practices include the use of different statistical analyses, automated surveillance alerts, CDI case identification and classification, genotyping practices, and use of biomarkers to track CDI virulence. Most of these studies are descriptive case studies with no comparison group. Several studies examined the utility and accuracy of International Classification of Diseases (ICD) code data alone or in combination with medication data to conduct HO-CDI surveillance. Overall, there is a gap in the literature with regard to facility practices for implementing surveillance to reduce CDI.

4.4.4.1 Surveillance To Identify CDI Outbreaks and Clusters

One study from the United Kingdom demonstrates how surveillance can be used to identify CDI clusters and trigger implementation of enhanced infection prevention practices. In this study, Hardy et al. (2010) described the use of an HO-CDI case threshold to identify CDI clusters at a 1,800-bed teaching hospital. The case threshold was two or more HO-CDI cases within a 28-day period. Two or more HO-CDI cases was considered a period of increased incidence. The studied intervention was implemented upon identification of a period of increased CDI incidence. It included a standardized set of interventions, including notifying staff of the increased incidence and auditing compliance with hand hygiene, using environmental decontamination practices, isolating patients, and providing clinical management of patients with confirmed or suspected CDI.

If the audit identified any shortcomings in these prevention practices, steps were taken to make improvements. Additional enhanced cleaning was also implemented upon identification of the period of

increased incidence (PII). If there were postaudit incident HO-CDI cases, a more detailed environmental audit was conducted by one of the head nurses. In the first 9 months of the study, isolates were ribotyped on PIIs with more than 10 cases; for the last 8 months of the study, isolates were ribotyped for all PIIs. In this case, an outbreak was defined as two or more cases of the same PCR ribotype within a 28-day period.

While less common in the United States outside of research contexts, ribotyping of *C. difficile* isolates helps determine transmission pathways and confirm presence of an outbreak. During roughly 1.5 years of the intervention, the number of PIIs investigated per month decreased from a peak of 14 per month in February 2008 to 1 in June 2009. For the first 9 months, five of seven periods with more than 10 cases were confirmed as outbreaks. In the final 8 months, ribotyping of the isolates confirmed nine (32%) of these periods to be outbreaks, with three being due to ribotype 027, two ribotype 078, and all the others distinct ribotypes.[22]

Two of the included studies examined different statistical methods for CDI surveillance.[23,24] Lavan et al. (2012) compared the value and efficiency associated with manual tracking and calculating the incidence and prevalence of CDI in two wards in an acute 751-bed hospital in Ireland that were experiencing an increase in the number of severe CDI cases. For 6 weeks, the researchers measured the prevalence of CDI, antibiotic use, and associated comorbidity, and then for 13 weeks identified all new CDI cases, all using manual data collection. CDI cases were assessed for CDI risk factors, disease severity, response to treatment, and outcomes at 6 months.

The researchers found that manual data collection and analysis took less time in their prevalence study than the incidence study. The prevalence study provided useful information about differences between the two wards in CDI prevalence and CDIs with MRSA colonization, the extent of multiple antibiotic prescriptions in CDIs, and areas that required more indepth surveillance. The incidence study permitted a more detailed evaluation of CDI risk factors, origin and severity of disease, and patient outcomes. Overall, researchers found that incidence analysis was more useful for their institution for planning preventive initiatives and focusing antibiotic stewardship efforts.[23]

Screening for outbreaks is often based on a relative increase in incidence or when incidence reaches an absolute threshold.[16] A temporal scan statistic approach examines new cases within a particular window of time and can be used prospectively or retrospectively. Faires et al. (2014) applied a retrospective scan statistic to identify several CDI clusters and potential outbreaks in a hospital based on 5 years of laboratory results and bacteriology reports. PCR was used to identify *C. difficile* isolates for the most recent year of data. CDI clusters were identified using the temporal scan statistic, and statistically significant clusters were compared with CDI outbreaks that had been identified using standard hospital surveillance. A negative binomial regression model identified associations between year, season, and month rate of CDI cases.

Results of the statistical analyses indicated that the incidence rate for CDI was significantly higher in the spring than in the fall and winter seasons. Overall, 86 CDI cases were identified, 18 specimens were analyzed, and 9 ribotypes were classified. The temporal scan statistic identified three significant clusters ($p \leq 0.05$), including potential outbreaks, not previously identified by hospital personnel using standard surveillance analyses. One outbreak was identified as starting a month before it had been recognized by the hospital. The researchers note that temporal analyses, applied prospectively and in tandem with other methods, could be useful in identifying clusters and outbreaks in a timely manner.[24]

4.4.4.2 Integrating Automation Into Surveillance

Over the last 10 years, CDI surveillance has become increasingly automated.[25] Automated and consistent measurement of CDI is preferable to disparate systems for surveillance of CDI.[21] Several studies in this review examined the feasibility and efficacy of electronic surveillance systems. Studies have found that the use of automated systems and EHR data assist in the rapid detection of cases and outbreaks,[12,13,26] and electronic strategies can provide timely alerts and help expedite contact precautions. Zilberberg et al. (2011) demonstrate that electronic patient data can be used to calculate risk-stratified HO-CDI rates to help inform practice.[27] Dubberke at al. (2012) and Benoit et al. (2011) found that automated surveillance using electronically available data (e.g., admission date) was accurate and more efficient than manual case review.[28,29]

4.4.4.2.1 Automated CDI Surveillance

Dubberke et al. (2012) developed and validated an automated CDI surveillance algorithm using 1 year of available electronic data from four U.S. hospitals located in different regions. Each hospital customized the algorithm to accommodate variability in datasets. Electronic surveillance was highly sensitive and specific and showed good agreement with manual review for HO; CO, study facility-associated; indeterminate; and recurrent CDI. The overall sensitivities, specificities, and kappa values of the algorithm compared with the manual case review were:

- HO: 92 percent sensitivity, 99 percent specificity, and 0.90 kappa;
- CO, study facility-associated: 91 percent, 98 percent, and 0.84;
- CO, CA: 96 percent, 94 percent, and 0.69;
- Indeterminate cases: 80 percent, 98 percent, and 0.76; and
- Recurrent cases: 94 percent, 99 percent, and 0.94.

The results for CO, other HCFA were less sensitive (57%), were highly specific (99%), and had a kappa value of 0.65. In discussing the lower sensitivity for CO, other HCFA infections, they note the challenges of accurately capturing previous healthcare episodes using the available data. Several hundred discordant cases (out of 1,767 patients with a positive CDI test) required review and correction due to misclassifications in the data. Overall, the researchers reported that automated surveillance reduces staff time and may help facilities better track CO CDI.[28]

While Dubberke et al. (2012) found that sensitivity and specificity for automated surveillance using EHR data was adequate, other researchers have found that, in practice, automated surveillance may overestimate the rate of HO CDI.[30,31] For example, Durkin et al. (2015) compared LabID reporting (for the NHSN) with traditional surveillance in 29 community hospitals in the southeastern United States. LabID is designed to use electronically captured laboratory data and hospital admission dates to determine HO versus CO surveillance CDI categories.

LabID surveillance resulted in a higher HO-CDI incidence rate than did traditional surveillance. The overall HO-CDI rate was 6.0 versus 4.4 per 10,000 patient days for LabID and traditional surveillance, respectively ($p<0.001$). After 6 months, 286 (23%) mismatched CDI events were detected. The most frequent causes of mismatched cases by LabID were:

- Diagnostic testing delay >3 days despite the presence of symptoms of CDI in the first 2 days of admission triggering an HO-CDI LabID categorization,
- Misclassification of recurrent or continuation episodes as incident events by LabID, and
- Lack of an indeterminate category in LabID definitions.

The differences based on surveillance method may affect hospital quality rankings.[31] Several hospitals in the study showed significantly lower rankings based on LabID surveillance (versus traditional surveillance). Once the coding was corrected, hospital rankings based on LabID HO rates were similar to rankings based on traditional surveillance.

In a recent study, Albert et al. (2018) examined the misclassification of HO CDIs reported to the NHSN by a large urban medical center. Using retrospective chart review of 212 HO-CDI cases, they found that only 62.2 percent of the cases reported to NHSN actually met the clinical definition of probable or possible HO CDI. The researchers estimate that the remaining cases may have been misclassified due to delays in testing, inappropriate testing, or use of stool softeners and laxatives. The researchers cite prior evidence that PCR testing is less able to distinguish between infection and colonization cases and that testing patients for CDI either too late or without clinically significant diarrhea contributes to overdiagnosis of HO CDI.[32] Truong et al. (2017) suggest real-time electronic tracking of diarrheal episodes and laxative therapy, to verify *C. difficile* testing criteria.[33]

4.4.4.2.2 Automated Alerts

Quan et al. (2015) explored the accuracy and efficiency of a system for five MDROs and *C. difficile* tracking in a 410-bed tertiary care center that automated the following: monitoring microbiology results and initiating chart-based flags, ordering contact precautions on admission, and ensuring appropriate removal of precautions. The system was initiated as an alternative to manual case review, which required the assessment of laboratory results and tracking prior history of MDRO carriage and *C. difficile* infection. The system automatically reviewed daily positive laboratory results for 110,212 patient days and identified 1,543 results representing either new incident CDI cases or cases not previously known to the system, which triggered organism-specific flags. The automated ordering of precautions for inpatients occurred immediately after laboratory results were finalized, without a delay for manual order submission.

To test the accuracy of the system, the researchers conducted a point-prevalence assessment and found that all precautions were appropriate. The advantages of the automated system included preventing missed precautions and timelier weekend and after-hours isolation precautions. The researchers estimated that the automated alerts could save 850 annual hours of staff time.[12] Automated alerts have also been shown to expedite contact precautions and significantly increase the rate of appropriately isolated patients for other HAIs.[26]

4.4.4.3 Using ICD Code Data for HO-CDI Surveillance

Automated surveillance of CDI can be conducted using clinical data (e.g., the LabID system) or administrative code data.[34] We found three studies and a systematic review that examined the accuracy of using ICD code data for the identification of CDI.[20,35-37] There are advantages to using ICD data since these codes are used by all facilities for insurance billing purposes and are stored in electronic formats.[20,35] One disadvantage is that the ICD coding rules may not match the standard surveillance

definitions or account for testing sensitivity[35] or clinical context.[38] While useful for tracking overall CDI burden, some research shows that ICD-9 codes are not adequately accurate in identifying the place of onset (i.e., HO CDI vs. CO-HCFA infection).

Use of present-on-admission (POA) criteria, which CMS required to better distinguish CO versus HO-CDI cases began on October 1, 2008. In a review of overall cases of CDI, ICD coding may be useful, as evidenced in a recent national report using Healthcare Cost and Utilization Project data that focused on the burden of CDI for hospitals (using ICD-9 codes) and provided quarterly and annual estimates of CDI hospitalization rates from 2011 through 2015.[6] The POA indicator in ICD codes can be used to help distinguish which cases originated in the facility. This report shows how the POA-CDI rate is associated with the HO-CDI rate. However, the numbers do not account for CDI infections that resolved without an inpatient stay and cases that originated in a different health facility. Another challenge when working with these data is that coding practices may differ across hospitals and States.[6]

To improve the accuracy of ICD data, Schmiedeskamp et al. (2009) examined the use of ICD-9 Clinical Modification code CDI data combined with medication treatment data, in an automated HO-CDI case identification system. The researchers examined a year of discharge data (23,920 adult patients) for over 300 hospitals. They identified adults discharged with an ICD-9-CM code for CDI and documentation of CDI therapy with oral vancomycin or metronidazole compared with ICD-9 code only. Case review was used to determine true cases. The sensitivity of the ICD-9-CM code alone for identifying nosocomial CDI was 96.8 percent, the specificity was 99.6 percent, the positive predictive value was 40.8 percent, and the negative predictive value was 100 percent. When CDI drug therapy was included with the ICD-9-CM code, the sensitivity ranged from 58.1 percent to 85.5 percent, specificity was virtually unchanged, and the range in positive predictive value was 37.9 percent to 80.0 percent, depending on the parameters of number of days of therapy and when therapy started.[36]

4.4.4.4 *C. difficile* Genotyping

Although primarily used in research, genotyping technologies can enhance investigations into *C. difficile* transmission, identify virulent strains, and assist in understanding antimicrobial resistance.[16] Methods for genotyping (also called molecular typing) include:

- PCR ribotyping,
- Pulsed field gel electrophoresis variable-number tandem-repeat analysis,
- Whole-genome sequencing,
- Next-generation sequencing, and
- Multilocus sequence typing.

One U.K. study explored how PCR ribotyping can be used to help identify local/facility outbreaks and virulent strains and inform infection prevention initiatives.[39] Wilcox et al. (2012) evaluated England's Clostridium difficile Ribotyping Network and changes in CDI rates in the country. From 2007 to 2010, the network received samples from facilities for 10.8 percent of all CDI patients in the country (12,603 fecal specimens), along with demographic information, the name of the requesting hospital, and antibiotic history in the 30 days before the onset of CDI symptoms.

Hospitals were notified of the ribotyping results with a targeted turnaround time of less than 2 weeks. Ribotype 027, a ribotype associated with increased complications and mortality, was the most frequently detected in all 3 years but decreased over the 3 years. After 3 years, there was a 61 percent reduction in reported *C. difficile* in England. The researchers believe that the Clostridium difficile Ribotyping Network helped facilities get control of ribotype 027 by providing timely data on ribotypes, enabling targeted interventions for ribotype 027.[39]

4.4.4.5 Innovations

Compared with PCR ribotyping, whole genome sequencing offers greater detail about diversity within genotypes. Next-generation sequencing is a rapid form of whole genome sequencing. These technologies identify differences between isolates usually using single nucleotide variants.[16,40] With PCR ribotyping only, there is a greater likelihood of cases being flagged as sharing the same genotype, simply by chance.[16]

Moloney et al. (2016) used next-generation sequencing to enhance epidemiological information and identify and resolve a *C. difficile* outbreak at an Irish hospital. Seven patients with CDI were all found to have ribotype 020 and *C. difficile* with a particular classification of bacterial isolates (sequence type 295). Using this information, the researchers were able to link the patients and track transmission back to a community hostel for homeless adults. Infection prevention and control measures were taken in the hostel under the guidance of public health personnel, and the outbreak was resolved. Of note, the standard surveillance definitions inaccurately classified three of the cases as HO CDI when in fact they were exposed in the hostel. For most patients in the study, the researchers suspected several weeks between ST-295 exposure and symptoms.[40]

Monitoring patient biomarkers is a potential research strategy for early detection of increasing *C. difficile* strain virulence. Schlackow et al. (2012) used an automated monitoring system to examine routinely collected laboratory hospital data at a group of U.K. hospitals. In particular, they used iterative sequential regression and monitored biomarkers of inflammation and neutrophil counts upon CDI diagnosis, because these measures are taken frequently prior to therapy and are associated with mortality in *C. difficile* colitis.

Examining over 10 years of data from 7,272 CDI-positive adults, the researchers found a strong association ($p<0.0001$) between a severe strain of *C. difficile*, ST1, and higher neutrophil counts at diagnosis. Mean neutrophil count among cases with the highly virulent ST1 strain was 13.5×10^9/L, while in the non-ST1 *C. difficile* isolates it was 10.7×10^9/L (difference in means 2.8; 95% CI, 1.5 to 4.5, $p=0.0001$). Molecular typing confirmed that an increase in CDI mortality was likely due to the ingress of ST1. The researchers found similar trends in difference between severe strain biomarkers using secondary data analyses of two multicenter studies. Because of the timely availability of the laboratory data, researchers found that monitoring biomarkers was a more rapid way to identify severe strains of CDI than using mortality data.[41]

4.4.5 Contextual Factors

Contextual factors include the type of setting in which *C. difficile* surveillance is conducted as participation in the NHSN expands beyond acute care facilities. In addition, the sensitivity and specificity of different testing methods impact surveillance rates. There is debate about the role of asymptomatic

colonized *C. difficile* carriers—how they impact surveillance data and whether they should be actively surveilled.

4.4.5.1 Surveillance Settings

In addition to acute care hospitals, current participants in NHSN *C. difficile* reporting include skilled nursing facilities, LTCFs, long-term acute care hospitals, inpatient rehabilitation facilities, and inpatient psychiatric units (NHSN, n.d.). Some argue that surveillance case definitions may overestimate LTCF-associated CDI. For example, current surveillance case classifications may overestimate the incidence of nursing home-associated CDI. Mylotte et al. (2012) found that of 75 incident CDI cases, 52 (69%) developed within 30 days of admission to an LTCF and 23 (31%) developed more than 30 days after admission.

Of the 52 cases that developed within 30 days, 68 percent were in residents admitted for subacute care. The mean number of days ± SD to develop CDI was 10.5 ± 2.5 in those who developed infection within 30 days, and 75 percent of these cases developed within 15 days of admission.[42] Jump and Donskey (2015) proposed surveillance definitions for LTCFs in which a case would not be considered as originating in the LTCF if a patient had been discharged from a hospital in the last 30 days; such a case would be considered LTCF onset, hospital acquired.[43]

4.4.5.2 Testing Methods and *C. difficile* Colonization

CDI testing methods have different sensitivities and specificities, which impact CDI rates. Therefore, the CDC adjusts for the different tests in NHSN reporting. A number of recent studies have shown that more sensitive molecular testing methods result in higher CDI surveillance rates. For example, Moehring et al. (2013) studied a change in testing from nonmolecular to molecular testing using PCR at 10 hospitals. The mean incidence rate of CO-HCFA CDI (using the 2007 case definitions) before the switch was 6.0 CDIs per 10,000 patient days compared with 9.6 CDIs per 10,000 patient days 18 months after the switch. The researchers stated that the improved sensitivity of molecular tests allows infected and colonized patients to be rapidly and reliably identified but can be "too good" at identifying patients who are colonized but not truly infected with *C. difficile*.[44] We explore the impact of testing type on CDI rates in more detail in Section 4.5, Testing (Indepth).

4.4.6 Resources To Assist With Implementation

CDC Targeted Assessment for Prevention (TAP) Strategy:
https://www.cdc.gov/hai/prevent/tap.html

CDC Updated Guidelines for Evaluating Public Health Surveillance Systems:
https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5013a1.htm

CDC Healthcare Associated Infections—Community Interface: *Clostridioides difficile* Infection Tracking:
https://www.cdc.gov/hai/eip/cdiff-tracking.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fhai%2Feip%2Fclostridium-difficile.html

Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA):

https://www.idsociety.org/globalassets/idsa/practice-guidelines/clinical-practice-guidelines-for-clostridium-difficile.pdf

Greater New York Hospital Association: Reducing *C. difficile* Infections Toolkit: https://apic.org/Resource_/TinyMceFileManager/Practice_Guidance/cdiff/C.Diff_Digital_Toolkit_GNYHA.pdf

How to: Surveillance of Clostridium difficile infections: https://www.ncbi.nlm.nih.gov/pubmed/29274463

NHSN Surveillance for *C. difficile* (CDI) and Multidrug Resistant Organisms (MRDO): https://www.cdc.gov/nhsn/ltc/cdiff-mrsa/index.html

4.4.7 Gaps

While there are numerous case studies on CDI surveillance and how surveillance practices may overestimate HO CDI, there is limited research on CDI surveillance implementation, best practices, and challenges. In addition, while several studies pointed to the cost-effectiveness of automated surveillance systems [12,29] a more robust economic analysis of CDI surveillance programs could be beneficial. As with other PSPs, most of the CDI surveillance studies are in the context of hospitals, and other settings are poorly represented. The IDSA/SHEA 2017 *C. difficile* guidelines[4] identified additional gaps in understanding the epidemiology of *C. difficile,* including the need to better understand sources for *C. difficile* transmission in the community and the incubation period for *C. difficile*. Finally, some researchers have called for a standardized surveillance classification to define an "outbreak" of CDI.[16]

4.4.8 Future Directions

The implementation and capabilities of automated surveillance will continue to grow[25] and global strategies may be implemented. In the future, integrated healthcare databases to track CDI patients across health systems could help track transmission outside a particular facility, ward, or healthcare system.[17] Increased research and tracking of CO CDI and CO-HCFA CDI will help to better understand CDI epidemiology outside of the healthcare setting. Although tracking CO-HCFA CDI is not mandated and requires the collection/evaluation of patients' prior healthcare facility admissions, it is useful in order to better understand the epidemiology of CDI.[45]

Strains of *C. difficile* have shown resistance to certain antimicrobials, and resistance plays a role in occurrence and recurrence of CDI.[46] According to Peng et al. (2017), with technological advances in the future, clinical microbiology laboratories could rapidly perform antimicrobial susceptibility testing to determine antimicrobial resistance and report the information to clinicians in real time.[46] Similarly, more rapid and affordable genotyping and molecular typing has the potential to identify cases that are part of an outbreak and improve response times.[4,16]

Efforts in Europe have shown the potential for more standardized *C. difficile* PCR ribotyping.[47] After examining *C. difficile* ribotypes from six locations across the United States, Waslawski et al. (2013) called for greater *C. difficile* ribotype data in order to better understand the impact of ribotype on sensitivity and specificity of testing and clinical treatment for CDI. They also recommend the establishment of an internationally recognized *C. difficile* ribotype reference collection.[48]

Participation in surveillance reporting will increase and include a broader spectrum of settings. For example, data from a larger group of LTCFs will be used to establish national benchmarks and track achievement of prevention goals.[49] A number of studies found discrepancies between surveillance definitions and clinical incidence.[40,50,51] Review and refining of surveillance definitions may be warranted as we continue to better understand CDI incubation periods. Finally, in the future, there is likely to be continued debate about "active surveillance" for *C. difficile*, i.e., the identification and isolation of asymptomatic carriers at hospital admission.[52,53] We explore this issue in more detail in Section 4.5, Testing (In-Depth).

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4.5 PSP 5: Testing

Reviewer: Andrea Hassol, M.S.P.H.

This section includes a summary of evidence published from 2008 to 2018 on diagnostic testing as a safety practice for CDI. After providing a brief practice description and testing recommendations by the IDSA/SHEA and others, we review how testing works as a safety practice for preventing CDI. In the evidence summary, we discuss testing criteria and whether to test asymptomatic patients, a summary of systematic reviews and meta-analyses on the accuracy of different testing methods, and studies on tools to predict CDI and CDI severity. Finally, we discuss gaps and future directions for CDI testing. Key findings are located in the box on the right.

Key Findings

- Some research supports universal *C. difficile* testing for hospitalized patients with diarrhea.
- Screening and isolating asymptomatic carriers can prevent CDI transmission but is resource intensive.
- NAATs of unformed stool have relatively accurate sensitivity and specificity.
- Concerns with NAATs include that they detect toxigenic *C. difficile* genes, not the actual damaging toxins and may capture colonized patients in addition to those infected with *C. difficile*.
- Certain multistep test algorithms (that include a test for *C. difficile* and for CDI toxins) perform as well as or better than NAATs but take longer.
- Tools that identify patient risk for CDI could be useful in preventing CDI.
- Tools that identify a high risk of severe CDI or mortality show promise for prevention of severe CDI outcomes.
- Future directions include improved diagnostic technology for increased efficiency and accuracy of diagnosis.

4.5.1 Practice Description

The IDSA and SHEA recommend the following testing practices for suspected *C. difficile* in adults (the recommendation and quality of evidence come from IDSA/SHEA):

- Use patients with unexplained and new-onset ≥3 unformed stools in 24 hours as the preferred target population for testing for CDI *(weak recommendation, very low quality of evidence)*.
- Use a stool toxin test as part of a multistep algorithm (i.e., glutamate dehydrogenase [GDH] plus toxin; GDH plus toxin, arbitrated by NAAT; or NAAT plus toxin) rather than NAAT alone for all specimens received in the clinical laboratory when there are no preagreed institutional criteria for patient stool submission (*weak recommendation, low quality of evidence)*.
- Use NAAT alone or a multistep algorithm for testing (i.e., GDH plus toxin; GDH plus toxin, arbitrated by NAAT; or NAAT plus toxin) rather than a toxin test alone when there are preagreed institutional criteria for patient stool submission *(weak recommendation, low quality of evidence)*.
- Do not perform repeat testing (within 7 days) during the same episode of diarrhea and do not test stool from asymptomatic patients, except for epidemiological studies (strong recommendation, moderate quality of evidence).

Recent published guidelines and systematic reviews recommend only testing symptomatic patients for *C. difficile*, except for the purpose of epidemiological studies.[1,2] The recommendations are somewhat flexible with regard to the number of episodes of diarrhea that justify the need for CDI testing, noting that providers should take into account whether the patient has risk factors for CDI, most notable of which is antimicrobial use.[3] Before testing, physicians should attempt to rule out other causes of diarrhea.[4] Considerations with regard to *repeat* testing include the background prevalence of CDI at the

facility.[1,4] SHEA/IDSA provide no recommendations for the use of biologic markers as an adjunct to diagnosis and do not recommend testing to determine if CDI has been cured.[1]

The guidelines also recommended that, while laboratory diagnosis is pending, treatment should be initiated empirically for patients who present with fulminant CDI or if obtaining the test results takes more than 48 hours. If test results cannot be obtained on the same day, patients with suspected CDI should be placed on preemptive contact precautions pending the *C. difficile* test results. As treatment recommendations differ, it is important to know the severity of the infection and whether it is an initial or recurrent episode.[1]

An abdominal CT scan may be used to differentiate between CDI and other causes of colitis and to determine the extent of the disease. However, to diagnose regular CDI (e.g., while test results are pending), when an abdominal CT has poor sensitivity, endoscopy can be used in certain urgent situations. The American College of Gastroenterology guidelines recommend endoscopy when a rapid diagnosis is needed or an initial negative toxin assay when CDI is strongly suspected, when there is an ileus and stool is not available, or when other colonic diseases are in the differential diagnosis.[5]

4.5.2 Testing as a PSP

Patients with *C. difficile* shed *C. difficile* spores, which contaminate the environment and may infect other patients.[6,7] Rapid identification of patients with CDI helps expedite contact precautions and isolation of these patients and prevent transmission to other patients.[8] The symptoms of CDI often match those of other causes of diarrhea[9,10]; therefore, early and rapid diagnosis is important to start the appropriate treatment and improve patient outcomes.[11] Starting treatment and infection protocols sooner may ultimately reduce hospital length of stay, thereby reducing healthcare costs.[12] Rapid diagnosis also ensures that providers modify any existing therapies, such as discontinuing antimicrobial agents, which could worsen a patient's condition.[13]

While testing accuracy and speed have improved in the last 10 years, there is currently no consensus on the best testing method.[1,14] It is helpful for clinicians to understand the strengths and limitations of the testing methods when interpreting test results. The testing methods have varying sensitivities and specificities, due to each test's detection ability and the tests' different detection targets.

Each class of test targets one of the following: *C. difficile* toxin, genes that produce toxin, or identification of toxigenic *C. difficile* in the stool. Detection of genes that produce toxins and toxigenic *C. difficile* indicates a patient may be colonized or infected with *C. difficile*. Detection of *C. difficile* toxin indicates infection. Each of the targets can indicate different stages in the progression of the disease.[9] Some patients may remain colonized and acquire protection from disease while others progress to the disease. Some with symptoms may be treated and become asymptomatic carriers.[15]

While the guidelines support accounting for *C. difficile* risk factors, Marra and Ng (2015) point out that the common risk factors for HA CDI are not as prevalent in CA CDI.[16] The criteria for whom to test for CDI such as the number and frequency of diarrheal stools that should trigger testing have decreased in the last few decades.[1] Whole genome sequencing and molecular typing indicate that most CDI is acquired from sources other than symptomatic cases.[17,18]

Asymptomatic colonized patients do not shed as many *C. difficile* spores as CDI patients; however, they still contaminate the environment.[7] Evidence supports identifying asymptomatic colonized *C. difficile*

patients for the purpose of isolation and contact precautions.[19-21] One study found that 29 percent of CDI cases were linked to transmission from colonized patients.[22]

In the last decade, the most commonly used standalone test method has shifted from enzyme immunoassays to tests that detect DNA. Known as nucleic acid amplification testing, or NAAT, these tests generally have better detection abilities than enzyme immunoassays.[3] A shift to more rapid and accurate testing results in less use of unnecessary CDI-targeted antimicrobials[23] and a decrease in laboratory testing volume.[24]

NAAT detects toxigenic *C. difficile* genes, not the damaging toxins, and may identify asymptomatic carriers as well as those with *C. difficile* disease; also, there is debate about whether the presence of toxigenic *C. difficile* alone is sufficient to diagnosis CDI. Guidelines therefore suggest that only *symptomatic* (i.e., those with diarrhea) patients should be tested.[25]

To improve accuracy, combinations of tests are being used. Particularly if laboratories lack clinical input on specimen criteria and accept any unformed stool for testing, it may be most appropriate to use a combination of tests such as a test for organism combined with a relatively sensitive test for toxin in the stool.[3] These combinations test for the toxigenic organism and test for the actual toxin. Some guidelines do not promote the use of NAATs as a singular method even when patients are symptomatic.[4,9]

We discuss the testing methods in more detail in the evidence summary. Some evidence from European studies shows that CDIs are being underdiagnosed due to lack of clinical suspicion or inaccurate testing.[26,27] It is likely that continued research will lead to improved testing methods and protocols.

4.5.3 Methods

The question of interest for this review is: What are the best testing methods and protocols for identifying and preventing CDI?

To answer this question, we searched the databases CINAHL and MEDLINE from 2008 to 2018 for ""*Clostridioides difficile*" and related MeSH terms and synonyms, as well as terms such as "diagnostic test," "testing algorithms," "rapid identification," "stool sampling," and "screening." The search string also included a variety of healthcare settings, including "hospitals," "inpatient," "long-term care," "transitional care," and "home health." The search yielded 732 results. After duplicates were removed, there were 710 papers, all of which were screened for inclusion. Articles were excluded if they were out of scope or were not primary studies, meta-analyses, or systematic reviews, leaving 78 full-text articles that were retrieved.

Reference lists of included articles were also screened to ensure thoroughness and seven additional studies were retrieved via this method. An additional systematic review was identified and retrieved when we researched background information on *C. difficile* testing.[28] Of the retrieved articles, 26 studies, 3 systematic reviews, and 4 meta-analyses were selected for inclusion in this review. Articles were excluded at each step if the outcomes were not relevant or precisely reported or if the study design was insufficient.

Due to the large number of search results for certain topics, we include a sample of studies rather than all results. Similarly, for the performance of individual test types, we chose to include a summary of published meta-analyses instead of reviewing individual studies.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

4.5.4 Review of the Evidence

This review includes 26 studies, 3 systematic reviews, and 4 meta-analyses that address key issues in diagnostic testing for *C. difficile*. Four studies examined CDI testing criteria, including whether to systematically test hospitalized patients with diarrhea and whether to conduct repeat testing for CDI. Four studies and one review examined the question of whether to screen for and isolate asymptomatic *C. difficile* carriers.

We summarize the CDI testing methods and implications outlined by several reviews and studies. The performance of the tests is summarized by five recent meta-analyses. We also review five studies that evaluated tools for measuring patient risk of CDI and five studies that evaluated tools for measuring risk of CDI severity, including mortality.

4.5.4.1 Testing Criteria

While the guidelines promote testing of patients with three unformed stools in a 24-hour period, some researchers advocate for a more systematic process for *C. difficile* identification. Reigadas et al. (2015) tested all diarrheal stool for 6 months at a 1,550-bed hospital in Spain, regardless of clinician request. They found that 45 (18.1%) positive CDIs would have been excluded from testing because they did not meet the testing criterion (three unformed stools in 24 hours). Community-acquired cases and young age were risk factors for underdiagnoses.

Reigadas et al. (2015) recommend that all patients hospitalized with diarrhea be tested for CDI.[27] The European Society of Clinical Microbiology and Infectious Diseases suggests that all submitted unformed stool samples (whether they are submitted for testing for other conditions or for CDI) from patients 3 years or older should be tested for CDI.[4]

Several studies evaluated the use of repeat testing. To better understand the factors that might contribute to a negative test followed by a positive test, Mostafa et al. (2018) examined 2 years of hospital laboratory test orders for *C. difficile* PCR, for which the test result, clinic-pathologic patient features, and previous test results were recorded. In a retrospective chart review, they found that 1,637 of 20,866 lab orders were repeat tests within the first 7 days of initial diagnosis. Out of 554 patients who first tested positive, 2.3 percent (13) of patients were retested as negative within 7 days. Of the patients who first tested negative (970), 4.5 percent (44) were positive on the repeat test. Prior *C. difficile* infection was the only factor significantly correlated with change from negative to positive *C. difficile* test result within 7 days.[29]

The likelihood of a change in test result after a repeat test within 7 days appears to be somewhat linked to the test type and whether the initial test was positive or negative. Aichinger et al. (2008) conducted an observational study and examined the results of patients who had been retested within 7 days of the initial test result. There were 792 patients tested twice by enzyme immunoassay samples and 351 patients tested twice by PCR samples. The patients were all retested within 7 days of the initial diagnosis.

The authors found that retesting patients who were initially negative by enzyme immunoassay and PCR tests resulted in positive tests in 1.9 percent and 1.7 percent of cases, respectively. Patients with positive enzyme immunoassays and PCR results retested as negative in 4.8 percent and 2.9 percent of cases, respectively.[30] The findings about retesting negative results are consistent with the findings of others; it is generally noted that that negative CDI tests are very unlikely to change within 7 days.[1] Repeat testing on negative tests may be helpful in an endemic or outbreak setting.[4]

4.5.4.2 Screening and Isolation of Asymptomatic Carriers

Preemptively identifying hospital patients at risk for CDI, and for severe courses of CDI, has been proposed as a patient safety strategy. At the patient level, it is recommended to screen symptomatic patients primarily so that providers can identify those in need of CDI treatment. The arguments in support of *only screening symptomatic patients* include:

- Screening asymptomatic patients requires significant laboratory resources,
- Studies on MRSA found that active surveillance was not more effective than enhanced infection control policies,
- Isolating asymptomatic CDI carriers requires additional hospital resources (e.g., single rooms), and
- Other interventions, such as hand hygiene, are effective at reducing multiple HAIs and are a better use of resources.[31]

In addition, cohorting symptomatic patients with colonized but asymptomatic patients increases risk of infection of the latter.[32]

Several published studies found public health benefits from screening asymptomatic carriers. One quasi-experimental study and three simulations found that detecting and isolating asymptomatic carriers was associated with prevention of future cases.[19-21,33] In the quasi-experimental study, Longtin et al. (2016) examined the impact of testing all patients admitted through the emergency room at a 354-bed Canadian acute care facility. Patients with a positive test were put into isolation (excluding patients who stayed less than 24 hours). Roughly 92.5 percent of eligible patients were screened over 17 months and 368 (4.8%) were identified as asymptomatic *C. difficile* carriers. During the intervention, 38 patients (3.0 per 10,000 patient days) developed an HA CDI compared with 416 patients (6.9 per 10,000 patient days) during the pre-intervention baseline period ($p<0.001$).[19]

In their simulation, Lanzas and Dubberke (2014) also found that testing asymptomatic carriers reduced the number of new colonizations and HO-CDI cases by 40 percent to 50 percent and 10 percent to 25 percent, respectively, compared with the baseline scenario.[20] In the simulations, factors that impacted the percentage of reduced cases include test sensitivity, test turnaround time (as it relates to delaying isolation), colonization prevalence at admission, strain, and effectiveness of patient isolation.[20,21]

Screening and treating high-risk populations (regardless of CDI symptomology) is also explored in the literature. Saab et al. (2015), for example, conducted a simulation model with cirrhosis patients to compare costs and outcomes of two strategies for screening CDI. The first strategy consisted of screening all cirrhosis patients (regardless of symptoms) for CDI and treating if *C. difficile* was detected. In the second strategy, only patients with symptomatic CDI were treated.

The results showed that screening all cirrhosis patients for CDI was consistently associated with improved healthcare outcomes and decreased healthcare utilization across all variables in the one- and two-way sensitivity analyses. Using baseline assumptions, the authors found the costs associated with only screening symptomatic patients for CDI were 3.54 times greater than the costs to screen all cirrhosis patients.[33]

Another approach, outlined by Furuya-Kanamori et al. (2015) in their review, suggests that patients at high likelihood of being asymptomatic carriers are not tested but medical staff should use enhanced infection control practices such as the use of gloves. In addition, units or facilities with high likelihood of asymptomatic carriers should carry out CDI cleaning protocols.[15]

4.5.4.3 Diagnostic Testing Strategies

In this segment, we start by providing an overview of the distinctions between "reference standard" tests and tests most commonly used in clinical practices. We then summarize recent meta-analyses on commercial diagnostic testing methods. These meta-analyses are highlighted in Table 4.5.

4.5.4.3.1 Reference Standards

The two most common reference standards for identifying *C. difficile* are toxigenic culture (TC) and cell cytotoxicity assay (CCTA). These are the "gold standards" against which commercial tests are compared.[3,9,10] Neither test is useful in a clinical setting as they take several days to complete and require specific expertise and equipment.[2,25]

TC is intended to detect whether *C. difficile* is present and whether it can produce toxins. This test takes between 4 and 7 days.[16] Typically, toxigenic strains of *C. difficile* cause symptoms and the disease of *C. difficile*; however, the presence of toxigenic strains may not always result in active infection.[9] Therefore, a positive test result is not entirely indicative of a CDI.

The other common reference standard, the CCTA, measures the presence of free toxin in feces. The detection of free toxin with CCTA indicates that the patient has diarrhea caused by *C. difficile.* This test takes about 2 to 4 days for results and has a higher specificity than TC.[16] Planche et al. (2013) sought to validate the reference methods according to clinical outcomes using test results, length of hospital stay, and 30-day mortality. In a study of 12,420 fecal samples from four U.K. laboratories, the researchers found no increase in mortality when toxigenic *C. difficile* was present (as indicated by a positive TC test). CCTA was positivity correlated with clinical outcomes, making this a better reference method to define CDI and *C. difficile*-associated disease.[14]

TC is useful for identifying patients who may be asymptomatic and capable of transmitting the organism to others. Culture for the organism of *C. difficile* (regardless of the potential for toxin production) was rarely mentioned in the reviewed studies and meta-analyses, except by Crobach et al. (2016) as a reference test for GDH immunoassays.[4]

4.5.4.3.2 Commercial *C. difficile* Tests Overview

Many studies compare and measure the performance of individual tests. We report here on systematic reviews and meta-analyses to summarize the accuracy of different diagnostic testing methods.[4,16,28,34] We focus on the testing methods and not distinctions between the brands of tests available for each method. However, performance of tests does vary across manufacturers.[2,10] Table 4.5 outlines the detection targets and drawbacks of common reference and commercial *C. difficile* testing methods.

Table 4.5: *C. difficile* Testing Methods

Test	Detects	Drawback
TC	Toxigenic *C. difficile*	Toxigenic *C. difficile* does not always produce toxins; may detect colonized carriers; takes several days
CCTA	CDI toxins	Takes several days and requires specialized equipment
Toxin immunoassay	CDI toxins	Inconsistent sensitivity (depending on particular brand and study)
GDH immunoassay	*C. difficile* enzyme common in toxigenic and nontoxigenic organism	Unable to tell if the *C. difficile* organism produces toxins
NAATs (PCR and loop-mediated isothermal amplification [LAMP])	Genes for toxigenic *C. difficile*	Toxigenic *C. difficile* does not always produce toxins; may detect colonized asymptomatic carriers

TC and CCTA were standard diagnostic practice when *C. difficile* was first discovered, but now faster and less expensive tests are widespread.[16,35] The first alternatives to TC and CCTA to be used widely were toxin enzyme immunoassays.[9] Studies and meta-analyses group the immunoassays generally into those that test for toxins A and B and those that test for GDH. Crobach et al. (2016) further characterized the immunoassays into well-type and membrane-type; well-type tests are used for testing samples in batches, and membrane-type tests are used for testing solitary samples.[4]

The enzyme immunoassays for *C. difficile* toxins A and B cost $5 to $15 per test[10] and take a few hours to complete.[16] It is most appropriate to compare toxins A and B tests against CCTA since these tests detect *C. difficile* toxins.[9] The immunoassays for toxins A and B were widely used as standalone tests until about 10 years ago. Because of very poor sensitivity, and moderately poor specificity, they are now primarily recommended as part of a two-step or three-step testing algorithm.[9,16,25,36]

GDH is a common *C. difficile* enzyme antigen produced in large amounts by all strains of *C. difficile*, independent of toxigenicity.[2] Like TC, the GDH test indicates the presence of the organism in feces and does not indicate toxin production. Although the GDH immunoassay is sensitive, it is not as specific for CDI since both toxigenic and nontoxigenic organisms produce GDH.[16] The cost per test is $5 to $15[10] and test time is 15 to 45 minutes.[16] Because the GDH immunoassay does not detect toxin-producing *C. difficile*, it is not recommended as a standalone test and should be paired with a test that detects toxin.[25]

After FDA approval in 2009, NAATs became available .[2] NAATs include rapid testing PCR and LAMP. NAATs test for the genes of *C. difficile* that produce toxins and identify the presence of toxigenic *C. difficile*.[25] NAATs are more expensive than the enzyme immunoassays for toxins A and B and GDH at about $30 to $50 a test.[10] NAAT testing is estimated to take about 1 to 2 hours.[9]

Due to the limitations of these individual tests, combinations of tests can be used to improve specificity and positive predictive value of diagnosis.[16] While the SHEA/IDSA guidelines support the use of NAATs as a single step, Crobach et al. (2016) found that none of the individual commercial methods was satisfactory as a single test to diagnose CDI.

Several strategies can be used for multi-step testing.[4] One is to do two simultaneous rapid tests and then retest concordant results. Another strategy involves testing for GDH and toxins A and B, then further testing concordant positive results with PCR.[25] In their prospective study of 12,420 fecal samples, Planche et al. (2013) found that the optimal algorithm when TC was the reference was a combination of

GDH and NAAT. For CCTA as the reference, the best algorithms were toxins A and B/NAAT and GDH/toxins A and B.[14]

4.5.4.4 Diagnostic Studies Meta-Analyses Overview

Table 4.6 presents a summary of sensitivities and specificities from six studies. Butler et al. (2016) reviewed and pooled results from 37 studies from 2011 to 2014.[28] For studies that used multiple reference standards, such as culture, TC, and cell cytotoxicity neutralization assay (CCNA), Crobach et al. (2016) conducted a meta-analysis of immunoassay tests, including those for toxins A and B and GDH, as well as NAATs. They found 56 studies that included sensitivity and specificity for toxins A and B, 31 studies with sensitivities and specificities for GDH tests, and 14 studies on NAATs.[4]

O'Horo et al. (2012) reviewed 11 databases and found 25 PCR studies going back to the mid-1990s and 6 LAMP studies going back to 2005. Heterogeneity in the LAMP studies did not allow meta-analysis.[34] Wei et al. (2015) conducted a meta-analysis of nine LAMP studies published before February 2014 and concluded that LAMPs were suitable as standalone tests for CDI.[37]

Bagdasarian et al. (2015) reviewed 13 studies on testing algorithms. In general, multistep algorithms using NAAT had good sensitivity (0.68–1.0) and specificity (0.92–1.0), but algorithms using only GDH or toxin enzyme immunoassay testing performed worse and had greater variability.[25] Four of the studies analyzed by Butler et al. (2016) involved multistep algorithms.

Table 4.6: Meta-Analyses of CDI Diagnostic Tests

Types of Tests	Study	Sensitivity (95% CI)	Specificity (95% CI)	Notes
Immunoassays for *Clostridium difficile* toxins A and B	**Butler et al., 2016[28]**	0.70 (0.66 to 0.74)	0.98 (0.97 to 0.99)	Summary reference; moderate strength of evidence; mixed reference, primarily TC
	Crobach et al., 2016[4]	0.83 (0.76 to 0.88)	0.99 (0.98 to 0.99)	Reference: CCNA
		0.57 (0.51 to 0.63)	0.99 (0.98 to 0.99)	Reference: TC
Immunoassays for GDH	**Butler et al., 2016[28]**	0.90, (0.78 to 0.96)	0.94 (0.89 to 0.97)	Moderate strength of evidence; mixed references
	Crobach et al., 2016[4]	0.94 (0.89 to 0.97)	0.90 (0.88 to 0.92)	Reference: CCNA
		0.96 (0.86 to 0.99)	0.96 (0.91 to 0.98)	Reference: TC
		0.94 (0.86 to 0.97)	0.96 (0.92 to 0.98)	Reference: Culture *C. difficile*
NAATS that include PCR and LAMP	**Butler et al., 2016[28]**	LAMP: 0.95 (0.90 to 0.97)	LAMP 0.98 (0.96 to 0.99)	High strength of evidence; mixed references
		PCR: 0.95 (0.93 to 0.96)	PCR 0.97 (0.96 to 0.98)	
	Crobach et al., 2009[4]	0.96 (0.93 to 0.98)	0.94 (0.93 to 0.95)	Reference: CCNA
		0.95 (0.92 to 0.97)	0.98 (0.97 to 0.99)	Reference: TC
	O'Horo et al., 2012[34]	PCR 0.92 (0.91 to 0.94)	PCR 0.94 (0.94 to 0.95)	Reference: TC
		PCR 0.87 (0.84 to 0.90)	PCR 0.97 (0.97 to 0.98)	Reference: CCNA
	Wei et al., 2015[37]	LAMP 0.93 (0.91 to 0.95)	LAMP 0.98 (0.98 to 0.99)	Mixed references
Two- or three-step algorithms	**Bagdasarian et al., 2015[25]**	(0.68 to 1.0)	(0.92 to 1.0)	13 studies; only CI is provided. Both TC and CCNA used as reference; mixed algorithms.
	Butler, et al., 2016[28]	0.73 (0.62 to 0.82)	1.00 (0.99 to 1.0)	Low strength of evidence; mixed references; mixed algorithms

4.5.4.5 Implications of More Sensitive Testing Tools

Because PCRs are highly sensitive, they may detect asymptomatic colonized patients as well as symptomatic infected patients.[38,39] Koo et al., for example, found that universal PCR testing of all 101 adult hospitalized patients resulted in 18 positive tests, and of these, 72 percent were for patients with asymptomatic *C. difficile* colonization, which, from a treatment perspective is a false positive.[38] Therefore, many experts recommend only testing symptomatic patients with PCR.[1,25]

Some researchers have pointed out that more sensitive testing methods result in an increase in reported HO CDI. Moehring et al. (2013) studied 10 hospitals (and 22 controls) that switched to PCR from immunoassays. The mean incidence rate of HCFA CDI before the switch was 6.0 CDIs per 10,000 patient days compared with 9.6 CDIs per 10,000 patient days a year and a half after the switch. After adjustment in the mixed-effects model, the overall IRR comparing CDI incidence after the switch to before the switch was 1.56 (95% CI, 1.28 to 1.90).[40] There is concern about lack of standardization in testing and higher HO-CDI reporting rates for those facilities using more sensitive methods.[41]

Other researchers found decreased or stable CDI rates after switching from enzyme immunoassays to NAATs and a decrease in laboratory testing volume. Casari et al. (2018) found that more sensitive testing methods had beneficial results in terms of reductions in the number of samples tested and minor reductions in positive CDI tests at a 750-bed hospital. In 2011, the hospital tested 2,746 samples and the following year, after switching from toxin A and B immunoassay to NAAT with sampling criteria, 677 samples. The rate of healthcare-acquired CDI infections decreased from 3.74 per 1,000 admissions to 2.92 per 1,000 admissions a year after the switch in testing method. Other hospitals in the region saw steady CDI rates.[42]

Napierala et al. (2013) found that 20 months after a switch from toxin A and B immunoassay to PCR for diagnosis of CDI at three hospitals, there was a significant decrease in laboratory testing volume (and decreased associated workload). Site-specific *C. difficile* testing volume decreased by 32.5 to 53.9 percent following implementation of PCR. *C. difficile* toxin detection rates were largely unchanged across the three hospitals.[24]

4.5.4.6 Testing Methods Financial Analyses

Schroeder et al. (2014) conducted an economic evaluation comparing eight algorithms for CDI testing in a hypothetical cohort of 10,000 adult inpatients suspected of having CDI. The testing methods included:

- Standalone PCR;
- GDH testing with positive results confirmed by PCR; and
- Both GDH and *C. difficile* toxin A and B with concordant positives treated, concordant negatives not treated, and discordant results confirmed by PCR.

For the model, the researchers assessed cost and effectiveness from the hospital/healthcare perspective (e.g., laboratory testing, isolation protocol, treatment, prolonged hospitalization, and transmission of disease). For traditional algorithms, in which the test results were available after 4 hours, the assumption was that patients would be placed in isolation and initiated on CDI treatment while awaiting CDI test results. For the rapid testing algorithms, the assumption was no presumptive isolation or treatment.

A cost analysis (including estimated costs of missed cases) favored standalone PCR in most contexts but favored immunoassays then PCR if:

- A missed CDI case resulted in less than $5,000 of extended hospital stay costs and <2 transmissions,
- GDH diagnostic sensitivity was >93 percent, or
- The symptomatic carrier proportion among the TC-positive cases was >80 percent.

The number of missed CDI cases was minimized by standalone PCR, whereas the number of false-positive diagnoses was minimized by GDH/PCR.[43]

4.5.4.7 Risk Prediction Tools

It is theorized that identifying patients at risk of CDI could help guide preemptive testing, infection prevention measures, and treatment.[44,45] As shown in Table 4.7, five studies developed or validated tools for predicting patients' risk of developing CDI.[44-48] In one study, researchers measured patient outcomes associated with a screening tool that identified high-risk patients and implemented enhanced infection control policies for these patients.[45] The screening tool was informed by literature on CDI risk factors and a retrospective examination of 1 year of data on healthcare-acquired CDI at a 20-bed vascular-thoracic ICU.

Patients who met certain criteria (e.g., over 55 years old, prescribed a fluoroquinolone agent for any duration or prescribed any other antimicrobial agents for ≥5 days, history of immunosuppression) were identified as high risk for CDI. Measures were taken to reduce risk, such as a review of medication, hand hygiene audits and enhanced environmental cleaning measures for the patients' rooms, and education for patients and families. During the first year, 1,066 patients were screened, and 157 patients were placed in the preventive model. During the pre-intervention phase, 10 cases of healthcare-acquired CDI occurred (overall incidence rate, 14.7) and during the 12-month study period, two cases of healthcare-acquired CDI were identified (incidence rate, 3.12) (p=0.025).

Other tools for predicting risk of CDI were validated retrospectively but were not implemented as a preventive measure. For example, Cooper et al. (2013) developed a tool that weighted certain EHR variables, such as admission from another facility, to provide a patient risk score. The variables were selected based on review of hospital data and previously published data on CDI risk factors. When a patient's score met the tool criteria, the risk factors and score, along with the patient's basic demographic data, appeared on a daily review report. The tool was validated over the course of a year and the final model resulted in an area under the curve (AUC) of 0.929 (95% CI, 0.926 to 0.932).

AUC is a measure of how well a tool can distinguish between two diagnostic groups. The AUC is calculated from a graph of the true positive rate (sensitivity) with the false positive rate for different cutoff points of the parameter. A perfect tool would result in an AUC of 1.0. The optimal cutoff score was 0.636, where both sensitivity and specificity were at 91.61 and 86.96, respectively. Of 4,927 patients identified as at risk for CDI, 254 (92.7% of total CDI cases in the study period) developed the disease.[44]

Table 4.7: Predictive Tools for CDI Incidence

Author	Setting/Population	Tool	Outcome
Cooper et al., 2013[44]	A 255-bed community hospital; 4,927 records identified as at risk for CDI.	An electronic screening tool to help identify patients at risk of CDI.	The final model resulted in an area under the curve of 0.929 (95% CI, 0.926 to 0.932).
Cruz-Betancourt et al., 2016[45]	A 20-bed vascular-thoracic ICU; 1,066 screened patients.	Predictive model for prevention of *C. difficile* infection in patients in ICUs. Evidence-based interventions (bundle) were implemented for patients identified as being at high risk for HA CDI.	During the pre-intervention phase, 10 cases of healthcare-acquired CDI occurred (overall incidence rate, 14.7) and during the 12-month study period, two cases of HA CDI were identified (incidence rate, 3.12) (p=0.025).
Kuntz et al., 2014[48]	Records of outpatient visits in a large healthcare system. Tool was validated with cohort of 296,550 patients.	Predicting CDI after an outpatient visit using electronic medical record.	The area under the receiver operating curve was 0.790.
Stites et al., 2016[46]	A large safety net hospital; prospective analyses for 10,990 admissions.	A predictive model that identifies patients at high risk for CDI at the time of hospitalization. Model to help inform antimicrobial stewardship.	The model identified 55% of patients who later tested positive as being at high risk for CDI at the time of admission (c-statistic 0.77, 95% CI, 0.69 to 0.84).
Tabak et al., 2015[47]	Six acute care hospitals; 78,080 adult admissions, 323 HO-CDI cases.	An HO-CDI predictive model using EHR clinical data present at time of admission.	The model had a c-statistic of 0.78 (95% CI, 0.76 to 0.81).

We found several other studies that validated tools to predict CDI severity or mortality; five of these studies are highlighted in Table 4.8. Van der Wilden et al. (2014), for example, studied and validated a risk scoring system to identify patients at risk for developing fulminant *C. difficile* colitis, which carries a high risk of mortality. Patients with *fulminant colitis* may have frequent bloody stools, abdominal pain, distension, and acute, severe toxic symptoms, including fever. It is possible that early surgical intervention may help improve outcomes for patients at risk of developing severe *C. difficile* colitis.[49]

The researchers sought to develop a simplified scoring system based on four weighted factors: age >70, white blood cell count ≥20.000 or ≤2.000/µL, cardiorespiratory failure (the need for mechanical ventilation or vasopressor support), and diffuse abdominal tenderness. Over the course of 2 years, all patients with fulminant *C. difficile* colitis (746) were prospectively enrolled in the study; 48 (6.4%) of them progressed to fulminant *C. difficile* colitis. The risk scoring system (RSS) successfully distinguished patients with CDI from those who went on to have fulminant *C. difficile* colitis (AUC, 0.98). The researchers found that the system performed as well as a more complex system based on 12 variables and suggested that it could be useful as a bedside tool for clinicians to identify patients at risk of fulminant *C. difficile* colitis.[49]

Table 4.8: Predictive Tools for CDI Severity and Mortality

Article	Setting/Population	Tool	Results
Archbald-Pannone et al., 2015[60]	A U.S. academic hospital; enrolled the 362 hospitalized adult subjects who did not have chronic diarrhea and followed them for 30 days after CDI diagnosis or until death.	A parsimonious predictive model for CDI mortality.	The area under the ROC curve was 0.804.

Article	Setting/Population	Tool	Results
Figh et al., 2017[63]	A hospital; the study group consisted of all cases that resulted in death (n = 79). The control group consisted of all surviving patients who were identified as having CDI based on ICD-9 documentation (n =192).	Two published clinical prediction tools, the Velazquez-Gomez Severity Score Index (VGSSI) and ATLAS (age, temperature, leukocytosis, albumin, and systemic concomitant antibiotic use) scores, were evaluated, and variables showing the greatest correlation with mortality in patients with CDI. were identified to further develop an objective, mortality-based clinical prediction tools.	Mortality indices in patients with CDI were strongly associated with VGSSI and ATLAS scores: Pearson's correlation coefficients r =0.9536 (p=0.002) and 0.9103 (p=0.0001), respectively. Did not hold for intermediate ranges.
Kassam et al., 2016[61]	Used data from the United States 2011 Nationwide Inpatient Sample (NIS) database to develop. Then a sample tool was validated in an independent sample of all CDI hospitalizations from the 2010 NIS dataset. All CDI-associated hospitalizations were identified using discharge codes (ICD-9-CM); 77,776 CDI hospitalizations were identified.	To develop a novel CDI risk score to predict mortality titled Clostridium difficile associated risk of death score (CARDS).	The severity scoring system had a c-statistic of 0.77.
Van Beurden et al., 2017[62]	A 750-bed tertiary care center; the validation cohort comprised 148 patients diagnosed with CDI between May 2013 and March 2014.	External validation of three tools to predict a complicated course of CDI.	The performance of all three prediction models was poor when applied to the total validation cohort with an estimated AUC of 0.68 for the Hensgens model, 0.54 for the Na model, and 0.61 for the Welfare model.
Van der Wilden et al., 2014[49]	Massachusetts General Hospital; all patients (746) with *C. difficile* colitis admitted to the hospital were prospectively enrolled in a specific database.	An RSS for patients at risk of developing fulminant *C. difficile*.	The RSS successfully discriminates patients with *C. difficile* infection from those who have fulminant *C. difficile* (AUC, 0.98).

4.5.5 Resources To Assist With Implementation

APIC Implementation Guide: Guide to Preventing *Clostridium difficile* Infections: Includes section on *C. difficile* diagnosis:
https://apic.org/wp-content/uploads/2019/07/2013CDiffFinal.pdf

CDC: FAQs for clinicians about *C. difficile*: Which laboratory tests are commonly used for diagnosis?
https://www.cdc.gov/cdiff/clinicians/faq.html#anchor_1529601768432

SHEA/IDSA Clinical Practice Guidelines for C. difficile: 2017 Update: These guidelines provide updated recommendations regarding *C. difficile* epidemiology, diagnosis, treatment, infection prevention, and environmental management. Each recommendation includes a brief summary of the literature on the practice:
https://www.idsociety.org/globalassets/idsa/practice-guidelines/clinical-practice-guidelines-for-clostridium-difficile.pdf

4.5.6 Gaps and Future Directions

It may be beneficial for further exploration into the range of factors that impact the speed and accuracy of testing. For example, Kundrapu et al. (2013) found that delays included not providing stool collection supplies to patients in a timely fashion, rejecting specimens due to incorrect labeling or leaking from the container, and holding samples in the laboratory for batch processing. A corrective intervention consisted of easier-to-use containers, prioritization of CDI testing at the laboratory, on-demand specimen pickup and delivery (rather than at scheduled pickup times), and clinician education. The intervention was associated with reduced average time from CDI test order to result from 1.8 to 0.8 days. Additional studies that help inform systems processes would help expedite CDI testing.[50]

Obtaining stool specimens may delay testing since it is not always possible to obtain specimens on demand, if a patient is not able to produce stool. Another study examined the use of rectal swabs (rectal swabs with liquid transport medium and nylon flocked dry swabs) for diagnosing CDI, with mixed results. The authors concluded that rectal swabs could not replace stool samples in the two-step laboratory diagnosis of CDI, as the sensitivities were too low, probably due to diluting effects of the fecal sample in the liquid medium. For simple PCR-based detection of *C. difficile*, however, dry swabs were a suitable alternative to stool samples.[51]

Factors that lead to case misclassification will continue to be studied, especially given financial penalties for HO CDI. One study addressed concern about overreporting of HO-CDI rates and examined the role of laxatives. As diarrhea in the hospital can have many causes, including the use of laxatives, Truong et al. (2017) evaluated a system in which lab testing criteria combined the presence of diarrhea (≥3 unformed stools in 24 hours) and absence of laxative intake in the prior 48 hours. The researchers found that 7.1 percent (164) and 9.1 percent (211) of 2,321 *C. difficile* test orders were canceled due to absence of diarrhea and receipt of laxative therapy, respectively. HO-CDI incidence rate decreased from an average of 13.0 cases to 9.7 cases per 10,000 patient days (p=0.008). Oral vancomycin days of therapy decreased from an average of 13.8 days to 9.4 days per 1,000 patient days (p=0.009).[52]

In the future, it is likely that the speed, accuracy, and convenience of CDI testing will continue to improve. One weakness of NAAT testing is that it does not detect *C. difficile* toxin. Some have proposed tests for toxin that are as accurate as CCTAs but fast and more practical for the clinical setting.[53] Other researchers examined lightweight, rapid, and portable CDI testing systems that could expedite and simplify the diagnostic process.[54,55]

Yet another rapid CDI identification strategy explored in the literature is the use of dogs to scent-detect patients with *C. difficile*. Bomers et al. (2014) conducted a study in which a trained 5-year-old dog was presented with patients and asked to identify those with CDI. During a total of nine hospital visits, the dog performed 651 screenings involving 371 patients and correctly identified 12 of 14 CDI cases (sensitivity 86 percent [95% CI, 56% to 97%]) and 346 of 357 CDI-negative participants (specificity of 97% [95% CI, 94% to 98%]). Of the 11 CDI-negative participants that were "falsely" indicated by the dog as positive, 2 (18%) developed CDI during the 3 months of followup after the detection period, compared with only 12 of the 346 participants (3.5%) that the dog identified as *C. difficile* negative (p=0.06).[56] More research on this technique with larger samples would be useful.

Currently, genotyping is used for CDI surveillance and understanding transmission pathways, but the technology also has potential diagnostic value. Identifying a patient's particular strain of CDI could help

inform antimicrobial treatment decisions.[57] Whole genome sequencing has shown promise in identifying whether recurrent infection is due to relapse or reinfection with CDI.[58] Durovic et al. (2017) used genotyping to determine whether CDIs were due to recurrent infection or reinfection. Among 750 patients with CDI, 130 (17.3%) were diagnosed with recurrence or reinfection and strains were available from 106 patients. The period that showed the best indication of when an infection might actually be a reinfection was 20 weeks. None of the independent clinical characteristics was statistically sufficient to indicate whether infection was due to relapse or recurrence.[59]

If *C. difficile* continues to be a common cause of infection and mortality, risk identification tools could be implemented for clinical use. In addition, understanding of differences in the symptomology of CA CDI may help improve diagnostic accuracy. Finally, the role of asymptomatic carriers as a source of CDI transmission will continue to be discussed and potentially addressed by actively screening for colonized carriers. More real-world research is needed to explore the potential of this practice.

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4.6 Multicomponent CDI Prevention Interventions

Reviewer: Katharine Witgert, M.P.H.

Our search for articles on individual CDI PSPs published from 2008 to 2018 uncovered studies that looked at patient outcomes associated with the combination of two or more CDI PSPs. To accurately reflect the number of articles on multicomponent CDI prevention interventions, we decided to include a review of these studies.

In this addendum to the CDI patient safety chapter, we provide a practice description and evidence summary of the research published from 2008 to 2018 on multicomponent CDI prevention interventions. We then discuss qualitative research on implementation barriers and facilitators, as well as gaps and future directions.

Most of the included articles were identified in the searches for the five other PSPs (hand hygiene, antimicrobial stewardship, environmental cleaning and decontamination, surveillance, and testing) or from reference lists of articles identified in these searches. To ensure thoroughness, we conducted a brief additional search for multicomponent interventions and identified three additional sources.[1-3]

Key Findings

- Multicomponent interventions to prevent CDI were associated with decreases in CDI rates.
- The most common component was environmental cleaning, followed by hand hygiene and patient isolation practices; antimicrobial stewardship and contact precautions; and CDI testing and surveillance.
- No single CDI prevention resource was used across studies.
- Information was limited on staff compliance and financial costs of interventions.
- Collaborations and teamwork were reported to be facilitators of implementation of multicomponent interventions.
- Additional facilitators of staff compliance included adequate supplies (e.g., gowns, soap), communication, signage, and institutional support. Barriers included time it takes to perform prevention practices (e.g., wash hands, put on gowns), inadequate staff education, inconsistency in testing criteria and unclear roles for ordering CDI tests, visitors not practicing contact precautions, and lack of isolation rooms.
- Real-world studies on the implications of different practice combinations, as well as studies on regional prevention efforts and nonhospital settings, will help improve understanding.

For all searches, we excluded articles without clearly stated methodology or a methods section. We also excluded studies that did not quantify or clearly report CDI outcomes, did not clearly explain the interventions, did not describe baseline prevention practices, or did not measure statistical associations with more than one of the interventions. The remaining eight studies and three reviews addressed multicomponent prevention interventions and CDI patient outcomes. Key findings are located in the box above.

4.6.1 Practice Description

Barker et al. (2017) describe a CDI bundle as any set of multiple (>1) interventions focused on reducing CDI in the inpatient setting. To guide their decision about which set of practices to implement, the researchers whose studies we reviewed cited different influences. Several cited prior research and recent IDSA/SHEA recommendations as guiding the decision.[4,5] In one study, a team of experts (assembled by the facility) reviewed facility epidemiological data and determined which practices to implement.[6] Two articles stated that the practices in their respective facilities were guided by government mandates or recommendations.[7,8]

Some studies and resources recommend that facilities assess their current practices to identify gaps and targets for improvement. Facilities should use multidisciplinary teams to oversee cross-cutting efforts and set achievable goals.[9,10] There are different contextual recommendations within the 2017 IDSA/SHEA guidelines.[11] Several of the guidelines are framed as minimum recommendations and some are tailored for outbreak or endemic situations.[11] Resources are available to assist facilities in identifying targets for a multicomponent intervention, for example, CDC's CDI Targeted Assessment for Prevention (TAP) tool, which helps facilities use surveillance data to inform prevention efforts.[12]

4.6.2 Review of the Evidence

Three reviews and eight studies found reductions in CDI rates following implementation of multicomponent CDI prevention interventions. In this evidence summary, we first provide an overview of the reviews and then examine the studies in depth and present the primary outcomes, different intervention components, cross-cutting factors, process measures, and economic outcomes. We then present two simulation studies that attempt to measure the impact of different combinations of prevention components.

4.6.2.1 Reviews

Three systematic reviews address multicomponent interventions and had sufficient methodologic quality for inclusion in this report.[1,2,13] The reviews found that studies on multicomponent interventions showed reductions in CDI, although Barker et al. (2017)[14] noted that p-values were not provided in 11 of the studies they reviewed. Barker et al. (2017)[14] reviewed 26 studies on multicomponent interventions published from database inception up to April 30, 2016. Seven of the studies they found are included in this review (many of the studies they included were published prior to 2008 and thus were not within the parameters of our searches). We include one study by Koll et al. (2014)[9] that was not included in the review by Barker et al. (2017).[14]

In another review, Louh et al. (2017) examined studies published from January 1, 2009, to August 1, 2015, on CDI prevention practices in acute care hospitals. They identified 14 studies on "bundled" interventions,[13] 5 of which we include in this review. Yakob et al. (2014)[2] conducted a meta-analysis of studies published up until March 2014 that measured CDI rates before and after implementation of multicomponent prevention interventions. Six studies were included, four of which are included in this review.[4,7,9,15] The six studies showed reductions in CDI from 33 to 61 percent. In addition to the review, they conducted simulations to assess the impact of different combinations of multicomponent interventions. These findings are described later in this section.

4.6.2.2 Studies

We found eight studies that measured CDI rates before and after implementation of a multicomponent CDI prevention intervention [3-9,15] and two simulation studies that explored different combinations of prevention components.[2,14] The eight real-world studies were observational or quasi-experimental with an interrupted time series or pre/post design. These studies are presented in Table 4.9.

Using $p<0.05$ as the cutoff, we found that the eight real-world studies showed significant declines in CDI rates following implementation of a multicomponent prevention intervention.[3-9,15] The studies are primarily in single hospital settings, except the studies by Koll et al. (2014), which evaluated a regional program implemented by 35 hospitals,[9] and Cheng et al. (2015), which assessed efforts in 4 hospitals.[3]

Two studies examined long-term hospital care, one in a long-term acute care hospital[5] and another in three extended-care hospitals (in addition to one acute care hospital).[3]

Across studies there was a range in the number of implemented components; the multicomponent intervention studied by Price et al. (2009) included two components (a dedicated CDI isolation ward and antimicrobial stewardship),[8] while the remaining studies we reviewed all included more than three components. Studies outside of the United States are noted as such in the "Setting" column of Table 4.9.

Table 4.9: Studies on Multicomponent CDI Prevention Interventions 2008–2018

Article	Setting	Interventions	CDI Outcomes
Abbett et al., 2009[4]	A 750-bed tertiary care university-affiliated hospital	All-staff education campaign Promotion of awareness of CDI testing Discontinuation of nonessential antimicrobials Contact precautions Promotion of hand hygiene Sign on CDI patient doors Dedicated stethoscopes Lab communication protocols Enhanced patient isolation Terminal bleach cleaning for CDI rooms CDI treatment checklist	The incidence rate of healthcare-associated CDI decreased from an average of 1.10 cases per 1,000 patient days (95% CI, 1.00 to 1.21) during the pre-intervention period (~2 years) to 0.66 cases per 1,000 patient days (95% CI 0.60 to 0.72) during the post-intervention period (~2.5 years).
Brakovich et al., 2013[5]	A 50-bed long-term acute care hospital	Environmental services education HPD Microfiber mops New diagnostic assay Removal of ABHRs from patient rooms Promotion of hand hygiene Private CDI rooms Dedicated equipment Antimicrobial stewardship CDI care coordination liaisons Data collection and feedback Surveillance education	The pre-implementation cumulative CDI rate was 46.86 per 10,000 patient days. The post-implementation cumulative infection rate after 12 months was 26.26 per 10,000 patient days ($p<0.001$).
Cheng et al., 2015[3]	A university-affiliated acute hospital and three extended-care hospitals with a total of 3,200 beds, Hong Kong	Environmental services education Patient cohorting Dedicated equipment Promotion of handwashing with soap and water Twice daily cleaning and cleaning at patient discharge (with bleach solution) of CDI patient rooms Terminal curtain change Outbreak investigation	Before the implementation of infection control interventions, the incidence rates of healthcare-associated CDI per 10,000 admissions and per 10,000 patient days increased significantly by 15.3% and 17.0%, respectively, per quarter ($p<0.001$) from 2008 1Q to 2010 1Q. Both healthcare-associated CDI rates per 10,000 admissions and per 10,000 patient days declined significantly by 47% ($p<0.001$) after the implementation of interventions in the second quarter of 2010.
Koll et al., 2014[9]	35 acute care hospitals	Regional multifacility collaborative (regional dissemination of CDI prevention bundle, baseline surveys, site visits, intrafacility strategizing, knowledge sharing, collaborative learning, data collection/feedback on CDI case definitions and bundle compliance) Contact precautions for patients with diarrhea Signs on CDI patient doors Dedicated rectal thermometer Patient isolation and/or cohorting Standardized cleaning protocol and checklists	A regression analysis demonstrated that the predicted HO-CDI reduction over time was significant over the course of the project ($p<0.001$). Based on the regression estimation, participating hospitals had 1,084 fewer cases of hospital-onset CDI than were expected (exact rates not provided) over the 22-month project.

Article	Setting	Interventions	CDI Outcomes
Power et al., 2010[6]	5 wards—850-bed university teaching hospital, UK	On five wards with high baseline CDI: • Formation of teams • Learning sessions on theory and practice of improvement • Selection of key drivers and development of test of change • Visits from executive team Hospitalwide: • Rapid response cleaning team • Promotion of handwashing (staff and patients) • Staff hand hygiene audits • Antimicrobial stewardship • CDI education • Disposable washbowls	In the five wards, there were 2.60 (95% CI, 2.11 to 3.17) cases per 1,000 occupied bed days at baseline. After 3 months of the intervention, a shift occurred representing a reduction of 73% (0.69, 95% CI, 0.50 to 0.91). In the rest of the hospital at baseline, there were 1.15 (95% CI, 1.03 to 1.29) cases per 1,000 occupied bed days. The cases decreased 56% from baseline (0.51, 0.44 to 0.60) after 6 months.
Price et al., 2009[8]	A 820-bed teaching hospital, UK	• Patient cohorting • New antibiotic policy restricting the use of cephalosporins and quinolones	The number of CDI cases each month was falling before the intervention; there was a significant increase in the rate of reduction after the intervention from 3% to 8% per month (trend: 0.92, 95% CI, 0.86 to 0.99, p=0.03).
Salgado et al., 2009[15]	A 610-bed, tertiary care, academic institution	• Placing patients with diarrhea into empiric contact precautions until CDI was ruled out as the cause of diarrhea • Cleaning equipment and the environment with a bleach solution in areas occupied by CDI patients • Requiring soap and water for hand hygiene for staff working with patients with CDI	The overall mean outbreak CDI rate was 3.90 per 1,000 patient days, and the peak outbreak CDI rate (November 2004) was 5.52 per 1,000 patient days. Immediate postoutbreak CDI rate was 1.84 per 1,000 patient days, and mean postoutbreak rate, maintained for 36 months beyond the outbreak, was 1.24 per 1,000 patient days (p <0.0001).
Weiss et al., 2009[7]	A 554-bed, acute care tertiary hospital, Canada	• Rapid *C. difficile* testing for all hospitalized patients who had at least one occurrence of liquid stool • Rapid isolation of CDI patients • Dedicated/trained housekeeping for CDI rooms • Increase in housekeeping hours • Patient cohorting • Handwashing in/out of CDI rooms • Limit of one visitor at a time • Promotion of gloves • Promotion of patient handwashing • Revised prescribing guidelines • Hiring of four infection prevention experts • Installation of 85 new sinks • CDI surveillance	Most interventions were implemented in late 2005. During the 2003–2004 period, there were 762 cases of CDI (mean annual rate, 37.28 cases per 1,000 admissions), compared with 292 cases of CDI (14.48 cases per 1,000 admissions) during the 2006–2007 period (odds ratio, 0.379 [95% CI, 0.331 to 0.435]; p <0.001), a 61% reduction.

4.6.2.2.1 Infection Prevention Practices

As shown in Table 4.10 below, in the reviewed studies, the most common component of the multicomponent interventions was environmental cleaning and decontamination, which was included in seven of the eight studies. Isolation of CDI patients and hand hygiene practices were the next most common components—each was included in five studies. Antimicrobial stewardship practices and contact precautions were each included in four studies. Testing and surveillance practices were included in three studies. In their review, Barker et al. (2017) found that in 26 studies, hand hygiene and environmental cleaning were the most common components (each in 23/26 studies) followed by patient

isolation/cohorting (20/26) and contact precautions (19/26) and antimicrobial stewardship (19/26).[1] Louh et al. (2017) did not quantify the individual components across studies.[13]

Table 4.10: Components in Multicomponent CDI Prevention Interventions

Intervention Component	Number of Studies	Specific Practices Mentioned
Environmental cleaning and decontamination	7	Increase in environmental services hours and training, dedicated CDI cleaning teams, cleaning equipment, dedicated equipment, disposable washbowls, daily and terminal cleaning with bleach solution, terminal hydrogen peroxide decontamination, terminal curtain change, protocols and checklists
CDI patient isolation	5	CDI patient cohorts, private rooms for CDI patients, wards for CDI patients, rapid isolation
Hand hygiene	5	Removal of ABHRs, promotion of handwashing with soap and water when working with CDI patients, patient hand hygiene, hand hygiene observations/audits, installation of sinks
Antimicrobial stewardship	4	Discontinuation of nonessential antimicrobials, restriction of the use of clindamycin, cephalosporins, and quinolones, revised guidelines and formularies
Contact precautions	4	Use of gowns and gloves when working with CDI patients, limits on patient visitors, empiric contact precautions
Testing	3	Testing at first sign of diarrhea, promotion of testing, new diagnostic assay
Surveillance	3	Tracking and classification of CDI cases, education, outbreak investigation

The individual practices deemed crucial to the multicomponent interventions varied across studies in this review. Some researchers felt that inclusion of antimicrobial stewardship as part of a multicomponent intervention was the primary factor in reducing CDI.[6,8] Conversely, Salgado et al. (2009),[15] Weiss et al. (2009),[7] Koll et al. (2014),[9] and Cheng et al. (2015)[3] all emphasized that they saw CDI reductions by focusing on *C. difficile* transmission prevention, without the inclusion of antimicrobial stewardship or reductions in antimicrobial use. Across the studies, the most common transmission prevention practices were use of gloves/handwashing with soap and water,[3,5,7,15] new training and protocols for environmental cleaning staff training,[3,5,7,9] and CDI patient isolation/cohorting.[3,8,9]

Notably, Louh et al. (2017) found that multicomponent interventions that included environmental cleaning and decontamination were more effective than multicomponent interventions that did not include a focus on environmental cleaning.[13] However, Brakovich et al. (2013) called out the importance of surveillance as part of a multicomponent intervention in a long-term acute care hospital.[5]

4.6.2.2.2 Cross-Cutting Practices

When discussing which cross-cutting practices facilitated the success of a multicomponent intervention, researchers highlighted several practices. The use of checklists and assigned roles was noted [4,5,9](as well as staff education).[3,5,6,9,15] Barker et al. (2017) and Abbett et al. (2009) stated the importance of improved workflow systems and Barker et al. (2017) also pointed out that staff compliance with bundle practices is highly important and rarely adequately measured.[4,14] Communicating laboratory results[4] and communicating CDI patient status through door signs[4,9] were also highlighted. Two studies spoke to the benefits of teams, inter- and intrafacility collaborations, data collection and feedback, and collaborative learning.[6,9]

In the study by Power et al. (2010),[6] an 850-bed hospital implemented a multicomponent intervention that included antimicrobial stewardship, hand hygiene, environmental cleaning and decontamination, and education about CDI. In five wards with higher baseline CDI rates, there was an implementation of an "improvement collaborative," in which staff were broken into teams who planned, implemented, and

measured the impact of selected PSPs as outlined by a systems improvement toolkit.[16] The five selected collaborative wards saw a 73 percent reduction in HA-CDI cases per 1,000 patient bed days after 3 months, and the rest of the hospital saw a 56 percent reduction in CDI cases per 1,000 patient bed days after 6 months (see Table 4.10).[6]

4.6.2.2.3 Process Measures

Process measures included antimicrobial use, CDI tests ordered, and staff compliance with intervention components. Although not all interventions included antimicrobial stewardship, antimicrobial use was a common process measure.[3,7,8,15] For example, following a multicomponent intervention that included antimicrobial stewardship (in addition to a new isolation ward), Price et al. (2010) found decreases in antimicrobial use. The multicomponent intervention took place in an 820-bed hospital in the United Kingdom. After 15 months, the level of cephalosporin and quinolone use declined (22.0% and 38.7%, respectively, $p<0.001$), and antipseudomonal penicillin use increased by 20.7 DDD per month ($p=0.011$).[8]

Abbett et al. (2009) measured number of CDI tests as a process measure. The multicomponent intervention was in a 750-bed hospital and included the promotion of testing of suspected CDI patients (in addition to several other practices). After 2 years, Abbett et al. (2009) found a 15 percent increase in the rate (tests per 1,000 patient days) of *C. difficile* testing (testing rate ratio, 1.15 [95% CI, 1.12 to 1.17]; $p<0.001$). Koll et al. (2014) collected data on compliance from 35 acute care hospitals participating in a regional CDI prevention effort. For the submitted data (based on staff observations), the mean reported compliance with a prevention bundle was 95 percent and the mean reported compliance reported for an environmental cleaning protocol was 96 percent.[4]

4.6.2.2.4 Economic Outcomes

Brakovich et al. (2013) and Weiss et al. (2009) provided financial information on the cost to implement the respective prevention interventions. Brackovich et al. (2013) reported that the cost of HPD equipment and contracted services was $1,800 per month. The cost of new microfiber mops and environmental services staff training was approximately $650.[5] While exact figures were not provided, Weiss et al. (2009) reported that costs of the intervention they studied included paying salary for four new infection preventionists and a 26.2 percent increase in staffing costs for environmental services personnel. They also reported an increase of 89.6 percent in cost of cleaning supplies, although this amount represented less than 0.03 percent of the total hospital budget.[7]

In addition, Koll et al. (2014) reported savings in healthcare costs associated with a regional multicomponent intervention. They noted that 35 hospitals prevented approximately 1,084 cases of HO CDI, resulting in cost savings of $2.7 million to $6.8 million on healthcare costs.[9]

4.6.2.3 Multicomponent Intervention Simulation Studies

To determine what combination of CDI prevention practices are most effective as a multicomponent intervention, Barker et al. (2017) conducted a simulation using a model of *C. difficile* transmission. The model was based on prior data to construct potential *C. difficile* transmissions by patients, visitors, nurses, and physicians and includes parameters such as patient antimicrobial use and length of stay. The interventions were "implemented" in a theoretical 200-bed hospital for 1 year.

After analyzing nine multicomponent intervention strategies, the researchers found that daily cleaning with sporicidal disinfectant and screening and isolating asymptomatic *C. difficile* carriers reduced CDI by

68.9 percent and 35.7 percent, respectively (both p<0.001). Combining these interventions into a two-intervention bundle reduced hospital-onset CDI by 82.3 percent and asymptomatic HO colonization by 90.6 percent (both, p<0.001). Adding patient hand hygiene to HCW hand hygiene reduced hospital-onset CDI rates an additional 7.9 percent (p<0.001).[14]

Yakob et al. (2014) conducted a series of simulations of different combinations of prevention methods based on their model of *C. difficile* transmission. The prevention methods included antimicrobial stewardship; administration of probiotics/intestinal microbiota transplantation; and improved hygiene and sanitation. They also examined the impact of reduced length of stay for inpatients. The researchers examined the impact of the prevention interventions on both colonization and CDI rates and found that, for infection control, the combined benefit of reducing length of stay and improving sanitation and hand hygiene significantly exceeds that achieved with either method alone. Antimicrobial stewardship showed greater efficacy in colonization control than it did in disease control. In terms of symptomatic disease incidence reduction, antimicrobials, probiotics, and intestinal microbiota transplantation proved substantially less effective than reducing length of stay and improving hygiene.[2]

4.6.3 Implementation

Two studies used a systems engineering framework to examine barriers and facilitators to prevention practices.[17,18] A systems engineering framework is one that examines workflow systems in relation to tasks, tools, and technologies, the physical environment, and the organization.[18] Yanke et al. (2018) conducted a qualitative analysis on barriers and facilitators of implementation of the VA *C. difficile* prevention bundle. The study consisted of four focus groups of healthcare staff in a variety of roles (e.g., physicians, nurses, and health technicians) at an 87-bed VA hospital. Bundle components included rapid PCR testing and diagnosis, hand hygiene promotion, and contact isolation precautions; facilitators and barriers were identified for each component.

For testing, facilitators included positive aspects of PCR testing (expedient, efficient, highly sensitive) and almost universal testing of newly admitted patients with diarrhea. Testing barriers included certain laboratory policies (e.g., only testing stool once per week, rejection of nonliquid stool), ambiguity between nurse practitioners and resident and attending physicians on who should order testing, inconsistent threshold for testing, and delays in obtaining specimens. For hand hygiene, facilitators were adequate soap supplies, extra sinks, and signage reminders. Multiple barriers were identified, such as:

- Uncertainty about where to wash hands (e.g., inside or outside of patient rooms),
- Sink water that was too hot,
- Lack of access to sinks in patient rooms due to clutter in and around sinks,
- Need to touch curtains with potentially contaminated hands,
- Time it takes to wash hands in a busy environment,
- Lack of education, and
- Broken soap dispensers.

Finally, facilitators of contact isolation precautions included proactive isolation of patients by nurses when testing was ordered, supply of clean gowns, institutional support for compliance, and clear signs on contact isolation rooms. Barriers to implementation of contact precautions included:

- Problems with location of equipment,
- Inconsistent compliance by patients' visitors, food service workers, and healthcare staff,
- Lack of clarity around responsibility for enforcing family member compliance,
- Time it takes to don or implement contact precautions,
- Electronic record functionality for identifying contact precaution patients,
- Lack of isolation rooms,
- Inappropriate removal of isolation stethoscopes, and
- Overloaded linen bags.

Certain overarching factors were identified in the focus groups, such as a desire by some staff for more information on the bundle and data on compliance. Perspectives varied depending on staff roles (i.e., nurses, residents, and attending doctors); the researchers highlight the importance of collecting interprofessional perspectives.[17]

Ngam et al. (2017) examined the perspectives of 10 nurses at a large academic teaching hospital. In a focus group, the nurses were asked questions about barriers and facilitators to the facility's CDI prevention bundle. Testing facilitators included the staff's commitment to testing and the ease of placing orders in the EHR, while barriers included challenges in collecting stool samples (e.g., patient discomfort) and lack of consistency/communication challenges around who orders the test. Contact precautions barriers included inadequate supplies, time it takes to practice contact precautions, and challenges with family/visitor compliance. Inadequate sink access was identified as a barrier to hand hygiene, while signage and sink foot pedals were facilitators. Barriers to disinfection of the environment included moving tools in and out of rooms and confusion around roles and policies and procedures for disinfection.[18]

4.6.4 Resources To Assist With Implementation

2017 IDSA/SHEA *C. difficile* Clinical Practice Guidelines:
https://www.idsociety.org/practice-guideline/clostridium-difficile/

CDC HAI Prevention Toolkits:
https://www.cdc.gov/HAI/prevent/prevention_tools.html

CDC Targeted Assessment for Prevention (TAP) Strategy:
https://www.cdc.gov/hai/prevent/tap.html

Greater New York Hospital Association United Hospital Fund: Reducing *C. difficile* Infections Toolkit:
https://apic.org/Resource_/TinyMceFileManager/Practice_Guidance/cdiff/C.Diff_Digital_Toolkit_GNYHA.pdf

Health Research and Educational Trust *Clostridium difficile* Change Package: http://www.hret-hiin.org/Resources/cdi/16/HRETHEN_ChangePackage_CDI.pdf

4.6.5 Gaps and Future Directions

Additional research into overcoming barriers to compliance with recommended CDI prevention practices as part of multicomponent prevention interventions would be useful as staff compliance is a major factor in intervention success.[1,19] More robust financial analysis that includes costs for staffing, trainings, supplies, delays in room turnover, testing, antimicrobials, patient treatment, and other items would also help facilities considering implementing a multicomponent intervention.

As with other CDI PSP studies in this report, higher quality, case-control/cohort/randomized, and longer term studies would also help improve knowledge and understanding.[1,13] In the future, studies of regional initiatives and multicomponent interventions in a variety of settings (e.g., outpatient, nursing home) will help improve CDI prevention.

Future efforts will benefit from improved resources to assist facilities in developing customized multicomponent interventions and determining which strategies to implement. This review found that intervention components, while informed by recent recommendations, varied across studies. Hospital resources and facility limitations are important considerations in implementing a tailored multicomponent strategy.[7]

As demonstrated by Barker et al. (2017), outcomes associated with multicomponent interventions are more complex than just the sum of their parts,[15] and different *combinations* of practices may be more effective than others.[2] To determine the most effective components in different contexts, McFarland (2017) recommended stepwise evaluation, with standardized outcomes, and measuring the efficacy attributable to each component, while accounting for compliance, over time.[19]

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Conclusion

The PSPs reviewed in this chapter aim to prevent CDI by:

- Reducing risk,
- Stopping the transmission of the *C. difficile* organism,
- Identifying and isolating patients with CDI as early as possible, and
- Tracking cases and identifying outbreaks, transmission pathways, and virulent strains.

The evidence in support of these practices, when implemented in real-world healthcare settings, ranges in depth, quality, and consistency:

- Environmental cleaning and multicomponent interventions had the most consistently positive outcomes across the reviewed studies.
- Antimicrobial stewardship shows promising results for reducing CDI, especially under certain conditions.
- Reducing CDI rates through hand hygiene (washing hands with soap and water) is well supported by in vitro studies but not well tested in real-world studies.
- Research on surveillance explores the accuracy of case definitions, automation, and innovations.
- Studies that address CDI testing explore sensitivity and specificity of testing methods and considerations of who and when to test.

Additional key findings from each of the PSPs in this chapter follow.

Antimicrobial Stewardship: The reviewed meta-analyses found ASPs were associated with decreases in CDI. Individual study outcomes were mixed, showing statistically significant decreases (6/15 studies) and statistically nonsignificant decreases/no change (9/15 studies) in facility- or ward-level CDI. Interventions included formulary restrictions, prescriber education, and audit and feedback/case review practices.

Significant reductions in CDI were associated with higher baseline CDI rates/outbreaks, ASPs developed specifically to reduce CDI (as opposed to ASPs focused on other clinical and microbiological outcomes), and ASPs that included restrictions to high-risk antimicrobials or a preauthorization component. Prescriber buy-in and staffing and technical resources were factors that impacted implementation.

Hand Hygiene: In laboratory testing, washing with soap and water outperforms ABHRs for removal of *C. difficile* spores from hands; ABHRs are not effective in killing *C. difficile* spores.[1,2] It is the mechanical action of washing that removes the organism; therefore, proper handwashing technique is important.[3] In the studies reviewed for this report, interventions targeted multiple HAIs or included the use of ABHRs, which made it difficult to draw concise conclusions about the impact of practices targeting *C. difficile*. The studies found statistically nonsignificant reductions in CDI following hand hygiene interventions.

Most studies took place in hospitals and interventions included: hand hygiene education, data collection/observation, and additional hand hygiene supplies/sinks. Hand hygiene is frequently

framed as an HCW compliance issue, with studies measuring the impact of sink location and education on hand hygiene compliance. Patient hand hygiene initiatives show promise for helping prevent the spread of CDI.[4]

Environmental cleaning and decontamination for *C. difficile* was associated with significant decreases in facility-level CDI rates in most studies. Practices with positive outcomes include daily and terminal cleaning of CDI patients' rooms with bleach solutions (typically 5,000 ppm), and terminal bleach cleaning plus the use of no-touch decontamination methods such as hydrogen peroxide or UVD. The UVD process takes less time than the hydrogen peroxide method. Both methods require the room or area be vacant, which is an implementation challenge.[5,6] Studies suggest that standardized cleaning protocols and training and observation of environmental cleaning services staff help improve cleaning and decontamination for *C. difficile*.[7]

For CDI **surveillance**, using standardized and accurate case definitions is an important practice.[8] Much research in the last 10 years has examined the accuracy of healthcare facility-onset/associated case definitions using different data and data collection methods. Studies also examined automated surveillance, laboratory alerts, risk stratification, statistical methods, and impact of the different testing methods on incidence. Research using new technologies for *C. difficile* genotyping and ribotyping has helped identify outbreaks.[9,10] Despite the role CDI surveillance plays in understanding epidemiology and informing prevention practices, CDI surveillance implementation is not well studied.

Testing for CDI was a frequent topic of research. Rapid and accurate identification of CDI is important in order to initiate treatment and discontinue antimicrobials (if appropriate) for CDI patients.[11] Our search yielded a relatively large number of studies on the performance of different test types and brands. Research also explored the best practices for when to test a patient based on symptoms, how to interpret results, and which methods have the most accurate, rapid, and useful outcomes. If test results cannot be obtained on the same day, patients with suspected CDI should be placed on preemptive contact precautions pending test results.[8]

The evidence indicates that NAATs and multistep test combinations show best results.[8] CDI risk-prediction tools show promise for preemptive intervention. There are different perspectives on whether to test for (and subsequently isolate) asymptomatic carriers; However, some studies show this practice is resource intensive.[12-15]

Multicomponent CDI prevention interventions included environmental cleaning, hand hygiene, patient isolation, antimicrobial stewardship, testing, and surveillance, as well as other PSPs and cross-cutting strategies. Studies consistently showed associations between multicomponent interventions and statistically significant reductions in CDI. Factors that facilitated implementation of multicomponent interventions included the use of checklists and assigned roles,[16-18] staff education,[17-21] and collaboration and teamwork.[17,20]

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5. Infections Due to Other Multidrug-Resistant Organisms

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Introduction

Background

Multidrug-resistant organisms (MDROs) are microorganisms, mainly bacteria, that are resistant to one or more classes of antimicrobial agents.[1] These include methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant Enterococci species (VRE), carbapenemase-producing Enterobacteriaceae, and Gram-negative bacteria that produce extended spectrum beta-lactamases (ESBLs). These last two types of pathogens produce chemicals that allow them to resist the effect of certain antimicrobials, and this adaptation is easily passed between different species.

Other species of note include MDR *Escherichia coli* and *Klebsiella pneumoniae*, *Acinetobacter baumannii* (abbreviated AB; some strains are resistant to all antimicrobial agents), and organisms such as *Stenotrophomonas maltophilia* that are intrinsically resistant to the broadest-spectrum antimicrobial agents.[1] MDROs' resistances limit treatment options for patients, making infection critical to preventing further harms.

Importance of Harm Area

The World Health Organization (WHO) now recognizes that MDROs are a growing threat in every geographic region of the world.[2] Drug-resistant bacteria pose a significant public health risk both domestically and abroad due to their ability to colonize individuals without causing symptoms, their endurance in the environment, and the clinical threat they pose.[3] The growing presence of resistant microbes is of particular concern for vulnerable patients, such as those who have received organ transplantation, those with cancer, preterm infants, and immune-suppressed and other medically vulnerable individuals.[2]

With treatment complicated by the limited availability of antimicrobials to treat these infections, MDROs are responsible for approximately 23,000 deaths annually from antibiotic-resistant pathogens in the United States alone.[4] The Centers for Disease Control and Prevention (CDC) (2018) states that 11 percent of individuals screened in healthcare facilities are asymptomatic carriers for a transmissible, "hard-to-treat" microorganism.[5]

Drug-resistant organisms are becoming increasingly present in all settings and geographic areas. As cited in Tacconelli et al. (2014), carbapenem resistance increased in five European countries from 2008 to 2011.[6] In the United States, infections caused by multidrug-resistant, Gram-negative bacteria have increased over the past decade, and one out of five hospitals reporting invasive infections implicated a carbapenem-resistant *K. pneumoniae*, one of the most common MDROs.[6] While rates of hospital-onset, MRSA-related bacteremia in the United States have declined, community-onset MRSA-related bacteremia has increased in recent years.[7]

The patient safety practices (PSPs) in this report have universal application for reducing the burden of colonization and infection. When differences are significant (e.g., Enterococci in the digestive tract vs. *S. aureus* on patient skin), we make a note in the findings. The large benefit of these practices, however,

comes from this universality: whether the organism is an extremely drug resistant *A. baumannii* or methicillin-susceptible *S. aureus,* infection prevention reduces risks and prevents patient harms.

Methods for Selecting PSPs

To determine the optimal methods for controlling MDROs and preventing MDRO-related infection, we reviewed CDC guidelines[8] and the compendium of strategies from the Society for Healthcare Epidemiology of America.[9,10] Using these systematic reviews and reports, we developed an initial list of 23 PSPs that target diagnostic errors, and the Technical Expert Panel, Advisory Group, and AHRQ reviewed it.

Based on the reviewers' recommendations, we identified six priority PSPs:

- Chlorhexidine bathing to control MDROs
- Hand hygiene to reduce MDRO transmission
- Active surveillance strategies for MDROs
- Environmental cleaning and disinfection strategies
- Minimizing exposure to invasive devices and reducing device-associated MDRO risks
- Communication of patients' MDRO status

What's New/Different Since the Last Report

The previous Making Health Care Safer reports included recommendations for infection control practices, including multicomponent interventions for device-associated infections as well as general infection prevention. In this report, we focus on the evidence for those practices (and some new practices) to reduce the transmission of and infections caused by MDROs.

As noted in previous Making Health Care Safer reports, the epidemiology of MRSA, VRE, and other MDROs has continued to evolve; this report updates the literature with responses to that emerging, evolving resistance in the following ways:

- Chlorhexidine bathing is a practice that can be combined with others (such as active surveillance and contact precautions) in response to MDRO outbreaks or added to routine patient bathing to control MDROs and prevent infection. Current guidelines focus mainly on acute care populations, especially critical care. In this report, we include studies of non-critical care populations and some studies on chlorhexidine in community settings. This review also includes information on chlorhexidine resistance and important considerations when adding chlorhexidine bathing to routine patient care.
- Hand hygiene is a universal strategy for preventing transmission of MDROs and MDRO-related infection, regardless of patient care risk factors. This review also includes new findings on the role of patient hand hygiene and mathematical models to measure the impact of hand hygiene (in combination with other PSPs or alone).
- For active surveillance, this review looks at specific strategies for identify MDRO-infected and MDRO-colonized patients, particularly active surveillance cultures/testing of patients and their environment, to prevent MDRO transmission.

- Environmental cleaning is a new practice in this report, and our review focuses both on the efficacy of different cleaning products and strategies to ensure thorough cleaning.
- Many practices and resources for minimizing the risk of harm due to device use were covered in the previous version of Making Health Care Safer; this review includes updated literature and any additional resources since that publication was written.
- Finally, communicating patients' MDRO status (also new in this report) allows facilities to take appropriate infection prevention precautions from the start of the patient encounter. This report provides evidence on the negative effects of missed communication and some examples of communication strategies.

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5.1 PSP: Chlorhexidine Bathing To Control MDROs

Reviewer: Sam Watson, M.H.A.

Chlorhexidine solutions have broad antimicrobial activity and are already commonly in use as topical disinfectants and antiseptics as part of recommended strategies for MDRO control and infection prevention.[1-3] Either universal or targeted chlorhexidine bathing can complement other infection control methods of screening, isolation, and eradication.[4]

This chapter examines specific efficacy of chlorhexidine to prevent different infections (by organism, by type of infection), the mode and frequency of successful chlorhexidine bathing for disease prevention, and considerations for or unintended consequences of general chlorhexidine use. The review' key findings are located in the box to the right.

Key Findings

- The strongest evidence supports using chlorhexidine bathing to reduce colonization and infection, particularly by multidrug—resistant Gram-positive bacteria (MDR-GPB) such as MRSA and VRE, and for healthcare-associated infections (HAIs) related to medical devices that create a break in the skin (e.g., central lines).
- Less evidence is available to support chlorhexidine bathing for preventing infection from MDR Gram-negative bacteria (MDR-GNB), such as carbapenem-resistant Enterobacteriaceae (CRE), and for other types of HAIs.
- As an intervention, chlorhexidine is low cost to implement (especially if routine bathing is already in place) and generally well received by staff, but compliance with bathing can wane over time.
- While the literature has not described any clinical effects of chlorhexidine resistance, this practice should continue to be monitored.

5.1.1 Practice Description

For the purpose of this review, we define "chlorhexidine bathing" as application of chlorhexidine to the skin or oropharyngeal surfaces to promote decolonization and to prevent infection. As described below, oropharyngeal surfaces represent a reservoir for MDROs in mechanically ventilated patients who cannot perform their own oral care. Since chlorhexidine bathing is recommended for patients at high risk for MDRO-related infections—generally intensive-care patients, many of whom may be mechanically-ventilated as part of their care—we include oral care as part of a chlorhexidine bathing routine.[3]

5.1.2 Methods

To investigate the current literature for chlorhexidine bathing—for which patients, in what form, how often, and with what effectiveness—we searched three databases (CINAHL, MEDLINE, and Cochrane) for a combination of the keywords "chlorhexidine bathing" and MeSH terms related to "cross infection prevention," "drug resistance, multiple, bacterial," and "drug resistance, microbial." Articles from 2008 through December 31, 2018, were included. (Any relevant articles published after the original search are included in the PRISMA diagram as additional sources.)

The initial search yielded 323 results (including 6 articles from other sources); after duplicates were removed, 300 were screened for inclusion, and 124 full-text articles were retrieved. Of those, 42 were selected for inclusion in this review. Articles were excluded if they did not mention chlorhexidine's role in preventing MDROs, mentioned a PSP other than bathing, or discussed use of chlorhexidine outside the healthcare environment. Chlorhexidine oral care was included in this review, as were in vitro studies that assessed the impact of chlorhexidine use on the selection or development of resistant organisms.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

5.1.3 Review of Evidence

One of the aims of this review is to better understand the nuances of chlorhexidine's efficacy for controlling and preventing infection caused by MDROs.

The questions of interest for this review are: Which chlorhexidine applications are most effective for decolonization and for infection control, against which organisms is chlorhexidine the most effective, and what are the potential outcomes related to chlorhexidine resistance? Further, which patients benefit the most from chlorhexidine bathing?

Many of the studies included in this report and in systematic reviews focus on intensive care unit (ICU) patients, who have the most risk factors for MDRO colonization and infection. While these patient populations show benefits in terms of reduced colonization, carriage, and infection, the studies that include relatively healthy populations (both in community and hospital settings) show more nuanced results without a clear benefit.

The studies summarized in this section include several well-designed, rigorous studies, some of which have very large populations (tens or hundreds of thousands). When findings are nuanced, we note where limitations may have contributed a null finding or if mediating factors showed benefit for one subgroup but not the whole population.

This summary indicates the best-supported uses of chlorhexidine and the level of evidence for other uses. Section 5.3.4 provides a list of resources for implementing chlorhexidine bathing protocols. Where the evidence is not definitive, such as using chlorhexidine bathing to prevent infection for relatively healthy patient populations or reduce MDROs in community settings, we hope this review will help clinical staff make their own determination on implementing chlorhexidine bathing.

5.1.3.1 Efficacy for Controlling MDROs and Preventing Infection

In the sections below, we summarize the clinical results of chlorhexidine bathing for major MDROs (MRSA, VRE, CRE), HAIs, and other results. This summary is accompanied by a table that briefly describes the supporting evidence for each section. Additional information can be found in the Chlorhexidine Bathing Evidence Table (see Appendix B).

5.1.3.1.1 MRSA

Evidence suggests that chlorhexidine bathing in the hospital setting reduces MRSA acquisition and carriage but may not always result in fewer MRSA infections. Three systematic reviews found evidence that chlorhexidine bathing alone reduces MRSA acquisition and carriage.[5-7] This finding is supported by five strong studies (four experimental, one quasi-experimental) that also found chlorhexidine bathing reduced MRSA carriage and acquisition.[8-12] While most of these studies found that bathing also reduced MRSA infections, Derde and colleagues' review (2012) included some studies that found no significant reduction in infections.[6]

One prospective cohort study found no reduction in MRSA colonization rates, specifically, but did find a significant reduction in the rates of infections caused by all MDROs (measured in aggregate, not by specific MDRO).[13] Interpreting these results is made more difficult by the fact that chlorhexidine bathing

is recommended as part of a multicomponent strategy that includes nasal mupirocin and, in a few studies, oral antibiotics, as described in general MDRO and MRSA control guidelines.[3,14]

In long-term care facilities, Peterson and colleagues' cluster-randomized study (2016) demonstrated that a thorough decolonization protocol that includes chlorhexidine bathing can reduce MRSA colonization without the need for patient isolation.[12] This is an important finding for implementation, because extended patient isolation and gown and glove use may not be feasible or desirable in long-term or residential care settings.

Table 5.1 below presents the results from each study.

Table 5.1: Summary of MRSA Results

Study	Type of Study	Setting	MRSA Results
Climo et al., 2013[8]	Multicenter, cluster-randomized, non-blinded crossover trial	Hospital (ICU)	Reduced MRSA acquisition: total MDRO acquisition (MRSA or VRE) decreased from 6.6/1,000 patient-days to 5.1/1,000 patient-days (p=0.03).
Denny & Munroe, 2017[5]	Systematic review	Hospital	Reduced MRSA acquisition, colonization, transmission, and infection rates (statistical findings not reported for all studies).
Derde et al., 2012[6]	Systematic review	Hospital	Reduced MRSA acquisition and carriage but not consistently reduced MRSA infections (statistical findings not reported for all studies).
Huang et al., 2019[9]	Cluster-randomized trial	Hospital, non-critical care units	No statistically significant reduction in MRSA-positive cultures, except for a subgroup of patients with invasive medical devices. The hazard ratio (HR)[f] for the decolonization group of those patients was 0.8 (95% CI 0.69 to 0.96) compared with the routine care group's HR of 1.17 (95% CI 1.00 to 1.37) for MRSA- or VRE-positive culture (p=0.0004).
Huang et al., 2013[10]	Cluster-randomized trial	Hospital (ICU)	Significantly reduced MRSA-positive clinical cultures in chlorhexidine decolonization groups (p<0.001 for test of all groups being equal) compared with a screening and isolation approach: 0.75 HR for targeted decolonization (3.2 vs. 4.3 isolates/1,000 days), 0.63 for universal decolonization (2.1 vs. 3.4 isolates/1,000 days), and 0.92 for screening and isolation (crude rate, 3.2 vs. 3.4 isolates/1,000 days).
Musuuza et al., 2017a[11]	Quasi-experimental, pre-test/post-test study	Hospital (ICU)	Reduced MRSA colonization, but not statistically significant (9.2% to 5.6%, p=0.119).
Peterson et al., 2016[12]	Prospective, cluster-randomized trial	Long-term care facility	Reduced MRSA colonization.
Ruiz et al., 2017[13]	Prospective cohort study	Hospital (ICU)	No reduction in MRSA colonization.
Sidler et al., 2014[7]	Systematic review	Hospital (ICU)	Reduced MRSA acquisition and carriage but not consistently reduced MRSA infections.

5.1.3.1.2 VRE

Several studies found evidence that chlorhexidine can reduce VRE acquisition and colonization. One rigorous, multicenter study found that chlorhexidine bathing can reduce VRE acquisition.[8] Three systematic reviews found that chlorhexidine can reduce VRE carriage in hospital patients.[5-7] Finally, two quasi-experimental studies found reduced VRE colonization among patients who were bathed daily with

[f]A hazard ratio represents the risk of a negative outcome (in this case, MRSA-positive clinical culture) at any point in the study, versus relative risk or odds ratio, both of which represent cumulative risk over the length of the study.

chlorhexidine, and the Mendes and colleagues study (2016) additionally observed reduced VRE infections.[11,15] Table 5.2 below presents the results from each study.

Table 5.2: Summary of VRE Results

Study	Type of Study	Setting	VRE Results
Climo et al., 2013[8]	Multicenter, cluster-randomized, non-blinded crossover trial	Hospital (ICU)	Reduced VRE acquisition: total MDRO acquisition (MRSA or VRE) decreased from 6.6/1,000 patient-days to 5.1/1,000 patient-days (p=0.03).
Denny & Munro, 2017[5]	Systematic review	Hospital	Reduced VRE carriage (statistical findings not reported for all studies).
Derde et al., 2012[6]	Systematic review	Hospital	Reduced VRE carriage (statistical findings not reported for all studies).
Huang et al., 2019[9]	Cluster-randomized trial	Hospital, non-critical care units	No statistically significant reduction in VRE-positive cultures, except for a subgroup of patients with invasive medical devices. The HR for the decolonization group of those patients was 0.8 (95% CI 0.69 to 0.96) compared with the routine care group's HR of 1.17 (95% CI 1.00 to 1.37) for MRSA- or VRE-positive culture (p=0.0004).
Mendes et al., 2016[15]	Quasi-experimental observational and in vitro resistance study	Hospital (transplant ward)	Reduced VRE colonization and infection rates (colonization change in trend: Beta-3=–0.040, p=0.001; infection change in trend: Beta-3=–0.086, p=0.001).
Musuuza et al., 2017a[11]	Quasi-experimental, pre-test/post-test study	Hospital (ICU)	Reduced VRE colonization (14.5% to 8.4%, p=0.030).
Sidler et al., 2014[7]	Systematic review	Hospital (ICU)	Reduced VRE carriage in one meta-analysis reviewed (VRE colonization: incidence rate ratio 0.51; 95% CI 0.36 to 0.73; VRE infection: incidence rate ratio 0.57; 95% CI 0.33 to 0.97).

5.1.3.1.3 CRE

Few studies directly addressed chlorhexidine effects on CRE specifically (a number focused on the larger category of MDR-GNB). Of those that did, two observational cohort studies found that chlorhexidine bathing could reduce CRE colonization.[13,16] Table 5.3 below presents the results from each study.

Table 5.3: Summary of CRE Results

Study	Type of Study	Setting	CRE Results
Abboud et al., 2016[16]	Observational pre-post cohort study	Hospital (surgery ICU)	Significant reduction in CRE colonization (26.8% pre-intervention, 9.3% post-intervention; p<0.001).
Ruiz et al., 2017[13]	Prospective cohort study	Hospital (ICU)	Reduction in MDRO colonization, including Enterobacteriaceae (22.0% vs. 18.4%; p=0.01).

5.1.3.1.4 HAIs

Many studies examined the effect of chlorhexidine bathing on rates of various HAIs, such as catheter-associated urinary tract infection (CAUTI), ventilator-associated pneumonia (VAP)[g], and central line-associated blood stream infection (CLABSI). Where possible, we specify whether all infections or MDRO-only infections are noted in the results, but not all studies provided that level of detail. Based on the studies included, chlorhexidine bathing is most effective at reducing colonization by and HAIs from

[g]A note on terminology: In this review, we used the authors' words describing the HAIs they studied, which may be different from the terms currently in use (for example, ventilator-associated events or VAE is preferred over VAP due to difficulties with the definition of "VAP").

Gram-positive MDROs in patients who have a break in the skin due to a needed medical device (e.g., central line). Table 5.3 and the paragraphs below summarize these findings.

One review and several studies, including two large studies (Huang et al., 2013, and Huang et al., 2019) with more than 10,000 patients and 400,000 patients, respectively, have found evidence that chlorhexidine bathing can reduce the risk of HAIs, especially in intensive care units.[9,10] Huang and colleagues' 2013 REDUCE MRSA trial found universal decolonization involving daily chlorhexidine bathing throughout the patient's entire ICU stay and twice-daily intranasal mupirocin for 5 days was more effective than targeted decolonization or screening and isolation in reducing MRSA-positive clinical cultures and all-cause bloodstream infections.[10]

In a subsequent study (the ABATE Infection trial, 2019), Huang et al. evaluated the impact of universal chlorhexidine bathing and targeted mupirocin use for MRSA carriers in non-ICU settings.[9] The authors found that the intervention did not significantly reduce MRSA- or VRE-positive clinical cultures for the overall study population. In a post-hoc analysis, patients with medical devices (including central lines, midline catheters, and lumbar drains) were found to experience a significantly greater benefit from the intervention.

Similarly, Denny and Munroe's systematic review (2017) found the strongest evidence for reducing surgical site infection (SSI) and CLABSI rates, as well as acquisition, colonization, and infection for MRSA and VRE.[5] Among ICU patients, Climo and colleagues' 2013 study found a significant reduction in CLABSIs (the only HAI outcome included in that study).[8] As mentioned above, only a few studies included in this review examined chlorhexidine bathing for CRE, and only one, Abboud and colleagues' observational cohort study (2016), looked at CRE-related HAIs. Abboud and colleagues found reductions in those HAIs in CRE-colonized patients after chlorhexidine bathing was implemented.[16]

While some studies did not show an effect of chlorhexidine bathing on HAIs, most of these studies were considerably smaller than the two studies by Huang and colleagues. A rigorous cluster-randomized trial by Noto and colleagues (2015) found no impact on CLABSI, CAUTI, VAP, or *Clostridioides difficile* infection rates among the 9,340 patients in the study.[17] Ruiz et al. (2017) reduced MDRO colonization with chlorhexidine wipes, but this did not lead to a reduction in HAIs in their single-site study. Ruiz and colleagues also noted that longer ICU stays (in one Spanish hospital) were associated with overall incidence of HAIs, suggesting that chlorhexidine bathing alone was not sufficient to reduce the infection risk posed by extended stays in intensive care.[13]

Two studies directly compared the use of chlorhexidine bathing against bathing with soap and water, finding no improvement in HAI rates when chlorhexidine was used. Kengen et al.'s study of 6,634 ICU patients (2016, Australia) found no statistically significant difference in HAIs when patients received daily bathing with chlorhexidine instead of soap and water.[18]

Similarly, Boonyasiri and colleagues' smaller study of 418 Thai ICU patients (2016) found no benefit to chlorhexidine bathing over soap and water bathing on HAI rates in environments where most HAIs were caused by MDR-GNB.[19] However, Camus and colleagues (2014) reduced HAIs from MDR-GNB by adding mupirocin application to chlorhexidine bathing.[20]

Most studies of chlorhexidine for HAI prevention focused on BSIs, but a few looked at VAP and SSIs. Duszynska and colleagues' observation study (2017) also found no reduction in intubation-related

pneumonia, nor in UTIs, although overall infections and catheter-related infections were significantly lower.[21] A randomized trial of oropharyngeal decontamination using chlorhexidine found no effect on reduced BSIs from MDR-GNB in mechanically ventilated patients.[22]

Although chlorhexidine is routinely used for preoperative antisepsis in surgical settings, Abboud and colleagues (2016) found no supporting literature that chlorhexidine bathing reduced SSIs (although they did observe a reduction in SSIs among CRE-colonized patients in their study).[16] In their systematic review, Denny and Munroe (2017) did not find clear evidence of the efficacy of chlorhexidine bathing for preventing SSIs.[5]

Finally, Urbanic and colleagues (2018) raise an important limitation that applies to all these studies: because of other HAI prevention initiatives, the absolute number of HAIs is, in some cases, very low.[23] The number needed to treat with chlorhexidine bathing in order to significantly reduce HAIs may be, in some cases, larger than the number of patients enrolled in studies. This finding suggests that chlorhexidine bathing has limited benefit for HAI reduction in settings where HAIs are already well controlled by other means.

Table 5.4 below presents the results from each study.

Table 5.4: Summary of HAI Results

Authors	Type of Study	Setting	HAI Results
Abboud et al., 2016[16]	Observational pre-post cohort study	Hospital (surgery ICU)	Significant reduction in CLABSI (2.07/1,000 line-days to 0.23/1,000 line-days, p<0.002), VAP, and UTI rates in CRE-colonized patients. Reduced SSIs only in noncolonized, bathed patients (2.4% to 0.8%, p<0.003).
Boonyasiri et al., 2016[19]	Randomized, open-label controlled trial	Hospital (ICU)	No impact on HAI rates in settings where >60% of HAIs were caused by MDR-GNB.
Camus et al., 2014[20]	Multicenter, placebo-controlled, randomized, double-blind trial	Hospital (ICU)	When combined with mupirocin and administration of oral antibiotics, reduction in HAIs caused by MDR-GNB (5.45% to 1.59%, p<0.0001).
Climo et al., 2013[8]	Multicenter, cluster-randomized, nonblinded crossover trial	Hospital (ICU)	Reduction in CLABSIs (6.60/1,000 patient-days to 4.78/1,000 patient-days, p=0.007).
Denny & Munro, 2017[5]	Systematic review	Hospital	Reduced CAUTI, VAP, and CLABSI rates, across all studies reviewed (statistical findings not reported for all studies).
Duszynska et al., 2017[21]	Observational study	Hospital (ICU)	Reduction in catheter-related infections (p=0.005); non-significant reductions in UTIs and intubation-associated pneumonia.
Huang et al., 2019[9]	Cluster-randomized trial	Hospital, non-critical care units	No statistically significant reduction in all-cause BSIs among total population (189,081 patients in the baseline period and 339,902 patients in the intervention period). However, a sub-group of high-risk patients (those with medical devices) did have a significantly reduced HR of all-cause BSIs in the decontamination group compared with the routine care group (0.81 [95% CI 0.70 to 0.94] vs. 1.13 [95% CI 0.96 to 1.33]; p=0.0032).
Huang et al., 2013[10]	Cluster-randomized trial	Hospital (ICU)	Significantly greater reduction of all-cause BSIs in universal decolonization group, compared with both targeted decolonization and screening with isolation. All-cause BSI HRs were 0.99 (crude rate, 4.1 vs. 4.2 infections/1,000 days) for screening and isolation, 0.78 (3.7 vs. 4.8 infections/1,000 days) for targeted decolonization, and 0.56 (3.6 vs. 6.1 infections/1,000 days) for universal decolonization (p<0.001 for test of all groups being equal). MRSA-related BSIs reduced in decolonization groups, but not significantly.

Authors	Type of Study	Setting	HAI Results
Kengen et al., 2018[18]	Single-site retrospective, open-label, sequential period, interrupted time series analysis	Hospital (ICU)	No reduction in rates of ICU-associated, clinically significant positive blood cultures, blood culture contamination, newly acquired MDRO isolates, and *C. difficile* infections (CDIs).
Noto et al., 2015[17]	Pragmatic cluster-randomized, crossover study	Hospital (ICU)	No difference detected between the rates of CLABSI, CAUTI, VAP, and *C. difficile* infections.
Ruiz et al., 2017[13]	Prospective cohort study	Hospital (ICU)	No reduction in CLABSI, VAP, or UTI rates.
Wittekamp et al., 2018[22]	Randomized trial of oropharyngeal decontamination	Hospital (ICU)	No reduction in BSIs caused by MDR-GNB.

5.1.3.1.5 Other Results

This section summarizes other relevant results that do not fall under the categories above. Most of these studies focused on MDRO generally or MDR-GNB specifically. The studies we reviewed do not support chlorhexidine use but also do not warrant a recommendation *against* using it for MDR-GNB, although it may not be the most effective precaution for those organisms. Table 5.5 below presents the studies and their results.

None of the systematic reviews recommended chlorhexidine bathing for preventing/reducing MDR-GNB colonization.[6,7,24] One review (Tacconelli et al., 2014) found only temporary decolonization of MDR-GNB using chlorhexidine, and one randomized, open-label controlled trial (Boonyasiri et al., 2016) found that chlorhexidine bathing offered no reduction or delay in MDR-GNB acquisition.[19,24] Kengen and colleagues' retrospective time study (2018) found no difference in MDRO acquisition with chlorhexidine bathing compared with soap and water, whereas Ruiz and colleagues (2017) saw a reduction in MDRO acquisition, including MDR-GNB.[13,18]

Musuuza and colleagues' pre-post study (2017) found lower colonization with MDR-GNB (specifically, fluoroquinolone-resistant GNB) after chlorhexidine bathing, but Mendes and colleagues' quasi-experimental observational study (2016) did not.[15,25] Maxwell and colleagues (2017) found no difference between chlorhexidine and soap bathing for lowering MDRO infection rates (from GNB or GPB).[26] Pedreira and colleagues (2009) observed no reduction in MDRO colonization rates when chlorhexidine was added to standard oral care (toothbrushing) in pediatric ICU patients.[27]

Table 5.5: Summary of Other Results

Study	Type of Study	Setting	Other Results
Boonyasiri et al., 2016	Randomized, open-label controlled trial	Hospital (ICU)	No reduction/delay in MDR-GNB acquisition.
Derde et al., 2012[6]	Systematic review	Hospital	Little evidence supporting chlorhexidine bathing for MDR-GNB.
Kengen et al., 2018[18]	Single-site retrospective, open-label, sequential period, interrupted time series study	Hospital (ICU)	No reduction in ICU-associated, clinically significant blood cultures or in MDRO acquisition.
Maxwell et al., 2017[26]	Prospective, randomized control trial	Hospital (ICU)	No difference between soap and chlorhexidine at reducing infectio26ns from GNB or GPB.
Mendes et al., 2016[15]	Quasi-experimental observational study	Hospital (transplant ward)	Not effective in r19educing colonization from MDR-GNB.
Musuuza et al., 2017[11]	Quasi-experimental, pre-test/post-test study	Hospital (ICU)	Reduced prevalence of colonization with fluoroquinolone-resistant GNB.

Study	Type of Study	Setting	Other Results
Pedreira et al., 2009[27]	Randomized control study	Hospital (PICU)	No reduction in MDRO colonization rates (compared with standard care) when chlorhexidine was added to oral care (tooth-brushing) in pediatric ICU patients.
Ruiz et al., 2017[13]	Prospective cohort study	Hospital (ICU)	Reduction in overall MDRO colonization, including MDR-GNB.
Sidler et al., 2014[7]	Systematic review	Hospital (ICU)	Little evidence supporting chlorhexidine bathing for MDR-GNB.
Tacconelli et al., 2014[24]	Systematic review	Hospital	Only temporary decolonization of MDR-GNB.

5.1.3.2 Process Outcomes

5.1.3.2.1 Application

Chlorhexidine bathing, as described in the literature, covers a range in terms of concentration used, mode of application, and frequency. Of those studies that described the frequency of application (24 of 42), almost all described daily chlorhexidine bathing, with a smaller number using multiple applications per day (4 out of 24, of which one was an oropharyngeal-only application of chlorhexidine).

In terms of concentration, the vast majority of reviews and studies used a 2% chlorhexidine gluconate solution (either in prepackaged wipes or applied using a soaked washcloth). The exception was one oropharyngeal application (Camus et al., 2016) that used a 4% aqueous solution.[28] For otherwise healthy patients outside a hospital setting, Whitman and colleagues (2010) found daily bathing with 2% chlorhexidine cloths to be ineffective in reducing soft skin and tissue infection.[29] Chlorhexidine's effectiveness includes prolonged residual disinfection, so it is important not to rinse after use.[5]

5.1.3.2.2 Adverse Effects

The most common adverse effect in the literature was skin irritation, as seen in one systematic review and several studies.[5,10,19] When use of chlorhexidine wipes was discontinued, pruritus stopped. Oral mucosa lesions were observed in 9.8 percent of the 8,665 mechanically ventilated patients in Wittekamp and colleagues' chlorhexidine mouthwash study (2018).[22]

More serious adverse effects can occur with exposure to sensitive areas (eyes, esophagus, intestinal lining, inner ear), as noted in one systematic review.[5] Severe anaphylaxis is possible but rare (only found in case reports), as reported in reviews by Denny and Munroe (2017).[5]

5.1.3.3 Economic Outcomes

Only one study (Peterson et al., 2016) addressed the cost of chlorhexidine bathing, which was negligible when chlorhexidine was incorporated into an established daily bathing routine.[12] Since staff are already accustomed to daily bathing, no additional time is required, and the only potential cost is the difference between chlorhexidine supplies and previous bathing solutions.

5.1.3.4 Evaluations of Chlorhexidine Resistance

The most important unintended consequence of the wide use of chlorhexidine is the development of resistance to chlorhexidine and other biocides.[30] None of the MDROs in the studies in this review showed biocide resistance at the concentrations typically used for chlorhexidine bathing; the in vitro studies compared survivability of resistant MDROs in low concentrations of chlorhexidine. An equal number of studies supported or refuted the hypothesis that chlorhexidine bathing increases the

prevalence of resistance genes in hospitals; however, many of these studies looked at isolates from a single hospital and may have limited generalizability. Regardless of changes in prevalence, these authors hypothesize that overdiluted concentrations or residual chlorhexidine may be selecting for resistant organisms (either resistant clones/strains or organisms less susceptible to chlorhexidine) and should be monitored for clinical impact.[31-33]

5.1.3.4.1 In Vitro Studies

Resistance to chlorhexidine is detected by observing higher minimum inhibitory concentrations (MICs) to inhibit bacterial growth and higher minimum bactericidal concentrations (MBCs) to eliminate the organisms. One Scottish and one U.S. study found chlorhexidine resistance to be more common in settings where chlorhexidine bathing was routine.[34,35] In one in vitro study of MDRO isolate cultures from U.S. ICUs with and without daily bathing, Suwantarat and colleagues (2014) found that hospital ICU units that bathed patients were more likely to have CLABSI-causing organisms that could withstand higher levels of chlorhexidine (compared with units that did not conduct bathing).[35]

Hijazi and colleagues' (2016) in vitro study of samples collected over 7 years from Scottish ICUs found that implementing chlorhexidine bathing increased the prevalence of resistance genes in those organisms.[34] One retrospective cohort study in the United States found no conclusive trends in the prevalence of chlorhexidine-resistant MDROs after implementing chlorhexidine bathing, but the authors hypothesize that some increases may be due to readmitted patients who were unsuccessfully decolonized in previous hospitalizations.[36]

McNeil and colleagues' study of *S. aureus* in a U.S. pediatric hospital environment (2014) showed that organisms with resistance genes had MICs twice as high and MBCs 8 to 16 times as high as the more susceptible organisms ($p<0.005$).[37] However, several studies found that prevalence of resistance genes did not always result in measurable resistance. One in vitro study of cultures from an ICU after implementing chlorhexidine bathing found that resistance genes were linked to higher MICs in one MRSA strain but not another.[38]

Similarly, Musuuza and colleagues' pre-post study (2017) did not show increased MICs in MRSA and fluoroquinolone-resistant GNB after a daily bathing intervention in their U.S. hospital.[11] While not genetically resistant, oral MRSA biofilms studied in vitro by Smith and colleagues (2013) show considerable resistance to chlorhexidine mouthwashes, which may account for failure of mouth washing to prevent VAP and for frequent MRSA recolonization.[39]

5.1.3.4.2 Clinical Implications

The clinical impact of chlorhexidine resistance genes is unclear. One in vitro study of MRSA isolates in a U.S. hospital found that MRSA strains showed more resistance to chlorhexidine than methicillin-susceptible strains.[40] Similarly, Alotaibi and colleagues (2017) found more chlorhexidine resistance in VRE than in vancomycin-susceptible Enteroccoci strains in isolates from Danish hospitals.[41] Hayashi and colleagues (2017) found that *A. baumanii* epidemic strains from Japanese isolates showed increased resistance to chlorhexidine in vitro but not at concentrations typically used for disinfection.[42]

Two studies found evidence that might suggest that chlorhexidine bathing can favor chlorhexidine-resistant MDROs (particularly MDR-GNB) by eliminating the "competition" from chlorhexidine-susceptible MDROs. Abboud and colleagues (2016) found an increase in colonization with *Pseudomonas aeruginosa* and *A. baumanii* after chlorhexidine bathing was implemented in a Brazilian hospital ICU.[16]

However, Camus and colleagues (2016, France) found no increase in MDR-GNB after implementation of a multicomponent chlorhexidine bathing intervention for ventilated patients that also included oral care, mupirocin ointment, and oral antibiotics.[28] In that study, however, it is unclear what effect the additional components, particularly mupirocin ointment use, had on MDR-GNB rates. Cho and colleagues (2018) and McNeil and colleagues (2014) also found that chlorhexidine resistance genes were associated with mupirocin resistance in both South Korean and U.S. isolates; this finding may be due to the frequent combination of chlorhexidine and mupirocin in hospitals' decolonization strategies.[37,43]

Importantly, no studies suggested that chlorhexidine bathing was ineffective due to resistance; at the concentrations typically used (1-4%), chlorhexidine still kills even the most resistant organisms. However, overdiluted solutions may fail to kill organisms as intended and create unwanted transmission and infection, especially in cases where biofilms have formed.

5.1.3.4.3 Alternatives to Chlorhexidine

Several of the studies mentioned above examined multiple biocides and alternatives to chlorhexidine. Some alternatives, such as triclosan and hydrogen peroxide, have their own risk of resistance selection, as detailed in Wesgate and colleagues' in vitro study (2016).[44] Grare and colleagues' (2010) in vitro study shows the effectiveness of alternative cationic compounds[h] that show promising effectiveness against MDROs, but it will be some time before these products are commercially available.[45]

5.1.4 Implementation

As described above, the most common frequency of chlorhexidine bathing was daily, and the most common application was a 2% chlorhexidine gluconate solution, either in prepackaged wipes or in soaked washcloths. One important aspect of chlorhexidine use is to allow long-term contact with the skin. Ekizoğlu and colleagues (2016) recommended a contact time of at least 5 minutes, and no-rinse applications can further take advantage of chlorhexidine's persistent antimicrobial effects on the skin.[31] DeBaun and colleagues' in vitro study of MRD isolates (2008) suggests that extreme dilutions (between 1:2,048 and 1:8,192) of chlorhexidine may still be effective against MRSA and *A. baumanii*, but such extreme dilutions may not always be sufficiently bactericidal or inhibitory for resistant organisms (as discussed above under chlorhexidine resistance).[46]

Chlorhexidine can be successfully used for MRSA decontamination, when combined with mupirocin and active surveillance.[6] However, the effectiveness of decolonization for otherwise healthy populations is unclear. While Whitman and colleagues (2010) successfully reduced skin and soft tissue infections in healthy populations by instituting daily bathing with 2% chlorhexidine-impregnated clothes, Huang and colleagues (2019) did not find benefits to introducing chlorhexidine in a non-critical care hospital setting.[9,29]

Interestingly, a study by Fritz and colleagues (2012) found that a household intervention of *S. aureus* decolonization and personal care hygiene (i.e., relegating personal care items to a single individual and frequent, hot-water washing of linens and towels) reduced skin and soft tissue infections in household members but not the index case patients. Fritz et al. hypothesized that the acquisition of new *S. aureus* strains may put someone at higher risk for infection, rather than simply being colonized; 20 percent of

[h]Negatively charged chemical compounds that bind to proteins and can disrupt microorganisms' membranes.

the index patients (pediatric patients with a skin or soft tissue infection) were not colonized with *S. aureus* at screening, despite having an *S. aureus* culture from the infection site.[47]

5.1.4.1 Barriers and Facilitators to Implementation

In general, daily chlorhexidine bathing is a low-cost strategy that is well received by staff. Chlorhexidine bathing also has the advantage of being easy and quick to implement, as noted by Huang and colleagues (2013).[10] Two studies found that the staff responsible for implementing a chlorhexidine bathing intervention rated chlorhexidine bathing positively (Boonyasiri et al., 2016; Duszynska et al., 2017), and Huang and colleagues noted high rates of compliance (over 80%) in their MRSA decolonization study (2013).[10,19,21] However, Musuuza and colleagues (2017) noted that compliance can wane over time.[11]

In a survey of Thai hospitals, Apisarnthanarak and colleagues (2017) found that good leadership support for an infection control program was statistically significantly associated with regular use of chlorhexidine bathing (that is, hospitals without that support were less likely to use chlorhexidine bathing).[48] When facilities implement chlorhexidine bathing, leadership support for infection prevention programs can help sustain compliance with bathing over time.

5.1.4.2 Resources To Assist With Implementation

- A universal ICU decolonization protocol from the Agency for Healthcare Research and Quality. This protocol was followed in Huang et al., 2013, in which the authors demonstrated a statistically significant reduction in BSIs.
  https://www.ahrq.gov/hai/universal-icu-decolonization/index.html
- A chlorhexidine bathing implementation toolkit from the University of Wisconsin.
  https://www.hipxchange.org/CHGBathing

5.1.5 Gaps and Future Directions

As covered in Denny and colleagues' systematic review (2017), additional research could include[5]:

- Studies on the frequency and duration of bathing (how many times a day, for what period);
- Evaluations of chlorhexidine bathing's role in multicomponent programs (also suggested in commentary by Horner et al., 2012)[49]; and
- Continued research on chlorhexidine resistance and related clinical outcomes, especially the role of biofilms (as noted in commentary by Grascha, 2014) and Gram-negative bacteria (also suggested in commentary from Strich & Palmore, 2017).[50,51]

Although none of the studies included in this report indicated negative clinical outcomes due to chlorhexidine resistance, commentary by Kampf (2016) cautions against use of chlorhexidine for general, nonspecific applications such as hand hygiene or instrument soaking, where insufficient concentrations are more likely to occur.[52] Further studies to prevent these vulnerabilities in chlorhexidine bathing would be valuable to establishing bathing protocols.

References for Section 5.1

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5.2 PSP: Hand Hygiene To Reduce MDRO Transmission

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Hand hygiene is one of the most fundamental and cost-effective infection control practices.[1] Yet despite over 150 years of efficacy evidence, hand hygiene opportunities continue to be missed in healthcare settings, with hand hygiene rates of only 40 to 60 percent in intensive care settings.[2] Johnston and Bryce (2009) identified several factors that support or impede hand hygiene compliance: environmental factors (making handwashing supplies accessible and convenient), individual factors (whether the person believes in the need for handwashing at the indicated opportunities), and organizational factors (whether a person's workflow allows proper handwashing to take place).[3]

The reasons for these missed opportunities are complex: patient care workload and limited time; inadequate staff education or knowledge about transmission risk; lack of convenient, accessible cleaning products and sinks; and even awareness that an opportunity for hand hygiene is occurring. In a nonsystematic review, Otter et al. (2013) found that although several MDROs (notably, *A. baumannii*) are known to contaminate the patient environment and survive on dry surfaces, healthcare personnel are less likely to conduct hand hygiene after environmental contact than after patient contact.[4] In addition, long artificial or natural nails can harbor harmful organisms, as can rings worn during care.[5-7]

Key Findings

- Hand hygiene is indispensable for preventing the transmission of MDROs. Hand hygiene compliance and compliance with other PSPs are complementary: high compliance with one practice is associated with high compliance with others.
- The World Health Organization's "My Five Moments for Hand Hygiene" was recommended or used by many studies in this review as the most effective tool for improving hand hygiene compliance, but many effective campaign materials are available.
- Staff can make existing campaigns even more effective by personalizing the implementation with educational and promotional materials and supporting each other in observing hand hygiene.
- The biggest barriers to hand hygiene compliance are: (1) realizing an opportunity for hand hygiene is occurring and (2) remembering to complete hand hygiene protocol, consistently, at every opportunity. Education can help with the first, and direct observation with immediate feedback helps improve the second.

New technology in the healthcare setting can aid hand hygiene (such as "smart badges" that remind staff to clean hands), but technological changes to workflow also introduce new hand hygiene opportunities (such as the use of personal cell phones in the clinical setting, as studied in Graveto and colleagues' 2018 review).[8] Hand hygiene interventions are generally well received and inexpensive to implement, and they align with medicine's principle of "first do no harm."[9] Several studies in this review demonstrate that it is possible to achieve very high rates of hand hygiene compliance. We include lessons learned from those studies for consideration when seeking to not just achieve but maintain those very high rates. The review's key findings are located in the box above.

5.2.1 Practice Description

Hand hygiene, as defined by the Centers for Disease Control and Prevention (CDC), is "cleaning your hands by using either handwashing (washing hands with soap and water), antiseptic hand wash, antiseptic hand rub (i.e., alcohol-based hand sanitizer including foam or gel), or surgical hand

antisepsis."[i] In this review, we include evidence-supported methods for disinfecting the skin of hands by using a cleaning solution (with or without water), with or without concurrent use of medical gloves. (This chapter does not focus on glove use.)

5.2.2 Methods

To investigate the role of hand hygiene in preventing transmission of MDROs and containing MDRO outbreaks, we searched three databases (CINAHL, MEDLINE, and Cochrane) for a combination of the keywords "hand hygiene," "hand disinfection," "hand sanitization," and "hand washing," as well as MeSH terms "cross infection prevention," "drug resistance, multiple, bacterial," and "drug resistance, microbial." Articles from January 1, 2008, through December 31, 2018, were included. (Any relevant articles published after the original search are included in the PRISMA diagram as additional sources.)

The initial search yielded 225 results (including 11 articles from other sources); after duplicates were removed, 207 were screened for inclusion, and 168 full-text articles were retrieved. Of those, 17 were selected for inclusion in this review. Articles were excluded if they did not mention hand hygiene's role in preventing MDRO transmission, described gown and glove use without also mentioning handwashing or hand disinfection, or did not include implementation in a healthcare setting. Outbreak response case studies are included in this review if they describe the role of hand hygiene in ending the outbreak.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

5.2.3 Review of Evidence

Consistent hand hygiene at all opportunities in patient care is essential, since MDROs can be acquired from contact with a colonized patient or contaminated surface and transferred to new patients or surfaces.[6,9] In their systematic review of prevention for MDR Gram-negative bacteria (MDR-GNB), Tacconelli and colleagues (2014) strongly recommend correct hand hygiene before and after patient contact, as well as before and after contact with the patient environment, regardless of gown and glove use.[6] Even in facilities where hand hygiene compliance rates are high (above 80%), outbreaks can be opportunities to achieve near-perfect compliance. Palmore and Henderson (2013) note, however, that compliance will eventually return to baseline levels after an outbreak ends, highlighting the challenge of sustaining universal hand hygiene.[10]

Of the 17 studies and reviews included in this report, 5 studies and 1 review explicitly examined the causal relationship between better hand hygiene compliance and reduced MDRO transmission. An additional four studies used mathematical models to estimate the role of hand hygiene in multicomponent MDRO prevention strategies. Two studies looked at the role of patient hand hygiene in preventing MDROs, one study reviewed hand hygiene costs and cost savings (due to infection prevention), and one review looked at hand hygiene opportunities related to cell phone use. Finally, two

[i]Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Division of Healthcare Quality Promotion. Accessed February 12, 2020 from https://www.cdc.gov/handhygiene/providers/index.html.

reviews and one study looked at factors influencing hand hygiene and best practices for increasing compliance.

5.2.3.1 Reducing MDRO Rates Through Hand Hygiene

Four studies found that improved hand hygiene reduced MDRO transmission and one found that the association between hand hygiene and reduced MDRO transmission varied by MDRO, as summarized in the table below. One review by Taconnelli et al. (2014) did not provide statistical findings but recommended hand hygiene for MDR-GNB based on the evidence of frequent hand contamination during patient care, MDRO survivability on hands, and risk of contamination due to fomites (objects or surfaces that are likely to carry infectious pathogens) in the patient environment.[6]

Table 5.6 summarizes the findings from studies evaluating the efficacy of hand hygiene for reducing MDRO transmission and infection.

Table 5.6: Summary of Clinical Outcomes of Hand Hygiene Interventions

Study	Sample Size, Population	Hand Hygiene Measures, MDROs	Outcomes
De la Rosa-Zamboni et al., 2018[11] Pre-post study of a hand hygiene communication campaign	All patients in a pediatric hospital in Mexico between January 2013 and October 2016	Direct hand hygiene observation MRSA, VRE, MDR-ESKAPE pathogens[j]	The authors observed a correlation between hand hygiene adherence and reduced attack rates for: • MRSA (coef, -17.10, 95% CI -30.67 to -3.53, p=0.019). • VRE (coef. -54.87, 95% CI -73.28 to -36.46, p=0.001). • *Enterobacter* spp. (coef. -33.04, 95% CI -51.14 to -14.94, p=0.002). • MDR-ESKAPE group (coef. -7.76, 95% CI -15.08 to 0.37, p=0.059.
Pires dos Santos et al., 2011[13] Pre-post study of a multi-component intervention, including hand hygiene and antibiotic stewardship	749-bed hospital in Brazil	Liters of alcohol-based hand rub consumed Carbapenem-resistant *P. aeruginosa* (CR-PA)	Antibiotic stewardship had little impact, but improved hand hygiene was significantly associated with reduced infection rates.
Sopirala et al., 2014[12] Pre-post quality improvement study including hand hygiene promotion and feedback, routine surveillance, and glove and gown use	All patients in a 1,191-bed hospital between January 1, 2006, and September 30, 2009	Direct observation of hand hygiene, volume of and soap/ sanitizer used MRSA	The program achieved high compliance with hand hygiene (93%) with reduced total MRSA cases from 0.49 to 0.34 per 1,000 patient-days (incidence rate ratio [IRR]=0.59, 95% CI 0.42 to 0.84, p=0.003) and MRSA-related bacteremia from 0.18 to 0.10 per 1,000 patient days (IRR=0.68, 95% CI 0.56 to 0.84, p<0.001).

[j] *Enterococcus faecium*, *S. aureus*, *K. pneumoniae*, *A. baumanii*, and *P. aeruginosa*.

Study	Sample Size, Population	Hand Hygiene Measures, MDROs	Outcomes
McLaws et al., 2009[15] Pre-post study of a hand hygiene promotion campaign	All public hospitals in the Australian State of New South Wales	MDR-AB, MRSA, and VRE	Hand hygiene rates increased in six of the nine hospital systems in the study (no change in two and a decrease in one). Between pre- and post-intervention periods, MRSA infections from nonsterile sites inside the ICU dropped by 16 percent, and those nonsterile sites outside the ICU dropped by 25 percent. MRSA infections in sterile sites (both within and outside the ICU) remained stable. VRE rates remained stable (except for an outbreak in some hospitals), and MDR-AB infections in ICU sterile sites fell (although not in other sites).
Vernaz et al., 2008[14] Interrupted time series analysis of increased alcohol-based hand rub use (as part of an intervention that included antibiotic use, patient isolation, screening on admission, automated computerized alerts, topical decolonization of MRSA carriers)	All hospital patients between February 2000 and September 2006, Switzerland	Hand rub use MRSA, *C. difficile* (not an MDRO but included in the study)	Consumption of hand rubs increased over the study period, from an average of 1.303 L per 100 patient-days in 2001 to 2.016 L per 100 patient-days. Only MRSA showed a temporal association between the increase in hand rub use and a decrease in MRSA rates.

De la Rosa-Zamboni and colleagues (2018) studied the efficacy of a hand hygiene intervention in a pediatric teaching hospital in Mexico. Alcohol-based hand rubs were placed in every patient unit and periodic education programs were individualized for each group of healthcare workers (attending physicians, nurses, residents, students, and ancillary staff) to highlight the mortality and costs associated with healthcare-associated infections and the evidence about efficacy of hand hygiene. Monthly monitoring and feedback were provided to each group about infection rates and hand hygiene compliance.

Hand hygiene adherence increased from 34.9 percent during the baseline period to 80.6 percent in the last 3 months of the pre-post study. The overall infection rate decreased from 7.54 to 6.46 per 1,000 patient-days (p=0.004), with central line-associated bloodstream infections declining from 4.84 to 3.66 per 1,000 central line-days (p=0.05).[11]

Sopirala and colleagues (2014) used a hand hygiene program that trained staff nurses in infection control and linked them to infection prevention staff for ongoing monthly education, achieving very high rates of hand hygiene compliance (93%) and reducing MRSA rates by almost half in the pre-post study.[12]

Pires dos Santos and colleagues (2011) studied multiple strategies to reduce CR-PA infections in a hospital in Brazil. They found that antibiotic stewardship had little impact, but improved hand hygiene (as measured by hospitalwide use of alcohol-based hand rub) was significantly associated with reduced infection rates.[13]

Vernaz and colleagues (2008) conducted an interrupted time series study of the temporal relationship between increased alcohol-based hand rub use (as part of multicomponent intervention) and reduced MRDOs. The authors established a temporal association between increased alcohol-based hand rub use and reductions in MRSA rates but not *C. difficile* rates. (This finding is consistent with evidence in this

report and in the guidelines reviewed, that alcohol-based hand rubs are not effective for spore-forming bacteria such as *C. difficile*.)[14]

Finally, one study of nine hospitals in Australia found that results varied across facility and different MDROs. McLaws and colleagues (2009) found mixed results across the sites included in their pre-post study of hospital regions in Australia. Hand hygiene rates increased in six of the nine hospital systems in the study. For the remaining three hospitals, one had a decrease and the other two had no observed change. Although hand hygiene increased overall, two of four clinical indicators of MRSA infection remained unchanged. The authors concluded that concurrent clinical and infection control practices at different facilities possibly influenced MRSA infection rates and modified the effects of hand hygiene compliance across the different locations.[15]

5.2.3.1.1 Mathematical Models of Hand Hygiene's Impact

We reviewed four studies that used mathematical models to estimate the impact of changes in hand hygiene compliance on MDRO acquisition and infection, controlling for the influence of other concurrent infection control or antibiotic stewardship interventions. To create these models, these studies used measurement from an existing facility or ICU; because these were based on single sites, the generalizability of these models may be limited. Still, these models offer examples of how to retroactively assess the effectiveness of individual components of multicomponent interventions, a common challenge given that few hand hygiene compliance programs are implemented without other concurrent practices or programs.[16]

Barnes and colleagues (2014) simulated scenarios of patient-to-patient transmission via the hands of transiently contaminated healthcare workers to quantify the effects of hand hygiene versus environmental cleaning on rates of MDRO acquisition. For all organisms studied (*A. baumannii*, MRSA, and VRE), increases in hand-hygiene compliance outperformed equal increases in thoroughness of terminal environmental cleaning. The authors estimated that a 20 percent improvement in terminal cleaning would be required to match the reduction in organism-acquisition achieved by a 10 percent improvement in hand hygiene compliance.[17]

D'Agata and colleagues (2012) modeled the impact of several distinct strategies for infection control. They found that improved hand hygiene compliance reduced MDRO colonization slightly more than improved compliance with contact precautions. They estimated that a 20 percent increase in hand hygiene compliance reduced colonization between 8 and 12 percent, while a similar 20 percent increase in contact precaution compliance reduced colonization between 6 and 10 percent.[9]

Harris and colleagues (2017) randomly assigned 20 ICUs to infection control interventions and used the resulting data to understand the relative contribution of the interventions. They found that approximately 44 percent of the subsequent decrease in the MRSA acquisition rate was due to universal glove and gown use, 38.1 percent of the decrease was due to improvement in hand hygiene compliance after exiting patient rooms, and 14.5 percent of the decrease was due to the reduction in physical contacts between healthcare workers and patients.[18]

Wares and colleagues (2016) modeled transmission in an outpatient dialysis unit and found that even with perfect compliance with hand hygiene, 13.4 percent of patients remained colonized with MDRO. They concluded that although the hands of healthcare workers are among the main vectors of MDRO

spread, transmission of MDRO occurs through numerous paths, including a contaminated environment and hospital-acquired colonization.[19]

5.2.3.1.2 Patient Hand Hygiene

Two studies examined the role of patient hand hygiene in reducing MDROs. Cheng and colleagues conducted two studies in Hong Kong of patient hand hygiene: one pre-post study (2015) in a hospital setting and one cluster-randomized trial (2018) in nursing homes.[20,21] In the hospital study, an intervention of single room isolation, strict contact precautions, and directly observed hand hygiene in conscious patients immediately before receiving meals and medications resulted in reduced bacteremia caused by MDR-AB. The rate decreased from 14 cases in 2013 to 1 case in the first 6 months of 2014 ($p<0.001$).[20]

In the second study, directly observed hand hygiene was performed in intervention nursing homes at 2-hour intervals during the daytime and before meals and medication rounds. The volume of alcohol-based hand rub used per resident per week was three times higher in the intervention nursing homes than in the controls ($p=0.006$), suggesting that hand hygiene education was effective in increasing use. Serial monitoring of environmental specimens revealed a significant reduction in MRSA in the intervention versus control nursing homes (13.2 percent vs. 32.8 percent; $p<0.001$) and a reduction in CR-AB species (9.3 percent vs. 15.7 percent; $p=0.001$).[21]

5.2.3.2 Process Outcomes

One study and one guideline review measured factors that can affect the efficacy of hand hygiene interventions. These factors include awareness of the need for hand hygiene in a given opportunity, knowledge of proper hand hygiene technique, and knowledge of what can make hand hygiene less effective even when performed correctly.

Rupp and colleagues' 2008 crossover trial in two ICUs demonstrated that hand hygiene compliance improved when alcohol-based hand rub was available on the unit. However, no improvement was seen in the rates of device-associated infection, infection due to multidrug-resistant pathogens, or infection due to *C. difficile* (for which alcohol-based hand rubs are not recommended). In addition, cultures of samples from the hands of nursing staff revealed that an increased number of both microbes and microbe species was associated with longer fingernails, wearing of rings, and lack of access to hand gel.[22]

Even after hand hygiene is improved, sustainability remains a challenge. In Palmore and Henderson's outbreak case study (2013), the authors achieved nearly perfect hand hygiene compliance from the hospital's already-high rate of 85 percent that was sustained for 6 months after the outbreak. However, after that point, the authors observed a return to baseline in the followup period.[10]

Ongoing observation and feedback are recommended for both increasing and sustaining compliance, but Ellingson and colleagues' (2014) guideline review notes a few challenges in carrying out this type of measurement and evaluation.[16] First, direct observation requires a trained observer, and no current guidelines note how frequently observation should take place to increase or sustain hand hygiene compliance. Indirect measurement can also be done by measuring the volume of hand hygiene solution used, with or without technological solutions such as "smart counters" that track and report dispenser use. These and other technological solutions, such as smart badges that alert remind healthcare personnel about an opportunity for hand hygiene, have programmatic limitations. They may be able to

alert on entry/exit but not for contact with surfaces or patients. In addition, there are costs in buying, installing, and maintaining this technology.

5.2.3.3 Economic Outcomes

Hand hygiene promotion programs can be very cost-effective in that they help reduce all infections (not just MDROs). One observational study provided economic findings: Sickbert-Bennett and colleagues studied a large U.S. teaching hospital (2016) before and after implementation of a hospitalwide initiative that included education about hand hygiene and instruction that all staff should provide immediate feedback and reminders to each other.

During the 17-month study period, there was a significant increase in the overall hand hygiene compliance rate ($p<0.001$) and a significant decrease in the overall HAI rate ($p=0.0066$). There were 197 fewer healthcare-associated infections and an estimated 22 fewer deaths, for an estimated saving of U.S. $5 million. The authors noted that while infections declined, there was no similar reduction in MDRO infections. They posit that many MDRO infections occur in patients who are colonized before admission to the hospital and cannot be prevented through better hand hygiene.[23]

5.2.4 Implementation

5.2.4.1 Summary of Evidence on Implementation

When practiced consistently, hand hygiene is an effective tool in reducing MDRO colonization and infections. The challenge is finding cost-effective strategies to increase hand hygiene compliance and sustain it over time. Lee and colleagues' systematic review (2019) found that, overall, implementing any infection control program reduces HAI rates; however, the greatest reductions come from interventions with multiple, reinforcing components that address:

- Knowledge (education),
- Consistency (monitoring and feedback), and
- Accessibility (providing supplies in places that make sense given the patient care workflow and hand hygiene opportunities).[24]

Maintaining hand hygiene requires education and culture change, creating workflows that support hand hygiene and technological solutions to automate monitoring and feedback. In some hospital settings, however, the time required for meticulous hand hygiene is a barrier. In their 2017 nonsystematic review, Strich and Palmore point out that if hand hygiene were performed in compliance with WHO guidelines (including 20–30 seconds per hand hygiene episode), each nurse would spend an estimated 58 to 70 minutes on hand hygiene for each patient during a 12-hour ICU shift, which conflicts with patient care duties. They also note that early-generation electronic monitoring systems have had mixed results in improving and sustaining hand hygiene compliance.[2]

In their guidelines for preventing HAIs through hand hygiene (including MDRO infections), Ellingson and colleagues (2014) recommend direct observation as the primary method for measuring hand hygiene compliance, combined with at least one other measurement method (self-report, technologically-automated tracking) to strengthen measurement against limitations from any single method.[16]

5.2.4.2 Barriers and Facilitators

Trautner and colleagues (2017) surveyed nursing home staff across 13 States and found large gaps in knowledge about proper hand hygiene procedures. Although all respondents reported receiving training in hand hygiene, less than 30 percent knew the correct length of time to rub hands (28.5 percent of licensed personnel and 25.2 percent of unlicensed personnel understood this fact) or the most effective hand cleaning agent to use (11.7 percent of licensed personnel and 10.6 percent of unlicensed personnel understood).[25]

One way to address the issue of organizational culture is to personalize a well-supported intervention to promote hand hygiene compliance. Luangasanatip and colleagues' systematic review (2015) recommends the WHO's "My Five Moments" intervention for its efficacy in increasing hand hygiene compliance. They also suggest that this intervention is even more effective and sustainable when goal setting, incentive rewards for achievement, and mechanisms to ensure accountability are added.[26]

A study of general infection prevention practices by Clock and colleagues (2010) found that individuals who adhered to one set of infection control behaviors were likely to adhere to all. They recommend focusing on changing the behaviors of those likely to be systematically noncompliant, such as visitors and staff not directly involved in patient care.[27]

Several studies in this review addressed compliance by improving access to hand hygiene equipment and supplies. However, if hand hygiene equipment becomes contaminated, the equipment itself can become a source of transmission. As observed by Hota and colleagues (2009) in their CR-PA outbreak response, handwashing sinks increased environmental contamination due to splashing from contaminated drains. In their study of ICU and transplant units, contaminated sink drains were implicated in 36 infections over a 15-month period, by organisms that were phenotypically similar; 17 of these patients died.[28]

Kotsanas and colleagues' (2013) investigation of a CR-*K. pneumoniae* outbreak found that once an MDRO is established in sink drains, it is difficult to eradicate without complete removal and redesign of sinks.[29] (Johnson et al., 2018, investigated a 2016 hospital outbreak of *Sphingomonas koreensis* and identified facility plumbing as a reservoir.[30]) The authors recommend that preventive efforts focus on appropriate sink design to minimize "spray" and enforcement of clear policies to use designated sinks for hand hygiene only, not for waste disposal. They also recommend frequent surveillance/testing of sink drains and surrounding environment for contamination.

5.2.4.3 Resources To Assist With Implementation

Since hand hygiene has a long, established history of efficacy and implementation, many promotional tools and campaigns have been developed. Below, we present the tools and campaigns described or evaluated in the above studies and reviews.

- The most frequent tool mentioned by the studies in this review was the WHO's "My Five Moments for Hand Hygiene" program, which can be found at https://www.who.int/infection-prevention/campaigns/clean-hands/5moments/en/.
- The Association for Professionals in Infection Control and Epidemiology also offers a number of implementation guides, educational tools, and articles to promote and support hand hygiene, available at https://apic.org/resources/topic-specific-infection-prevention/hand-hygiene/.

- The U.S. Department of Veterans Affairs' "Infection: Don't Pass It On" campaign materials are available at https://www.publichealth.va.gov/infectiondontpassiton/index.asp.
- Materials from the "Clean Hands Save Lives" campaign studied by McLaws et al. (2009) can be found at http://www.cec.health.nsw.gov.au/topics/concluded-projects/clean-hands.[15]
- Materials and guides from the "Clean In, Clean Out" program implemented by Sickbert-Bennett et al. (2016) is available at http://news.unchealthcare.org/empnews/handhygiene.[23]
- The CDC offers resources to support hand hygiene in healthcare settings under the "Clean Hands Count" campaign, available at https://www.cdc.gov/handhygiene/index.html.
- Additional health promotion materials from the CDC's "Life is Better with Clean Hands" campaign can be found at https://www.cdc.gov/handwashing/campaign.html.
- Commentary from Landers and colleagues on suggested moments for patient hand hygiene can be found in their 2012 article.[31]

5.2.5 Gaps and Future Directions

As described in the process outcomes section above, it is important to understand the systemic reasons that hand hygiene is not successfully completed at all opportunities. One of these is awareness that a hand hygiene opportunity is occurring, such as touching contaminated surfaces (as mentioned in Otter and colleagues' 2013 nonsystematic review).[4]

Graveto and colleagues' systematic review (2018) found that in addition to known fomites such as patient linens and healthcare personnel's clothing, cell phones are frequently used in clinical settings, are often colonized with infectious organisms, and are rarely sanitized.[8] While this finding represents a threat to successful hand hygiene, cell phones have important clinical utility, and it would be impractical to ban cell phones in all healthcare settings. The authors note that data are limited about the connection between cell phone contamination and HAIs. The authors recommend that cell phone use be incorporated into hand hygiene promotion, including handwashing before and especially after cell phone use, and routine disinfection of cell phones.

Even when hand hygiene compliance is nearly perfect, resistance to antimicrobial solutions is an increasing concern, given the widespread and rapid rise of antibiotic resistance. In Kampf's nonsystematic review (2016), the frequency of handwashing events greatly increased the exposure of MDROs to low levels of chlorhexidine and the selective pressure for resistance.[32] Although Ho and Brantley's commentary (2012) on a pre-post study of chlorhexidine resistance genes in MRSA did not demonstrate a correlation between increased antiseptic use for hand hygiene and increased resistance gene prevalence, the authors note that other studies have shown some association and recommend further study.[33]

Outside the clinical setting, alcohol-based hand rubs are also used as a hand hygiene alternative when soap and water washing is not available. At the time of this report, the Food and Drug Administration was investigating benzalkonium chloride, ethyl alcohol, and isopropyl alcohol for safety and efficacy in over-the-counter hand rubs when used in place of soap and water washing among the general population. These ingredients are deferred from further rulemaking as data are gathered on their

general safety and efficacy, and future research should include considerations about which solutions to use or avoid in community settings.[k]

[k]More information on this final rule can be found on the *Federal Register* website at: https://www.federalregister.gov/documents/2017/12/20/2017-27317/safety-and-effectiveness-of-health-care-antiseptics-topical-antimicrobial-drug-products-for.

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5.3 PSP: Active Surveillance for MDROs

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"Active surveillance" is a broad practice that encompasses many activities, including sample collection, laboratory testing, data collection, data analysis, and reporting and feedback. Active surveillance helps prevent the spread of infection by identifying when an MDRO enters a healthcare facility and quickly triggering infection control measures. Active surveillance can also help with diagnosis and appropriate treatment of infections and antibiotic stewardship by generating data that can be used to create a local profile of antibiotic susceptibility or antibiogram.[1]

Key Findings

- Targeted active surveillance performs as well as universal active surveillance for many MDROs and uses fewer resources. However, in places where universal active surveillance is already in place, screening for other MRDOs using the same sample may be cost-effective, as patients colonized with an MDRO share risk factors for others.
- Some consensus exists for screening high-risk patients (those with a history of MDROs or risk factors associated with MDRO colonization/infection) on admission, but any screening approach will require compliance with infection prevention protocols when a patient's culture result is positive.
- Surveillance may improve compliance with other PSPs when it is part of a multicomponent intervention, but more research is needed on the mechanisms and circumstances of this association, as it can be confounded by the coimplementation of other, bundled practices.

5.3.1 Practice Description

With the infection prevention and healthcare practitioner in mind, this report provides evidence to support strategies for "active surveillance"—the collection and culturing of samples specifically for identifying MDRO colonization and infection among patients. However, "active surveillance" is a broad practice that encompasses many activities (sample collection, lab testing, data collection, data analysis, and reporting and feedback) and occurs at many levels.[1]

Considering the broad scope, we also include best practices for active surveillance that continue beyond obtaining laboratory results. Where described in the literature, we include best practices in using active surveillance results to:

- Direct infection prevention responses;
- Evaluate the effectiveness of IP practices;
- Track and communicate MDRO status, prevalence, and risk to prevent intra- and inter-facility transmission; and
- Develop local, regional, and global datasets of MDRO prevalence that inform risk-based approaches to active surveillance and infection prevention.

Epidemiologically, genotyping of active surveillance samples can help identify potential modes of transmission or assess need for patient bathing/deeper environmental cleaning by identifying related organisms from multiple sample sites.[1,2] These genotyping data can also be used to identify whether the MDROs identified in screening are endemic to the environment or are imported by asymptomatic carriers. However, this practice requires access to labs with the capacity to do quick-turnaround, real-time genotyping.[1]

Integration of active surveillance programs into electronic medical records can help automate identification and analysis but requires facilities with those capacities or access to them. However,

generating larger, regional and even global surveillance systems allows individual facilities to identify risk factors for incoming patients (for example, knowing what areas of the world have high prevalence of certain MDROs).[1]

Many resource challenges arise in creating sophisticated laboratory and data integration systems that can identify, genotype, and share information on MDROs. At the same time, investing in these systems benefits other infection control practices by generating the data that allow facilities to take a risk-based approach to screening, isolation, and contact precautions, which represent an opportunity for cost saving.[1] Finally, facilities must make decisions about when to stop active surveillance, balancing the costs of an active surveillance program against the possibilities of failed eradication and recolonization.[3] Key findings are located in the box above.

5.3.2 Methods

To investigate how active surveillance has been implemented to prevent transmission of MDROs and contain MDRO outbreaks, we searched three databases (CINAHL, MEDLINE, and Cochrane) for a combination of the keywords "monitoring," "surveillance," and "monitoring and surveillance," as well as MeSH terms "cross infection prevention," "drug resistance, multiple, bacterial," and "drug resistance, microbial." Articles from January 1, 2008, through December 31, 2018, were included. (Any relevant articles published after the original search are included in the PRISMA diagram as additional sources.)

The initial search yielded 392 results (including 24 articles from other sources); after duplicates were removed, 352 were screened for inclusion, and 175 full-text articles were retrieved. Of those, 23 were selected for inclusion in this review. Articles were excluded if they did not mention active surveillance's role in preventing MDRO transmission, only described surveillance for determining treatment, or did not include implementation in a healthcare setting.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

5.3.3 Review of Evidence

The Key Findings box presents a high-level summary of the findings in this review. Although the ideal method for active surveillance varies by MDRO (based on how the organism is acquired and shed by patients), one common theme is using targeted, active surveillance based on MDRO risk factors, such as recent hospitalization or history of MDRO colonization. Screening results should then be used to guide other infection control practices, such as contact precautions or decolonization protocols. Without adherence to these practices, the value of active surveillance is limited.

Screening decisions for facilities should be based on the available epidemiological surveillance data on which organisms are likely to be prevalent in a facility's patient population. Rare MDROs will result in far higher screening costs to prevent one infection/colonization event, compared with MDROs with higher prevalence. For MDROs or other pathogens frequently present on admission (such as MRSA or *C. difficile*), screening results may be useful in identifying a patient at risk for other MDROs. Conducting tests for multiple MDROs on one sample may reduce the materials and time needed for sample collection but may increase costs related to lab processing.

Where active surveillance may provide the most value is in improving compliance with other PSPs in multicomponent interventions. However, it is not clear how strong that association may be or why an association appears in some studies but not others. As mentioned above, identifying patients colonized or infected with an MDRO is only valuable if the correct procedures to reduce transmission (such as hand hygiene or decolonization) are followed consistently based on that knowledge. More research is needed to understand the synergistic effect of active surveillance to maximize its benefits.

5.3.3.1 Active Surveillance To Control MDRO Transmission

Active surveillance for MDROs is necessary because routine surveillance of clinical samples will undercount colonized or infected patients.[3,4] The proportion of clinically evident cases also varies by organism and susceptibility of the patient population, which means many asymptomatic carriers will go unnoticed without active surveillance.[4] In addition, an accurate screening process will reduce the number of patients on isolation or contact precautions unnecessarily.[5] In an outbreak of an MDRO in an otherwise low-prevalence setting, active surveillance is needed to verify that the outbreak has been successfully contained.[6]

It should be noted that in each of the studies included, active surveillance was combined with other infection control preventions. Tacconelli et al. (2014) strongly recommend always pairing surveillance with other infection prevention practices.[4] Cipolla et al., in their 2011 commentary, suggest that active surveillance results can be used to build a local antibiogram to complement antibiotic stewardship initiatives.[7] Gasink and Brennan's nonsystematic review (2009) further found that active surveillance without preemptive isolation has not been shown to be effective.[8]

This variation in practice makes it difficult to evaluate the effect of infection prevention with and without active surveillance, as noted in Strich and Palmore's commentary (2017).[9] While Strich and Palmore suggest that universal contact precautions may ultimately be more effective for MDRO prevention than active surveillance, these universal measures come with extra costs and potential for additional negative outcomes (discussed below).

In this summary, we present ways healthcare facilities used these strategies, including both successful and unsuccessful approaches. Several organizations have produced evidence-based recommendations on the best ways to use active surveillance to identify and contain MDROs, links to which can be found in section 5.3.4.4. However, the field of MDRO research continues to evolve, and we provide recent findings to supplement existing recommendations. We also present lessons learned from outbreak responses, especially lessons learned about challenges that threaten the validity and effectiveness of active surveillance.

5.3.3.1.1 Screening Methods for Detecting MDROs

Although screening is widely used, findings are mixed as to the correct screening method (patient sites, type of swabs used), frequency, target population, and culturing of samples. The sensitivity and specificity of a sample collection site or type varies by type of MDRO.

Given the costs associated with active surveillance and subsequent patient isolation, Freire and colleagues (2017; prospective cohort study) recommend universal surveillance in facilities where the incidence of MDROs is moderate to high and for patients for whom the rate of conversion from colonization to infection is high (e.g., transplant patients).[10] In universal surveillance, Barbadoro and colleagues' 2017 time series analysis found that skin, blood, and respiratory samples performed better

at initially identifying the presence of an MDRO than did urine samples.[11] The CDC (2019) offers guidelines for surveillance based on different categories of organisms and resistance mechanisms, with a recommended approach for each.[12]

Based on the findings in our review, we summarize the evidence for active surveillance around five topic areas, comparing both universal and targeted approaches (when findings are available):

- Surveillance for general MDR Gram negative bacteria (MDR-GNB)
- Surveillance for methicillin-resistant *Staphylococcus aureus* (MRSA)
- Surveillance for vancomycin-resistant Enterococci (VRE)
- Surveillance for carbapenem-resistant or carbapenemase-producing Enterobacteriaceae (CRE/CPE)
- Surveillance for MDROs using environmental sampling

General MDR-GNB: No consensus exists on frequency of screening or timing of screening for MDR-GNB. A nonsystematic review by Gasink and Brennan (2009) showed that screening during admission with weekly followup prevented the spread of MDR-*A. baumanii*.[8] However, a similar program for MDR-*K. pneumoniae* was not successful.[4] In epidemic settings, targeted screening on admission for high-risk patients is recommended. Screening can also be used to reinforce other prevention practices in the outbreak response, such as hand hygiene.

In the endemic setting, active surveillance should be used as an additional measure to control the spread of MDR-GNB between facilities or units. Otter and colleagues, in their 2015 commentary review, suggest using surveillance data from endemic settings to build risk assessment protocols and implement targeted screening policies that will catch MDR-GNB carried by transferred patients without adding unnecessary costs or burden.

As far as sampling sites, Tacconelli and colleagues (2014) found that rectal swabs, urine, or respiratory secretions were sufficient for almost all MDR-GNB, with rectal swabs being the most sensitive and groin being most specific. However, one study in that systematic review showed that sensitivity of screening is low (29%) even when six body sites are included. Finally, Tacconelli and colleagues note that (as of writing in 2014) rapid polymerase chain reaction-based methods to identify MDR-GNB were still in development, so culture-based tests remain the standard.[4]

Once an MDR-GNB pathogen is identified, Tacconelli and colleagues recommend weekly screening until no cases of colonization/infection or cross-transmission are observed.[4] Several outbreak responses have noted that MDR-GNB pathogens, particularly MDR-AB, produce significant environmental contamination due to their method of shedding (shed skin cells, stool, and/or urine).[13,14] However, the mean colonization time for MDR-GNB in their reviewed studies was 144 days, representing a significant length of time. Tacconelli and colleagues also noted that the efficacy of screening was linked to the level of compliance, so screening must be maintained over time.[4]

Methicillin-resistant *Staphylococcus aureus* (MRSA): Given the increasingly endemic nature of MRSA in both healthcare and community settings, questions have emerged about the clinical value of screening for MRSA, especially among asymptomatic carriers.[15,16] If conducting screening for MRSA, Lin and colleagues (2018) found nasal screening to be most sensitive: nasal culturing alone identified 84 percent

(327/388) of MRSA positive patients; only 61 patients (16%) were both nasal-culture negative and groin-culture positive. Nasal screening also had a strong negative predictive value of 98 percent (95% CI, 97.6% to 98.5%).[16]

MRSA screening may be a useful tool for identifying colonization of other, nonendemic MDROs. Evidence supports some association between MRSA status at admission and later discovery of MDRO colonization. Jones and colleagues' retrospective cohort study (2015) found that 2.4 percent of patients with positive MRSA screening later had a positive MDR-GNB culture, compared with 0.9 percent of patients with a negative MRSA screening ($p<0.001$). This association was strongest for *Acinetobacter* species of MDR-GNB. Jones et al. also found that 85.5 percent of those with a subsequent MDR-GNB negative culture also had an MRSA-negative screen.[17]

In facilities where universal MRSA screening is already in place, a positive result may be considered a risk factor for other MDROs. By knowing risk factors associated with colonization by MDROs other than MRSA, hospitals and other facilities can develop risk-based testing approaches for screening on admission, reducing costs in time and materials.[18]

Vancomycin-resistant Enterococci (VRE): Active surveillance for VRE can help detect asymptomatic carriers, but the clinical benefit of this strategy is unclear and methods for VRE surveillance can vary widely in practice.[19] Active surveillance helps detect asymptomatic VRE colonization in patients with *C. difficile* infection (CDI) in facilities with a high VRE prevalence, given high correlation between colonization with the two organisms. More than 50 percent of patients with CDI were also colonized with VRE.[20]

Despite this finding, it is not clear whether surveillance for asymptomatic VRE carriers reduces VRE-related infections. Almyroudis and colleagues' interrupted time series study (2016) found that active surveillance with precautions for sporadic (not horizontally-transmitted) VRE did not protect patients against VRE bacteremia.[21] Huskins et al. (2011) also observed no difference in mean colonization and infection rates between the active surveillance and control groups in a cluster-randomized trial of active VRE and MRSA surveillance upon admission.[22]

Carbapenem-resistant/carbapenemase-producing Enterobacteriaceae (CRE/CPE): Although the global prevalence of CRE/CPE is increasing, not all regions or all facilities in a region share the same risk for CRE outbreaks. Active surveillance following identification of CRE can reveal additional asymptomatic cases, as Banach and colleagues learned in their 2014 observational study using *C. difficile* samples to test for concurrent CRE carriage. Rescreening of clinical samples collected for other testing (such as Banach et al.'s approach to perform testing for CRE on *C. difficile* stool samples) is one way to efficiently screen patients who have risk factors for multiple MDROs and identify asymptomatic carriers.[23]

Karampatakis and colleagues' quasi-experimental study (2018) showed that a multicomponent intervention, including active surveillance, reduced rates of *K. pneumoniae* and *P. aeruginosa* infection but not of other MDR-GNB (*A. baumannii*), further highlighting the importance of tailoring infection prevention response to the organisms.[24] As described below in environmental surveillance, *A. baumannii* may require enhanced environmental cleaning protocols compared with CRE, due to the increased environmental contamination from colonized patients.

In light of no clear evidence for or against universal screening for CRE, one commentary by Asensio and colleagues (2014) recommends active surveillance on admission for patients in any of the following elevated risk groups:

- Patients transferred from a healthcare facility in any foreign country (in light of a lack of data on global CRE prevalence
- Patients transferred from acute or long-term care facilities with known high CRE prevalence
- Patients previously colonized or infected with CRE
- Patients who have had close contact with a person with CRE.

Finally, any surveillance must have clear definitions to avoid under- or over-reporting of CRE cases.[25] In Mayer and colleagues' retrospective laboratory audit (2016), underreporting due to misunderstanding definitions was far more frequent than overreporting.[26]

Environmental Sampling for MDRO Surveillance: Active surveillance of the environment, in addition to patients, combined with monitoring staff's adherence to infection control practices, can identify the transmission patterns and expose areas for improvement. For example, Sui and colleagues' 2013 outbreak response found that, compared with MRSA, MDR-AB patients were more likely to contaminate their environment.[27]

Environmental sampling as part of active surveillance can be used to identify areas in need of intensive cleaning or where cleaning has been missed, as identified by Lesho and colleagues (2018) and Liu and colleagues (2014) in their respective outbreak responses.[28,29] Nusair and colleagues' observational study (2008) found that evaluating the outcomes of different types of sampling (such as the most frequently positive patient body sites) can also help streamline the sample collection process for future surveillance.[30]

Cheng and colleagues (2018; outbreak response case study) found that environmental surveillance may serve as an indicator of MDRO carriers, at least in the case of MDR-AB, where the organism is consistently shed by patients.[31] In another outbreak (of MDR-*E. coli*), however, environmental surveillance failed to identify an environmental source.[32] The outbreak was successfully contained only after it was moved to a temporary neonatal ICU, showing that negative environmental samples do not reliably indicate that the environment is free of MDROs. In addition, the Healthcare Infection Control Practices Advisory Committee recommends culturing environmental samples when epidemiological evidence shows an environmental source of ongoing transmission.[33]

5.3.3.1.2 Genotyping MDRO Cultures

Genotypic testing can help determine whether MRDOs identified in active surveillance are horizontally transmitted between patients, coming from a common environmental reservoir, or are imported from other facilities. One interrupted time series study of active screening of high-risk patients by Borer and colleagues (2011) found that 45 percent of CR-*K. pneumoniae* infections and 57 percent of all positive cultures were community acquired.[34] Benenson and colleagues' 2013 screening of neonates in an Israeli ICU found both imported and horizontally-transmitted strains of ESBL-producing *K. pneumoniae*. The authors significantly decreased the number of positive cultures using surveillance in combination with cohorting of neonates with positive cultures.[35]

In Kohlenberg and colleagues' outbreak report (2010), active surveillance detected environmental reservoirs of CR-PA unrelated to the outbreak strain, based on genotyping results of the cultured organisms.[36] Finally, Wendel and colleagues' MDR-*P. aeruginosa* outbreak response case study (2015) used genotyping to confirm transmission through shared hair washbasins, which allowed the authors to halt the epidemic and prevent further transmission by discontinuing their use.[37]

5.3.3.2 Surveillance for Process Outcomes

Surveillance, by its nature, is a practice that gathers process and outcome data, allowing evaluation of other patient safety practices. This section describes how different modes of active surveillance have been evaluated for effectiveness and how active surveillance can be used to evaluate the effectiveness of other practices or bundles.

Tracking MDRO isolates over time and between different units allows hospitals to evaluate the effectiveness of their infection control protocols. In Ahern and Kemper's 2009 case study, the authors showed reduction in MDROs despite increased rate of antibiotic prescription.[l] Bryce and colleagues' pre-post study (2015) found that risk-based active surveillance could be as effective as universal surveillance in reducing the target MDRO, VRE, as well as MRSA and *C. difficile* infection.[38] In D'Agata and colleagues' mathematical model simulation (2012), targeted screening for MRSA and VRE for patients receiving antimicrobials (a known risk factor for MDRO acquisition) reduced MDRO acquisition while universal screening did not.[39]

Active surveillance programs have been observed indirectly enhancing compliance with other patient safety practices, but more research is needed to understand when and why adding active surveillance helps compliance with other practices, as our review also uncovered examples of no association.[40] For example, Evans et al. (2017) observed decreases in transmission and HAIs related to MRSA in U.S. Veterans Affairs hospitals after implementing an infection prevention bundle. The authors speculate that universal screening for MRSA as part of the bundle served as a reminder to comply with other practices such as hand hygiene and contact precautions. Other hand hygiene and device-placement bundles were already in place, but MRSA transmission and infection rates did not drop until the active surveillance bundle was implemented.[41]

Mawdsley et al. (2010) found that weekly surveillance rounding successfully improved compliance with contact isolation initiation and required minimal resources (two person-hours of work per week, split among six infection preventionists).[42] Compliance surveillance in Palmore and colleagues' outbreak response effort (2011) helped identify a staff subpopulation that were more likely to fail to comply with infection control policies (in this case, physicians).[43]

Conversely, Huskins et al. (2011) observed that reporting culture results did not yield high compliance with contact precaution requirements. Despite being aware of patient's colonization status, healthcare providers used clean gloves only 82 percent of the time, gowns 77 percent of the time, and hand hygiene 69 percent of the time during observed periods.[22] Similarly, Lin and colleagues' observational study of 25 Illinois hospitals (2018) found that only 54 percent of patients whose point prevalence

[l]Ahern JW and Alston, WK (2009). Use of Longitudinal Surveillance Data to Assess the Effectiveness of Infection Control in Critical Care. Infection Control and Hospital Epidemiology, 30, 11, 1109-12.

culture was positive for MRSA were on contact precautions, despite new State legislation mandating active MRSA surveillance on admission and contact precautions for any patients with a positive result.[16]

5.3.3.3 Economic Outcomes

Cost-effectiveness of active surveillance interventions depends on how many infections are reduced (or are likely to be reduced) by the intervention, which varies by facility and even within facilities. Early detection and containment of MDROs reduces the costs associated with decontamination and eradication.[44] In cases where an MDRO is already endemic, such as in Zarpellon and colleagues' (2018) prospective study of active surveillance, the authors took a modified, risk-based approach. MRSA was considered endemic in the study hospital, except in pediatric and neonatal wards. Accordingly, the authors screened for MRSA only in pediatric and neonatal wards, where the MDRO was not yet established.[45]

Cost avoidance in targeted active surveillance can also take the form of reduction in products needed for contact isolation (gloves, gowns, hospital linens), laboratory reagents, and lost revenue (due to needing private rooms for patient isolation), as described by Bryce and colleagues in their 2015 pre-post study of targeted monitoring for VRE.[38] Johnston and Bryce's nonsystematic review (2009) found that screening patients at high risk for colonization with MRSA or VRE may be cost-effective if coupled with barrier precautions.[3]

The more accurate the active surveillance methodology, the fewer patients will be put on contact precautions unnecessarily.[46] Morgan and colleagues' 2009 systematic review also notes that faster screening tests can reduce the time patients are kept on preemptive precautions or in single-patient rooms.[47]

Finally, Banach and colleagues' observational study (2014) demonstrated the efficacy of a low-cost strategy to screen for CRE using sampling already being done for CDI, as both organisms share risk factors. The total cost of detecting one CRE-colonized patient ranged from $580 to $649 and required between 68 and 76 samples to be tested (based on the prevalence at the facilities in the study).[23]

5.3.3.4 Unintended Consequences

5.3.3.4.1 Negative

Active surveillance is used to identify patients to be placed on contact precautions, which reduce transmission but may have unintended adverse effects on the patient. Morgan and colleagues' systematic review (2009) found that contact precautions were associated with less contact from healthcare workers, delays in care, adverse events (non-infection- associated), increased symptoms of depression and anxiety, and decreased patient satisfaction with care.[47] This finding was also noted in commentary from Lemmen & Lewalter (2018).[5]

A study by Day and colleagues (2013) found that patients on contact precautions were not at any greater risk of developing depression or anxiety, although they may have more symptoms of anxiety and depression at the start of contact precautions.[48] Rapid-result genetic testing can also reduce any potential adverse effects of contact isolation by limiting the time spent in preemptive isolation pending screening results.[8]

Palmore and Henderson found an unintended negative consequence of public education in their 2013 outbreak response report: coverage of the outbreak in the wider media emphasized mortality rates,

which increased community anxiety when information was shared about the outbreak.[49] When sharing information on outbreaks and infection prevention responses with patients and families, one must convey the importance of preventing transmission and managing patients' understanding of their individual morbidity and mortality risk. Publications on techniques used to control the outbreak in a facility as well as media coverage of the outbreak, for example, could be shared.

5.3.3.4.2 Positive

Active surveillance has shown positive unintended effects. Bryce and colleagues' pre-post study (2015) found that risk-management surveillance reduced other infections (MRSA, CDI) in addition to the target organism (VRE).[38] In one observational study, environmental surveillance for MDROs led to discovery of a leaking water pipe that led to significant mold growth that could have resulted in additional harm among the immunocompromised patients.[30] Finally, Sánchez García and colleagues' active surveillance for MRSA during an outbreak (2010) identified a novel strain that was resistant to linezolid and allowed implementation of protocols to contain and ultimately eliminate it.[50]

5.3.4 Implementation

5.3.4.1 Summary of Evidence on Implementation

Reduction in MDRO infection rates does not come from active surveillance alone; rather, it should guide healthcare staff in informed decision making, such as implementing patient isolation and contact precautions. Regular monitoring through clinical sampling is a simple way to detect emergent pathogens, but it has limitations. Orsi et al. (2011) and Sandora et al. (2010) describe tradeoffs between routine surveillance of clinical samples and active surveillance.[51,52]

Routine clinical surveillance of already-collected samples is less costly in terms of collection time, but active surveillance testing can determine presence on admission or temporality of colonization, as well as identifying asymptomatic carriers (as mentioned above). Therefore, Orsi et al. (2011) recommend active surveillance to close the gaps in clinical sampling during outbreaks or for MDROs not endemic in a facility.[51]

5.3.4.2 Barriers and Facilitators

Adding weekly dissemination of the results of active surveillance (MDRO rates, location of acquisition) was key to successfully controlling MDROs. Although other components (active surveillance, patient isolation) had been in place already, Quan and colleagues (2015) demonstrated that automated systems could support enforcement of contact precautions and save considerable infection preventionist time.[53]

Horizontal transmission of MDRO strains may not need universal active surveillance, but MDRO acquisition or infection between facilities warrants communication to identify patients at elevated risk. In a retrospective analysis using a regional surveillance system for MDROs based on an existing MRSA and VRE alert system, Rosenman and colleagues (2014) observed several crossovers between institutions.[54]

Coordination with regional and national public health agencies can help with interfacility transmission by coordinating notification and infection prevention efforts across all facilities. Grundmann's 2014 commentary recommends a stepwise approach (local to regional to national to global) for creating a global surveillance network.[55]

Investing in active surveillance can require expenditures for laboratory and computer resources, as noted in O'Brien and Stelling's systematic review (2011), but these investments can help reduce the cost of other infection prevention efforts.[1] If a facility cannot absorb the costs of running a laboratory, partnering with public health agencies for surveillance may be an option.

In addition to the costs associated with conducting active surveillance, a few other challenges are described in the literature. Faster results can be available using molecular testing methods such as polymerase-chain reaction, but these tests can be costly, have limited specificity in some cases, and are not available in all facilities.[51]

5.3.4.3 Additional Important Contextual Factors

Santos et al., in their 2008 commentary review, note that although active surveillance for MDROs has significant benefits for infection prevention and treatment for the patient, it can also be considered quality improvement (research). Therefore, surveillance and isolation precautions do not require specific patient consent.[56] However, education and clear communication about the need for and impact of active surveillance on patients are critical. In addition, the financial burden of active surveillance should be assumed by the facility, not the patient.

5.3.4.4 Resources To Assist With Implementation

- The CDC offers MDRO surveillance and reporting instruction modules for its National Healthcare Safety Network system, available for a range of healthcare facilities at https://www.cdc.gov/nhsn/enrolled-facilities/index.html.
- The CDC also offers a series of recommendations for containing MDROs, based on the categories of MDRO sorted according to type of organism, prevalence, and resistance mechanisms. These recommendations (*Interim Guidance for a Public Health Response To Contain Novel or Targeted Multidrug-Resistant Organisms*) can be found at https://www.cdc.gov/hai/pdfs/containment/Health-Response-Contain-MDRO-H.pdf.
- Evidence-based recommendations from the Healthcare Infection Control Practices Advisory Committee (HICPAC; last updated in 2006) on surveillance and other practices for managing MDROs can be found at https://www.cdc.gov/infectioncontrol/guidelines/MDRO/index.html.
- The Health Research & Educational Trust Hospital Improvement Innovation Network offers many resources for addressing MDROs, including surveillance guidelines, in the MDRO Change Package available from its website: http://www.hret-hiin.org/topics/multi-drug-resistant-organisms.shtml.

5.3.5 Gaps and Future Directions

The greatest challenge to active surveillance cultures/testing for MDROs is understanding which surveillance protocols are the most sensitive and specific for correctly identifying carriers while minimizing the burden for collecting samples and processing data. Although evidence-based recommendations exist for MRSA, VRE, and CRE, numerous pathogens (particularly other MDR-GNB such as *K. pneumoniae* and emerging MDR pathogens such as *Candida auris*) lack a consistent recommendation for whom and when to screen.

Duffy and colleagues (2011), in their synopsis of a working group of infection prevention professionals, recommend strengthening partnerships between healthcare facilities and public health departments to

build capacity for identifying and tracking emerging MDROs.[57] Further studies that evaluate targeted surveillance protocols based on risk factor analysis would give healthcare facilities another tool for effective, lower cost surveillance.

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5.4 PSP: Environmental Cleaning and Disinfection

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Key Findings

- Cleaning with chlorine-based solutions (e.g., bleach) was studied as part of enhanced cleaning methods for MDROs. Research is lacking on cleaning with bleach as a single intervention.
- Moderate evidence supports the use of quaternary ammonium compounds for certain MDROs, although evidence is mixed in support of their usefulness in the targeted disinfection of high-touch surfaces.
- More studies are needed in clinical settings that examine the different cleaning and disinfecting agents.
- No-touch disinfection technologies are promising additions to disinfection practices but must be further studied to determine the most efficacious and cost-effective options.
- Environmental screening is a useful tool for auditing and monitoring ongoing cleaning practices and for identifying highly contaminated surfaces for targeted cleaning during outbreak scenarios.
- Efficacy of approaches varied against different species of bacteria and for sensitivity versus drug-resistant strains.

This section reviews research from 2008 to 2018 on environmental cleaning and disinfection as a strategy to prevent the transmission of multidrug-resistant organisms (MDROs) and reduce healthcare-associated infections (HAIs). Following a practice description and methods, the evidence summary reviews the research on different disinfectant agents, no-touch decontamination methods, and antimicrobial surfaces. Next, we explore several implementation facilitators, including environmental screening, audit and feedback, education, and facility policies. Finally, we look at gaps and future directions. Key findings are located in the box on the right.

5.4.1 Practice Description

Environmental surfaces serve as an intermediate vector for transmitting MDROs in healthcare settings.[1] Environmental contamination can occur from contact with MDRO-infected individuals or their body fluids and can result in transmission to another individual. The "environment" includes furniture and other surfaces in patient rooms; medical equipment; personal items belonging to patients, visitors, or staff; and structural components of the facility (e.g., sinks, air vents).

To remove MDROs or disinfect the environment, healthcare facilities use specific cleaning and disinfection practices. Enhanced or standard cleaning may be implemented on a daily basis or when a patient vacates a room (called terminal cleaning). In the event of an outbreak or increased rate of transmission, facilities may perform a more thorough, one-time environmental cleaning. The latter is frequently done when other infection control practices or standard environmental cleaning does not reduce infection rates or when a specific source of contamination is suspected or identified by environmental screening. Enhanced environmental measures also include reinforcing training of environmental services staff and monitoring adherence to environmental cleaning protocols.[2]

Before a disinfectant is applied, cleaning is required to manually scrub and wash any visibly soiled surfaces because disinfectants cannot typically penetrate organic matter or thick substances to eradicate microbes beneath.[3] After cleaning, a disinfectant is applied and left in contact with a surface for the amount of time designated by the manufacturer as necessary to kill/deactivate microorganisms. The variations and efficacy of these environmental cleaning and disinfection practices—highlighting MDROs in healthcare settings—are the focus of the following systematic literature review.

5.4.2 Methods

To determine the most effective environmental cleaning and disinfection practices for reducing the spread of MDROs, three databases (CINAHL, MEDLINE, and Cochrane) were searched for "bacterial drug resistance," "microbial drug resistance," and synonyms, in combination with "disinfection methods," "environmental monitoring," "environmental cleaning," and associated phrases. Articles from 2008 through 2018 were included.

The initial search yielded 375 results (including 9 from other sources); after duplicates were removed, 347 were screened for inclusion, and 130 full-text articles were retrieved. Of those, 58 were selected for inclusion in this review. Articles were excluded if they were outside the scope of this review, included insufficient detail on a patient safety practice, did not describe an intervention (e.g., surveillance only), demonstrated insufficient rigor, or were included in another PSP section of this report.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

5.4.3 Review of Evidence

This review includes evidence from 4 systematic reviews and 54 studies. Of the studies:

- Twenty-one were before-and-after intervention studies (one of which was a mathematically modelled and simulated intervention),
- Thirteen were outbreak studies,
- Nine were laboratory studies,
- Five were cross-sectional surveys,
- Two were cluster-randomized controlled trials,
- Two were cluster-randomized crossover studies,
- One was a prospective cohort study, and
- One was a prospective controlled quasi-experimental study.

Of all included articles, 25 took place or reviewed studies that took place in the United States, 31 occurred outside the United States, and 2 included studies from both the United States and abroad. The included studies focused on cleaning and decontamination agents to reduce MDROs and infection from MDROs, as well as facilitators and barriers to cleaning and sterilization in the healthcare environment.

5.4.3.1 Disinfection Products

5.4.3.1.1 Chlorine-Based Disinfectants

The most commonly referenced disinfectants were chlorine-based products (e.g., bleach), which were used in various studies for deep, terminal, or daily routine cleaning and often as part of multicomponent interventions.

Standard or enhanced environmental cleaning with chlorine-based disinfectants has been associated with controlling outbreaks and reducing MDROs.[4-6] In one study, a sink trap was determined as the likely source of an increased number of patient infections with multidrug-resistant *A. baumannii*.[4] As a response to the outbreak and the results of environmental sampling, bleach was used to disinfect sinks and plumbing. During the 6 months after the intervention, the number of new cases greatly declined. In an in vitro study, sodium hypochlorite at 0.5% concentration, standing for 30 seconds, was found to successfully eradicate imipenem-resistant *A. baumannii*, but the article noted that an overdiluted bleach solution (0.08%) was insufficient to reduce environmental contamination.[7]

Cleaning with chlorine-based agents was a component of several multicomponent interventions to decrease MDRO transmission.[8-16] For example, cleaning with chlorine-based disinfectants was part of a multicomponent intervention to reduce pandrug-resistant *A. baumannii*.[16] The intervention included hand hygiene, surveillance, and patient isolation. In another multicomponent intervention, enhanced cleaning with a chlorine-based detergent, combined with patient isolation, chlorhexidine bathing, and staff education was associated with ending an outbreak of linezolid-resistant *Enterococcus faecium*.[17]

A multifacility cluster-randomized crossover study in nine U.S. hospitals compared bleach with the detergent used at baseline (quaternary ammonium),[m] ultraviolet-C light (UV-C), and a combination of bleach and UV-C in preventing transmission of several MDROs. The incidence of target organisms among exposed patients was not significantly changed with the use of bleach alone, or the combination of bleach and UV-C, compared with quaternary ammonium.[18]

A before-and-after study in a burn ICU found that adding a chlorohexidine-alcohol disinfectant to standard cleaning with sodium hypochlorite was more effective than standard cleaning with sodium hypochlorite alone, although other implementation variables (e.g., frequency of cleaning, targeted cleaning) were also altered and may have contributed to the results.[19]

5.4.3.1.2 Quaternary Ammonium Compounds

Quaternary ammonium compounds (QACs) have demonstrated mixed success in environmental cleaning and disinfection. In one study, terminal cleaning with QAC reduced environmental contamination with MDR-AB in patient rooms within ICUs at an American teaching hospital.[20] QACs were also incorporated into environmental cleaning practices as a part of successful multicomponent outbreak interventions for MDR-AB.[11,15] Lastly, in one before-and-after study, the use of Bio-Kil (which contained QAC) compared with manual surface cleaning with 500 ppm sodium hypochlorite was found to disinfect and provide ongoing microbial activity, resulting in reduced environmental bacterial contamination and sepsis incidence in the ICU.[21]

QACs have also been included in interventions that use enhanced environmental cleaning practices. One cluster-randomized controlled trial supplemented routine cleaning of ICU rooms with a one-time disinfection of high-touch surfaces in each room. Both routine and enhanced cleaning used a QAC disinfectant. Adding the supplementary cleaning did not result in a significant difference in the

[m]Quaternary ammonium is commonly used in ordinary sanitation of patient care equipment and healthcare facility surfaces. Manufacturers indicate that it is generally fungicidal, bactericidal, and active against some viruses, but not sporicidal or tuberculocidal. For more information, refer to Rutala WA, Weber DJ. Disinfection, sterilization, and control of hospital waste. In: Bennett JE, Dolin R, Blaser MJ, eds. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 8th ed. Philadelphia, PA; 2015.

subsequent colonization of healthcare workers' gowns and gloves with MRSA or MDR-AB and thus was not determined to add value to environmental cleaning and disinfection practices.[22] While no clinical outcomes were reported, the contamination of healthcare workers' gowns and gloves is a suspected source of transmission to patients. This study did not provide sufficient evidence to support the use of QACs to target high-touch surfaces.

QACs are not sporicidal and thus should not be relied on to eradicate spore-producing organisms such as *C. difficile* from the environment.[18] They are also considered to have very low, if any, toxicity to humans.[21] Lastly, a cross-sectional in vitro study of 12 vancomycin-susceptible *E. faecium* and 37 vancomycin-resistant *E. faecium* isolates found that the resistant isolates had decreased susceptibility to benzalkonium chloride. Further research is needed to investigate the potential for MDRO cross-resistance with antibiotic resistance and QAC-based disinfectants.[23]

5.4.3.1.3 Hydrogen Peroxide

Several studies examined hydrogen peroxide in various forms for reducing/eliminating MDROs. Hydrogen peroxide was tested in four variations in a laboratory study. In this study, a novel hydrogen peroxide disinfectant including anionic and nonionic surfactants in an acidic product was compared in vitro with traditional hydrogen peroxide disinfectants. The "improved" hydrogen peroxide product was more effective in reducing bacteria than QAC or any of three tested concentrations of hydrogen peroxide.[24]

In a cross-sectional study of clinical isolates, vancomycin-resistant and vancomycin-sensitive bacteria were not found to differ in their minimum inhibitory concentrations for hydrogen peroxide (in contrast to chlorohexidine and benzalkonium chloride).[23] No further studies directly addressed the use of hydrogen peroxide in its liquid state for environmental disinfection of clinical settings. We discuss the use of hydrogen peroxide vapor and no-touch methods below.

Silver ions are used on antimicrobial surfaces and in cleaning products for their antibacterial properties. One in vitro study by De Giglio et al. (2014) investigated the use of a combination of 0.1% silver ion and 5% hydrogen peroxide disinfectant on sensitive and resistant strains of *Staphylococcus aureus* and *P. aeruginosa*. The disinfectant was effective for both sensitive and multidrug-resistant strains, although it took twice as long for the latter (10 minutes versus 5 minutes). The efficacy decreased in the presence of organic matter, doubling the required contact time for both sensitive and resistant strains.

This study indicates that use of silver ion solutions for disinfecting surfaces should be preceded by cleaning of any soiling or organic matter. In addition, close attention should be paid to contact time of the disinfectant, especially if multidrug-resistant strains are known to be contaminating the environment.[25]

5.4.3.1.4 Chlorhexidine

We found several before-and-after and outbreak studies of chlorhexidine and alcohol-based disinfectants, used separately or in conjunction. For example, one before-and-after study in an Italian burn ICU compared standard environmental cleaning using sodium hypochlorite with a chlorohexidine-60% isopropyl alcohol disinfectant. Additional changes were made to the daily cleaning regimen, including increased focus on high-touch surfaces and more frequent disinfection.

After the intervention, there was a decline in the percentage of positive carbapenem-resistant *A. baumannii* environmental cultures from 13 percent to 4 percent and a reduction in samples exceeding the acceptable adenosine triphosphate (ATP) limits from 21.7 percent to 14 percent.[19] A cross-sectional study of chlorohexidine for vancomycin-sensitive and vancomycin-resistant Enterobacteriaceae clinical isolates found a lower susceptibility to chlorohexidine in vancomycin-resistant isolates than in the drug-sensitive isolates.[23]

5.4.3.1.5 Multiple Disinfectants

Chlorine-based disinfectants have been used in combination with other disinfectant chemicals in outbreak settings. Enhanced cleaning was initiated at the start of an outbreak of *A. baumannii* during which the organism was isolated from 22 neonates in a neonatal ICU.[26] Infection control measures included disinfection with bleach for surfaces, hydrogen peroxide gas plasma for reusable equipment, and disinfection of nursery incubators with 4% chlorhexidine. The intervention also included closure of the ward and hand hygiene promotion. The last case occurred 8 months after the first identified *A. baumannii* isolate. The source of the outbreak was likely a mother admitted to the adult ICU.[26] The researchers credit control of the outbreak to enhanced infection control measures.

5.4.3.1.6 Other Disinfectant Agents

Sodium dichloroisocyanurate was used as part of a multicomponent intervention in a Korean ICU to stop an outbreak of carbapenem-resistant *A. baumannii.* The disinfectant was used for terminal and indepth cleaning, and effectiveness was audited with environmental cultures. Additional measures included contact precautions, patient isolation, and change to a closed suctioning mechanical ventilation system. Within 5 months of implementing these more intensive disinfection and isolation practices, there were no new colonizations or infections,[27] but it is not possible to separate whether this finding was due mainly to the disinfectants used or to other components of the intervention.

Glucoprotamin was investigated in one in vitro laboratory study included in our review. This disinfectant had varying levels of efficacy against several MDROs. For example, glucoprotamin was more effective against Gram-negative than Gram-positive bacteria. In addition, tetracycline-resistant *P. aeruginosa* was found to be more resistant to glucoprotamin disinfectant than was tetracycline-sensitive *P. aeruginosa,* but not at levels typically used in environmental cleaning.[28]

Phenolic agents were used in one pre-post intervention study in a large Thai tertiary care hospital. In the baseline period, no interventions were performed other than standard infection control practices. In the second intervention stage, sodium hypochlorite (bleach) was used for environmental cleaning. In the third intervention stage, phenolic agents with detergent were used for environmental cleaning instead of bleach, without any other changes to the intervention.

Compared with the pre-intervention period, the second stage that used sodium hypochlorite had a 67 percent reduction in colonization and infections by pandrug-resistant *A. baumannii* (from 3.6 to 1.2 cases per 1,000 patient-days; $p<0.001$) and the third stage using phenolic agents with detergent had a 76 percent reduction in infections and colonizations (from 3.6 to 0.85 cases per 1,000 patient-days; $p<0.001$).[16]

A separate before-and-after study tested similar stages for control of extensively drug-resistant *A. baumannii* (XDR-AB). The same researchers found that the use of sodium hypochlorite decreased clinical and surveillance isolates of XDR-AB compared with the use of detergent-disinfectant in the baseline

period. The rate decreased from 11.1 to 1.74 cases per 1,000 patient-days for clinical isolates (p<0.001); and from 2.11 to 0.98 per 1,000 patient-days for surveillance isolates (p<0.001).[8]

5.4.3.1.7 No-Touch Disinfection Methods

While traditional methods of disinfection require the manual application of chemicals to a contaminated surface, new no-touch disinfection methods are being developed. These techniques often supplement existing cleaning and disinfection policies or are implemented in outbreak situations in which routine cleaning practices have not been sufficient to reduce transmission. The two most common no-touch disinfection methods are hydrogen peroxide vaporization (HPV) and ultraviolet light-C decontamination (UV-C). We also briefly discuss studies about no-touch methods that use gas plasma, argon, helium, hydrogen peroxide/peracetic acid, and steam.

Ultraviolet disinfection was investigated by one before-and-after study, one cluster-randomized crossover study, three in vitro studies, two systematic reviews, and three nonsystematic reviews. One systematic review recommended that no-touch technologies such as UV (wavelength range not specified) should be used to augment traditional cleaning methods, especially for *C. difficile* and VRE.[29] A second systematic review stated that there is very low-quality evidence to support the efficacy of UV-C or xenon UV disinfection.[30]

Only two studies on no-touch methods included in this review took place in clinical settings. One before-and-after study found that UV-C radiation at close range was effective in reducing Gram-negative bacilli, *C. difficile*, *S. aureus,* and *Enterococcus* on computer keyboards.[31] The other study, a cluster-randomized crossover study found that adding UV-C room decontamination after standard cleaning reduced incidence of several target organisms, including three MDROs and *C. difficile*. The incidence of colonization or infection among exposed patients was lower after the addition of UV-C disinfection (relative risk [RR] 0.70, 95% CI 0.50–0.98; p=0.036).[18]

Two in vitro studies found UV-C disinfection effectively reduced bacterial load on environmental surfaces, although both concluded that the technology was more effective against MRSA than for *Candida* or *C. difficile*.[32,33] Presence of organic matter was also found to reduce UV-C efficacy,[33] indicating the importance of thoroughly cleaning soiled surfaces before UV-C disinfection.

Another study in a laboratory setting found 405 nanometer violet light (a slightly longer wavelength than UV light) was effective in reducing presence of ampicillin-resistant *E. coli*.[34] In summary, some evidence suggests that UV disinfection of patient rooms can reduce hospital-acquired infections caused by common MDROs and *C. difficile*, but much of the evidence comes from laboratory research and not clinical settings. In addition, standard cleaning and disinfection practices should be augmented and not replaced by this technology, especially if there is soiling of the surface being disinfected.

HPV was the focus of five before-and-after studies, one prospective cohort study, one cluster-randomized crossover study, and one systematic review. The five before-and-after studies [35-39] found HPV effectively reduced contamination from MRSA (two studies), VRE (one study), multidrug-resistant *A. baumannii* (four studies), multidrug-resistant Gram negative bacteria (MDR-GNB) (one study), and OXA-48 carbapenemase-producing Enterobacteriaceae (one study). HPV was also found to inactivate spores and to be effective for both porous and nonporous surfaces.[35]

A cluster-randomized crossover study by Blazejewski et al. (2015) found that HPV reduced MDRO contamination in patient rooms.[40] A prospective cohort study found patients admitted to rooms decontaminated using HPV were 64 percent less likely to acquire any MDRO ($p<0.001$) and 80 percent less likely to acquire VRE ($p<0.001$); acquisition of *C. difficile*, MRSA, and MDR-GNB were also reduced, although not statistically significantly.[n] In addition, one systematic review found evidence to support HPV effectiveness in decreasing VRE colonization and infection.[29] The studies suggest that HPV room decontamination both reduced environmental contamination by MDROs and MDRO transmission/acquisition in healthcare facilities.

Other no-touch technologies were each mentioned by one study, and additional research and evidence are needed before their safety and efficacy can be validated for use in reducing MDROs in healthcare settings. First, in a laboratory setting, Park et al. (2015) demonstrated that two types of plasma (an ionized gas), argon gas-feeding dielectric barrier discharge and nano-second pulsed plasma, effectively inactivated sensitive and resistant bacteria. The article did not discuss implementation or clinical applications.[41]

Helium and helium-air plasma are two other plasma decontamination technologies that were found by one in vitro study to reduce *S. aureus* and methicillin-resistant bacteria on glass surfaces,[42] but this technology was not effective for *C. difficile* spores. One last plasma technology, hydrogen peroxide gas plasma, was used as part of a multicomponent infection control intervention to stop an outbreak of XDR-AB in an Italian neonatal ICU.[26] This plasma technology successfully decontaminated the assisted-ventilation equipment that was partially implicated in the outbreak.

Another technology, aerosolized hydrogen peroxide and peracetic acid, had similar efficacy as HPV, in one cluster-randomized crossover study in a French ICU.[40] Lastly, steam vapor has been tested in laboratory studies on MDROs and has been found to be successful at decontaminating glass surfaces, even in the presence of organic matter.[43]

At present, HPV and UV decontamination are the most well-studied no-touch technologies and are discussed in the implementation section below because they differ in the time and effort each requires in a clinical setting. While other no-touch technologies have been developed and successfully tested in vitro to disinfect surfaces contaminated with MDROs, more studies will be needed before these can be applied in clinical settings.

5.4.3.2 Tools: Microfiber Cloths and Mops

Three before-and-after studies investigated the use of microfiber cloths in combination with one or more strategies to enhance cleaning. The use of microfiber cloths in daily cleaning and disinfection, in addition to patient cohorting, was implemented in a before-and-after study in a Spanish ICU. Care was taken not to reuse dirty cloths, and clean microfiber cloths were soaked in a bleach solution prior to use. This intervention was associated with a significant reduction in XDR-AB carriage.[44]

Another before-and-after study found that using microfiber cloths to clean along with fluorescent markers to identify the presence of organic matter to aid with cleaning reduced MDRO environmental

[n]Passaretti CL, Otter JA, Reich NG, et al. An evaluation of environmental decontamination with hydrogen peroxide vapor for reducing the risk of patient acquisition of multidrug-resistant organisms. Clin Infect Dis. 2013;56(1):27-35. doi: 10.1093/cid/cis839.

contamination of high-touch surfaces significantly, compared with a baseline period.[45] As part of another multicomponent intervention, microfiber cloths were used for daily cleaning in an ICU in the United States, resulting in decreased incidence of MDRO infections.[9]

5.4.3.3 Antimicrobial and Easy-To-Disinfect Objects and Surfaces

While certain contaminated areas are easy to clean and disinfect because of their accessibility and composition (e.g., flat, untextured, nonporous surfaces), other surfaces in a healthcare facility are more prone to harbor bacteria and are more difficult to decontaminate. Several innovations may decrease MDRO contamination of the environment and make cleaning and disinfection more efficient and effective.

In response to an outbreak of *A. baumannii*, an ICU in the United Kingdom implemented deep cleaning and disinfection, replaced items that were difficult to clean, and devised strategies to prevent contamination of regularly used medical equipment. For example:

- Patient binders were replaced with plastic-coated binders that could be wiped with disinfectant;
- Dressing trolleys—movable storage cabinets—were replaced with trolleys that had sealable doors to ensure they were only externally decontaminated; and
- Single-use bags were used to store equipment that was previously exposed. No additional cases of *A. baumannii* occurred after these interventions.[14]

Although not statistically rigorous, this study demonstrates that innovative strategies that replace everyday objects and tools can reduce MDRO transmission and make environmental disinfection simpler and more efficient.

Textiles, especially those frequently touched by infected or colonized patients (e.g., gowns, bed sheets, and blankets), can become contaminated and may be overlooked during standard cleaning operations. Two studies evaluated interventions that included replacing, decontaminating, or improving the antimicrobial properties of textiles found in patient rooms.

One before-and-after trial by Lee et al. (2017) disinfected all textiles and nurses' clothing in addition to other objects and surfaces with Bio-Kil (3-[Trimethoxysilyl] propyloctadecyldimethyl ammonium chloride), and found a statistically significant decline in the environmental bacterial burden compared with control rooms without this extra disinfection.[21]

Copper-oxide-impregnated woven linens were tested in six hospitals in a before-and-after study (the only textile intervention that was not combined with other interventions).[46] This fabric was used to produce patient gowns, pillowcases, sheets, washcloths, towels, and blankets. Compared with a prior period, after 180 days, there was a statistically nonsignificant 36.4 percent reduction in HAIs caused by MDROs ($p>0.05$). Using the combined metric of HAIs from both MDROs and *C. difficile,* the intervention had a statistically significant 39.9 percent reduction ($p<0.05$).

The use of antimicrobial materials for environmental surfaces was mentioned in one systematic literature review. Copper or silver ion surfaces were found by Tacconelli et al. (2014) to have ambiguous support in the literature reviewed in their study.[1]

5.4.4 Implementation

Overall, many of the studies reviewed included environmental cleaning and disinfection as part of a multicomponent intervention. With the use of multicomponent interventions, it is difficult to attribute the success of the intervention to any one component. However, in general, multicomponent interventions have been demonstrated to be very effective when measuring reductions in a variety of MDRO-related clinical outcomes. In one systematic review, researchers found that environmental cleaning interventions were most effective when implemented in conjunction with antimicrobial stewardship, evaluation of standard care, and source control for reducing acquisition of several MDROs.[47]

5.4.4.1 No-Touch Disinfection Implementation

In a cross-sectional survey of healthcare workers and patients in a hospital testing UV-C disinfection, 84 percent responded that the purpose of UV-C room decontamination was well explained to them. However, 39 percent of responding patients had at some time refused UV-C disinfection in their room or bathroom due to not feeling well (25%), wanting to sleep (13%), not wanting to be bothered (11%), and not liking the smell (5%).[48] This survey demonstrates the importance of educating patients that may be affected by no-touch disinfection interventions that take place in occupied patient rooms.

Time requirements need to be considered when selecting no-touch disinfection methods. HPV requires sealing off rooms and vents and can take as long as 1 hour and 45 to run. However, HPV is a favored no-touch method for some who cite its advantages of portability, lack of harmful residue, and low vapor temperature.[38]

5.4.4.2 Environmental Screening Methods

Detecting the presence of MDROs in the environment can be helpful as a tool to audit the thoroughness of cleaning and disinfection, determine a source of contamination and targeted cleaning and disinfection during outbreaks,[49] and test or compare methods of cleaning and disinfection.

Healthcare facilities can monitor the thoroughness and efficacy of cleaning and disinfection by testing for MDROs on environmental surfaces using fluorescent gel, microbial culturing, UV detectable powder, or ATP detection. For example, fluorescent gels and powders are visible only with UV light and can be applied to a variety of surfaces before environmental cleaning to illuminate surfaces that are missed.

We reviewed six studies that used one of these methods to monitor cleaning and disinfection thoroughness. Five studies used microbial cultures to monitor cleaning [7,20,49-51] and three studies used UV-detectable powders or gels for monitoring purposes.[22,49,50]

In outbreak and endemic settings, environmental screening may be useful in some situations, for example, to help determine a point source of contamination contributing to new cases or to enhance general cleaning and disinfection to prevent additional cases. One systematic review recommends environmental screening only if standard infection control practices (e.g., contact precautions, enhanced cleaning and disinfection) fail to stop an ongoing outbreak.[1]

Microbial culturing as a method of environmental screening is helpful in endemic situations where the environmental strain must be compared with the outbreak strain to understand their relatedness. ATP testing can also differentiate between bacterial species, although it does not provide an isolate that can be sequenced to compare strains. Five studies in this review used microbial culturing in outbreak or

endemic situations to locate point sources contributing to new cases, or gaps in routine cleaning, and target those surfaces for disinfection.[7,11,20,52,53]

In addition, two studies used environmental screening to inspect rooms for bacterial contamination before new admissions. If any samples were positive, new patients were not admitted to those rooms. These studies used microbial culturing[27] and ATP detection[9] for this purpose. However, microbial culturing can take hours to complete after collection of environmental samples, and although fluorescent substances provide a real-time method of monitoring cleaning practices, they are not as useful in detecting the presence of bacteria.

5.4.4.3 Unintended Outcomes

Deep environmental cleaning of patient rooms, cleaning or replacement of equipment, and other major changes or interventions can impact daily activities within healthcare facilities. During an outbreak, one ICU had to relocate all patients for 1 week during an intensive cleaning, with accompanying logistical challenges and inconveniences.[14]

The implementation of no-touch technology for room decontamination has budget and staffing implications. As mentioned by Haas et al. (2014), the regular use of technology such as UV disinfection requires planning to ensure that resources are not depleted, staff are trained and available, and attention is not diverted from other tasks and responsibilities.[54]

It is important to assess the appropriateness of a cleaning or disinfection strategy for the specific pathogens of concern in a facility. One report by Passaretti et al. (2013) noted that HPV demonstrated "incompatibility" with the paint in some hospital rooms. It may be prudent to investigate compatibility of new disinfection methods with paint or other sensitive surfaces in rooms where they will be used.[55] Testing could also be done in a small number of rooms before widely implementing a new technique, to avoid widespread damage.

In general, efficacy against MDROs should not be the only outcome of interest in laboratory or preliminary clinical studies. Biodegradability, toxicity, and phenotypic changes to pathogens of interest should be studied and considered when introducing new chemicals or technologies.

A cross-sectional study of environmental service workers in U.S. hospitals found that only 60 percent of respondents reported "always" knowing the type of isolation precautions to be followed when entering a room to perform terminal cleaning; 27 percent also responded that they were "often" or "always" worried that cleaning products might be harmful to them.[56] These responses highlight the importance of the health and safety of staff performing environmental cleaning and disinfection.

5.4.4.4 Education, Monitoring, and Feedback

Education, reeducation, monitoring, and feedback all contribute to successful interventions. One before-and-after study examined a monitoring and feedback program for 27 facilities and their environmental cleaning staff. After an initial education period and several feedback cycles of analysis and objective performance feedback, thoroughness of cleaning improved from 50 percent of surfaces cleaned to 85 percent of surfaces cleaned.[57]

In another before-and-after trial, staff were reeducated with detailed instructions for cleaning and disinfection. This approach resulted in decreased incidence of carbapenem-resistant *K. pneumonia*e.[10]

Reeducation was also featured in other studies found in this review.[12,52] A modeled intervention study also found that improving terminal cleaning thoroughness reduced patient acquisition of MDROs.[58]

Monitoring and feedback can help address any confusion that environmental cleaning workers may have. In a cross-sectional study of U.S. hospital environmental workers, 28 percent reported "never" or "sometimes" knowing when to use UV disinfection, 37 percent reported that it was "always" clear what items they were responsible for cleaning, 39 percent reported that they "often" or "always" avoided cleaning near patients to avoid disturbing them, and 40 percent reported that the over-bed table was "often" or "always" too cluttered to clean properly during daily cleaning.[56]

Monitoring and feedback of daily cleaning and disinfection practices could help identify and change these simple lapses in cleaning procedures and reduce HAIs. Unannounced audits were implemented in one outbreak study to encourage ongoing, thorough cleanliness.[14] After a pass rate was achieved for 3 consecutive weeks, auditing was stopped. This strategy could be useful for improving thoroughness of cleaning and during the initial phase of implementing new practices or policies.

Specific staff training to target problematic practices has also been studied in effective before-and-after study interventions. One study in a U.S. hospital used an initial observation period to identify problem areas, then educated staff on hemodialysis-related cleaning and disinfection and avoiding cross-contamination with personal objects.[49] Paired with other changes, this intervention significantly reduced colonization with *K. pneumoniae carbapenemase*-producing isolates.

Monitoring and auditing can be done via visual inspection of cleaning and disinfection practices or with the use of any of the environmental screening methods described above. Fluorescent markers and ATP detection are more commonly used for cleaning and disinfection auditing than are microbial cultures.[45,49,59]

5.4.4.5 Facility Policies

Policy changes in healthcare facilities can also help reduce environmental contamination and improve patient outcomes. In endemic or outbreak situations, some facilities have implemented policies requiring that rooms be certified as clean either by inspection[10] or by a series of negative environmental cultures before new patients can be assigned to the vacated room.[27] Some facilities also may determine that current cleaning and disinfection practices are insufficient and choose to revamp entire policies for environmental cleaning and disinfection. This approach is most common in outbreak situations when traditional practices have not been enough to stem transmission.[51,53]

With the implementation of no-touch disinfection technologies or other labor-intensive interventions, management may need to readjust staffing and assignments[49,60] and otherwise ensure appropriate staffing levels. These changes in policies may require additional staff education (e.g., how to set up a room and use an HPV machine) or additional funding for new staff or equipment purchases.[54,59]

5.4.4.6 Resources To Assist With Implementation

The following resources include information on environmental cleaning, monitoring, program implementation, and other infection control:

- The Agency for Healthcare Research and Quality's Effective Health Care publication *Environmental Cleaning for the Prevention of Healthcare-Associated Infections* is available at https://www.ncbi.nlm.nih.gov/books/NBK311016/pdf/Bookshelf_NBK311016.pdf.
- The CDC's *Guidelines for Environmental Infection Control in Health-Care Facilities* is available at https://www.cdc.gov/infectioncontrol/pdf/guidelines/environmental-guidelines-P.pdf.
- The CDC's Options for Evaluating Environmental Cleaning web page includes links to toolkits for evaluating environmental cleaning and monitoring terminal cleaning and instructions for creating an environmental cleaning program, available at https://www.cdc.gov/hai/toolkits/evaluating-environmental-cleaning.html.
- The CDC's *Chemical Disinfectants—Guideline for Disinfection and Sterilization in Healthcare Facilities* is available at https://www.cdc.gov/infectioncontrol/guidelines/disinfection/disinfection-methods/chemical.html.
- The Association for Professionals in Infection Control and Epidemiology provides Environmental Services resources at https://apic.org/resources/topic-specific-infection-prevention/environmental-services/.
- The U.S. Environmental Protection Agency, Office of Pesticide Programs, publishes a list of recommended cleaning products, "List H: EPA's Registered Products Effective Against Methicillin Resistant *Staphylococcus aureus* (MRSA) and/or Vancomycin Resistant *Enterococcus faecalis* or *faecium* (VRE)," available at https://www.epa.gov/sites/production/files/2018-01/documents/2018.10.01.listh_.pdf.

5.4.5 Gaps and Future Directions

Most of the evidence presented above is taken from outbreak studies and before-and-after interventions or from in vitro studies, and the evidence is weak to draw conclusions about efficacy and implementation. Randomized studies are a more rigorous approach and should ideally be designed with one or two variable changes between the study and control groups. Multicomponent interventions make it difficult to understand which specific elements are responsible for success. More single intervention studies on environmental cleaning for MDROs would be useful.

Of particular importance for future research is comparing disinfectants for use in environmental disinfection. A handful of studies have found that QACs reduce environmental contamination with MDROs and provide residual antimicrobial properties. Although they are low toxicity to humans, evidence is mixed to support their usefulness in disinfecting high-touch surfaces and textiles that are in close contact with HCWs and patients. In addition, they cannot be used for spore-forming organisms, such as *C. difficile*, and are not yet used or studied as commonly as sodium hypochlorite. Lastly, many of the no-touch disinfection technologies are relatively new and have not been rigorously compared with traditional cleaning methods in clinical settings to determine which are most advantageous.

References for Section 5.4

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5.5 PSP: Minimizing Exposure to Invasive Devices and Reducing Device-Associated Risks

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Key Findings

- Using devices minimally and appropriately and practicing hygiene and infection control precautions when inserting them are basic steps that can be taken to reduce device-associated infections.
- Further research is needed to determine the safest and most effective uses of antimicrobial locking solutions and catheter materials.
- Antimicrobial resistance has not been eliminated as a concern when using antibiotics in antibiotic locking solutions, impregnated catheters, or prophylactic treatment to prevent infections.
- Ongoing implementation education, monitoring, and feedback for medical staff, patients, and caregivers are recommended for improving adherence to recommended PSPs.

An invasive device is any medical device that is introduced into the body, either through a break in the skin or an opening in the body. Invasive devices include catheters, such as urinary catheters or central venous catheters, and endotracheal tubes used for mechanical ventilation. Medical catheters are tubes that serve purposes such as administering fluids, blood products, medications, and nutritional solutions; providing hemodynamic monitoring; and collecting urine and measuring urinary output.[1,2,o] Endotracheal tubes are inserted into a patient's trachea to provide an unobstructed passageway for oxygen and other gases (e.g., anesthesia) while a patient is mechanically ventilated.

The use of invasive devices in patients, while often medically necessary, has been associated with increased risk of invasive infections (e.g., bloodstream infections) and overall mortality.[3] From 2011 to 2014, catheter-associated urinary tract infections (CAUTIs), central-line associated blood stream infections (CLABSIs), and ventilator-associated pneumonias (VAPs) accounted for 38 percent, 24 percent, and 2 percent of all healthcare-associated infections, respectively.[4] The treatment of these infections is often complicated by resistance to commonly used antibiotics. Within these three categories of infections (i.e., CAUTIs, CLABSIs, and VAPs), the percentage of pathogens that exhibited drug resistance varied depending on species and antibiotic, but an estimated 14 percent were caused by an antibiotic-resistant pathogen.[4]

5.5.1 Practice Description

Because medical devices provide direct access for bacteria to enter the human body, they pose a significant risk for invasive MDRO infections. Although many of the studies in this review focus on infections that are not specifically MDROs, they were included for their relevance to the prevention and control of MDROs. This review identifies and discusses opportunities to reduce device-associated risks during a patient's care in a health facility. Key findings are presented in the box above.

[o]The most recent recommendations for catheter use (as of June 2019) from the CDC's HICPAC generally recommend against using indwelling urinary catheters to manage urinary incontinence in place of nursing care. However, the committee also acknowledges that further research is needed for non-indwelling (e.g., condom-style) catheters and for patients at risk of skin breakdown. This approach is in keeping with the overarching recommendation for appropriate indwelling urinary catheter use: only when necessary and only for as long as needed. For more information, refer to Gould C, Umscheid C, Agarwal E, Kuntz G, Pegues D. Guideline for prevention of catheter-associated urinary tract infections Atlanta, GA: Centers for Disease Control and Prevention; 2009. https://www.cdc.gov/infectioncontrol/pdf/guidelines/cauti-guidelines-H.pdf.

5.5.2 Methods

To answer the question, "What are the best device reduction and harm minimization practices?" three databases (CINAHL, MEDLINE, and Cochrane) were searched for "catheter-related infections," "endotracheal tubes," and synonyms in combination with "infection control," "microbial drug resistance," and associated phrases. Articles from 2009 to December 2018 were included.

The initial search yielded 396 results; after duplicates were removed, 342 were screened for inclusion, and 139 full-text articles were retrieved. Of those, 17 were selected for inclusion in this review. Articles were excluded if they were outside the scope of this review, included insufficient detail on a PSP, were unable to be retrieved, or were used in the review of another PSP.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

5.5.3 Review of Evidence

The resulting 17 studies that were selected for review include 6 systematic reviews, 4 laboratory studies, 3 before-and-after intervention studies, 3 retrospective cohort studies, and 1 randomized control trial. The six systematic reviews included studies from various international settings. Of the 11 individual studies, 5 took place in the United States or its territories, and 6 took place abroad.

The settings for these individual studies include patient homes, surgical wards, ICUs, dialysis units, tertiary care hospitals, teaching hospitals, and laboratories. The settings covered in this review span community and primary care, long-term acute care hospitals, rehabilitation centers, hospitals, and general healthcare settings.

5.5.3.1 Least Harmful Device Use—Catheters

To reduce the harms associated with catheter use (intravascular or urinary catheters), interventions can target several stages of their use:

- Avoiding unnecessary and inappropriate catheter use,
- Ensuring aseptic placement of catheters,
- Maintaining awareness and proper care of catheters in place, and
- Promptly removing unnecessary catheters.[5]

A systematic review by Patel et al. (2018) reviewed 102 studies with interventions aiming to reduce CAUTIs and CLABSIs. The review determined that the most successful interventions targeted multiple stages. For both CAUTIs and CLABSIs, successful interventions included protocols to remove by default based on certain criteria (e.g., time).[5] Other aspects of successful interventions (e.g., monitoring, auditing, and staffing) will be addressed in section 5.5.4.

The CDC also has a published set of guidelines for reducing both intravascular catheter-related infections and CAUTIs.[1,6] These guidelines have various recommendations for reducing harm throughout the phases of the patient's care, including:

- Timing of catheter placement,
- Selection of the appropriate catheter device,
- Use of hand hygiene,
- Aseptic technique strategies,
- Barrier precautions during device placement and care, and
- Use of systemic antibiotics (not recommended) and antibiotic lock solutions.

Several of these interventions will be addressed below, with additional information provided in section 5.5.4.4.

5.5.3.1.1 Urinary Catheters

Specific to urinary catheters, Mody et al (2017) conducted a large-scale before-and-after intervention study of 404 nursing homes that implemented a multicomponent strategy that included targeting multiple stages of device use. This study of community-based nursing homes used the Comprehensive Unit-based Safety Program (CUSP) toolkit for CAUTI, developed as part of the Agency for Healthcare Research and Quality Safety Program for Long-Term Care. The intervention targeted urinary catheter removal, aseptic insertion, incontinence care planning, and various training programs for staff, patients, and family.

The intervention reduced UTIs, perhaps indicating success in aseptic techniques, but did not reduce overall catheter utilization. The authors theorized that catheter utilization in nursing homes across the country was already relatively low at the start of the study, leaving little room for further reductions.[7]

The low utilization of urinary catheters in nursing homes was also confirmed in a systematic review by Meddings et al. (2017). The same review found that nursing home interventions involving improving hand hygiene, reducing catheter use, and enhancing barrier precautions were all effective at reducing UTIs in nursing home residents.[8] In an ICU setting, Patel et al. (2018) assessed that many successful interventions included a focus on removing a urinary catheter.[5]

Another systematic review compared methods of short-term (14 days or less) bladder catheterization (indwelling urethral catheterization, intermittent urethral catheterization, and suprapubic catheterization) in hospitalized adults.[9] For the outcome of UTI, evidence was not sufficient enough to support the use of one route of catheterization over the others to reduce infections.

Meddings et al. (2015) used the RAND/UCLA Appropriateness Method, a method for evaluating the appropriateness of medical technology, to refine criteria for the use of urinary catheters (indwelling Foley catheters, intermittent straight catheters, and external condom catheters) in hospitalized medical patients. Using the literature, the authors developed a list of potential indications for each catheter type and created different scenarios illustrating their use. A multidisciplinary panel of subject matter experts ranked the scenarios as appropriate, inappropriate, or uncertain; appropriateness is defined as use for which benefits outweigh risks. The authors conclude that Foley catheters should only be used to measure urine or manage incontinence if other methods have been exhausted or if there are medical indications where nonbarrier methods would increase harm (e.g., to improve healing of sacral ulcers).[10]

5.5.3.1.2 Intravascular Catheters

With respect to intravascular catheters, certain patient safety practices can be used to reduce the risk of infection when vascular access cannot be avoided. The practices included in our review focus on the use of antibiotics or specialized catheters that contain antimicrobial substances. The section below discusses these practices in further detail and their implications for antimicrobial resistance and other potential patient harm.

The CDC guidelines for preventing intravascular catheter-related infections provide recommendations for antibiotic and antiseptic use.[6] In general, for intravascular catheters, the CDC does not recommend the use of systemic antimicrobial prophylaxis. Instead, the CDC recommends the use of certain antiseptic ointments at the catheter exit site for dialysis catheters and recommends antibiotic locking solutions (discussed below) in certain situations.[6] For details on the strength of the evidence for each of these recommendations, please view the CDC guidelines referenced in section 5.5.4.

Regarding site placement of central venous catheters (CVCs), one systematic review of published ICU infection outbreaks found strong evidence to support the use of subclavian insertion sites compared with jugular or femoral sites to reduce the risk of CLABSI.[11] This practice is strongly supported by the CDC guidelines to avoid use of jugular or femoral insertion sites.[6]

As with most medical procedures that are physically invasive, sanitary practices are necessary and may reduce the risk of infected wounds and invasive infections. While no study in this review specifically addressed sanitary practices as an intervention, the CDC guidelines include detailed instructions on appropriate infection control procedures for intravascular catheters.[6] The strongest CDC recommendations include:

- Using sterile gloves when inserting arterial, central, and midline vascular catheters;
- Frequently performing hand hygiene,
- Using sterile gauze or sterile, transparent, semipermeable dressing to cover the catheter site; and
- Using chlorhexidine antisepsis for insertion sites in specific cases (see guidelines for details).[6]

One method of combating invasive infections associated with catheters is to reduce and restrict the growth of bacteria within the catheter itself. Bacteria often form biofilms within catheters that can inhibit catheter function and increase the risk of infection. In addition to preventing bacterial infections and biofilm formation, antibiotic lock (ABL) therapy reduces costs and vein damage associated with device replacement. ABL therapy is the insertion of a concentrated antibiotic solution into a catheter lumen (its internal channel or tube) to prevent the development of microbial biofilm on catheter surfaces.

In a study by Dixon et al. (2012), ABL therapy, as an adjunct to systemic antibiotic therapy, vs. systemic antibiotic therapy alone in patients with tunneled hemodialysis catheters, reduced CLABSI incidence by over 50 percent (RR 0.50 +/- 0.03; $p<0.0001$) and reduced treatment failure and relapses in the study group compared with the control group.[12] The CDC recommends that ABL prophylaxis only be used for hemodialysis patients with long-term catheters who have a history of multiple CLABSIs despite appropriate aseptic techniques during catheter care and insertion.[6]

In two studies identified in this review, no antibiotic resistance was found to be associated with their use in ABLs. One retrospective cohort study in the homes of patients in the Netherlands found taurolidine to be safe for up to 702 days.[13] Another retrospective cohort study in a dialysis unit in the United Kingdom found no increased risk of drug resistance when using vancomycin and gentamicin ABL solutions paired with systemic vancomycin and gentamicin.[12] However, increased prevalence of *S. aureus* and antimicrobial-resistant Enterobacteriaceae was found.

5.5.3.1.3 Catheter Innovations To Reduce Risk of Infection

Various catheter materials have been studied to determine their effectiveness at reducing biofilm formation and preventing catheter-related infections. Urinary catheters can be made of hydrophilic materials—which reduce friction during insertion, thus reducing the need for lubrication and the risk of urethral damage—or impregnated with antimicrobial chemicals to prevent colonization of the catheter with bacteria or fungi. Catheters can be constructed of latex, silicone, or other components; however, antimicrobial silver alloys may bind more readily to latex than to other materials.[14]

Table 5.7 summarizes the evidence found in two systematic reviews and five studies regarding the use of alternative urinary and intravascular catheter materials and antimicrobial-impregnated catheters. Three technologies were found to be successful in laboratory experiments: gum arabic capped-silver nanoparticle-coated devices[15]; catheters impregnated with rifampicin, triclosan, and trimethoprim[16]; and CVCs impregnated with minocycline and rifampicin (M/R) + chlorohexidine (CHX).[17] One review found gel reservoir and hydrophilic catheters to be safer than traditional sterile noncoated catheters.[18]

Silver-impregnated catheters were determined to have mixed evidence.[11] Catheters impregnated with both silver and chlorohexidine have been demonstrated to reduce colonization and CLABSIs, especially in settings with high background rates of CLABSIs[11] and are highly recommended by CDC if the CVC is expected to stay in place for more than 5 days.[6]

Lastly, M/R-impregnated catheters were the most well studied, cumulatively mentioned in five different abstracted articles. Use of these antimicrobial catheters was backed by one laboratory study[19] and one retrospective cohort study.[20] One systematic review concluded that evidence was mixed to support the use of M/R catheters.[11] Another innovation for increasing catheter safety is the use of needleless connectors, which were mentioned in one review as having mixed evidence regarding their efficacy.[11]

While some studies found a reduction in catheter contamination with needleless connectors, others observed an increase in infection rates temporally associated with their introduction. If needleless connectors are used, the CDC strongly recommends that an antiseptic be used to scrub the access port and that it be accessed only with sterile devices.[6]

The CDC guidelines previously referenced also include recommendations on urinary catheter materials. The CDC acknowledges the benefits of antibiotic-impregnated or antiseptic-impregnated urinary catheters in certain situations but also addresses a mix or lack of evidence demonstrating that they reduce UTI. The CDC also states that silicone and hydrophilic catheters may be preferable in certain situations (e.g., hydrophilic catheter use for intermittent catheterization).[1]

Table 5.7: Studies of Alternative Materials and Antimicrobial-Impregnated Catheters

Author, Year	Study Type	Patient Safety Practice	Evidence
Ansari et al., 2014[15]	Laboratory study	Use of gum arabic capped-silver nanoparticles (GA-AgNPs), as an antimicrobial surface coating material for surgical implants and instruments	The results of this laboratory experiment found that GA-AgNPs successfully penetrated biofilms, reduced biofilm formation, reduced biofilm coverage, and reduced bacterial colonization overall. The lowest minimum inhibitory concentration for extended spectrum beta-lactamase (ESBL), non-ESBL, and metallo-beta-lactamase *P. aeruginosa* was determined to be 11.25 mg/mL, indicative of a very strong bacteriostatic activity. The minimum bactericidal concentration was found to be in the range of 11.25–45mg/mL. At a concentration of 30 mg/mL, it arrested the biofilm formation without affecting the cell viability, whereas at a concentration of 60 mg/mL, the biofilm formation was completely blocked and the bacterial growth completely ceased.
Bayston et al., 2009[16]	Laboratory study	Impregnation of continuous peritoneal dialysis catheters using rifampicin, triclosan, and trimethoprim	Long-lasting ability to kill ~99% of pathogens associated with infection was seen in patients on continuous ambulatory peritoneal dialysis, even after very large challenge doses. In vitro challenge tests confirmed that this long-lasting activity could prevent colonization of the catheters in flow conditions for prolonged periods. Catheters stopped growth with no signs of resistance for 30 days, had a >98.9% reduction after 280 days' release of antimicrobials from the material, and after 72 hours failed to show bacterial migration down the track.
Bermingham et al., 2013[18]	Systematic review	Use of various materials and practices for urinary catheters, including: clean versus sterile noncoated intermittent self-catheterization, hydrophilic catheters, gel reservoir catheters, and clean noncoated catheters	People using gel reservoir and hydrophilic catheters were significantly less likely to report one or more UTIs compared with those using sterile noncoated catheters (absolute effect for gel reservoir = 149 fewer per 1,000 (95% CI, −7 to 198, p=0.04); absolute effect for hydrophilic = 153 fewer per 1,000 (95% CI, −8 to 268, p=0.04). However, the confidence intervals for these values were wide and overlapping. There was no significant difference in the incidence of symptomatic UTI for people using clean versus sterile noncoated catheters for long-term intermittent self-catheterization.
Doyle et al., 2011[11]	Systematic review	M/R and silver or chlorohexidine-silver sulphadiazine (CHX/SS) impregnated CVCs	This systematic review of outbreak studies reported a reduction in colonization and CLABSIs with both technologies, especially in settings with high background rates of CLABSIs.
Raad et al., 2008[19]	Laboratory study	CVCs impregnated with M/R, silver-platinum and carbon (SPC), and CHX/SS	M/R-CVCs were superior in antiadherence activity and prolonged antimicrobial durability against MDR *S. aureus* and other MRD Gram-negative bacteria.
Raad et al., 2012[17]	Laboratory study	Second-generation CVCs impregnated with M/R and CHX	CHX-M/R-coated catheters have unique properties in completely inhibiting biofilm colonization of MRSA, VRE, *P. aeruginosa*, and *Candida* spp. in a manner superior to that of M/R- or CHX-treated catheters.
Ramos et al., 2011[20]	Retrospective cohort study	CVCs coated with M/R	The incidence of CLABSI per 1,000 patient-days in the medical ICU significantly and gradually decreased from 8.3 in 1998 to 1.2 in 2006 (p<0.001) during the course of the intervention.

5.5.3.2 Reducing Ventilator-Associated Infections

A small number of articles identified and abstracted in this literature review focused on ventilator-associated infections, mainly referring to pneumonia. This is not an intensive review of ventilator-

associated infection reduction, but several PSPs were identified as well-supported or somewhat supported by the current literature to reduce risk of infection. The references listed below have up-to-date recommendations.

A systematic literature review by Doyle et al. (2011) found overall support in the literature for bed elevation of 30 to 45 degrees for mechanically ventilated patients. They also found supporting evidence for selectively decontaminating patients' digestive tract to prevent VAPs. These PSPs—bed elevation and selective decontamination—aim to reduce aspiration of bacteria in respiratory fluid and thus reduce pneumonia in ventilated patients.[11]

Subglottic secretion drainage (SSD) refers to removing bacteria-laden secretions that pool below the vocal cords but above the cuff of the endotracheal tube in mechanically ventilated patients was found by one randomized control study to be associated with lower rates of VAP and overall lower length of required ventilation.[21]

The same systematic literature review found only mixed evidence to support using topical antibiotics to decontaminate the oropharynx of patients on mechanical ventilation.[11] A before-and-after intervention study of 925 patients in an ICU administered polymyxin/tobramycin/ amphotericin B in the oropharynx and the gastric tube plus a mupirocin/chlorhexidine regimen in all intubated patients. This regimen lowered the incidence rates of intubation-related pneumonia (5.1 vs. 17.1 per 1,000 ventilator-days; $p<0.001$) in the experimental group.[22]

The Society for Healthcare Epidemiology of America (SHEA) and Infectious Diseases Society of America (IDSA) guidelines, "Strategies to Prevent Ventilator-Associated Pneumonia in Acute Care Hospitals," includes several recommendations covering the topics addressed by this literature review, as well as other PSPs. The recommendations are delineated for different populations (e.g., adults vs. neonates) and can be viewed at the link referenced in section 5.5.4.4 below.

The SHEA/IDSA guidelines state that there is moderate evidence to support the use of endotracheal tubes with a subglottic secretion drainage port for patients ventilated for more than 2 to 3 days and consider it a best practice. These guidelines also note that the quality of evidence was low to support the bed elevation discussed by Doyle et al. and that the quality of evidence was high for selective oral or digestive decontamination.

Additional guidelines from the SHEA/IDSA publication suggest additional PSPs for adult patients. PSPs with high quality of evidence include:

- Assessing the readiness to extubate daily,
- Interrupting sedation daily,
- Performing spontaneous breathing trials with sedatives turned off, and
- Changing the ventilation circuit only if visibly soiled or malfunctioning.

PSPs with moderate quality of evidence include managing patients without sedation whenever possible, facilitating early mobility, administering regular oral care with chlorhexidine, and providing prophylactic probiotics.[23]

5.5.3.3 Evaluation and Monitoring of Device Use

To reduce duration of device use, clinicians often must regularly reevaluate the need for the device and monitor any changes (e.g., the patient's dependence on the device). In the previously referenced systematic review, Patel et al. (2018) found that successful interventions aiming to reduce CLABSIs and CAUTIs often used checklists, auditing, and monitoring and focused on removal of devices. These checklists and monitoring procedures help reduce human error during the maintenance and removal of devices.[5]

The CDC guidelines for intravascular catheters also provide recommendations on device removal and care. These include assessment of an insertion site infection, removal of unnecessary catheters, quick replacement of catheters when aseptic technique cannot be ensured, and appropriate length of time to use certain types of catheters (e.g., up to 14 days for umbilical venous catheters).[6]

The CDC also has various recommendations on the evaluation and monitoring of device use for urinary catheters. These guidelines include the removing urinary catheters for operative patients as quickly as possible (<24 hours if possible), reducing kinking and obstruction of catheter tubes, and implementing guidelines to advise on proper catheter maintenance.

Lastly, the SHEA/IDSA guidelines include several recommendations on evaluation and monitoring of ventilator use. Some of these recommendations include changing the ventilator circuit if it is visibly soiled or malfunctioning, minimizing breaks in the ventilator circuit, and assessing the readiness to extubate daily. These recommendations are expanded on and delineated for certain populations in the full report, which can be viewed at the link provided in section 5.5.4.4 below.[23]

5.5.4 Implementation

5.5.4.1 Unintended Outcomes

Some of the above interventions, such as ABL solutions, topical skin ointments, and oropharynx decontamination involve the use of antibiotics. As with any antimicrobial use, overuse and inappropriate use can lead to increased drug resistance and increased risk of MDRO colonization or infection.

Regarding ventilator-associated antibiotic use, one before-and-after study discussed the effectiveness of selective digestive decontamination using polymyxin, tobramycin, and amphotericin B in the oropharynx and the gastric tube plus a mupirocin and chlorhexidine regimen in intubated patients. This study maintained that use of antibiotics in this scenario did not confer antibiotic resistance, but evidence showed that this practice increased the risk of MRSA infection and tobramycin resistance in aerobic Gram-negative bacilli such as *P. aeruginosa* and Enterobacteriaceae.[22] The SHEA/IDSA guidelines recommend that facilities with high levels of antimicrobial resistance not use digestive decontamination until higher quality, long-term studies are performed to assess the risks.[23]

Regarding ABL solutions, a retrospective cohort study in a dialysis unit found that after vancomycin and gentamicin catheter lock solutions were used, there was no statistically significant evidence of increased antimicrobial resistance. However, there was some change in the antimicrobial resistance profiles of

monitored pathogens, showing that the drug pressure did influence microbial flora and may need to be studied for longer periods.[12]

Another study investigated resistance to the antibiotic taurolidine and found that it was safe for use for up to 1,394 days. Resistance to the drug was most commonly seen in *Candida albicans*, although bloodstream infections were more commonly caused by *S. aureus* and other *Staphylococcus* species.[13] Although there is some evidence of the interaction of antibiotics in locking solutions and a patients' microflora, the CDC suggests (as a lower priority guideline) ABL prophylaxis, antimicrobial catheter flush, and catheter lock prophylaxis only for high-risk patients. High-risk patients have long-term catheters, have a history of CLABSI, and already adhere to maximal aseptic precautions.[6]

For intravascular catheters, the CDC states that antibiotic ointments and creams should not be used on insertion sites (other than dialysis catheters) because of the risk of conferring antimicrobial resistance and fungal infections. Chlorhexidine dressings are appropriate in some cases.[6]

In summary, this review highlighted potential increases in the antimicrobial resistance prevalence of clinically important pathogens. When considering the use of antibiotics to prevent CLABSIs, CAUTIs, or VAPs, clinicians should exercise caution and be diligent about referencing the existing guidelines, which specifically warn against or promote antibiotics for certain uses and populations. Further research is needed on long-term effects of antibiotic use for selective digestive decontamination and long-term use of locking solutions.

5.5.4.2 Cost-Effectiveness

Although not the focus of this section, two articles touched on cost-effectiveness of interventions discussed above. Doyle et al. (2011) found evidence that antibiotic-impregnated catheters were cost-efficient compared with standard catheters in high-risk populations.[11]

In a systematic review of the evidence to support gel catheters or hydrophilic catheters versus clear noncoated catheters, Bermingham et al. (2013) found that clear noncoated catheters were more cost-effective than single-use gel reservoir catheters. The review identified evidence that these clear noncoated catheters were less effective in preventing UTIs, so this information on cost-effectiveness will be important when considering the implementation of alternative materials.[18]

5.5.4.3 Interventions and Education To Reduce Device-Related Infection Risk

Ongoing education of patients, staff, and caregivers can also help reduce the harms associated with device use. The CDC recommends several education and implementation interventions for staff and patients to help improve outcomes associated with device use. Further, the CDC advises allowing only individuals (including family and at-home caregivers) trained in appropriate techniques for catheter insertion and maintenance to perform these tasks. Other agency recommendations include quality improvement programs to provide ongoing training for staff on all the PSPs discussed above: automated alerts to reassess the need for device use, written guidelines, auditing and feedback of staff practices, and periodic training on insertion, maintenance, and removal.[1]

The SHEA/IDSA guidelines also state that staff education can help maintain high levels of compliance with recommended practices. Staff educational activities include workshops, hands-on training, and use of multiple modalities to convey information. Making information accessible in pocket pamphlets,

posters, flowsheets, and other readily available modalities is also suggested. Finally, these guidelines state that educating patients and family on ventilator-associated guidelines can help them engage with and support the medical team's care.[23]

Within this review, two studies addressed education interventions for preventing CAUTIs. In a multifacility intervention within U.S. nursing homes, Mody et al. (2017) found success in reducing CAUTIs with a multicomponent intervention that included patient training on catheter care and a socioadaptive bundle emphasizing leadership, resident and family engagement, and effective communication.[7]

Lastly, Saint et al. (2016) performed a multifacility before-and-after study of implementation of the CUSP for CAUTI protocol (also known as On the CUSP: Stop CAUTI) to reduce CAUTIs in 603 hospitals across the United States. The multicomponent intervention included staff education on technical and socioadaptive factors, providing feedback to the units on CAUTI rates and catheter use, and addressing gaps in knowledge of urinary management processes.[24]

5.5.4.4 Resources To Assist With Implementation

The following resources include information on prevention of device-related infections; proper catherization use, duration, and removal; insertion site assessment and infection prevention; and other precautions to be taken when using catheters:

- AHRQ Toolkit To Reduce CAUTI and Other HAIs in Long-Term Care Facilities is available at https://www.ahrq.gov/professionals/quality-patient-safety/quality-resources/tools/cauti-ltc/index.html.
- AHRQ Toolkit for Reducing CAUTI in Hospitals is available at https://www.ahrq.gov/professionals/quality-patient-safety/hais/tools/cauti-hospitals/index.html.
- AHRQ Toolkit for Reducing Central Line-Associated Blood Stream Infections is available at https://www.ahrq.gov/professionals/education/curriculum-tools/clabsitools/index.html.
- The Ann Arbor Criteria for Appropriate Urinary Catheter Use in Hospitalized Medical Patients: Results Obtained by Using the RAND/UCLA Appropriateness Method includes guidelines for uses of various urinary catheters, a summary of their most common uses, and a daily ICU checklist for appropriateness of Foley catheter use (Meddings et al., 2015).
- CDC Guideline for Prevention of Catheter-Associated Urinary Tract Infections 2009 is available at https://www.cdc.gov/infectioncontrol/pdf/guidelines/cauti-guidelines-H.pdf.
- CDC Guidelines for the Prevention of Intravascular Catheter-Related Infections, 2011, is available at: https://www.cdc.gov/infectioncontrol/pdf/guidelines/bsi-guidelines-H.pdf).
- AHRQ Toolkit To Improve Safety for Mechanically Ventilated Patients is available at https://www.ahrq.gov/professionals/quality-patient-safety/hais/tools/mvp/index.html.
- TAP Catheter-Associated Urinary Tract Infection (CAUTI) Implementation Guide: Links to Example Resources is available at https://www.cdc.gov/hai/prevent/tap/cauti.html.
- SHEA/IDSA Strategies to Prevent Ventilator-Associated Pneumonia in Acute Care Hospitals: 2014 Update is available at

https://www.jstor.org/stable/pdf/10.1086/677144.pdf?refreqid=excelsior%3A71370b2e020eaf1ce0b6a59683810314.

5.5.5 Gaps and Future Directions

Gaps in evidence are listed within the guidelines cited above (e.g., CDC, SHEA/IDSA), and this review identified several gaps that require further research. In addition, further research is needed on the safety and efficacy of novel technologies such as GA-AgNPs,[15] the triple antibiotic combination discussed by Bayston et al. (2009),[16] and the newly developed M/R + CHX impregnated catheter discussed by Raad et al. (2012).[17] Further study is also needed on ABL solutions. Specifically, long-term studies on antibiotics in ABLs are needed to determine the risk of conferring drug resistance and increasing risk of infection.[12]

Kidd et al. (2015) stated larger sample sizes are needed to create adequately powered studies on alternative catheterization methods, such as suprapubic catheterization and intermittent self-catheterization compared with indwelling urinary catheters.[9] These methods are often cited as reducing risk of infections, but further research is needed to confirm and repeat the results of preliminary studies.

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5.6 PSP: Communication of Patients' MDRO Status

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A patient's positive MDRO status must be promptly communicated to patient care staff to ensure proper infection control practices are implemented and to protect patients against improper treatment (e.g., inappropriate antibiotic use). The timely and accurate dissemination of this information to all clinicians, visitors, and others in the facility who interact with those patients protects these individuals against MDRO transmission. Communication of an individual's past MDRO infections, documented asymptomatic carriage, and relevant high-risk healthcare exposures (such as transfer from a facility with a suspected or identified MDRO outbreak) should occur at every admission or transfer.

Key Findings

- Communication failures have been linked to poor patient outcomes, especially for vulnerable patient populations (e.g., immunosuppressed patients).
- Multimodal and redundant communication policies can improve communication compliance in settings with complex communication (e.g., organ donation) or with multiple care providers (e.g., transfers). Modes of communication can include checklists, brightly colored leaflets attached to medical records, and electronic or automated communication.
- Revisiting policies to ensure they are meeting a facility's needs, performing ongoing monitoring and feedback of policy compliance, and involving staff from multiple disciplines in policymaking are all important for improving patient status communication.

Effective communication also requires decisions about who needs to be notified, what information they need, and what privacy concerns exist in sharing this information. As soon as positive laboratory testing results are available, the laboratory should notify key clinicians and infection control personnel. These personnel should then communicate the appropriate precautions to all other staff, visitors, and others whose interaction with patients puts them at increased risk of MDRO acquisition. By implementing effective communication and infection control strategies, each healthcare facility can play a role in preventing local and ultimately global spread of MDROs. Key findings are presented in the box to the right.

5.6.1 Practice Description

The CDC recommends that all facilities have a system in place to communicate a patient's MDRO status to all necessary personnel before transfer of the patient.[1] Communicating a patient's MDRO status occurs at several points during the patient's interaction with the healthcare system. Intrafacility communication must begin when a positive laboratory test occurs or is highly suspected based on a patient's risk or previous exposures. The information must be disseminated to all clinicians interacting with the patient, visitors, and anyone whose patient interaction increases his or her exposure risk.

When patients are transferred between facilities, interfacility communication of patient status is required. Special care and attention to patient status communication must be taken in situations where patients are immunosuppressed and vulnerable to infection and where facilities may not have preexisting relationships or communication channels. Examples of information sharing strategies from case studies include electronic communication, a highlighted or annotated medical record or patient file, a transfer form, a brightly colored leaflet, verbal communication, and an automated alert.

5.6.2 Methods

The question of interest for this review is: What are the methods of MDRO status communication in a healthcare setting?

To answer this question, we searched three databases (CINAHL, MEDLINE, and Cochrane) for "information dissemination," "information sharing," "patient transfer," or "communication" in combination with "cross-infection," "prevention and control," "drug resistance," and relevant synonyms or similar phrases. Articles from 2009 to December 2018 were included.

The initial search yielded 140 results (including 8 from other sources). After duplicates were removed, 128 were screened for inclusion, and 54 full-text articles were retrieved. Of those, we selected 12 for inclusion in this review. Articles were excluded if they were out of scope or had insufficient detail about the topic of status communication or if the full article was not accessible.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

5.6.3 Review of Evidence

Of the 12 articles were selected for review, 2 were case studies, 2 were outbreak studies, 2 were cross-sectional studies, 2 were retrospective cohort studies, 1 was a systematic review, 1 was a prospective interrupted time series study, 1 was a prospective observational study, and 1 was a randomized controlled trial. Nine of the 13 included studies that took place in the United States, 1 took place in Australia, 1 took place in Italy, and 1 took place in Denmark. The systematic literature review was a review of German studies.

5.6.3.1 Intrafacility Communication

Timely and accurate dissemination of a patient's MDRO infection or carrier status is the first step that should be taken to control transmission within a healthcare facility. If a patient is high risk or highly suspected to harbor an MDRO, or if a positive test is received from a clinical laboratory as the result of active screening or routine clinical testing, steps should be taken to communicate the patient's status to all necessary staff. Examples of ways to communicate a patient's MDRO status include:

- Physical signs at the entrance to a patient's room or at the foot of the bed,
- Documentation in a patient's file (e.g., a brightly colored leaflet or note in the front of the file), and
- Checklists, policies, or electronic notifications that prompt providers to check patients' MDRO laboratory test results before interacting with and treating them.

In a prospective observational study of 101 inpatient transfers to radiology, Ong and Coiera (2010) identified and quantified the errors that occurred during intrafacility transfer. The Australian teaching hospital used a transfer form for continuity of care and a patient identity verification process when transferring a patient's care from one individual to another. The most common error that occurred during this process was "inadequate handover," which occurred 43.1 percent of the time and included a missing transfer form or omitted or incorrect information on the form.

While the results did not specifically report on communication of patient MDRO status, these lapses and inaccuracies in communication demonstrate weaknesses or failures in current practices that likely impact the transfer of knowledge about a patient's infectious status. This problem is reinforced by the fact that 2.9 percent of transfers had inappropriate infection control precautions, such as contact precautions.[2] This study demonstrates that despite an existence of facility policy, implementation and compliance were inadequate, even though four redundant stages of the communication process were identified. Strategies for improving implementation will be discussed in section 5.6.4.

A randomized crossover study in the same hospital compared the use of a checklist with the use of a colored cue card to communicate that a patient was highly infectious. Both strategies improved compliance with infection control precautions similarly compared with the control group (38% compliance). The colored cue card increased compliance to 73 percent, and the pretransfer checklist increased compliance to 71 percent. However, adherence to the checklist was low at 40 percent and was anecdotally reported to be criticized by staff as annoying or redundant.[3]

One Danish university hospital used a leaflet in the front of each patient file and distributed it to the patient's visitors, as well as positioning a sign at the patient's bedpost so that anyone reviewing the file or entering the patient's room was alerted to the patient's status and appropriate precautions.[4] This hospital placed patients on contact isolation precautions if they were positive for an MDRO, putting the patient in rooms only with other MDRO-positive patients, and using personal protective equipment (PPE) when in direct contact with the patient. This intervention of leaflets and signs contributed to a decrease in the number of patients needing isolation per 1,000 occupied bed-days, which declined from 0.94 (95% CI 0.74 to 1.14) to 0.65 (95% CI 0.43 to 0.87; p=0.021) for ESBL-*K. pneumoniae* (ESBL-KP). Researchers also noted a reduction in the rate of isolated ESBL-KP from 39.5 percent to 22.5 percent, although this finding was not statistically significant.[4]

This study showed that improved signage and documentation within a patient's file can improve compliance with contact precautions, thus reducing transmission and the need for additional patients to be put on contact precautions. Ultimately, reducing the number of patients on contact precautions can allow hospitals to conserve resources, such as single-use gowns, gloves, and individual patient rooms. It can also conserve the time of staff who would otherwise need to don and doff PPE and thoroughly decontaminate surfaces and equipment.

Intrafacility communication can be crucial during an outbreak situation, when communicating a patient's infection with a highly transmittable pathogen is necessary to implement proper infection control and prevent further spread. Enhanced communication was part of a multicomponent intervention implemented to stem an outbreak of carbapenem-resistant *K. pneumoniae* among severely immunocompromised ICU patients at the NIH Clinical Center in Maryland.[5] An interdisciplinary team held daily staff meetings to discuss the outbreak investigation and control methods, held weekly meetings to share new findings or developments, and provided email notifications with updates and infection control reminders. An information sheet about transmission of MDROs was also given to patients upon admission.

This successful multicomponent intervention included educating staff, patients, and families on proper infection control practices and keeping everybody updated and informed about the selected infection control practices to ensure understanding and compliance. This intervention involved thorough and constant intrafacility communication using electronic, paper-based, and person-to-person

communication.[5] This case study demonstrates that redundant communication and education through multiple modes were effective at reducing transmission.

The studies above demonstrate several methods of intrafacility communication that contributed to successful interventions. These methods included a visual cue (leaflets, signage), electronic record alerts,[6] continuity of care checklists (examples of which can be found in section 5.6.4, and intensive staff involvement and daily communication to heighten awareness during an outbreak among high-risk patients.

5.6.3.2 Interfacility Communication

Patients may be transferred between healthcare facilities for a variety of reasons, including a need for specialty care not offered at the current facility, cost or insurance coverage of medical procedures, or a shift from needing acute care to long-term care. These transfers become moments of vulnerability and possible failed communication regarding the status of a patient who may have an MDRO infection or colonization. Steps should be taken to strengthen communication between facilities in these situations to ensure that transmission does not occur. Specifically, the Council of State and Territorial Epidemiologists recommends that interfacility communication include information on patients' infection or colonization status, the organism with which they are infected, the recent and current antibiotic treatments used, and risk factors (e.g., invasive medical devices).[7]

Several outbreaks have been associated with lapses of communication during patient transfers. One outbreak study in Oregon[8] identified 21 cases of extensively drug-resistant *A. baumannii* in patients transferred between several skilled nursing facilities, acute care hospitals, and long-term acute care hospitals. Despite Oregon Health Department's recommendations for interfacility status communication, diagnosed cases were transferred between facilities with no communication of the patients' diagnosis. Transmission of the extensively drug resistant pathogen at other facilities was ultimately only detected due to voluntary surveillance and detection of other cases and a subsequent epidemiological investigation. This outbreak was the direct result of ineffective interfacility communication and the resulting failure to implement appropriate infection control practices.[8]

Oregon's example cautions that despite policies on interfacility communication, implementation was not adequate and an individual facility's own active surveillance program was needed to halt an outbreak. Implementation strategies such as periodic audits and monitoring and feedback may help improve compliance with existing facility guidelines.

Medicare and Medicaid require long-term care facilities (LTCFs) to communicate specific information when a patient is transferred to another facility or discharged.[9] While this requirement is only for LTCFs, it can be used as an example for other healthcare facilities to ensure proper continuation of care, especially infection control precautions such as contact precautions.

5.6.3.3 Communication During the Process of Organ Transplantation

A unique infection prevention challenge is posed by organ donation. Several organ donation-associated transmissions have been documented, despite existing policies that require communication of positive culture results by organizations such as the United Network for Organ Sharing (UNOS) and the Organ Procurement and Transportation Network (OPTN).[10]

A retrospective cohort study by Miller et al. (2015) found that poor communication could be implicated in several adverse outcomes after organ transplantation. The researchers investigated 56 infection events due to donor-derived transmission over a 2-year period and found that 18 were associated with errors in communication. Of these 18 infection events, 12 resulted in poor patient outcomes, including 6 deaths.

The communication errors included:

- A delay in communication of suspected donor-derived infection from the transplant center to the organ procurement organization (OPO) or OPTN,
- A failure to communicate positive laboratory results from the laboratory to the OPO or OPTN,
- A delay in communication from the OPO to the OPTN or transplant center, and
- Incomplete communication or erroneous test results.

This study points out the many complexities of communication in the organ donation process due to the many organizations and players involved. To improve communication during organ transplantation, the authors recommend continuous education of all involved clinicians on communication policies, evaluation and monitoring of compliance and failures in the system, safeguards to prevent errors in medical records or lab result reporting, and expedited donor autopsies and lab results.[11]

Ariza-Heredia et al. (2012) documented a successful case of interfacility status communication, where four organ recipients were exposed to *K. pneumoniae* carbapenemase from a donor's kidney, liver, and heart. The positive culture result of the donor was communicated before the transplants occurred, and appropriate antibiotics and contact precautions were implemented for the two recipients who developed infections. The donor's institution initially contacted OPTN, who then facilitated the prompt interinstitutional communication.[10]

In another U.S. case study,[12] two kidney transplants failed when the donor's positive *E. coli* infection was miscommunicated. The donor's laboratory results were incorrectly entered into the chart accompanying the donated organ, and no procedure was in place to ensure that the information was correct and communication of those results occurred. To prevent such failures in the future, the authors recommended multiple redundant communication strategies. These strategies include:

- The donor facility highlighting any positive MDRO results in the charts that accompany an organ,
- The donor facility noting expected dates of pending test results in documentation accompanying an organ, and
- Both the donor and recipient facilities following up to obtain any pending test results.

Doublechecking the donor's medical records for MDRO information is also a prudent step the OPO could take. These interfacility communication procedures and redundancies would protect organ donation recipients from life-threatening infection and failed organ transplants due to improper antibiotic administration or other inappropriate medical care.[12]

A retrospective cohort study performed in Italy (Mularoni et al., 2015) found that from 2012 to 2013, four organ recipients acquired a carbapenem-resistant Gram-negative bacterial infection due to donor

infection that was not communicated, unrecognized, or underestimated.[13] This error delayed the appropriate antibiotic treatment for these recipients. In one example, a patient was discharged from an ICU and antibiotic treatment was discontinued due to failed communication of the patient's positive blood culture result. In another case, a donor had an unrecognized UTI that was detected with a positive urine culture but not communicated to the recipient's caregivers. Lastly, underestimation of the risk of transmission from the donor's MDR infection resulted in inappropriate medical treatment of the recipient.

Lapses in communication during organ transplants may pose a serious threat to recipients and can result in rejected or failed organs as demonstrated in these reports. By improving this process of communication, clinicians promote patient safety and can improve post-transplant outcomes.

5.6.3.4 Unintended Consequences

Negative outcomes associated with inefficient or inaccurate status communication were observed in a handful of the studies in this review. A statewide registry created for CRE carriers in Illinois demonstrates a resource burden imposed by a communication system. Participants reported that manual data entry and manual queries for patients were burdensome and time consuming, so researchers are working to create an automated notification system.[14]

5.6.4 Implementation

As several examples in this review have pointed out, having policies in place does not guarantee effective implementation of patient status communication, be it during transfers, during organ transplantation, or within a facility itself. Engaging staff in new procedures and educating them on the steps involved are all important when applying new policies.

Methods for engaging staff in implementation could include:

- Performing needs assessments before developing new procedures,[15]
- Hosting multidisciplinary meetings to facilitate collaborative thinking or elicit feedback,[4,5]
- Distributing reports on infection rates and trends since implementation of communication procedures,[4] and
- Informing managers and other leaders of procedural changes.[4]

A cross-sectional survey of 448 infection control professionals in the United States reiterates the findings above. The factors that were found to improve implementation included:

- Distribution of copies of the policy to providers ($p=0.03$),
- Use of forms (i.e., checklists) to enhance infection control adherence ($p=0.0008$),
- Administrator-directed infection control activities ($p<0.0001$),
- A culture of data-driven decision making ($p<0.0001$),
- Communication of antimicrobial resistance trends to physicians ($p<0.0001$), and
- Interdepartmental coordination of patient care ($p<0.0001$).[16]

These tools used for changes in infection control policies can just as easily be applied to interfacility or intrafacility communication of patient MDRO status. Educating providers and staff on new policies by distributing educational resources can be part of continuing education on communication protocols. Checklists can be used to facilitate more thorough information exchange when patients are transferred within a facility. Improved communication and improved coordination of patient care foster an environment more conducive to continuity of information when interfacility communication occurs. Lastly, the reporting of data to demonstrate improvements in patient outcomes can reinforce making positive changes in facility practices that are connected to patient communication.

When implementing interfacility communication protocols, facilities may benefit from reaching out to State health departments or national organizations such as UNOS. Many already have relationships with healthcare facilities, know the appropriate contacts there, and can facilitate meetings or discussions among facilities. For example, the Oregon Health Department helped create a form and process for facilities to use with newly admitted and transferred patients. State health departments should continue to encourage and facilitate interfacility discussion about MDRO communication practices, and smaller local health departments or healthcare facilities should reach out to these larger organizations to ask for assistance in improving intrafacility communications.

5.6.4.1 Resources To Assist With Implementation

Additional resources and tools to aid in the implementation of patient status communication and infection control are listed below.

- CDC's Inter-Facility Infection Control Transfer Form for States Establishing HAI Prevention Collaboratives is available at https://www.cdc.gov/hai/pdfs/toolkits/Interfacility-IC-Transfer-Form-508.pdf.
- The CDC's Interim Guidance for a Public Health Response To Contain Novel or Targeted Multidrug-Resistant Organisms (MDROs) is available at https://www.cdc.gov/hai/containment/guidelines.html.
- CDC's MDRO Management Guidelines is available at https://www.cdc.gov/infectioncontrol/guidelines/mdro/index.html.
- Oregon's Guidance for Control of Carbapenem-Resistant Enterobacteriaceae: 2016 Oregon Toolkit is available at https://www.oregon.gov/oha/PH/DISEASESCONDITIONS/DISEASESAZ/CRE1/cre_toolkit.pdf.

5.6.5 Gaps and Future Directions

More rigorous research studies in a variety of geographic areas and healthcare settings are needed to evaluate the most effective ways to communicate patient status (e.g., checklists vs. brightly colored leaflets in patient files). Facilities that often exchange patients or are part of larger health systems are encouraged to develop relationships with one another to develop strategies and policies for patient MDRO status communication, if not regulated by the government as in the case of LTCFs.

More research and innovation are needed to promote consistent use of technology-based and paper-based communication of patient MDRO status, such as laboratory results in organ transplantation. Lastly, an iterative review of status communication policies is important to ensure that policies are

useful, easy to implement, and meet the needs of the ever-changing world of infection control and prevention.

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Conclusion and Comment

In this review, we examine the evidence supporting the use of individual safety practices. However, many of the studies on the efficacy of patient safety practices examine bundled approaches or implementation of multiple practices at once, making it difficult to assess the effectiveness of any one practice. Further, improving compliance with one practice (for example, hand hygiene at every opportunity) can reinforce compliance with others, making each practice more successful when combined with others. Understanding the limitations of the available evidence, we make the following recommendations:

- The level of evidence to support hand hygiene for MDRO infection prevention is high. What is needed is further study about the best ways to sustain high compliance with hand hygiene at every opportunity. Increasing compliance may require new technologies, institutional policies, and approaches to reducing the barriers that result in missed opportunities for hand hygiene.
- While active surveillance has evidence to support its use in preventing MDRO acquisition and infection, there is no consensus on the optimal surveillance strategy, due to variation in patient risk factors, local epidemiology, and facility laboratory capability. Some cost-effective suggestions include active surveillance testing of samples (including routine clinical samples) for multiple MDROs and developing risk-based surveillance protocols based on which MDROs are likely to be encountered.
- There is a high level of evidence supporting the use of chlorhexidine bathing, both for preventing MDRO acquisition and as part of decolonization strategy (to reduce transmission opportunities). Chlorhexidine bathing is relatively low cost to implement, and adverse events are rare and resolve when chlorhexidine use is stopped. There is some evidence that the use of chlorhexidine may be selecting for resistance, but no clinical impacts have been documented in the literature reviewed.
- While some evidence supports the efficacy of different solutions for environmental cleaning in laboratory settings, more studies are needed evaluating the relative efficacy of disinfection agents against different MDROs in a clinical setting. These studies should also control for other infection control practices.
- Bundle approaches for reducing device-associated infections have strong evidence to support their use for infection prevention, regardless of the type of pathogen. More evidence is needed to understand the risks of increased resistance introduced by the use of antimicrobial solutions and devices.
- There is strong evidence to suggest that failure to communicate patients' MDRO status can lead to poor patient outcomes, but there are no rigorous analyses or comparisons of optimal communication approaches for MDROs.

6. Carbapenem-Resistant *Enterobacteriaceae*

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Introduction

Background

Carbapenem-resistant *Enterobacteriaceae* (CRE) encompass a family of gram-negative bacteria that cause infections with high mortality rates and few therapeutic options due to their ability to confer resistance to many different antibiotics.[1] Different mechanisms cause the carbapenem resistance, with carbapenemase-producing CRE (CP-CRE) considered primarily responsible for the increase in the spread of CRE.[2] CP-CRE produce enzymes that break down many antibiotics: penicillins, cephalosporins, monobactams, and carbapenems. This trait is most commonly seen in *Enterobacteriaceae*, which include clinically important bacterial species such as *Escherichia coli* (*E. coli*) and *Klebsiella pneumoniae*.[3]

Because of the public health risk CRE poses, predominantly attributed to the rapidly spreading CP-CRE, healthcare facilities must implement stringent infection control practices to reduce CRE-associated transmission and to ensure that healthcare settings remain safe for patients. Many toolkits and guidance documents exist to assist healthcare workers and infection control specialists to design and implement their CRE prevention policies. This systematic literature review assesses the implementation and effectiveness of contact precautions to prevent CRE in healthcare settings. The review's key findings are located in the box on the next page.

Importance of Harm Area

CRE is commonly associated with clusters and outbreaks in healthcare settings and is responsible for increasing morbidity, mortality, and healthcare costs worldwide.[3] In the United States, 42 States over the past decade have had at least one type of CRE infection diagnosed in their medical facilities. About 4 percent of hospitals and 18 percent of long-term acute care hospitals (LTACHs) had a patient with a CRE infection in 2012.[4] A study of blood and cerebrospinal fluid isolated from invasive *Klebsiella pneumoniae* infections in Europe showed an increase in carbapenem resistance from 4.6 percent in 2010 to 8.3 percent in 2013.[5]

Carbapenem resistance can be transferred between patients and between different species of bacteria via plasmids, allowing the rapid spread of the resistance gene within healthcare and community settings.[6] Although CRE are largely associated with nosocomial transmission, species within the *Enterobacteriaceae* family (such as *E. coli*) have been associated with community-acquired infections and outbreaks in the past.[2] Therefore, as CRE becomes more prevalent, both nosocomial and community transmission should be considered when developing prevention efforts.

Mortality among patients with CRE infections can be as high as 40 to 50 percent due to both the severity of the infections and the lack of effective antibiotics with which to treat them.[2] Because of their increasing global incidence and associated morbidity and mortality, the World Health Organization recently identified CRE as critical pathogens requiring focused prevention research.[7]

Prolonged inpatient stays increase the risk of exposure to and colonization by CRE.[8] Additionally, patients in long-term care facilities or those who received medical care in CRE-endemic regions are at increased risk for colonization.[2] Other risk factors include intensive care unit (ICU) stay, poor functional status, underlying medical conditions, and receipt of antibiotics.[9]

Methods for Selecting Patient Safety Practices (PSPs)

CRE are predominantly transmitted through person-to-person contact in healthcare settings (the other route being contact with environmental fomites). Transmission-based precautions are the most important means of eliminating nosocomial transmission. Organism-independent PSPs (such as general hand hygiene and environmental cleaning practices) are covered in greater detail in Chapter 5 of this report, "General MultiDrug-Resistant Organisms." This chapter specifically focuses on transmission-based precautions for CRE prevention.

Key Findings:

- Contact precautions have been shown to reduce transmission of CRE as part of infection control bundles in a variety of healthcare settings, including long-term care facilities and acute care facilities.
- Active surveillance is recommended in outbreak scenarios, in highly endemic regions, and in healthcare facilities or units with ongoing transmission.
- Further research is needed to develop accurate risk assessment tools for determining risk of CRE colonization at hospital admission in order to inform preemptive contact precaution policies.
- Comprehensive policies are needed to ensure appropriate use of contact precautions, regular compliance monitoring, and ongoing staff education.
- Additional research is needed to determine whether there is an appropriate time to discontinue contact precautions based on duration of CRE carriage.

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6.1 PSP: Contact Precautions To Prevent CRE Infections

Contact precautions are one of three types of transmission-based precautions to control the spread of infectious diseases, the other two being airborne and droplet precautions. Contact precautions are currently recommended to prevent nosocomial transmission of CRE for patients with known or suspected infections or at an increased risk of infection with CRE.[1,2] Maintaining appropriate contact precautions can be challenging for patients undergoing procedures or those who are critically ill and require intensive patient care. Contaminated stool and bodily fluids can transmit CRE, making environmental contamination a concern for patients who are incontinent, who have draining wounds or secretions, or who require high levels of care.[1] Patient transport within and between healthcare facilities also complicates strict adherence to contact precautions. However, when successfully implemented, contact precautions have been shown to reduce transmission of CRE in healthcare facilities.

6.1.1 Practice Description

Contact precautions include appropriate patient placement (e.g., single-patient spaces), use of personal protective equipment, a reduction in the movement and transportation of the patient, the use of disposable or dedicated patient-care equipment, and the frequent and thorough cleaning of patient spaces (especially high-touch surfaces and equipment in close proximity to the patient).[3] Variations on implementation of contact precautions differ by setting, risk of transmission, and the type of care being provided.

Some level of patient isolation should also be a part of contact precautions when feasible. This may include:

- Isolating carriers or individuals infected with CRE in single rooms with attached bathrooms.
- Isolating carriers into rooms shared only by other patients colonized or infected with the same pathogen.
- Cohorting staff (to reduce staff-to-patient transmission), defined as using a dedicated team of healthcare staff to care for patients infected with a particular multi-drug resistant organism (MDRO).
- Prioritizing patients at higher risk of transmission for single rooms, and rooming the remaining carriers or infected individuals together.

Of these options, single patient rooms are always preferred whenever possible. The placement of appropriate signs outside patient rooms is essential to alert staff and visitors to the isolation status of the patient(s) whose room(s) they are entering.

In addition to the contact precaution practices described above—particularly during invasive procedures—contact precautions may include full-head protection and/or face masks. Molter and colleagues advised, when feasible, individual supplies and equipment dedicated to a colonized patient should be used.). However, more studies are needed to determine which variations or additions to contact precautions improve control of CRE transmission.

6.1.2 Methods

To answer the question, “What are effective contact precautions for CRE in healthcare settings?” we searched three databases (CINAHL®, MEDLINE®, and Cochrane) for “Carbapenem-resistant

Enterobacteriaceae" as a keyword term, as well as "cross-infection," "contact precautions," "dedicated staff," "prevention and control," "patient isolation," and similar synonyms. English-language articles published from January 2009 through December 2018 were included. The initial search yielded 69 results. After 13 duplicates were removed, the remaining 56 articles were reviewed and 52 full-text articles were retrieved. Of those, 21 were selected for inclusion in this review. Articles that were excluded had insufficient detail, were of limited rigor, or were not available in English.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

6.1.3 Review of Evidence

Of the 21 articles we reviewed, 3 were systematic reviews and 18 were studies. One of the systematic reviews had a general focus on CRE in healthcare settings, whereas the other two focused specifically on hospitals and outbreaks in acute care hospitals. Of the 18 studies, 11 took place in international settings and only 1 took place in the United States. These studies included:

- 10 pre-post intervention studies.
- 3 outbreak investigations.
- 2 cross-sectional surveys.
- 1 model-based study.
- 1 prospective observational study.
- 1 ambidirectional cohort study.

All but one study included contact precautions as part of an intervention with multiple PSPs. Studies also included active surveillance (n=7), staff/patient/equipment cohorting (n=7), patient isolation (n=6), staff education (n=5),hand hygiene (n=4), monitoring and feedback (n=4), and other topics (n=6). Other topics included: environmental cleaning, chlorhexidine bathing, personal protective equipment use, staff attitudes toward contact precautions, an interdisciplinary outbreak intervention team, and antimicrobial stewardship.

6.1.3.1 Initiating Contact Precautions

Contact precautions are often initiated following a positive screening test. Active screening using perirectal swabs or swabs of other body sites may be used to screen patients for CRE colonization for the purpose of initiating contact precautions. The European Centers for Disease Control and Prevention (ECDC) recommends active screening on admission to specific wards or units (e.g., oncology units), during outbreak scenarios, and upon admission to a hospital.[4]

Active surveillance (upon admission) may not be appropriate in all settings. In units that regularly perform contact precautions, such as ICUs, active screening may be unnecessary. For some organisms, such as extended-spectrum beta-lactamase (ESBL)-producing bacteria, active surveillance has not been found to reduce transmission.[5] Active surveillance also may not be appropriate in settings where the prevalence is low. A study in a large tertiary care hospital in South Korea found that transmission of CRE

was reduced without implementing active screening, which they deemed inefficient given the hospital's location in a low-prevalence setting.[6] That hospital's multi-faceted intervention included antibiotic stewardship measures, contact isolation, and enhanced monitoring of hand hygiene practices. Passive surveillance may be sufficient to reduce transmission in low-endemicity settings—initiating contact precautions only if a CRE infection is identified during the course of clinical care, as opposed to screening upon admission.

Pre-emptive isolation relies on identifying CRE carrier risk factors at admission to the facility, which requires information about potential risks. The Centers for Disease Control and Prevention (CDC, 2015) recommends isolating patients who transfer from high-risk settings (e.g., hospitals in endemic areas or facilities with known outbreaks).[1] Djibré et al. (2017) used risk factors to predict carrier status and to reduce unnecessary additional contact precautions in an ICU setting. Their prediction model had a low positive predictive value of 18 percent but a relatively high negative predictive value of 93 percent for predicting carriage of any MDRO, which allowed them to reduce unnecessary contact precautions. The risk factors in their model included: exposure to antibiotics within the preceding 3 months (odds ratio [OR]: 1.64, 95% confidence interval (CI), 0.68 to 3.94, p=0.27), chronic dialysis (OR: 2.16, 95% CI, 0.53 to 8.69, p=0.28), and recent (within the past year) prior hospital stay for more than 5 days (OR: 2.38, 95% CI, 1.04 to 5.46, p=0.04).[7]

A meta-analysis performed by van Loon et al. (2017) pooled ORs from 43 studies to assess risk factors for acquiring a CRE. This meta-analysis found that the greatest pooled ORs were for carbapenem exposure (OR = 4.71, 95% CI, 3.54 to 6.26) and cephalosporin use (OR = 4.49, 95% CI, 2.42 to 8.33).[8]

Further research is needed to design a decision tree or risk score that can be used as a simple and accurate screening tool in a variety of settings. A study performed at the Johns Hopkins Hospital found that despite their assessed risk factors at admission (history of vancomycin-resistant *Enterococcus,* methicillin-resistant *Staphylococcus aureus*, and/or multi-drug-resistant gram-negative organisms), 57 percent of CRE-colonized patients and 50 percent of patients colonized with CP-CRE were not isolated with contact precautions (Goodman et al., 2018).[9] The Johns Hopkins study demonstrates that even with a review of a patient's history at the time of hospital admission, many CRE carriers are missed, and are placed on contact precautions only after a positive clinical culture is isolated. This type of study is valuable for determining the positive predictive value of existing methods for preemptively assessing risk, and similar research is needed to assess the risk prediction models suggested in other studies and guidance documents.

6.1.3.2 Contact Precautions Examples and Summary

The literature we reviewed included many examples of successful contact precautions that reduced CRE transmission in various settings, as shown in Table 6.1. All these interventions combined contact precautions with other interventions, including screening, patient and staff cohorting or isolation, staff education, pre-emptive contact isolation using risk factor analysis, environmental cleaning, compliance monitoring, and/or hand hygiene. Studies reporting on bundled interventions are limited in their ability to attribute successful reductions in transmission to any one intervention. This weakens the evidence in support of contact precautions significantly and should be taken into consideration when reading this review. Additionally, most of these studies were pre-post interventions and took place during nosocomial outbreaks of CRE.

Table 6.1: Summary of Studies on Contact Precautions

Study	Intervention(s)	Results
Arena et al., 2018[10]	• Presumptive and standard contact precautions and cohorting • Admission/weekly screening	At admission, 11.6% of patients were colonized, and 9.9% of those negative at admission subsequently became colonized. The intervention was associated with a decline in the incidence of carbapenem-resistant *Enterobacteriaceae* (CRE) colonization in the Severe Brain Injury ward (from 17.7 to 7.2 acquisitions/100 at-risk patient-weeks, p<0.05), but not in other wards. The change was not statistically significant.
Ben-David et al., 2014[12]	• Contact isolation • Active surveillance • Periodic on-site assessments of infection control policies and resources	In long-term acute care hospital (LTACHs), prevalence among those not known to be carriers decreased from 12.1% to 7.9% (p=.008[1]). Overall carrier prevalence decreased from 16.8% to 12.5% (p=0.013[1]). Appropriate use of gloves was independently associated with lower incidence of new CRE carriers.
Ben-David et al., 2019[13]	• Population-tailored contact precautions • Staff education • Active surveillance • Real-time notification of healthcare facilities when cases were detected upon transfer or admission screening, by establishing a repository of all CRE carriers and events of acquisition	Incidence per 10,000 patient-days declined to approximately 50% of baseline (p<0.001), from 2.5 to 1.2 for post-acute care hospitals, from 2 to 0.8 for skilled nursing facilities (SNFs and from 0.5 to 0.3 for nursing homes (NHs. The number of SNFs and NHs experiencing ≥ 5 CRE acquisitions annually decreased from 35 to 11. The incidence of CRE acquisition declined between 2009 and 2015 in all facility types, as expressed by an incidence rate ratio (IRR) of <1/year (PACHs: 0.90, 95% confidence interval (CI), 0.88 to 0.92, p< 0.001; SNFs: 0.87, 95% CI, 0.85 to 0.90, p<0.001; NHs: 0.93, 95% CI, 0.91 to 0.95, p<0.001).
Borer et al., 2011[15]	• Pre-emptive and standard contact precautions • Patient cohorting • 1:4 nursing ratio • Improved signage • Dedicated staff and equipment • Visitor education	CRE incidence declined from 5.26 to 0.18 per 10,000 patient-days (p<0.001[2]) with carbapenem-resistant *Klebsiella pneumonia* in a tertiary care teaching hospital.
DalBen et al., 2016[20]	• Contact precautions • Hand hygiene • Compliance monitoring of hand hygiene and contact precautions (audit and feedback)	CRE R_0 decreased from 11 to 0.42 (range, 0-2.1[2]); and median prevalence of patients colonized with CRE decreased from 33% to 21%.[2] The authors used a mathematical model to provide a real-time decision report to an ongoing before-after trial in an ICU.
Djibré et al., 2017[7]	• Reductions in preemptive advanced contact precautions based on risk factors	The rate of acquired multi-drug resistant organisms (MDRO) (positive screening or clinical specimen) was similar during both periods (respectively, 10%, n=15 and 11.8%, n=15; p=0.66[2]).
Jalalzaï et al., 2018[5]	• Universal contact precautions • Active surveillance cultures (ASCs)	Intensive care unit (ICU)-acquired extended-spectrum beta-lactamase (ESBL)-positive clinical *Enterobacteriaceae* infections occurred in 1.1% of patients admitted during the ASC period and 1.5% of patients admitted during the no-ASC period (p=0.64). An admission during the no-ASC period had no impact on the risk of ESBL infections (odds ratio, 1.16, 95% CI, 0.38 to 3.50, p=0.79), in-ICU death (hazard ratio, 1.22, 95% CI, 0.93 to 1.59, p=0.15), and extended length of stay (standardized hazard ratio[3] of discharge for admission during the no-ASC period, 0.89, 95% CI, 0.79 to 1.01, p=0.08).
Kim et al., 2014[6]	• Contact precautions • Hand hygiene • Monitoring and feedback	In a South Korean teaching hospital, CRE incidence increased from 1.61 in 2008 to 5.49 in 2009, and 9.81 per 100,000 patient days in early 2010. After intervention, CRE incidence declined to baseline levels in 2011 and the decrease was sustained (p<0.001).

Study	Intervention(s)	Results
Molter et al., 2016[17]	• "Extended" contact precautions (hand hygiene, gowns, gloves, face masks, head protection, cohorted staff and patients, individual supplies/equipment, separate communal facilities for carriers) • Weekly staff education • Interdisciplinary outbreak intervention team	After the implementation of the intervention during an outbreak in a tertiary care hospital, there was no contamination of environmental surfaces or equipment and no new cases after 4 days.
Robustillo-Rodela et al., 2017[11]	• Contact precautions • Staff education • Environmental cleaning • Chlorhexidine bathing	During an ICU outbreak, the cumulative incidence of OXA-48-like carbapenemase producing *Enterobacteriaceae* decreased 77% ($p<0.05$), from 3.48% to 0.79%. Incidence of multidrug-resistant *Acinetobacter baumannii* did not change following the intervention.
Rossi Gonçalves et al., 2016[16]	• Contact precautions • Bedside alcohol gel • Active screening	A CRE outbreak in a university hospital in Brazil was not contained. Poor compliance with infection control measures such as contact precautions and hand hygiene led to the dissemination of colistin-resistant KPC-producing *Klebsiella pneumoniae*.
Schwaber et al., 2011[14]	• Contact isolation • Evaluation and feedback • Patient/staff/equipment cohorting	Pre-intervention, the monthly incidence of nosocomial CRE was 55.5 cases per 100,000 patient-days. During intervention, increase in incidence stopped and eventually reduced to 11.7 cases per 100,000 patient-days ($p=0.001$). There was a direct correlation between compliance with guidelines and success in containment of transmission (effect estimate -0.06, 95% CI, -0.11 to -0.1, $p=0.02$) (as shown in Table 1 in article).
Sypsa et al., 2012[18]	• Contact precautions • Hand hygiene • Active surveillance • Isolation/cohorting	Mathematical modeling of the interventions suggested that, assuming 60-80% hand hygiene compliance, this multifaceted intervention would result in a 60-90% reduction in number of colonized patients.
Toth et al., 2017[19]	• Enhanced contact isolation • Active surveillance	The model's intervention effect on transmission reduction ranged from 79% to 93%.
Viale et al., 2015[28]	• Contact precautions • Cohorting carriers • Staff education • Antimicrobial stewardship • Active surveillance	In an Italian teaching hospital, CRE colonization incidence reduced significantly over 30 months, with risk reductions of 0.96 (95% CI, 0.92 to 0.99, $p<0.0001$) and 0.96 (95% CI, 0.95 to 0.97, $p<0.0001$), respectively.

Four of these studies reported on the effects of preemptive contact precautions, active screening, cohorting, and advanced contact precautions in ICU settings. One study found no statistically significant change in transmission after implementing active surveillance in an ICU. This ward already used universal contact precautions due to the sensitive population.[5] Two other studies found that implementing preemptive contact precautions had no effect on CRE transmission, including one study in an ICU[7] and one hospital-wide study that included a severe brain-injury unit.[10] The latter study also included active screening and patient cohorting as part of the multi-faceted intervention, which was not found to have a statistically significant effect either facility-wide and within individual units. Thus, this review found little evidence to support preemptive contact precautions, advanced contact precautions, and active screening in ICU settings. However, one study in an ICU found a reduction in cumulative incidence of CRE as a result of a multi-faceted intervention that included staff education, environmental cleaning, and chlorhexidine bathing in addition to contact precautions.[11] Further research is needed to strengthen the evidence in support of these other practices to reduce CRE transmission in ICU settings.

Seven facility-wide studies reported on variations in CRE infection control practices in settings ranging from long-term care (e.g., LTACHs, skilled nursing facilities [SNFs], and nursing homes [NHs]) to tertiary

care hospitals. Three of these studies reported on the successful multi-faceted intervention in Israeli healthcare settings. These national interventions included active surveillance, on-site policy and implementation assessments, and contact isolation. With this large-scale and heavily resourced intervention, Israel successfully reduced CRE transmission in LTACHs, post-acute care hospitals, SNFs, and NHs.[12-14]

Two teaching hospitals also successfully reduced CRE transmission with their multi-faceted interventions: one included preemptive contact precautions, cohorting (staff, equipment, and patients), improving signage, and visitor education,[15] and one included standard contact precautions and hand hygiene monitoring.[6] Because of the multifaceted nature of these interventions—which also included antibiotic stewardship, new emergency flagging systems, and environmental cleaning policies—it is difficult to associate success with any one factor. Another study (of implementing active screening and contact precautions during a CRE outbreak) found that poor implementation of contact precautions impeded the intervention and resulted in a continuation of the outbreak.[16] This is a cautionary tale of the importance of monitoring ongoing infection control practices as well as CRE-positive cultures. Lastly, one outbreak study implemented extended contact precautions and used an interdisciplinary outbreak intervention team to successfully stem a CRE outbreak.[17]

In addition to studies, this review included three mathematical models.[18-20] One model of a hyperendemic surgical unit found that a multi-faceted approach was necessary to reduce colonization prevalence.[18] This model found that hand hygiene alone was insufficient, and had to be paired with contact precautions and patient isolation/cohorting to successfully reduce prevalence. Active surveillance and enhanced contact isolation were found to be successful in one model of LTACHs, Acute Care Hospitals (ACHs), and NHs in Utah.[19] This model lends support to these practices in facilities in regions with ongoing outbreaks. Lastly, one mathematical model was used to provide real-time decision support and to predict observed outcomes during a successful before-after study in an ICU.[20]

6.1.3.3 Discontinuation of Contact Precautions

There is currently no global consensus on whether it is appropriate, or when it is appropriate, to discontinue contact precautions. A study of 15 hospitals in Canada found that 6.7 percent discontinued contact precautions after one negative specimen, 26.7 percent discontinued after three negative specimens separated by 1 week, and 53.3 percent continued until the patient was discharged.[21] Even within this review, several different strategies on discontinuation of contact precautions were mentioned. In post-acute care hospitals in Israel, discontinuation of contact precautions is recommended only in sub-acute medical wards when 3 months have passed since the last positive culture. For all other wards in post-acute care hospitals, discontinuation is not recommended.[13] Current Israeli national guidelines state that contact precautions should not be discontinued less than 1 month after a positive culture, and state that 3 months since the last culture is recommended for community, general hospital, and long-term care facility (LTCF) settings.[22] In a pre-post intervention study in a South Korean tertiary care hospital, contact isolation was discontinued after three consequent negative cultures were taken at least 3 days apart.[6] In a literature review by French et al. (2017), one study kept patients on contact precautions for the duration of their hospitalization.[23]

The CDC (2015) recommends that contact precautions be continued indefinitely.[1] However, Banach et al. (2018) recommend discontinuation on a case-by-case basis if: (1) at least 6 months have elapsed since a positive culture, and (2) at least two consecutive negative cultures were collected at least 1 week

apart.[24] This guidance does not recommend discontinuation for organisms found to be susceptible to two or fewer antibiotics, when a symptomatic patient is infected with a known or suspected CRE, or when a patient is treated with a broad-spectrum antibiotic (which could select for CRE).

Zimmerman et al., (2013) produced an ambidirectional cohort study in an Israeli teaching hospital on the length of CRE carriage to help inform discontinuation of contact precautions. They found that the mean time to CRE negativity was 387 days (95% CI, 312 to 463). They also found that repeat hospitalization was positively associated with increased carriage time (p=0.001).[25] More studies like this are needed to assess risk factors for increased carriage in a variety of settings and populations. By creating more specific models on the length of CRE carriage for different patients, we can make safer and more responsible recommendations on the discontinuation of contact precautions, which are burdensome to patients, staff, and the healthcare system.

6.1.4 Implementation

Fostering a workplace environment that encourages consistent use of contact precautions requires multi-institutional stakeholder involvement. Local health departments and large health systems may mandate contact precautions for patients with CRE infections. On a facility level, administrators and infection control specialists should encourage appropriate contact precautions by implementing monitoring and compliance audits as well as education of staff, patients, and visitors. This section focuses on the evidence identifying key supporting factors and systemic challenges to consistent use of contact precautions.

6.1.4.1 Staff Compliance With Contact Precautions

Cross-sectional surveys have been used to better understand how workplace environments can improve staff compliance with contact precautions and thus reduce transmission of CRE. A study of 420 healthcare workers in an acute care hospital and post-acute care hospital in Israel found that CRE acquisition was negatively correlated with workplace factors such as lack of staff engagement in infection control efforts ($r = -0.25$; $p < 0.05$) and the impression that the work environment is overwhelming, stressful, and chaotic ($r = 0.22$; $p = 0.06$).[26] Efforts should be made to engage staff in infection prevention and to ensure that understaffing and disorganization are not hindering these efforts.

Training, monitoring, compliance auditing, and feedback systems are also effective for improving compliance and appropriate use of contact precautions. An impressive example is the work that has been done on a national level by Israel's Ministry of Health task force.[14] To control CRE transmission among 27 acute care hospitals, the task force visited hospitals to evaluate infection control policies and intervened when compliance and implementation were poor. This led to reduced nosocomial CRE transmission from a monthly incidence of 55.5 cases per 100,000 patient-days to 11.7 cases per 100,000 patient-days (p<0.001). Other Israeli research involved a prospective cohort interventional study that scored 16 infection control features, with feedback reported to 13 post-acute care hospitals. Overall carrier prevalence in the 13 facilities declined from 16.8 to 12.5 percent (p=0.013).[12] This study also found that appropriate use of gloves was independently associated with lower CRE carrier incidence (New carrier prevalence is defined as the prevalence of carriers detected during screening who were not previously known to be carriers. Thus, the denominator of this measure excludes known carriers.). As another example, one quasi-experimental study by DalBen et al. (2016) found that weekly audit and feedback improved compliance with hand hygiene and contact precautions from 66 percent to 84

percent over a 24-week intervention period, and reduced weekly median R_0 from 11 during the baseline period to 0.42 during the intervention period.[20]

6.1.4.2 Facilitators

6.1.4.2.1 Policy

Infection control policies vary at a national, regional, or facility level and can influence use of contact precautions to prevent CRE. For example, in a 13-facility intervention in Israel, a task force monitored infection control policies and resources during periodic site visits, and developed national guidelines for CRE prevention. By the end of this national intervention, CRE carrier prevalence in post-acute care hospitals had decreased from 16.8 percent to 12.5 percent ($p=0.013$).[12] Schwaber et al. (2011) also found that because of this intervention in Israel, the incidence of nosocomial transmission decreased among 27 acute-care hospitals ($p<0.001$).[14] Additionally, a study of 15 hospitals in Canada found that only one-third of the facilities had written infection control policies for CRE.[21] However, this study was conducted in 2012, only shortly after Canada had released guidance for CRE. It is possible that additional hospitals have developed policies since then.

The CDC recommends that healthcare facilities implement policies for important CRE prevention practices such as hand hygiene and antibiotic stewardship, and that policies be enforced through continuous monitoring, auditing, and feedback.[1] Additionally, the CDC recommends that facilities "strictly enforce CDC guidance for CRE detection, prevention, tracking, and reporting."[27] Guidance documents are available on the CDC website.

6.1.4.2.2 Education

The presence of a policy alone may not be enough to facilitate consistent control methods for CRE. Education must accompany any new policy to ensure effective implementation. Awareness about infection control policies is crucial to consistently and successfully implementing these procedures. Staff education has been part of several intervention bundles that have been successful in reducing CRE transmission.[11,13,17,28] Additionally, the CDC recommends that all staff working with patients with CRE should be educated on practicing appropriate contact precautions.[1]

6.1.4.3 Other Challenges

Adherence to contact precautions alone may not be enough to reduce transmission of CRE. An ICU in Brazil had to halt new admissions when contact precautions failed to stem an outbreak (compliance was not reported).[16] Delay of implementation can reduce the efficacy of contact precautions and may be to blame in some of the outbreaks. In a model for CRE transmission in LTACHs, delaying interventions until the 20th CRE case reduced transmission to 60 to 79 percent, below the reduction rate for immediate intervention of 79 to 93 percent.[19]

6.1.4.4 Resources To Assist With Implementation

There are many toolkits to aid facilities in implementing institution-specific infection control programs specifically targeting transmission of CRE or other important multi-drug resistant organisms.

- The CDC healthcare facility guidance lists recommendations for specific types of healthcare facilities, excluding certain long-term care facilities such as nursing homes and assisted living facilities.[1]

- A systematic review performed by the European Centre for Disease Prevention and Control also lists recommendations based on findings from several studies, including contact precautions (n=6), dedicated/cohorted staff (n=6), isolating patients (n=4), and educating staff (n=3), all of which are effective methods for reducing CRE transmission.[4]
- Additional guidance documents and reviews available for CRE prevention are by Banach et al. (2018), Carmeli et al. (2010), Magiorakos et al. (2017), Friedman et al. (2017), and Parker et al. (2014).[2,24,29-31]

6.1.5 Gaps and Future Directions

Future research is needed to improve the sensitivity of risk factor analysis at patient intake in order to determine whether pre-emptive contact precautions should be implemented. A number of risk factors are being used to determine the risk of carriage, such as international travel to areas with increased transmission and prevalence of MDROs in healthcare settings, history of dialysis or chemotherapy, or history of CRE carriage.[29] However, quantitative analysis of the predictive value of these risk factors is needed to focus resources and avoid inconveniencing patients who ultimately test negative upon screening.

Currently there is no consensus on an appropriate timeline for discontinuation of contact precautions, although a handful of studies address average length of CRE carriage, and one guidance document was found containing discontinuation recommendations.[24] Only one study in this review investigated the average length of carriage of CRE to inform discontinuation policies. Zimmerman et al. (2013) obtained follow-up cultures from 97 patients who had a positive culture during a hospitalization at an Israeli teaching hospital. Using Kaplan-Meier survivor analysis, the authors found a mean time to culture negativity of 387 days (95% CI: 312–463 days; range: 26–1,025 days) and a median time of 295 days (95% CI: 192–398 days). Seventy-eight percent of the patients had positive cultures at 3 months, 65 percent had positive cultures at 6 months, and 39 percent had positive cultures at 1 year. Repeat hospitalization was an independent risk factor for CRE carriage ($p<0.001$), reemphasizing that healthcare exposure is a crucial factor in CRE transmission.[25] This study and future studies may help predict the length of carriage for patients with varying risk factors and contribute to more-evidence-based recommendations on an appropriate timeline for discontinuation of contact precautions.

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Conclusion

Based on the evidence found in this review, contact precautions are strongly recommended for patients infected with or colonized by CRE. There is little evidence to support universal active surveillance for CRE. However, active surveillance is recommended in outbreak scenarios, in highly endemic regions, and in healthcare facilities or units with ongoing transmission. In units already using universal contact precautions, the evidence suggests that active surveillance does not have a significant impact on reducing transmission. There was little evidence in this study to support preemptive contact precautions for high-risk patients. However, it is recommended that CDC guidelines be followed for this practice.

In all settings, ongoing monitoring, staff feedback, and education on the implementation of contact precaution and infection control policies are highly recommended. Although no study singles out the association of these practices with a successful intervention, they are often part of successful multi-faceted interventions.

There is no strong support for discontinuation of contact precautions when an individual has been placed on contact precautions due to a positive CRE culture. Such patients should remain on contact precautions at each healthcare facility they are admitted to until they are discharged into the community.

7. Harms Due to Anticoagulants

Authors: Sarah J. Shoemaker-Hunt, Ph.D., Pharm.D., and Brandy Wyant, M.P.H.

Introduction

Anticoagulants are a critical therapy in the prevention and treatment of various types of thromboembolic disorders. Key indications for anticoagulants include the prevention of stroke among patients with chronic atrial fibrillation, and prevention and treatment of venous thromboembolism (VTE), including deep vein thrombosis and pulmonary embolism. Anticoagulants include vitamin K antagonists (e.g., warfarin); heparin (unfractionated and low-molecular weight heparin); and novel oral anticoagulants (NOACs), such as direct thrombin inhibitors (e.g., argatroban and dabigatran) and factor Xa inhibitors (e.g., apixaban, rivaroxaban).

Anticoagulants have been consistently identified as the most common cause of adverse drug events (ADEs) in health care settings, such that an entire chapter of the National Action Plan for ADE Prevention is devoted to anticoagulants.[1] Bleeding is the primary ADE of concern for anticoagulants, but they require "a careful balance between thrombotic and hemorrhagic risks" (National Action Plan for ADE Prevention).[1]

Methods for Selecting Anticoagulant PSPs

The following three patient safety practices (PSPs) specific to addressing the potential harms of anticoagulants, particularly bleeding and thromboembolic events, were selected. They were among the list of nine specific PSPs that were compiled from various sources, particularly the National Action Plan for ADE Prevention, on recommended practices and potential gaps. Practices relevant to inpatient, ambulatory and long-term care settings were considered. Based on the survey of the Technical Expert Panel described in the methods section, the following PSPs were selected:

- PSP 1: Anticoagulation management service in the ambulatory setting
- PSP 2: Use of dosing protocols or nomograms for NOACs
- PSP 3: Interventions to support safe transitions and continuation of patients' anticoagulants post-discharge from a hospital or emergency department

What's New/Different Since the Last Report

In the Making Health Care Safer II report, a few chapters examined anticoagulants for specific thromboembolic disorders. It examined PSPs for intravenous anticoagulants and reviewed prevention of VTE.

References for Introduction

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7.1 Patient Safety Practice 1: Anticoagulation Management Service in the Ambulatory Setting

Reviewer: Scott Winiecki, M.D.

7.1.1 Practice Description

An anticoagulation management service is a systematic and coordinated approach to anticoagulation care delivery by a single provider following a physician-approved protocol. For example, these may be pharmacist- or nurse-led "anticoagulant clinics," in which patients are seen in an ambulatory setting on a regular basis to closely monitor bleeding and clotting laboratory values and adjust medications accordingly.

Note that many of the systematic reviews and studies compared different models of anticoagulation management services in terms of which professional provided the service as well as the specific model aims and mode (e.g., telephone) or how the model compared with usual care, which was not always described.

Key Findings:

- A range of models for anticoagulation management services are examined in the literature. Most are pharmacist led, but some are led by nurse practitioners, physician assistants, nurses, or pharmacy technicians.
- Some models examined different modes of providing anticoagulation management services (e.g., telephone).
- Overall quality of individual studies and studies within the systematic reviews is moderate to high, given the number of randomized controlled trials and non-randomized controlled trials with comparison groups or pre/post designs.
- There have been several recent systematic reviews of pharmacist-led anticoagulation management services compared with usual care or other models.
- Evidence shows that the effect of anticoagulant management services on time to therapeutic range is moderately positive, but evidence is low or mixed on bleeding events and thromboembolic events.

7.1.2 Methods

The question of interest for this review is, "What is the effect of an anticoagulant management service in the ambulatory setting on bleeding events and thrombotic events compared with usual care or different models of anticoagulant management service?"

Two databases (CINAHL® and MEDLINE®) were searched for articles published during the past 10 years using a combination of (1) terms related to anticoagulant and (2) pharmacist, nurse, nurse practitioner, or physician assistant, and (3) the outcomes of interest (bleeding or hemorrhage or patient safety, generally). Detailed search terms are provided in Appendix C.

Studies were included if they were empirical studies (or systematic reviews) of a systematic and coordinated anticoagulation care delivery service by a single clinician following a physician-approved protocol in an ambulatory setting. Studies were included if they used experimental, quasi-experimental, or observational study designs, examining anticoagulation management services pre/post, compared with usual care or different service models. Key findings for this review are located in the box above.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

7.1.3 Review of Evidence

Six systematic reviews and five single studies met the inclusion criteria and are characterized in terms of their setting, specific clinician and mode of delivery, and key outcomes in Appendix B. A synthesis of the evidence by outcome is shown below.

The majority of studies examined anticoagulation management services provided by pharmacists, although a few examined other professionals, including a nurse practitioner, nurse-pharmacist-dietician model, and a pharmacy technician versus a pharmacist-led model. Five of the systematic reviews examined the pharmacist-led model of anticoagulation service. The review by the Canadian Agency for Drugs and Technologies in Health (2011) also examined what they called "specialized anticoagulation services," defined as "tertiary or community hospital-based anticoagulation clinics, primary care settings, point-of-care (POC) testing and dose adjustment by community pharmacies, and patient self-testing and patient self-management."[1] These models were provided by pharmacists, other professionals, and patients themselves (i.e., patient self-testing).

The studies of anticoagulation management services were provided across a range of settings, including within an integrated health care delivery system; academic medical center; and safety-net, primary care, or ambulatory clinics; as well as for home-bound patients. Three studies specifically examined telephone-based models of anticoagulation management services—managed by nurse practitioner, clinical pharmacist, and patient self-testing, with various comparators.

The single studies examined the anticoagulation management services pre/post or compared with usual care or other models. Overall strength of the evidence is moderate to high given the inclusion of six recent systematic reviews, although few single studies had significant findings.

7.1.3.1 Clinical Outcomes

The clinical outcomes examined in the studies included time to therapeutic range (TTR), bleeding, and thrombotic events. The studies also examined patient-reported outcomes (satisfaction, quality of life), utilization and cost, and mortality. The findings for each of these are synthesized below.

7.1.3.1.1 Time to Therapeutic Range

TTR or percentage of time in therapeutic range were commonly reported in the studies and reviews.

Systematic reviews of pharmacist-led anticoagulation management services compared with usual care or other models found mixed results for significant differences in TTR. Entezari-Maleki et al. and Hou et al. found significant differences across observational studies in pharmacist models versus comparators (72.1% vs. 56.7%; p=0.013 for Entezari-Maleki et al.), although not for randomized controlled trials (RCTs).[2,3] However, Zhou et al.'s meta-analysis and Manzoor's review reported significantly higher percentages of anticoagulants within the therapeutic range as compared with all other models.[4,5] For "specialized anticoagulation services," which could include pharmacist-led models as well as other models such as patient self-testing, their review found significantly more favorable TTR compared with usual care.[1]

In the Duran-Parrondo et al. study of a pharmacist-involved model with patient education, compared with the control group, the intervention group improved its proportion of individuals' international normalized ratio (INR) results by 25 percent (relative risk [RR]=0.75; 95% confidence level [CI], 0.69 to

0.82) for those within 0.5 units of the target range and by 26 percent (RR=0.74; 95% CI, 0.67 to 0.81 for those within 0.75 units of the target range).[6]

Hawkins et al. examined the difference between a pharmacist-led versus a pharmacy technician-led model of anticoagulation management. They found that the technician-led group had a higher percentage of in-range INRs (mean difference=6.8%; 95% CI, 5.0% to 8.7%) and patients with 100-percent TTR (mean difference, 10.5%; 95% CI, 7.0% to 14.0%) during followup. They also found that the propensity-weighted 6-month followup mean TTR was 83.3 percent (95% CI, 82.4% to 84.2%) in the technician group and 77.7 percent (95% CI, 76.4% to 78.9%) in the usual care (pharmacist-managed) group, resulting in a mean difference in the followup mean TTR of 5.7 percent (95% CI, 4.1% to 7.2%).[7]

Three studies examined the use of telephone-based anticoagulation management services and found few differences from other models.[8-10] Lee et al. found that face-to-face management resulted in significantly greater INR TTR than did distance management using local laboratory testing (69.0% vs. 60.5%, p=0.0032). This study also found no difference in INR TTR between face-to-face management and patient self-testing (69.0% vs. 68.0%, p=0.25).[8] The Philip et al. study examined a telephone-based clinical pharmacist model to augment the clinical pharmacy service that was in high demand; the authors found no difference between the two groups in percentage of INR values in the therapeutic range.[9] Hassan et al. reported the percentage of INR values in therapeutic range (58.39%) and the mean TTR (62.75%) for homebound patients receiving telephone-based anticoagulation management but did not have a comparison group.[10]

7.1.3.1.2 Bleeding

Systematic reviews of pharmacist-managed anticoagulation service compared with other models or usual care found somewhat positive results on the number of bleeding events. Entezari-Maleki et al., Hou et al., and Zhou et al. found no significant differences in RCTs but observed significantly fewer bleeding events in non-RCTs (0.6% vs. 1.7%, p<0.001)[2] and a significantly lower risk of hemorrhage.[2,3,4] Manzoor et al. noted that 10 of the 12 studies that reported on bleeding found that the pharmacist-managed group had lower or equal risk of major bleeding as compared with usual care.[5] Saokaew et al. found that in RCTs, pharmacist-led management was significantly associated with substantial reductions in total and major bleedings (29% reduction in total bleedings, RR, 0.71; 95% CI, 0.52 to 0.96; p=0.028; 51% reduction in major bleedings, RR, 0.49; 95% CI, 0.26 to 0.93; p=0.030).[11] The Canadian review of specialized anticoagulation services did not find a reduction in bleeding or hemorrhage compared with usual care.[1]

In terms of the single studies, Duran-Parrondo et al. found that patients receiving followup by a pharmacist had a 75-percent reduction in bleeding (hazard ratio [HR]=0.25; 95% CI, 0.18 to 0.36).[6] When comparing a prior clinical pharmacist model with a telephone-based service led by a clinical pharmacist, bleedings were not significantly different, indicating comparable quality of anticoagulation management with either mode of delivery.[9] Hawkins et al. found that bleeding (HR=0.60; 95% CI, 0.39 to 0.94; p=0.026) was lower in the pharmacy-technician group during followup compared with the pharmacist-led model.[7]

7.1.3.1.3 Thromboembolic Events

Systematic reviews of pharmacist-managed anticoagulation service compared with other models or usual care found limited positive results in terms of the effect on thromboembolic events. Three reviews

found no significant differences in RCTs,[2-4] although the review by Saokaew et al. found that the risk ratio for pharmacist-led anticoagulation versus usual care on thromboembolic events was 0.79 (95% CI, 0.33 to 1.93; p=0.610).[11] Three reviews found significantly fewer thromboembolic events in the non-RCT studies versus usual care.[2,3,11] Manzoor et al. found that in 9 of 10 studies that reported on the outcome, the pharmacist-managed group had lower or equal risk of thromboembolic events as compared with usual care.[5] The Canadian review of specialized anticoagulation services found significant differences in the occurrence of thromboembolism.[1]

Of the four single studies that examined thromboembolic events, none observed a significant difference from the comparators—either usual care or different models.

7.1.3.2 Patient-Reported Outcomes

Some reviews examined patient-reported outcomes, including patient satisfaction and quality of life. In a pooled meta-analysis, Zhou et al. found that pharmacist-led models had significantly higher patient satisfaction as compared with all other models.[4] One study in the Entezari-Maleki et al. systematic review found no significant difference in quality of life between pharmacist-managed and usual care.[2]

7.1.3.3 Utilization and Cost

7.1.3.3.1 Utilization

The review by Entezari-Maleki et al. found significant differences in emergency department (ED) visits compared with usual care (7.9% vs. 23.9%; p<0.0001) and instances of hospitalization (3% vs, 10%; p<0.001) in non-RCTs, but no significant differences in RCTs.[2] Similarly, Manzoor et al. found decreased rates of hospitalization, shorter length of hospital stay, and fewer ED visits as compared with usual care in their review.[5]

Specialized anticoagulation services were not found to affect use.[1]

Duran-Parrondo et al. found that the intervention group had an—percent reduction (odds ratio=0.92; 95% CI, 0.88 to 0.96) in the number of medical consultations required to maintain individual patients' INR within the correct range.[6] Philip et al. did not find significant differences between the telephone-based clinical pharmacist service and previous in-person service in terms of percentage of clinical pharmacy visits for anticoagulation management, elapsed time to the third available clinic appointment (a measure of access to care), and number of clinical pharmacy visits for anticoagulation management, or pharmacist work hours per prescription volume.[9]

7.1.3.3.2 Cost

Three reviews reported a cost savings with a pharmacist-managed model.[2,3,5] The study by Hassan et al. of a telephone-based service for homebound patients led by a nurse practitioner determined the costs per visit to be $82, as compared with $300 for standard in-person visits to the hospital-based anticoagulation clinic.[10]

7.1.3.4 Mortality

Five systematic reviews that synthesized the evidence on mortality found no significant differences in RCTs or non-RCTs. The single study by Hawkins et al. examining a pharmacy technician model found that all-cause mortality (HR=0.44; 95% CI, 0.25 to 0.77; p=0.004) was lower in the technician group than in the pharmacist-managed group during followup.[7]

7.1.4 Implementation

No studies formally evaluated effective approaches for implementing anticoagulation management services.

7.1.5 Gaps and Future Directions

There is rather substantial literature on the effects of anticoagulation management services, in particular pharmacist-led services, as indicated by the six systematic reviews and five studies described above. Many of the studies and reviews examined the comparative effectiveness of different models, potentially exploring perhaps more cost-effective models (e.g., pharmacy technician model or telephone provided) with comparable quality and safety. There are still opportunities to expand the evidence and improve the safety of anticoagulants. An et al. (2017) is an example of expanding the evidence on anticoagulation management services beyond comparisons with usual care to quality improvement efforts within a management service, assessing the associations between management patterns and clinical outcomes.[12] Additional studies could expand the evidence looking at mixed models, especially to reach rural populations. For example, Hodge et al. (2008) studied a rural county in Australia, where a program "incorporated an anticoagulation clinic, point of care INR testing in remote centers, development of anticoagulation dosing protocol for GP use, and a comprehensive patient education program over 3 years."[13] With the NOACs, there are likely to be more therapeutic options with less direct management; however, they may also pose other challenges.

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7.2 Patient Safety Practice 2: Use of Dosing Protocols or Nomograms for Newer Oral Anticoagulants

Reviewers: Katharin Witgert, M.P.H., and Scott Winiecki, M.D.

Anticoagulants have consistently been identified as the most common causes of ADEs in healthcare settings.[1] While bleeding is the primary ADE of concern, anticoagulants require "a careful balance between thrombotic and hemorrhagic risks."[1] The introduction of NOACs, including the direct thrombin inhibitors (DTIs) (e.g., dabigatran, argatroban) and factor Xa inhibitors (e.g., rivaroxaban, apixaban), may be associated with lower rates of some bleeding events compared with warfarin;[2-5] however, the direct thrombin inhibitors are associated with a higher risk of major bleeding when used for management of heparin-induced thrombocytopenia.[6] While NOACs may offer different risks and benefits from older oral anticoagulants, careful dosing to balance the risks of thrombotic and hemorrhagic adverse events is required for NOACs, just as it is for older drugs. The Joint Commission National Patient Safety Goal (NPSG) 03.05.01[7] and the Institute for Safe Medication Practices (ISMP) Pathways for Medication Safety toolkit identify standardized anticoagulation dosing protocols as a potentially helpful PSP. This review focused on examining the use of dosing protocols and nomograms for NOACs.

7.2.1 Practice Description

A protocol or nomogram is a dosing tool that specifies the proper amount of drug (e.g., dose, infusion rate) to be given to a patient based on specific criteria (e.g., patient characteristics such as weight, kidney or liver function, laboratory results). The goal of a dosing protocol or nomogram is "to rapidly achieve and maintain a therapeutic range while guiding dosage adjustments and minimizing subtherapeutic or supratherapeutic concentrations."[8] The use of dosing nomograms has been shown to improve the safety and effectiveness of older anticoagulants, particularly heparin therapy.[9-13] Dosing protocols or nomograms are used for many drugs with a narrow window between their effective doses and doses at which they produce adverse effects; examples include several antibiotics (e.g., gentamicin, vancomycin) as well as anticoagulants (e.g., warfarin, heparin). Dosing protocols or nomograms may reflect different patient characteristics, such as kidney or liver function, depending on how a drug is metabolized. This PSP review was focused on the use of dosing protocols or nomograms for NOACs.

7.2.2 Methods

The question of interest for this review is, "What is the effect of dosing protocols or nomograms for NOACs on bleeding events?"

Two databases (CINAHL® and MEDLINE®) were searched for articles published during the past 10 years using a combination of (i) specific NOAC drug classes and drug names and (ii) terms for protocols or nomograms, and (iii) the outcomes of interest (bleeding or hemorrhage or patient safety, generally).

Studies were included if they were empirical studies of the use of nomograms or protocols for dosing NOACs, regardless of the specific clinical aim or target of the protocols. Studies were included if they used

Key Findings:

- There is a paucity of studies on the use of dosing protocols or nomograms for the NOACs.
- The few empirical studies that examine the effectiveness of protocols or nomograms for NOACs are observational, non-randomized studies without control groups or tests of significance and with very small sample sizes.
- At present, there is insufficient evidence to indicate the effectiveness of using dosing protocols/nomograms for NOACs to prevent bleeding.

experimental, quasi-experimental, or observational study designs. This review also includes studies without a test of significance, since there were few relevant, more rigorous studies identified in the literature. Key findings are located in the box above.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

7.2.3 Review of Evidence

The four studies that met the inclusion criteria are characterized in terms of their setting, the specific anticoagulant(s) targeted, the aim of the nomogram or protocol, and key outcomes. A summary of the study characteristics and key outcomes is provided in Table 7.1, with a detailed overview of each study provided in the Evidence Table in Appendix B.

Three of the four studies examined the use of protocols or nomograms for various NOACs to treat heparin-induced thrombocytopenia (HIT) within hospitals.[8,14,15] HIT is a "dangerous, potentially lethal, immunologically-mediated adverse drug reaction to unfractionated heparin or, less commonly, low molecular weight heparin. HIT can be associated with thrombosis formation in the more serious forms."[16] While somewhat rare (0.1%–5% prevalence in patients receiving heparin), of those who have HIT, 35 to 50 percent develop thrombosis (Salter et al., 2016).[16] Cessation of heparin therapy is paramount in HIT; other management or treatment considerations are alternative anticoagulants.

The fourth study examined adherence to a protocol for NOAC prescribing in an outpatient setting and whether there were differences between patients enrolled in an anticoagulation service and those who were not.[17]

The overall strength of the evidence on the effect of dosing nomograms or protocols for NOACs on bleeding is extremely low.

Table 7.1: Summary of Study Setting, Indication, Anticoagulant, Protocol Tested, and Outcomes

Author, Year	Setting, Study Design, Sample Size	Indication, Anticoagulant(s)	Protocol or Nomogram Tested	Outcomes
Ansara, et al., 2009[8]	• Community hospital • Observational, retrospective • N=51 patients	• Treat heparin-induced thrombocytopenia (HIT) • Argatroban	• Weight-based standard dosing nomogram • Hepatic/critically ill nomogram	• 16.25 hours mean time to activated partial thromboplastin time (aPTT) stabilization(standard) • 27.05 hours mean time to aPTT stabilization (hepatic) • 0 cases of major bleeding (standard) • 3 cases of major bleeding (hepatic), although not all attributable to drug • 0 thrombotic events after initiation of argatroban

Author, Year	Setting, Study Design, Sample Size	Indication, Anticoagulant(s)	Protocol or Nomogram Tested	Outcomes
Burcham et al., 2013[14]	• One academic medical center intensive care unit • Observational, retrospective • N=65 patients	• Treat HIT • Bivalirudin	• Dosing nomogram with fixed adjustments based on aPTT for use by nurses for intravenous bivalirudin	• 11.00 hours median time to steady state (range, 5.0–31.8 hours) • 53.7% of the aPTT values were in the target range • Bleeding occurred in 20 (30.8%) patients: 7 (10.8%) major bleed and 13 (20%) minor bleed. • All-cause mortality was 41.5%, and the median hospital length of stay was 28 days (range, 2–104 days).
Draper et al., 2017[17]	• One large multicenter, multispecialty group practice • Observational, retrospective cohort study • n=1,518 prescriptions	• Use of novel oral anticoagulants • Apixaban • Dabigatran • Rivaroxaban	• Anticoagulation service to encourage protocol NOAC adherence	Overall, the following percentages were prescribed per protocol: • 72% of apixaban • 52% of dabigatran • 70% of rivaroxaban Enrollment in the anticoagulation service was not associated with increased adherence to protocols.
Smythe et al., 2012[15]	• One academic medical center • Pre-/post-evaluation • N=49 patients	• Treat HIT • Argatroban • Lepirudin	• HIT recognition and management protocol	Correct dose per direct thrombin inhibitors protocol for initial dose ordered for 100% of patients post implementation vs. 31% pre implementation.

7.2.3.1 Clinical Outcomes

The clinical outcomes examined in the studies included measures of coagulation (activated partial thromboplastin time, aPTT), bleeding, and thrombotic events. The findings for each of these outcomes is synthesized below. The studies reported that clinical outcomes were not compared with usual care or a control group, so whether the time to coagulation and occurrence of bleeding and thrombotic events should be considered high or low for this patient population is unknown. The following are the descriptive findings on the reported outcomes.

7.2.3.1.1 Activated Partial Thromboplastin Time

Two studies evaluated the effect of the nomograms on the time to aPTT stabilization, a measure of the coagulation of blood.[8,14] Of the 51 patients in the study by Ansara et al. (2009), the *mean* time to aPTT was 16.25 hours and 27.05 hours for patients with the standard and hepatic/critically ill nomogram, respectively. Burcham et al. (2013) found a *median* aPTT of 11.00 hours (range, 5.0–31.8 hours) for intravenous bivalirudin with the use of a dosing nomogram in the intensive care unit.[14]

7.2.3.1.2 Bleeding

Two studies examined the occurrence of bleeding events with use of the nomograms or protocols.[8,14] With the standard nomogram, Ansara et al. (2009) observed no bleeding events. They observed three cases of major bleeding for the hepatic/critically ill nomogram, but the authors asserted these were not attributable to the argatroban.[8] In the study by Burcham et al., bleeding occurred in 20 (30.8%) patients, 7 (10.8%) meeting the criteria for a major bleed and 13 (20%) meeting the criteria for a minor bleed.[14]

7.2.3.1.3 Thrombotic Events

Ansara et al. (2009) reported no thrombotic events for patients after initiation of argatroban and during the hospital stay.[8]

7.2.3.2 Process Outcomes

The primary process outcome examined was adherence to the nomograms or protocols.

At a large multicenter, multispecialty group practice, Draper et al. (2017) examined prescribing adherence overall and whether enrollment of a patient in an anticoagulation service, specifically, would improve adherence to a protocol for direct acting oral anticoagulants (DOACs), including apixaban, dabigatran, and rivaroxaban. Of 1,518 DOAC prescriptions, 72 percent of apixaban, 52 percent of dabigatran, and 70 percent of rivaroxaban prescriptions were per protocol. Therefore, 24 to 45 percent of prescriptions were not per protocol, with some variance in reasons for classifying as not per protocol (e.g., off-label indication, renal impairment, hepatic impairment, dose too low, dose too high, or advanced age) across the different DOACs. Enrollment in the anticoagulation service was low (22% to 27% across the DOACs). Enrollment in the anticoagulation service was not associated with improved adherence to the DOAC protocols based on tests of significance.[17]

Smythe et al. (2012) found that after implementation of a dosing nomogram, 100 percent of patients' initial doses for DTIs were concordant with the protocol, as compared with only 31 percent before the protocol was implemented.[15]

7.2.4 Implementation

No studies formally evaluated effective approaches for implementing nomograms; however, Smythe et al. (2012) describe in detail their quality initiative for improving DTI prescribing as part of a protocol for recognizing and managing HIT. They describe the establishment of a multidisciplinary HIT working group led by the pharmacy department of an academic medical center that conducted a needs assessment, developed and revised dosing protocols, optimized HIT documentation in the electronic health record, expanded pharmacists' role in HIT, and provided education across disciplines on the protocols.[15]

7.2.5 Gaps and Future Directions

There are very few rigorous studies of the use of nomograms or protocols for NOACs in the literature, despite their expanding use and the remaining complexities of balancing between the risks of thrombotic and hemorrhagic adverse events with these newer agents and with the older anticoagulants (i.e., warfarin, heparin). There are many opportunities to expand the evidence, particularly in understanding whether and how use of nomograms or protocols improve aPTT and bleeding outcomes compared with normal care, and for what specific indications and/or patient populations.

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7.3 Patient Safety Practice 3: Interventions To Support Safe Transitions and Continuation of Patients' Anticoagulants Post Discharge

Reviewer: Scott Winiecki, M.D.

Transitioning patients from one setting to another is a particularly vulnerable time when safety lapses can result in negative clinical outcomes,[1-4] preventable adverse events,[5-9] and avoidable hospital readmissions.[10,11] The Joint Commission describes transitions of care as "the movement of patients between healthcare practitioners, settings, and home, as their conditions and care needs change."[12] Care transitions can also be cause for concern with anticoagulants, given they are the most common causes of ADEs in healthcare settings.[13] While bleeding is the primary ADE of concern, anticoagulants require "a careful balance between thrombotic and hemorrhagic risks."[13] Anticoagulants vary in their complexity, dosing, and requirements for transitioning to home from a hospital or ED.

7.3.1 Practice Description

Any intervention, service, or program that focuses on the safe transition and continuation of a patient's anticoagulant medications after discharge from a hospital or ED.

Key Findings:

- There is a paucity of literature and strong evidence on interventions, services, or programs for the safe transition of patients receiving anticoagulants after discharge from hospital or ED.
- Three studies of education and pill packs for rivaroxaban on dose transition (transitioning to daily at Day 22) found no significant improvements or differences.
- Two studies of low to moderate rigor examined a home-based service and a multi-component model for an ED.

7.3.2 Methods

The question of interest for this review is, "What is the effect of interventions to support care transitions for patients on anticoagulants discharged from emergency departments or hospitals?"

Two databases (CINAHL® and MEDLINE®) were searched for articles published in the past 10 years using a combination of (i) terms for anticoagulant and (ii) medication reconciliation and various terms for discharge, transfer, or handoff, and (iii) the outcomes of interest (bleeding or hemorrhage or patient safety, generally). Detailed search terms are provided in Appendix C.

Studies were included if they were empirical studies of an intervention specific to anticoagulants of any class for any indication upon discharge from an ED or hospital. Studies were included if they used experimental, quasi-experimental, or observational study designs with tests of significance. Key findings are located in the box above.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

7.3.3 Review of Evidence

The five studies that met the inclusion criteria are characterized in terms of their setting, study design, sample size, indication, anticoagulant(s), intervention, and outcomes in Table 7.2 and the findings synthesized below. A detailed overview of each study is provided in the Evidence Table in Appendix B.

Table 7.2: Summary of Study Setting, Indication, Anticoagulant, Intervention Tested, and Outcomes

Author, Year	Setting, Study Design, Sample Size	Indication Anticoagulant(s)	Intervention Description	Outcomes
Barbic et al., 2018[17]	• Emergency department (ED) discharge (Canada) • Pre/post • N=301 (n=129 pre; n=172 post)	• Atrial fibrillation (AF) or atrial flutter • Anticoagulants	• A coordinated, evidence-based ED AF pathway consisting of a care map, decision aids, medication orders, management suggestions, and electronic consultation or referral documents, all embedded into the electronic health record.	• Rates of new anticoagulation discharge for patients incorrectly not on anticoagulants upon ED admission significantly increased. • Median ED length of stay decreased from 262 to 218 minutes (44 minutes [p <0.03; 36.2–51.8]). • The 30-day ED revisit rate for congestive heart failure decreased from 13.2% (pre) to 2.3% (post) (absolute difference of 10.9%; p <0.01[(95% confidence interval, -8.1% to -13.7%]). • No significant differences between pre and post on: 30-day ED revisit for stroke, major bleeding, or atrial fibrillation; death within 30 days; outpatient clinic referral.
Castelli et al., 2017[14]	• Hospital discharge • Randomized controlled trial • N=25 patients	• Venous thromboembolism (VTE) • Rivaroxaban	• Rivaroxaban Patient Assistance Kit (R-PAK) is a novel discharge tool that includes reminder card stating dates of dose transition and a customizable pill box. Patients were also taught by a pharmacist how to use the pill box. • Control group received pharmacist education alone.	• No significant difference between the two groups on any outcomes: adherence, proper transition to daily administration on Day 22, percentage of patients who stopped rivaroxaban for any reason, patient understanding of correct timing and dose of medication, overall patient satisfaction, self-reported side effects, recurrent VTE, death.
Chu and Limberg, 2017[15]	• ED discharge • Retrospective cohort • N=41	• VTE • Rivaroxaban	• Patients discharged were counseled and provided a blister pack with dose instructions for the first 30 days • Control: usual care	• No statistically significant differences were found between the two groups on: adherence beyond the first month after discharge, 90-day readmission for recurrent VTE due to nonadherence or treatment failure, 90-day readmission due to bleeding or adverse event.
DiRenzo et al., 2018[16]	• ED discharge • Prospective cohort • N=17	• VTE • Rivaroxaban	• Intervention: outpatient VTE pharmacist-managed clinic under a collaborative practice agreement with a physician • Control: primary care provider management	• There were no significant differences 6 months following diagnosis between groups in major bleeding, recurrent thromboembolism, fatal event due to either bleeding or thromboembolism, number of hospitalizations after diagnosis, adverse events, or Morisky medication adherence score.

Author, Year	Setting, Study Design, Sample Size	Indication Anticoagulant(s)	Intervention Description	Outcomes
Stafford et al., 2011[18]	• Hospital discharge (Australia) • Prospective cohort • n= 236 patients (n=108 intervention)	• Newly initiated on warfarin, or continuing preadmission therapy with indication of at least 3 months of therapy • Warfarin	• Intervention: Collaborative, home-based post-discharge service. First visit within 2–3 days post discharge, subsequent visits based on risk assessment • Control: Usual care of the patient's community health care providers	• Persistence with warfarin improved (95.4% vs. 83.6%; p=0.004). • Significant decrease in major and minor hemorrhagic events at 90 days post discharge (5.3% vs. 14.7%; p=0.03) and at 8-day followup (0.9% vs. 7.2%; p=0.01). • Rate of combined hemorrhagic and thrombotic events at 90 days post discharge decreased (6.4% vs. 19.0%; p=0.008).

7.3.3.1 Outcomes

Three studies examined the effect of an intervention targeted at patients discharged on rivaroxaban for VTE from the hospital[14,15] or ED.[16] These three studies were observational and had quasi-experimental designs, had very small sample sizes (25, 41, and 17 intervention patients) and reflect a very low strength of evidence. The studies found no significant differences in bleeding, thromboembolic events, readmission, mortality, adherence, or dosing transition.

Barbic et al.'s multicomponent intervention of a coordinated ED approach for atrial fibrillation (pathway) significantly improved the rates of new anticoagulation for patients incorrectly not on anticoagulants upon ED admission. The median length of stay decreased significantly, as did the 30-day ED revisit rate for congestive heart failure. The study found no significant differences between pre and post intervention on: 30-day ED revisit for stroke, major bleeding, or AF; death within 30 days; or outpatient clinic referral.[17]

Stafford et al.'s collaborative, home-based post-discharge service significantly improved warfarin persistence/adherence (95.4% vs 83.6%; p=0.004), significantly decreased major and minor bleeding at 8-day followup (0.9% vs. 7.2%; p=.0.01) and 90 days post discharge (5.3% vs. 14.7%; p=0.03); and decreased the rate of combined hemorrhagic and thrombotic events at 90 days post discharge (6.4% vs. 19.0%; p=0.008).[18]

7.3.4 Implementation

No studies formally evaluated effective approaches for implementing anticoagulation management services.

7.3.5 Gaps and Future Directions

The available studies on safety practices for discharging patients on anticoagulants from hospitals and EDs are extremely few and reflect poor-quality evidence. Additional research is warranted to further understand the evidence-based approaches for successfully transitioning patients upon discharge to safely continue their anticoagulants and monitor appropriately for the specific anticoagulant. However, the paucity of studies may be a function of most care transition programs focusing on all of a patients' medications, not just anticoagulants.

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Conclusion

Evidence was sought on patient safety strategies to mitigate against bleeding and other adverse events associated with anticoagulants. There appears to be moderate evidence of pharmacist-provided anticoagulation management services, as well as some, albeit limited, evidence of different models being as effective, as described in Section 7.1. The studies of dosing protocols for the NOACs are largely observational, non-RCT studies without control groups or tests of significance, and with very small sample sizes. Thus, there is insufficient evidence to indicate the effectiveness of using dosing protocols/nomograms for NOACs to prevent bleeding. There is a paucity of literature and strong evidence on interventions, services, and programs for the safe transition of anticoagulant therapy post discharge from the hospital or ED. While this review may expand what we know and do not know about some patient safety practices to address the harms associated with anticoagulants, there are still many opportunities to improve the evidence base.

8. Harms Due to Diabetic Agents

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Introduction

In this chapter, two different kinds of diabetes patient safety practices are addressed—both intended to improve diabetes medication management. One practice focuses on provider administration of medication in the hospital setting when patients are ill. The other focuses on patient self-management in settings where patients are well enough to comprehend information about diabetes medication, typically outpatient settings.

The research on standardized protocols to reduce insulin administration errors that result in hypoglycemia is more robust than the research on the teach-back method, a communication confirmation method. However, in both cases, additional research is needed that is adequately powered and presents a study design that can detect an effect on hypoglycemia in the inpatient setting due to standardized protocols or a change in blood glucose levels in the outpatient setting due to teach-back. Key findings for both practices are located in the box on the next page.

Background

Individuals who have diabetes are not usually hospitalized for glucose control but are for other acute and chronic conditions. As inpatients, they are at risk for hypoglycemia and hyperglycemia by having their blood glucose levels (BGL) outside the recommended ranges for hospitalized patients (a target glucose range of 140–180 mg/dL); they may not have available or be consulting with a specialized diabetes or glucose management team skilled in diabetes medication administration.[1,2] Diabetes exacerbations are known to contribute to morbidity and mortality, and can be avoided through better medication management, including through the use of standardized insulin protocols. During the past decade, the United Kingdom—more than any other Nation—has documented diabetes medication errors through the National Diabetes Audit and instituted quality improvement projects to reduce errors and improve outcomes.[3] The data compiled through the National Diabetes Audit constitute one of the best sources of information on safety practices and are referred to below.

Diabetes is a growing chronic condition in the United States. Ambulatory patients with diabetes too frequently experience poor management of BGL, hypoglycemia (blood glucose below 70 mg/dL) and hyperglycemia (200 mg/dL or a fasting blood glucose level above 126 mg/dL).[4] In the 2013 Making Health Care Safer report, the Agency for Healthcare Research and Quality (AHRQ) focused on diabetes management as a patient safety practice. In this update, we more narrowly focus on medication management in hospitals and how to better equip both providers and patients to maintain recommended BGL levels and avoid instances of hypo- and hyperglycemia.

In addition, we examine the teach-back method used in settings where patients are able to self-manage their diabetes, generally in outpatient settings. The teach-back method is used for many different conditions and diseases, and has shown promise in helping patients and caregivers avoid medical mistakes.[5,6]

Importance of Harm Area

The clinical standards regarding BGL have evolved over the past two decades, beginning with a 2001 landmark study by Van den Berghe[7] that documented increased morbidity and mortality due to hyperglycemia in the inpatient setting. The study catalyzed a change in inpatient diabetes medication management toward standard protocols based on the American Diabetes Association's recommendations and away from the practice of sliding-scale insulin. In addition, there has been a move away from aggressive glycemic targets; adherence to strict targets has led to an increase in episodes of hypoglycemia. Tight glucose control is not indicated in the hospital setting. BGL <180 mg/dL is associated with lower rates of mortality and stroke compared with a target glucose <200 mg/dL, whereas no significant additional benefit was found with more strict glycemic control (<140 mg/dL).[8,9] Thus, the ranges for acceptable BGL have eased over time.[10,11]

There are numerous reasons that standardized insulin protocols or other ways of reducing medication administration errors are important patient safety practices (PSPs). A growing number of aging U.S. residents have diabetes, contributing to increases in the number of inpatients with multiple chronic conditions, which make diabetes even more difficult to manage and control.[4] If diabetes is well controlled during inpatient stays, other conditions can be more effectively treated and instances of BGL out of recommended range can be reduced.[12] These practice changes have implications for inpatient costs, quality of care, readmission rates, and patient reported outcomes.

The United Kingdom has made safety for diabetes inpatients a priority through DiabetesUK, a program that has collected data on medication errors and worked to decrease error rates. In 2017, one in six people in a hospital bed in England had diabetes, an estimated 270,000 individuals with diabetes suffered a medication error, 58,000 suffered an episode of severe hypoglycemia, and 9,600 required rescue treatment after falling into a coma as a result of severe hypoglycemia.[3] The country has been conducting the National Diabetes Audit since 2010, and based on the results, England instituted a multipronged patient safety program that includes: multidisciplinary diabetes teams in hospitals with strong clinical leadership, diabetes training, patient support and empowerment, better technology for identifying diabetes patients and those at increased risk for hypoglycemia, electronic prescribing, monitoring medication, and learning techniques to help hospitals learn from mistakes.

Key Findings for Insulin Protocol:

- Several studies have found that standardized protocols reduce hypoglycemic events in hospitalized patients in both acute and intensive care.
- Results are not uniform, and some studies using standardized protocols did not lead to a reduction in hypoglycemic events.
- Nurses are able to administer new, standardized protocols in most cases, even if the protocols take more time and are more complicated than prior protocols.
- The existing studies suffer from small numbers and weak study designs.
- The diversity of types and modes of protocols, study settings, and study designs makes the studies difficult to compare or synthesize.

Key Findings for Teach-Back:

- Teach-back has not been proven to improve Hemoglobin A1c levels or other clinical outcomes for diabetes patients.
- A greater number of studies and higher quality studies in diverse settings are needed to test the effects of teach-back in diabetes medication management.

There are several other trends that underscore the importance of reducing diabetes medication management errors. The Centers for Medicare & Medicaid Services (CMS) has established quality measures, and financial penalties in some cases, for unnecessary hospital readmissions. The pressure to

avoid readmissions has intensified, and hospitals and hospital systems are creating and using new protocols that can improve care coordination and healthcare access and help keep patients, including diabetes patients, out of the hospital. Since 2010, the Centers for Disease Control and Prevention (CDC) has funded the National Diabetes Prevention Program, a public-private partnership to disseminate a research-based lifestyle change program intended to prevent or delay type 2 diabetes. In recognition of the importance of diabetes prevention, CMS is currently conducting a project that implements and evaluates the diabetes prevention program among Medicare and Medicaid recipients on a large scale.

Methods for Selecting PSPs

Initial literature searches for PSPs in the harm area of medication management and diabetes agents were conducted, focusing on systematic reviews and guidelines. Results of these searches were reviewed by harm-area task leads to identify PSPs, and as needed, searches were refined. Then the project Technical Expert Panel and Advisory Group were engaged via a survey to prioritize PSPs for inclusion in the report. These survey results, along with refined recommendations for PSP inclusion, were submitted to AHRQ for review. After several rounds of review with AHRQ, two PSPs on medication management—diabetes agents were selected.

What's New/Different Since the Last Report?

The focus of PSPs has shifted from the last report to the current report, which more narrowly highlights diabetes medication management in inpatient settings. Recent studies to predict which patients are likely to experience hypoglycemia while hospitalized have led to development of screening tools,[13] identification of risk factors, [14,15] and identification of specific phenotypes[16] to help address this important potential patient-harm area.

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8.1 PSP1: Use of Standardized Insulin Protocols To Reduce Risk of Serious Hypoglycemia in Hospitals Due to Administration Errors

8.1.1 Practice Description

Standardized protocols are used in many situations because they reduce variability in human behavior and thus reduce the chance of error. Standardized insulin protocols and the insulin regimens to which they apply are intended to maintain relatively constant BGL in a person and reduce fluctuations. However, insulin medication must be adjusted based on an individual's activity and nutrition intake; an insulin bolus may be needed at mealtime, for example. Insulin regimens include basal insulin or a basal plus bolus correction insulin, which is the preferred treatment for non-critically ill hospitalized patients with poor oral intake. An insulin regimen with basal, prandial, and correction components is the preferred treatment for non-critically ill hospitalized patients who are able to intake nutrition orally. Standardized protocols are implemented through different forms, including specialized medical teams and paper and electronic order sets. Sole use of sliding-scale insulin in the inpatient hospital setting is strongly discouraged.[1]

8.1.2 Methods

Two databases (CINAHL® and PubMed/MEDLINE®) were searched for "insulin," "insulin administration," "hypoglycemic agents," and related synonyms, as well as "standing orders," "standard order set," and "standardized insulin protocol." Articles included were published from 2008 to 2018. The initial search yielded 145 results. Once duplicates were removed and additional relevant articles from selected other sources were added, a total of 132 articles were screened for inclusion, and full-text articles were retrieved. Of those, 14 were selected for inclusion in this review. Articles were excluded if the outcomes were not relevant to this review, the article was out of scope, or the study design was insufficiently described.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in report appendixes A through C.

8.1.3 Review of Evidence

Fourteen studies met the evidence criteria for this review in that they involved a standardized insulin protocol intended to reduce insulin medication administration errors in the inpatient setting and specifically targeted hypoglycemia. The types of studies were diverse in terms of populations, settings, countries, study design, sample size, type of standardized protocol, and outcomes (implementation and clinical).

Populations included individuals with type 1 or 2 diabetes who were admitted to acute care, intensive care, surgical, emergency department, and critical care units. Sample sizes ranged from 47 to 5,530, but most were small studies; eight of the studies included 200 or fewer patients.

The study designs included one interrupted time series (Wong et al., 2017),[2] three comparative effectiveness studies,[3-5] four prospective studies that used retrospective controls,[6-9] three pre-post studies,[10-12] one retrospective review,[13] one intervention with control group,[14] and one prospective

observational study in conjunction with a quality improvement effort. There were no randomized control studies.

8.1.3.1 Clinical Outcomes

Of the 14 studies, 7 demonstrated lower hypoglycemia rates when a standardized protocol was introduced. (Two of the studies drew findings from the same overall study.[6,8]) In some of these studies hypoglycemia was reduced, although time in target BGL was not statistically significant between the intervention and nonintervention groups. The seven studies are briefly described below.

In a study of 131 intensive care unit (ICU) patients, 65 received a static sliding-scale protocol, and 66 received a dynamic insulin infusion protocol. The dynamic protocol resulted in a lower rate of hypoglycemic events than the static protocol, although the time in target BGL ranges was low compared to other computer-assisted protocols. Twice as many nurses felt that the dynamic protocol, although more time consuming, was more effective than those who preferred the static one. However, the study population was small and conducted in a single hospital.[5]

A study of 552 acute and subacute trauma intensive care unit (TICU) patients who received an automated nurse-driven computer-based protocol was compared with retrospective data from patients at the same hospital who were treated with a manual, paper-based protocol. Hypoglycemia was lower in the computerized protocol group, and more patients were in the target BGL range. The computerized protocol worked with nursing workflows, and overall compliance was good.[9]

Two pilot studies were conducted—one in the cardiology and the other in the nephrology units of a Canadian hospital. Both studies used pre-printed insulin orders intended to standardize insulin prescribing practices, promote basal and mealtime insulin, reduce reliance on sliding-scale insulin, and standardize hypoglycemic management. Hypoglycemia rates decreased after the first pilot of 47 patients but not after the second.[10]

A small study of 96 ICU patients receiving parenteral nutrition compared a group receiving a transition order set with a retrospective comparison group (n=153) that did not receive the transition order set. Hypoglycemia rates decreased for the intervention group, and nurses reported that the new protocol was more time consuming but was a useful and instructive tool for maintaining BGL.[6]

In another sub-study based on the same overall study described above, a nurse-led self-adjusting standardized intravenous insulin protocol in an ICU led to a substantial reduction in hypoglycemic events, and fewer patients experienced more than one hypoglycemic event. The study examined the outcomes for the intervention compared with a retrospective control group. ICU length of stay was also lower for the protocol group.[8]

Another study using retrospective controls implemented a basal-bolus-booster insulin protocol in 57 patients known to be hyperglycemic in non-critical hospital units. Hypoglycemia was lower in the intervention group. Staff compliance with implementation of the basal-bolus portion of the protocol was good, while compliance with the bedtime booster was poor.[7]

In a study embedded in a quality improvement effort, 5,530 inpatients in an academic medical center were given a structured subcutaneous insulin order set that encouraged the use of scheduled basal and nutritional insulin, and provided guidance for monitoring glucose levels and insulin dosing. A hypoglycemia protocol and standardized correction insulin table were embedded in the order set. The

intervention was conducted over three time periods with slight changes each time. The percent of patients who suffered one or more hypoglycemic events over the course of their inpatient stay was 11.8 percent, 9.7 percent, and 9.2 percent, for time points (TP) 1, 2, and 3, respectively. The rate ratio (RR) of patients suffering from a hypoglycemic event was significantly improved in the intervention time periods compared to baseline, with an RR of TP3:TP1=0.77 (confidence interval [CI], 0.65-0.92). TP3 to TP2 showed no statistically significant difference. Of the monitored patient days in the baseline, TP1, 3.8 percent contained a hypoglycemic value. With the introduction of the structured insulin orders, TP2 hypoglycemia decreased to 2.9 percent, and in TP3 it was 2.6 percent.[15]

8.1.3.2 Process Outcomes

Four of the studies measured whether or not the protocol could be easily administered by nurses.[4-7] In all four cases, the new protocol was acceptable to nurses and integrated into workflows. However, in two of the studies, the nurses found the new protocol to be more time consuming than the prior protocols.[5,6]

8.1.3.3 Summary of Evidence on Implementation

Most of the studies were small, and several used retrospective data as the comparison group. Most suffered from weak designs. Standard protocols included both electronic and paper versions. None of them used sliding-scale methods. Nurses found the standardized protocols to take more time. In some cases, they were more complicated than usual care yet could be integrated into the workflow, and nurses supported them.

8.1.3.4 Gaps and Future Directions

8.1.3.4.1 Gaps

Studies with stronger designs and larger sample sizes were more likely to show an effect in terms of reducing hypoglycemia.

8.1.3.4.2 Future Directions

The evidence that standardized inpatient protocols lead to reduced hypoglycemia is growing. However, larger prospective studies with more robust methods are still needed. Other areas of future research include examination of standardized protocols that include intravenous insulin protocols versus subcutaneous protocols. Similarly, for the future, standardized protocols that include real-time continuous glucose monitoring (CGM) may improve patient safety. Real-time CGM would provide frequent measurements of interstitial glucose levels, as well as direction and magnitude of glucose trends, and may have an advantage over point-of-care glucose testing in detecting and reducing the incidence of hypoglycemia in the hospital setting. A recent review has recommended against using CGM in adults in a hospital setting until more safety and efficacy data become available.[16]

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8.2 PSP2: Use of Teach-Back in Diabetes Medication Management

8.2.1 Practice Description

The teach-back method is also called "closing the loop" and can be effective in increasing patients' ability to retain knowledge that helps them manage health conditions.[1,2] Teach-back tests comprehension by asking patients to say in their own words what they understand the clinician has instructed them to do. Teach-back has been utilized with many different kinds of patients; we sought to find examples of using teach-back with diabetes patients to improve their self-care. A recent AHRQ publication, Guide to Improving Patient Safety in Primary Care Settings by Engaging Patients and Families, includes a section on the teach-back method.[3] It is important to note that teach-back can occur in multiple settings, but to be effective, the patient must have the cognitive ability to comprehend the information, the physical skills to successfully self-administer insulin and other diabetes medication, be able to perform self-monitoring of blood glucose, and have adequate oral intake. The setting for teach-back is typically an outpatient setting.

8.2.2 Methods

Two databases (CINAHL® and PubMed/MEDLINE®) were searched for "diabetes" or "diabetes mellitus" as well as "teach-back communication," "teach-back," "teach back," and other related terms. Articles included were published from 2008 to 2018. The initial search yielded 161 results. Once duplicates were removed and additional relevant articles from selected other sources were added, a total of 155 articles were screened for inclusion, and full-text articles were retrieved. Of those, four were selected for inclusion in this review. Articles were excluded if the outcomes were not relevant to this review, the article was out of scope, or the study design was insufficiently described.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in report appendixes A through C.

8.2.3 Review of Evidence

Four studies that used the teach-back method for diabetes patients met the inclusion criteria for this review. Three were small studies with 12 to 171 subjects,[4-6] and one included 442 subjects.[7] Most studies were conducted in one or two provider organizations and consequently were difficult to generalize. Two studies measured clinical outcomes, and the others measured changes in knowledge. A main purpose of three of the studies was to assess the effectiveness of specific education methods in patient cohorts with low literacy. Below we review each of the four studies.

Coulter's (2018) study of 12 patients with type 2 diabetes in a rural clinic in Northern Illinois used a pre- and post-test design. Patients received standard teaching at baseline during face-to-face office visits, and the teach-back method was delivered via phone. Patients filled out surveys to assess their perceived understanding of diabetes management, patient actions that would help manage diabetes, and participant goals. The study found statistically significant decreases in hemoglobin A1C (HbA1c) cover the 3-month study period. While the authors noted that patients improved their understanding of diabetes management, no data were provided on measures of understanding or statistical significance.[4]

Kandula et al. (2011) conducted two experiments with patients in a health center and academic medical center, both located in Chicago. In one experiment, 112 patients were tested before and after receiving diabetes education Module One, and tested again after receiving diabetes education Module Two. In the second experiment with 58 patients, a pre- and post-test were administered before and after Module One, and the patients discussed their answers with a provider and were allowed to correct them. Both groups were tested 2 weeks after the initial test. The teach-back method did not have a statistically significant effect on diabetes knowledge scores.[5]

Negarandeh et al. (2013) conducted a randomized control trial in Kurdistan with 45 type 2 diabetes patients in each of three arms: one that received usual care, one that received diabetes education with a pictorial representation, and one that received diabetes education with teach-back. The analysis of variance indicated that there were statistically significant differences between the three groups in terms of knowledge, adherence to medication, and adherence to dietary regimen in the followup measurement ($p<0.05$). Both the pictorial and teach-back groups had better self-reported medication and dietary adherence than the control group. There was no statistically significant difference in HbA1c outcome measures.[6]

The largest study we identified randomized patients from the Carilion Clinic Department of Family and Community Medicine in southwest Virginia into two groups. One group included 217 patients who viewed a 60- minute DVD on diabetes prevention and then received a teach-back telephone call, while 225 patients attended a 120-minute group seminar and then received a teach-back telephone call. DVD participants performed significantly better across teach-back questions, demonstrated comprehension in fewer teach-back rounds, and answered more questions correctly on the first try. Among participants with low health literacy (LHL), the differences between the DVD and class groups were not significant. The approximately 18 percent of DVD participants and 16 percent of class participants with LHL did not achieve the teach-back goal after the teach-back was completed.[7]

8.2.3.1 Clinical Outcomes

Two of the studies measured changes in HbA1c levels over the course of the education and teach-back periods. One included only 12 patients, but there was a positive and statistically significant change in the patients BGL before and after teach-back was applied.[4] A second study found no difference in HbA1c levels before and after the intervention.[6]

8.2.3.2 Process Outcomes

All four studies measured changes in knowledge, and all found an increase in knowledge. However, the knowledge change could be attributed to the teach-back method in only two of the studies.[4,7]

8.2.3.3 Economic Outcomes

None of the studies investigated economic costs or outcomes.

8.2.4 Gaps and Future Directions

The studies with diabetes patients using teach-back as a method to improve diabetes medication knowledge or HbA1c levels are limited, and the results are mixed. However, most of the studies suffer from small numbers and weak study designs. Larger, more robust studies might be able to shed more light on this patient safety practice. Additionally, adaptations for health literacy and cultural and other social barriers need to be controlled for.

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Conclusion and Comment

Diabetes is a growing chronic condition in all age groups, and strategies for improving medication management will have significant impact on mortality and morbidity. Using standardized insulin protocols to reduce hypoglycemia in the hospital and teach-back methods in other settings to improve the ability of diabetes patients to better understand and self-manage their own insulin and other antihyperglycemic medication needs are both patient safety practices that have potential. There is more and stronger evidence to support standardized hospital insulin protocols to prevent hypoglycemia than there is to support teach-back methods to improve medication management. However, better-designed studies on both patient safety practices are needed to establish a firm evidence base.

Larger, better-designed studies on reducing hypoglycemia would lead to stronger clinical evidence and also to improved implementation of feedback. Teach-back is in a formative stage in that enhanced definitions and typologies of teach-back methods are needed before it will be possible to collate the clinical evidence.

9. Reducing Adverse Drug Events in Older Adults

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Introduction

Background

People are living longer than ever. In the United States, the number of Americans age 65 years and older increased from 37.2 million in 2006 to 49.2 million in 2016 (33% increase) and is projected to reach 98 million by 2060.[1] With age comes the likelihood of increasing morbidity. An estimated 98 percent of people age 65 years and older have at least two chronic diseases and take at least five prescription medications.[2]

As the medical field develops clinical therapies, protocols, and treatments to help the elderly population better manage, prevent, and/or enhance quality of life, there are also risks. For instance, polypharmacy—taking multiple medications concurrently—and the use of potentially inappropriate medicines (PIMs) pose the greatest risk of drug-related adverse drug events (ADEs) for older adults, who are more likely than younger people to take multiple medications at the same time.[3,4] Broadly defined as injuries that result from drug-related medical interventions (e.g., medication errors, adverse drug reactions, allergic reactions, or overdoses), ADEs have been associated with thousands of visits to the emergency department (ED) and hospitalizations.[5] However, up to half of identified ADEs are preventable,[6] and ADEs are one of the most common types of preventable adverse events across all healthcare settings.[7]

Importance of Harm Area

Common consequences of ADEs include drug-related morbidity and mortality, heart and/or renal failure, gastrointestinal and internal bleeding, and negative drug-drug interactions.[8,9] Given the prevalence of ADEs, preventing them is an important public health priority. The Joint Commission's 2019 revised National Patient Safety Goals on anticoagulant medicines identifies ADE prevention—in both hospital and ambulatory clinic settings—as a primary objective.[6,10] In addition to potential harm to patients, the estimated cost of treating ADEs in hospital settings was more than $76 billion in 2014 and has likely increased since.[11,12]

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9.1 Reducing ADEs in Older Adults

This chapter summarizes articles published from 2008 to 2018 that describe strategies that effectively reduce ADEs in older adults. Across all studies, the targeted population was adults aged 65 years and older, and the desired outcome was reduced inappropriate medication use or polypharmacy. We describe two approaches that inform how best to identify inappropriate medicines and reduce ADEs. We then describe our literature review strategy and conclude by identifying potential gaps, challenges, and future directions to consider in this field. Resources for future implementation efforts are also included.

9.1.1 Practice Description

Polypharmacy and the use of inappropriate medications present a risk for ADEs. Driven by the need to identify the most precise way to identify ineffective and/or unnecessary medications, several intervention strategies report varied success in implementation and effectiveness. As described in the overview box to the right, this review focuses on two emerging approaches: (1) deprescribing to reduce polypharmacy and (2) the use of the Screening Tool of Older Person's inappropriate Prescriptions (STOPP) criteria to reduce PIMs. Deprescribing involves reducing doses or stopping medications that are not useful or are no longer needed in order to reduce polypharmacy, reduce harm, and improve health. STOPP is a validated, evidence-based list of 80 criteria for potentially inappropriate prescribing in older adults, first published in 2008 and revised in 2014. The box to the right provides an overview.

PSP Overview

Deprescribing

- **Setting(s)**: acute hospital care, ambulatory care (primary care, long-term care, residential aged care facilities, skilled nursing facilities), community pharmacies
- **Patient Population Targets**: older adults, patients at high risk for polypharmacy and comorbidities
- **Provider Targets**: clinical community pharmacists, hospital pharmacists, geriatricians, general practitioners, geriatric nurse practitioners

STOPP Criteria

- **Settings**: acute hospital care, ambulatory care (home care, long-term care, skilled nursing facilities)
- **Patient Population Target**: adults aged 65 or older taking multiple medications
- **Provider Targets**: geriatricians, general practitioners, pharmacists, prescribing physicians

While it is a fairly new tool, evidence suggests that STOPP may be better at predicting PIMs in older adults than other tools, such as the American Geriatrics Society's Beers Criteria®, hereafter referred to as the Beers Criteria.[1] While this patient safety practice (PSP) specifically emphasizes the use of the STOPP criteria, it is often used with a companion screener, the Screening Tool to Alert to Right Treatment (START). START includes a set of 34 evidence-based and validated prescribing indicators for common diseases for the same population. Both have been more commonly used in non-U.S. settings. For the purposes of this review, we focus on STOPP and reference START as appropriate.

9.1.2 Methods

This section describes the literature search and review methods specific to this PSP area. The general methodology used across the project is available in the methods chapter of this report.

We applied search terms in two databases (CINAHL®) and MEDLINE®). Terms used to find deprescribing literature included "deprescribing," "adverse reactions/PC," "adverse drug events," "drug-related side effects," "inappropriate prescribing/PC," "polypharmacy," "polymedication," "cessation," "discontinuation," and "withdrawal." The search terms for STOPP included "STOPP," "potentially inappropriate medication list," "research studies," "prepost," "interventional," "randomized," and "non-

randomized." We further refined each search to focus on the priority population by including "older adult," "aged," "senior," and "elderly."

To make sure we identified all relevant articles, we reviewed the reference lists of systematic literature review articles and read abstracts or full-text of apparently relevant articles to screen them for inclusion.

Methods prescribed by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines guided the review. PRISMA flow diagrams illustrate the process for both the deprescribing and STOPP searches. Overall, 988 publications were identified and 131 articles were considered eligible for further review. Priority was given to intervention studies as opposed to prevalence, incidence, or observational studies. Studies were included if they were published in English; explicitly focused on deprescribing, polypharmacy, PIMs, and/or STOPP; targeted older adults; and effectively (i.e., statistically significantly) reduced medication use as a result of implementing an intervention related to deprescribing and/or using the STOPP criteria. Articles were excluded if the focus was on children/pediatric care. Ultimately, we selected for the evidence summary the 27 studies that are listed in alphabetical order in the evidence tables.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

9.1.3 Review of Evidence for Reducing ADEs in Older Adults

This section presents evidence from the 27 studies we reviewed related to the use of deprescribing or using the STOPP criteria to reduce the unnecessary medications that could lead to ADEs in older adults. It is important to note that deprescribing and the STOPP criteria are not actual interventions. Rather, deprescribing is an approach and STOPP is a screening tool. The evidence in this section specifically highlights intervention studies as opposed to prevalence, observational, or incidence studies.

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9.2 Patient Safety Practice: Deprescribing To Reduce Polypharmacy in Older Adults

9.2.1 Clinical Outcomes

Key Findings

- Geriatrician and clinical pharmacist reviews can effectively reduce the use of unnecessary medications.
- Educating patients and their families helps them better communicate their medication use to providers in order to discontinue unnecessary medications.
- Deprescribing reduces medication-related costs for patients and healthcare systems.

As previously discussed, deprescribing addresses polypharmacy by reducing inappropriate prescriptions and can lead to improved clinical outcomes. However, clinical outcomes can vary with the specific approach to deprescribing. Ocampo et al. (2015) found that a pharmacist-led medication review with an 18-month follow-up period in community pharmacies identified 408 negative outcomes related to prescriptions and resolved 393 of these problems, resulting in a significant decrease in hospitalizations (p=0.039) and ED visits (p=0.001). Physical and mental health summary scales increased from 65.8 to 82.7 (p<0.0001) and 66.2 to 81.1 (p<0.0001), respectively, while patients who were nonadherent decreased from 68 to 1 (p<0.0001).[1] Others reported that discontinuing multiple medications simultaneously was significantly associated with reductions in both the number of reported falls and frailty scores for older adults.[2] These researchers also examined collaborative medication reviews with general practitioners of patients age 65 years and older in a residential care facility. Their study noted a significant reduction in drug burden index scores, by 0.34 (p<0.001), reflecting a decrease in the cumulative exposure to medications, and the number of falls and frailty measured using the Edmonton frailty scale dropped by a mean difference of 1.35 (p<0.05). Additionally, the number of adverse drug reactions decreased by 4.24 (p<0.05) after 6 months.[2] However, in a multidisciplinary geriatric specialist medication review panel intervention including registrars in geriatric medicine, hospital pharmacists, and geriatric nurse practitioners, no significant difference was found in mortality (p=0.226) or frequency of hospital transfers (p=0.213) between intervention and regular care groups.[3] A summary of key findings are located in the Key Findings box above.

9.2.1.1 Process Outcomes

Many studies focused on process-related outcomes such as a decrease in the number of medications prescribed, which is expected to lead to clinical outcomes. Findings from the studies are subsequently presented by topical area.

9.2.1.1.1 Protocols, Algorithms, and Clinical Decision Support Systems

Among the studies focusing on the use of protocols, algorithms, and clinical decision support systems to promote deprescribing, patients had a significant decrease in the number of medications prescribed. A patient-centered deprescribing protocol called Shed-MEDS is implemented in four phases: (1) confirm medication history and list, (2) evaluate medication for deprescribing, (3) decide with the patients, (4) synthesize and communicate recommendations. Petersen et al. (2018) found that, among Medicare beneficiaries prescribed five or more medications, the mean number of prescribed medications was significantly reduced, from 11.6 to 9.1 (p=0.032), for those receiving the protocol.[4] Garfinkel et al. (2010) worked with elderly patients in Israel to implement the Good Palliative-Geriatric Practice algorithm, an evidence-based flow chart for drug discontinuation, which recommended discontinuing a total of 311 medications for 64 patients.[5] McKean et al. (2016) worked with patients age 65 or older taking eight or

more medications to implement an intervention consisting of a formal medication review among rounding clinicians, followed by receipt of a paper-based or computerized form listing clinical and medication data linked with a five-step clinical decision support tool to determine drugs eligible for discontinuation. The intervention led to a 34.3-percent decrease in regular medications, a small but nonsignificant decrease in PRN (as needed) medications, and a significant decrease in the number of medications per patient at discharge compared with admission (median change: 7 vs. 10 medications [p<0.001]).[6]

9.2.1.1.2 Interventions

Education-improvement interventions, which directly educate consumers, have also been associated with medication discontinuation to reduce polypharmacy. Tannenbaum et al. (2014) found that a direct-to-consumer education intervention using an 8-page booklet to describe the risks of benzodiazepine use and a step-wise tapering protocol led to a 27 percent discontinuation of benzodiazepines among community pharmacy patients age 65 or older in the intervention group, compared with 5 percent in the control group (95% confidence interval [CI], 14% to 32%), at 6 months after the intervention.[7] Martin et al. (2018) studied a consumer-based education intervention led by pharmacists in community pharmacies providing an educational brochure to patients age 65 and older. The study resulted in 43 percent of the intervention group no longer filling inappropriate medications, compared with 12 percent of the control group (95% CI, 23% to 38%).[8]

9.2.1.1.3 Pharmacist-Led Medication Reviews

Pharmacist-led medication review interventions across a number of settings have also promoted deprescribing. Lenander et al. (2014) found that a pharmacist-led medication review in a primary care setting targeting patients 65 and older with five or more different medications led to a decrease in drug-related problems. Using the Beers Criteria, after 12 months, drug-related problems decreased for the intervention group from 1.73 to 1.31 (p<0.05). There was also a larger reduction in the number of drugs prescribed in the intervention group (p<0.046).[9] Veggeland and Dyb (2008) observed the effect of adding a clinical pharmacist performing medication reviews to a geriatric care hospital team, finding it led to improved medication changes, extensive discontinuation of drugs, dose reductions, or decisions to revise medications at a later stage of hospitalization.[10]

9.2.1.1.4 Clinician-Led Medication Reviews

We found one study of a clinician-led medication review. Tamura and colleagues (2011) worked with geriatric medicine fellows in a nursing facility to implement a medication review using the updated Beers Criteria for patients (average age: 83 years old) with nine or more medications, leading to an average reduction of total medications from 16.64 to 15.53 (p<0.001), average number of scheduled medications from 11.3 to 10.99 (p<0.001), average number of PRN medications from 5.33 to 4.56 (p<0.001), and average number of high-risk medications from 5.33 to 4.56 (p<0.001).[11]

9.2.1.1.5 Pharmacist and Clinician Medication Reviews

Medication reviews involving both pharmacists and clinicians effectively decreased medication use in two studies. Chan and others (2014) determined the effectiveness of a medications safety review clinic for geriatric outpatients age 65 or older who were prescribed eight or more chronic medications or who had visited at least three different physicians at the two participating hospitals within 3 months. Four medication review sessions were performed by two research assistants, one clinical pharmacist, and one

geriatrician, leading to a mean decrease in chronic medications from 9.0 to 8.6 ($p<0.05$).[12] Wouters et al. (2017) sought to improve prescribing in nursing home residents by implementing the Multidisciplinary Multistep Medication Review, also referred to as the 3MR intervention. The randomized controlled trial took place on nursing home wards and consisted of an evaluation of the patient's perspective, medical history, and use of medications; a meeting between the physician and pharmacist; and the execution of medication changes. Results showed that successful discontinuation, without relapse or severe withdrawal symptoms, of at least one inappropriate medication was greater in the intervention group than the control group (39.1% vs. 29.5%; 95% CI, 1.02 to 1.75). In the 4 months after the baseline assessment, there was no deterioration of clinical outcomes, such as neuropsychiatric symptoms, cognitive function, or quality of life, in either group.[13]

9.2.1.2 Economic Outcomes

One study assessed the economic impact of deprescribing. Kojima et al. (2012) evaluated the effect on medication costs of a physician intervention using two tools, the Beers Criteria and the Epocrates online drug-drug interaction program, to reduce polypharmacy among long-term care residents. Findings showed that residents undergoing the intervention had significantly lower health care costs after the intervention. Average monthly medication costs declined from $874 to $843 ($p<0.0001$), scheduled medication costs from $814 to $801 ($p=0.007$), PRN medication costs from $60 to $42 ($p<0.0001$), and nursing medication administration costs from $483 to $461 ($p<0.0001$).[14]

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9.3 Patient Safety Practice: Using the STOPP Criteria To Reduce the Use of PIMs in Older Adults

9.3.1 Clinical Outcomes

The studies evaluating STOPP did not focus on clinical outcomes. There has been more emphasis on assessing the process of implementing or using STOPP criteria to more accurately identify PIMs.

9.3.2 Process Outcomes

Four studies demonstrate the effectiveness of STOPP. Campins et al. (2017) reported that the STOPP tool helped pharmacists determine that 27 percent of the intervention population's prescriptions were potentially inappropriate. The majority of these prescriptions were then changed, as follows: 43 percent were discontinued, 33 percent received a dose adjustment, 14 percent were substituted for more appropriate medications, and for 10 percent, the patient received a new prescription.[1] Similarly, Gibert et al. (2018) used STOPP in primary care consultations in France, resulting in a 38-percent reduction in the number of PIMs (n=170 vs. 106) across about 45 percent of patients (n=44) ($p<0.001$).[2] Hannou et al. (2017) introduced a part-time ward-based clinical pharmacist to a psychiatric unit's multidisciplinary team and screened prescriptions for potentially inappropriate drug prescribing (PIDP) using the STOPP/START criteria. The intervention was measured by the acceptance rate of pharmacist interventions (PhIs).The global PhI acceptance rate was 68 percent and the rate based on STOPP/START was 47%. When two STOPP criteria, the prescription of benzodiazepines or of neuroleptic drugs to patients who had fallen in the last 3 months, were removed from analysis, the acceptance rate for STOPP/START-based PhIs increased to 67 percent.[3] In Ilic et al. (2015), an education intervention targeting both physicians and nursing home residents provided information about the START/STOPP and Beers Criteria, as well as adherence, adverse drug reactions, and drug-drug interactions. According to the STOPP criteria, 70 drugs were inappropriately prescribed before the intervention, and 20 drugs after 6 months. The median number of inappropriately prescribed drugs according to the STOPP criteria before education was 3.5 (range 1.0-20.0), and the median number after education was 1.5 (range 0.0-6.0; $Z=2.823$; $p<0.005$).[4]

9.3.3 Economic Outcomes

STOPP has the potential for positive economic outcomes. After implementing a comprehensive geriatric assessment (CGA) that included the STOPP criteria, Unutmaz et al. (2018) suggested that the tool saved patients about $13 per month in medication costs, as well as reducing polypharmacy, PIMs, and potential prescribing omissions (PPOs).[5] O'Connor et al. (2016) reported significant reductions in medication costs. At discharge, median medication cost was significantly lower in the intervention group than in the control group ($p<0.001$).[6] Frankenthal et al. (2017) found that when pharmacists and prescribing physicians discussed medication reviews rather than communicating in writing, the reviews were more effective. Furthermore, the authors reported that the costs of medications were significantly lower in the intervention group than the control group ($p<0.001$) at the 24-month followup.[7] Hill-Taylor et al. reviewed three studies on the direct costs of potentially inappropriate prescribing (PIP). One study, Barry et al., found that the wholesale cost of the PPO instances identified by the START criteria in their study population was €188 per patient per year in 2007. Another, Cahir. et al, reported that the cost associated with the PIP instances identified by condensed STOPP criteria in their study population was

€318 per patient per year. The third study, Byrne et al., determined that the cost associated with PIP instances identified in their study population was €263 per patient per year.[8]

9.3.4 Unintended Consequences

9.3.4.1 Deprescribing: Negative Unintended Consequences

Deprescribing interventions do not always lead to an improvement in cognition scores.[9] One potential unfavorable effect of deprescribing interventions is that, while the interventions have reduced medication costs, they do not always lead to a decrease in healthcare utilization, such as hospital admissions and primary care visits.[10]

9.3.4.2 Using the STOPP Criteria: Negative Unintended Consequences

With the exception of longer lengths of stay found in one study,[6] no other unintended negative consequences were reported in the studies that examined the use of STOPP criteria to reduce ADEs. Although some researchers caution about risks related to cognitive declines when medications are reduced and/or eliminated, such findings were not discussed in the studies noted in this review.

9.3.4.3 Deprescribing: Positive Unintended Consequences

In addition to the clinical and process outcomes reported above, deprescribing also led to more positive quality of life in areas such as health transition, bodily pain, and general health.[11]

9.3.4.4 Using the STOPP Criteria: Positive Unintended Consequences

No unintended positive consequences were reported in our review of the studies that examined the use of STOPP criteria to reduce ADEs.

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9.4 Implementation

9.4.1 Summary of Evidence

We reviewed 27 studies, including 2 systematic reviews and 4 randomized controlled trials. Study interventions were heterogeneous, but most share common features. Interventions were delivered by pharmacists and/or physicians either in step-wise fashion (e.g., pharmacist conducts screening and makes recommendations; physicians review and accept/reject recommendations) or in collaboration (pharmacists and physicians review recommendations together). All studies were restricted to older adults (age 65 and older), but only three explicitly relied on geriatricians in the intervention. All STOPP interventions involved a screening step where STOPP criteria were used and included steps for making and accepting or rejecting recommendations generated from STOPP screening.

9.4.2 Barriers and Facilitators

This section describes barriers and facilitators to implementing interventions that focus on deprescribing or using STOPP criteria to reduce ADEs in older adults.

In the deprescribing literature, notable barriers to implementation included:

- Pharmacists not adhering to study protocols.[1]
- Inadequate documentation of medication history.[2,3]
- Limited communication between pharmacists and physicians.[1,4]
- Patients being discouraged from discontinuing medications by individual providers.[5]
- Patients perceiving deprescribing as contradicting their provider's recommendations.[6]
- Scheduling conflicts, competing demands, and general lack of time, which impacted medication review meetings between pharmacists and physicians.[4,6,7]
- Nonprescription medications (i.e., over-the-counter) that were not documented in medical databases, which prevented providers from seeing the full-range of medication use per patient and therefore not being able to accurately identify and include all patients who were at risk of polypharmacy in the study.[1]
- Lower acceptance rates of pharmacist interventions based on the STOPP criteria due to the lack of discontinuation of benzodiazepines.[3,8,9]

Key facilitators for deprescribing involved communication and collaboration between pharmacists and prescribing physicians during medication reviews,[4,6,10] and educating pharmacists and physicians about the risks of polypharmacy and the use of unnecessary medications in older adult patients.[11]

9.4.3 Resources To Assist With Implementation

The following resources were cited in our review of the evidence and can be used to implement future deprescribing practices:

- Good Palliative Care Algorithm[11]
  - A flow chart developed for use in nursing home settings to inform options for deprescribing.

- Epocrates Online Drug-Drug Interaction Tool[12]
  - Free web-based drug interaction tool that assists in identifying combinations of medications that could be harmful. Visit https://online.epocrates.com/interaction-check for more information.
- Canadian Deprescribing Network Patient and Pharmacist-Physician Materials[1]
  - A compilation of materials to inform and educate patients and prescribing physicians about ways to reduce the use of inappropriate medications, including alternative treatment options and evidence-based pharmaceutical opinions. Visit https://www.deprescribingnetwork.ca/patient-handouts for patient materials and https://www.deprescribingnetwork.ca/pharmaceutical-opinions for physician information.

The following resources were cited in our review of the evidence related to using the STOPP criteria:

- STOPP/START Toolkit Supporting Medication Review[13]
  - Designed to be used by healthcare professionals as a reference tool to support medication review for older adults. Developed by a consortium of professionals at the *National Health Service North of England Commissioning Support Unit* in the United Kingdom, the tool was validated for adults 65 years of age and older and can be downloaded at: https://www.herefordshireccg.nhs.uk/your-services/medicines-optimisation/prescribing-guidelines/deprescribing/748-stopp-start-herefordshire-october-2016/file.
- Comprehensive Geriatric Assessment (CGA) Toolkit Plus[14]
  - A series of rules/suggestions related to high-yield problems in prescribing for older people in terms of both reducing medication burden (STOPP) and adding in potentially beneficial therapy (START). Visit https://www.cgakit.com/m-2-stopp-start for more information.

9.4.4 Gaps and Future Directions

9.4.4.1 Gaps

9.4.4.1.1 Deprescribing

There are notable gaps in the research of implementation efforts related to deprescribing. While many interventions have applied the use of specific criteria, algorithms, and protocols, only a few studies have considered other patient-related factors, including cost, patient preference, compliance and convenience, life expectancy, and other health outcomes associated with deprescribing. Furthermore, most interventions take place in either the acute care setting or ambulatory care setting. Finally, few interventions focus on the transition from acute care to ambulatory care and primary care settings.

9.4.4.1.2 STOPP Criteria

Research in STOPP is advancing rapidly, and increasing numbers of well-designed randomized or prospective studies are being published. Little if any progress has been made, however, in examining the impact of these interventions on short- and long-term clinical,[15] utilization, and economic outcomes. Additionally, consensus is lacking on the most appropriate structure, format, and staffing, leading to heterogeneity of interventions.

9.4.4.2 Future Directions

9.4.4.2.1 Deprescribing

Recommendations for future deprescribing efforts include: factoring in perspectives and preferences of patients during the deprescribing process;[7] developing protocols that target multiple rather than specific medications and/or diseases;[7] and, with the expanding role of pharmacists, focusing on involving community pharmacists.[16] More rigorous, long-term examination is necessary to further support the promise of this approach on reducing polypharmacy and ADEs.[7,17,18]

9.4.4.2.2 STOPP Criteria

Based on the emergent evidence, STOPP appears to be most effective in reducing PIMs in older adults when used in concert with other approaches. Recommendations for future investigations call for the integration of the STOPP criteria with clinical decision support procedures as part of electronic health records as a means to improve efficiency during the screening process.[19] Combining STOPP—especially the 2014 revised version—with, or comparing it with, other screening tools such as the As Beers Criteria or the Medication Appropriateness Index could improve clinical appropriateness.[20] Researchers also recommend that future research examine the long-term clinical effects of using the STOPP criteria to reduce inappropriate medications and reduce ADEs.[21]

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Conclusion and Comment

Being able to prevent unnecessary ADEs that are associated with the use of inappropriate medication use or polypharmacy is especially important for older adults who are affected by multiple ailments and who inevitably traverse multiple healthcare settings and providers for treatment. As the evidence reviewed in this chapter suggests, deprescribing to reduce polypharmacy and use of the STOPP criteria to reduce PIMS are two approaches to consider. Albeit still emerging, studies on deprescribing highlight its potential in helping providers adjust down and/or eliminate medications based on the condition/need of patients. However, more research is needed to assess deprescribing in relation to patient adherence, compliance, and preference, as patients play a key role in a provider's ability to effectively monitor and adjust medication and treatment plans.

With regard to using the STOPP criteria to reduce PIMS, evidence suggests it is the most effective approach, but also note that it often does not—and should not—stand alone. In order to ensure that older adults are given the best possible care, in addition to screening their prescriptions for PIMS (i.e., using STOPP), it is equally important to identify more appropriate treatment options, thus also including the START criteria. More appropriate medication selection is also achieved through the use of the Beers Criteria or the Medical Appropriateness Index (MAI), which are other interventions that often accompany the use of STOPP.

While the literature in this review expands the existing knowledge of practices to reduce harm and preventable ADEs for elderly patients, in particular, the field will undoubtedly benefit from more studies that examine the short- and long-term clinical effects of reducing polypharmacy and PIMS through deprescribing and using the STOPP criteria.

10. Harms Due to Opioids

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Reviewer: Scott Winiecki, M.D.

Introduction

Background

Prescription opioids are commonly used in the treatment of pain in the United States. In 2016, an estimated 20.4 percent of U.S. adults (50 million) had chronic pain.[1] Although opioids are a key treatment option in the management of acute, post-operative, procedural, and cancer pain, there is limited evidence of their efficacy for chronic pain.[2,3]

Importance of Harm Area

In the past 20 years, there has been a dramatic increase in opioid prescribing, peaking in 2012 with 255 million prescriptions, or a rate of 81.3 opioid prescriptions per 100 persons.[4] From 1999 to 2017, nearly 400,000 drug overdose deaths involved opioids (including prescription and illegal),[5] signaling three waves of an opioid epidemic. The first wave of the opioid overdose deaths began in 1999 with increased prescribing of opioids in the 1990s.[6] The second wave began in 2010 with the increase in heroin-related overdose deaths, and the third wave in 2013 with the increase in overdoses involving synthetic opioids (e.g., illicitly manufactured fentanyl). Accordingly, in the National Action Plan for Adverse Drug Event Prevention, opioids are one of three drug classes targeted.[7] In 2017, the Department of Health and Human Services declared the opioid epidemic a public health emergency.[8]

Methods for Selecting Patient Safety Practices

Given the importance of harms due to opioids, we identified potential patient safety practices (PSPs) for both primary care practice and other settings. PSPs that were not fully addressed in existing guidelines, systematic reviews, or standards were prioritized. The candidate safety practices were discussed with the Agency for Healthcare Research and Quality (AHRQ) for consideration and final selection.

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10.1 Patient Safety Practice 1: Opioid Stewardship

10.1.1 Practice Description

Key Findings:

- The majority of studies examined multicomponent opioid stewardship, which often consisted of guideline-recommended clinical interventions or care processes, as well as implementation strategies.
- Most studies examined the effect of opioid stewardship interventions on reducing the potential risks of opioids with judicious prescribing and guideline-concordant care.
- The overall strength of the evidence on opioid stewardship is low to moderate, with variation by outcome examined.
- The strength of the evidence for opioid stewardship producing significant reductions in opioid dosages was moderate.
- Two studies examined whether their opioid stewardship initiatives reduced overdoses; neither study observed significant reductions.

Opioid stewardship—similar to antibiotic stewardship—consists of a range of risk-reduction interventions or strategies, often used in combination, to prevent adverse consequences from prescription opioids, including misuse, abuse, and overdose.[1,2] The range of opioid stewardship interventions or strategies includes the following, several of which are recommended in the Centers for Disease Control and Prevention's *Guideline for Prescribing Opioids for Chronic Pain*:

- Conduct of an individualized assessment of risks and benefits of opioids, and the appropriateness of a tapering (tapering slowly to minimize withdrawal symptoms).[3]
- Avoid coprescribing opioids and benzodiazepines or other sedative hypnotics (as appropriate).
- Use of treatment agreements (also known as controlled substance agreements or pain contracts).
- Urine drug screening (UDS).
- Checking Prescription Drug Monitoring Programs (PDMPs).
- Pain and functional assessment.
- Registry of patients with chronic pain or patients on chronic opioid therapy (COT).
- Limiting number of days supply for acute pain opioid prescriptions.
- Pill counts to detect aberrant drug-related behavior.
- Referrals to nonpharmacologic treatment providers (e.g., physical therapy), pain management, behavioral health, or addiction specialists.
- Risk assessment.

Besides recommending these specific interventions, most opioid stewardship initiatives also include *implementation strategies* to actually change practice; these implementation strategies are not necessarily unique to opioid stewardship efforts.[4,5] The studies included in this review used a range of implementation strategies to change practice, including electronic health record (EHR) tools (e.g., clinical decision support, templates, alerts, integrated PDMP, autopopulated fields), dashboards for monitoring and/or audit and feedback, provider and staff education and training, academic detailing, committee or task force on opioids, telehealth, and nurse care management.

10.1.2 Methods

The question of interest for this review is: "What is the effect of opioid stewardship interventions on key process outcomes (e.g., PDMP, treatment agreement, UDS, referrals), intermediate and clinical outcomes (e.g., opioid dosage, opioid prescriptions, overdose), and unintended consequences (e.g., change in pain)?" The review's key findings are located in the box above.

Two databases (CINAHL® and MEDLINE®) were searched for articles published in the past 10 years using terms for opioids, the outcomes of interest (opioid abuse, overdose, death), and several terms for opioid stewardship and opioid stewardship strategies.

The initial search yielded 392 abstracts; an additional 16 studies were identified from authors' knowledge of the field, expert recommendation, and reference lists. After removing duplicates, records of 408 studies were screened, from which 24 studies were reviewed for full text. Fourteen individual studies and one systematic review met the inclusion criteria, as shown in the PRISMA flow diagram in Attachment.

Studies were included if they evaluated an opioid stewardship strategy or a multicomponent opioid stewardship initiative to address potential harms of opioids. Studies that examined only effective pain management approaches were excluded if they did not concurrently address potential opioid harms. Studies of naloxone (opioid overdose reversal drug) prescribing alone were excluded from this review due to their focus on tertiary prevention (overdose reversal) versus risk reduction with primary and secondary prevention strategies; no studies included in this review had naloxone prescribing as part of their initiatives.

Studies were included if they used experimental or quasi-experimental designs with pre/post, with or without a control group. If studies were observational or qualitative studies without tests of significance or had fewer than 50 patients, they were excluded.

Studies were excluded if the outcomes were not relevant to this review (e.g., focused only on clinician outcomes, e.g., knowledge or perceptions), if the article was out of scope, or if the report did not describe an intervention.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report A through C appendixes.

10.1.3 Review of Evidence

The 14 single studies that met the inclusion criteria were characterized in terms of their setting, opioid stewardship strategies examined, study design, and outcomes. They are described in the Evidence Tables in Attachment.

Ten studies examined opioid stewardship interventions in primary care settings, of which three were in federally qualified health centers (FQHCs) or safety-net settings and two were in Veterans Administration (VA) clinics. One of the 10 studies in primary care settings examined a health system-wide opioid stewardship initiative, which included primary care practices, as well as emergency departments (EDs) and hospitals. Two studies examined opioid stewardship in EDs, one in a hospital outpatient surgery and the other in an urgent care setting.

The majority of studies examined multicomponent opioid stewardship interventions, which often consisted of guideline-recommended clinical interventions or care processes (e.g., use UDS, check PDMP), as well as implementation strategies (e.g., dashboards, audit and feedback), which are described in Section 9.1.1. There was variation in the level of detail provided in the descriptions of the various opioid stewardship initiatives. See Table 10.1 for an indication of the specific components of the opioid stewardship interventions reflected in the literature included in this review.

Table 10.1: Overview of Articles' Opioid Stewardship and Implementation Strategies, by Setting

Author, Year	Setting	Opioid Stewardship Interventions or Strategies	Implementation Strategies
Anderson et al., 2016[15]	• Primary care; Federally Qualified Health Center (FQHC)	• Treatment agreement • Urine drug screening (UDS) • Pain interference • Behavioral health visit • Project ECHO	• Education • Dashboard • Policy • Electronic Health Records (her) templates
Anderson et al., 2015[11]	• Primary care; FQHC	• Treatment agreement • Urine drug test/testing (UDT) • Document functional status • Behavioral health visit	• Dashboard
Dorflinger et al., 2014[18]	• Primary care; Veterans Affairs (VA)	• Treatment agreement • Shared decision making • Pain specialty care services • Use of nonpharmacologic treatments • Referrals	• EHR templates
Dublin et al., 2019[8]	• Primary care; integrated group practices	• Dose reduction • Risk stratification • Increased monitoring • Opioid care plans • UDS • Pain specialist consultation	• Education • Dashboard • Audit and feedback
Jacobs et al., 2016[19]	• Primary care; VA	• Pharmacist telephonic monthly assessment of medication use and aberrant drug-related behaviors at prescription renewal • Informed consent • UDT • Prescription Drug Monitoring Program (PDMP) • Electrocardiography monitoring	• EHR assessment and recommendations to provider
Liebschutz et al., 2017[6]	• Primary care; safety-net	• Nurse care management • Assessment of pain, addiction, misuse • UDTs • Pill counts • PDMPs • Electronic registry	• EHR tools • Education • Academic detailing • Electronic decision tools (intervention and control)
Von Korff et al., 2016[9]	• Primary care; integrated group practices	• Dose reduction • Risk stratification • Increased monitoring • Opioid care plans • UDS • Pain specialist consultation	• Education • Dashboard • Audit and feedback

Author, Year	Setting	Opioid Stewardship Interventions or Strategies	Implementation Strategies
Von Korff et al., 2019[10]	• Primary care; integrated group practices	• Dose reduction • Risk stratification • Increased monitoring • Opioid care plans • UDS • Pain specialist consultation	• Education • Dashboard • Audit and feedback
Weimer et al., 2016[17]	• Primary care	• Pain task force • Dose limitation • Initiation of taper for >120 morphine equivalents per day • Patient list of patients with high dosage	• Education • Policy
Weiner et al., 2019[16]	• Health system-wide	• Opioid Stewardship Committee • Prescribing, addiction, education task forces • Non-pharmacologic treatments • Referral for opioid use disorder (OUD) treatment • Naloxone	• Education • Patient education • EHR template • Integrated PDMP in EHR • Autopopulate patient discharge instructions • Connection to emergency department (ED) information exchange • Dashboard • Audit and feedback • Monitoring with opioid-related metrics
Kahler et al., 2017[12]	• ED	• Transfer "superusers" of ED to outpatient chronic pain program	• EHR alert of superusers
Neven et al., 2016[7]	• ED	• Citywide care coordination with EDs for patients' opioid-seeking behavior	• Information exchange across systems
Hartford et al., 2018[14]	• Hospital outpatient surgery	• Intra- and postoperative pain care bundle • Opioid reduction strategies	• Education • Patient education
Young et al., 2018[13]	• Urgent care	• Dose reduction • Increased monitoring	• Education • Guideline • Monitoring
Starrels et al. 2010[1] (systematic review, 11 studies)	• Pain specialists • Primary care	• Treatment agreement (10 studies) • UDT (8 studies)	• N/A

Fourteen single studies and one systematic review were included in this review. Six of the 14 studies had a control group: 2 studies were randomized controlled trials (RCTs),[6,7] 3 were interrupted time series with control groups,[89,10] and 1 was a one-way crossover intervention study with patients serving as their own control. Six pre/post intervention studies did not have a control or comparison group, and the remaining two studies were observational studies with tests of significance. The post-intervention time periods in these studies ranged from months to years.

The overall strength of the evidence on opioid stewardship was ranked low to moderate, with some variation by outcome examined.

The most clinically significant harms of opioids are opioid addiction or opioid use disorder (OUD), overdose, and death. Most studies did not examine the effect of opioid stewardship initiatives on OUD or overdose, although there were a few exceptions.[10] The majority of studies examined the effect of

opioid stewardship interventions on reducing the potential risks of opioids with judicious prescribing and guideline-concordant care (e.g., reduce inappropriate high opioid dosages; avoid coprescribing opioids and benzodiazepines; use UDS, treatment agreements).

The outcomes are presented by intermediate outcomes, process outcomes and utilization, overdose, and other outcomes.

10.1.3.1 Intermediate Outcomes

Most studies examined intermediate outcomes, including opioid prescribing, high opioid dosages and potential misuse.

Seven studies examined effects of opioid stewardship on prescribing any amounts of opioids. The evidence is low to moderate that opioid stewardship efforts decrease numbers of opioid prescriptions, the proportion of patients on long-term opioids, or days' supply.

Six of seven studies observed significant reductions in opioid prescribing either in pre/post studies or compared with control groups,[7,11-14] with the exception of Anderson et al. (2016), who observed no significant decline in opioid prescribing.[15]

Anderson et al. (2015) observed reductions in the proportion of patients on COT after their opioid stewardship intervention (from 3.4% to 3.1%; p=0.057).[11] Von Korff et al. (2016) found a significant decline in the proportion of patients receiving excess opioid days supplied (from 24.0% to 10.4% among COT patients in interventions and from 20.1% to 14.7% among COT patients in the control practices).[9]

Weiner et al. (2019) found a reduction in the number of unique patients with an opioid prescription each month (-52.6 patients; p<0.001).[16]

Hartford et al. examined a hospital outpatient surgery opioid stewardship initiative and found that only 78 of 172 (45%) patients in the post-intervention group filled their opioid prescription (p<0.001), with no significant difference in prescription renewals.[14]

Six studies examined the effect of their opioid stewardship interventions on opioid dosages, measured as morphine milligram equivalents (MMEs).[6,9,14,16-18] Four were in primary care settings,[6,9,17,18] one was health system-wide,[16] and one was in a hospital outpatient surgery.[14] The strength of the evidence for opioid stewardship initiatives producing significant reductions in opioid dosages was moderate.

While the opioid stewardship strategies varied and the post-intervention time periods ranged from months to years, the studies observed reductions in MMEs of varying magnitudes and measured in various ways. The following is a summary of the findings by the different measures of dosage used in the studies. Several studies also reported dosage in more than one way.

Mean daily MMEs decreased by 47 percent compared with control at 30 percent.[9] Weimer et al. reported that an average daily dose decreased by 64 mg (95% confidence interval [CI], 32 to 96]; p<0.001).[17]

In terms of dosage reduction, Liebschutz et al. found that intervention patients had a mean MME 6.6 mg lower than controls (p<0.001), and intervention patients were more likely than controls to have either a 10-percent MME dose reduction or opioid treatment discontinuation (adjusted odds ratio [AOR], 1.6).[6]

Studies examined high dosage by the proportion of patients on high dosages and observed a range of reductions in patients on high dosages. Von Korff et al. (2016) reported greater reductions in the intervention versus the control group (16.8% to 6.3%, a 63% reduction, vs. 20.6% to 13.6%, a 34% reduction).[9] Dorflinger et al. found that the proportion of patients receiving high-dose opioids decreased from 27.7 percent to 24.7 percent.[18]

In the health system-wide study, Weiner et al. (2019) found a significant decrease in mean MME per prescription (-0.4 MME per month, p<0.001) and prescriptions containing ≥90 MME also decreased (-48.1 prescriptions/month; p<0.001), which may or may not be statistically significant.[16]

In the study of the opioid stewardship initiative in general outpatient surgery, MMEs for prescriptions filled for the intervention group were significantly fewer than for the controls.[14]

Few studies included in this review examined misuse outcomes. One ED study found that the total number of unique controlled-substance prescribers at this specific health provider decreased from 11 to 7 (31% decrease, 95% CI, 23 to 38).[12] Another study in primary care found no difference in early refills in their intervention group compared with the control group.[6]

10.1.3.2 Process Measures and Utilization

The primary outcome targeted by most opioid stewardship initiatives was to improve use of recommended clinical interventions or care processes, or "guideline-concordant care." Five studies examined these various process outcomes.

In the randomized trial by Liebschutz et al., it was found that intervention patients were more likely than controls to receive guideline-concordant care (65.9% vs 37.8%; p<0.001; AOR, 6.0; 95% CI, 3.6 to 10.2).[6] Similarly, Jacobs et al. found significant improvements in guideline-concordant care after the pharmacist-led intervention in a VA setting.[19]

Five studies examined the effect of opioid stewardship initiatives on the use of annual UDS and observed significant increases.[6,15,18-20] In their systematic review, Starrels et al. (2010) found low to moderate evidence of the effectiveness of urine drug testing for reducing opioid misuse.[1]

One study (Jacobs et al.) found a significant increase in the use of a PDMP with opioid prescribing after implementation of a pharmacist-led risk assessment cliniced.[19]

Four studies examined the effect of opioid stewardship initiatives on the proportion of patients on COT with a treatment agreement and found significant improvements.[6,15,18,19] The systematic review by Starrels et al. (2010) found opioid misuse was modestly reduced after treatment agreements (with or without urine drug testing).[1]

Weiner et al. (2019) found that the number of prescriptions (+6.0 prescriptions/month; p<0.001) and prescribers (+0.4 providers/month; p<0.001) for the film version of buprenorphine/naloxone for OUD increased.[16]

Several opioid stewardship initiatives aimed to increase referrals to behavioral health and other specialists. Anderson et al. (2016) found significant increases in the percentage of patients with pain who had a visit with a behavioral health provider in their FQHC,[15] while Dorflinger et al. did not observe an increase.[18] Anderson et al. (2016) observed a significant increase in referral to a chiropractor,[15] and

Dorflinger et al., to physical therapy and pain management.[18] Anderson et al. (2016) also observed a significant decline in referrals to neurosurgery or orthopedic surgery and to pain specialists.[15]

The opioid stewardship initiative studied by Anderson et al. (2016) aimed to improve documentation, and significant increases were observed in the documentation of the presence of pain (64% to 82%; p=0.001), the source and/or cause of pain (62% to 74%; p=0.025), functional status (5% to 19%; p=.0.001), treatment plan (92% to 98%; p=0.002), and pain reassessment (17% to 39%; p=0.001).[15]

Two studies examined opioid stewardship initiatives in EDs and observed significant decreases in ED visits of 34 percent (from 14 to 4, a 58% decrease; 95% CI, 50 to 66)[12] and 58 percent (incidence rate ratio [IRR]=0.663; p<0.001; 95% CI, 0.569 to 0.775).[7]

10.1.3.3 Overdose

Two studies examined whether their opioid stewardship initiatives reduced overdoses. Neither study observed significant reductions.[10,16]

Von Korff et al. (2019) found that changes in overdose rates among patients did not differ significantly between intervention and control groups with the implementation of two different opioid stewardship initiatives (dose reduction and risk stratification/monitoring). Secondary analyses revealed that overdose rates decreased significantly (17% per year) with the dose reduction opioid stewardship initiative for patients on COT in intervention settings (relative annual change, 0.83; 95% CI, 0.70 to 0.99), but not in control settings (relative annual change, 0.98; 95% CI, 0.70 to 1.39). Von Korff et al. (2019) argued that the results are inconsistent given the differences observed in primary versus secondary analyses.[10]

While Weiner et al. (2019) observed a downward trend in overdoses, it was not statistically significant.[16]

10.1.3.4 Other Outcomes

Dorflinger et al. (2014) measured pain intensity over the 4-year study of a pain care and opioid stewardship model within the VA, and did not see differences from year to year.[18]

10.1.4 Implementation

Most opioid stewardship initiatives are multicomponent interventions, involving clinical interventions or care processes and often implementation strategies as well. The implementation strategies included education, policies, dashboards, audit and feedback, monitoring and metrics, health information exchange, and EHR tools. The EHR tools included an embedded PDMP, registry, alerts, autopopulation features, and templates.

The studies in this review examined multicomponent interventions and did not examine the differential effectiveness of different components.

10.1.4.1 Barriers and Facilitators

The included studies were not implementation or implementation-effectiveness designs that afforded a systematic evaluation of different implementation strategies' effectiveness.[21] The researchers of selected studies offered reflections and informal observations on facilitators and barriers to implementation of their opioid stewardship initiatives.

Anderson et al. (2015) fielded a survey of the participating primary care providers about their opioid dashboard. Respondents found the dashboard helpful for identifying patients on long-term opioids and gaps in services (85%), clinically useful (77%), and easy to use (69%).[11]

EHR tools were identified as key facilitators to opioid stewardship.[12,16,18] On the other hand, Dorflinger et al. also found EHRs limiting because of the challenges with capturing complementary health approaches (e.g., chiropractic).[18]

Weiner et al. (2019) reflected on several lessons learned. They found that it is critical to determine metrics and gain access to data at the beginning in order to guide the opioid stewardship effort. They also experienced a mismatch when primary care providers referred patients to pain specialists with the expectation that the pain physicians would prescribe opioids, whereas the specialists would only recommend opioid regimens and provide injections. Additionally, while their health system had increased access to substance use disorder treatment, their outpatient practices perceived there was inadequate access. Finally, they learned that many of these implementation challenges could be addressed by convening the various stakeholders to resolve the issues.[16]

Buy-in and administrative support were identified as key for two opioid stewardship initiatives, also.[7,12]

10.1.4.2 Resources To Assist With Implementation

- Centers for Disease Control and Prevention: Quality Improvement and Care Coordination: Implementing the CDC Guideline for Prescribing Opioids for Chronic Pain
- A Stakeholder-Driven Action Plan for Improving Pain Management, Opioid Use, and Opioid Use Disorder Treatment Through Patient-Centered Clinical Decision Support
- Six Building Blocks: A Team-Based Approach to Improving Opioid Management in Primary Care
- AHRQ: Clinical Decision Support (CDS) Connect Artifacts on Opioids and Pain Management

10.1.5 Gaps and Future Directions

This systematic review expands the evidence on opioid stewardship initiatives beyond what was known from previous reviews of specific opioid stewardship interventions or recommended strategies, but still points to several gaps and future directions for reducing the potential harms due to opioids:

- Seek out more detailed descriptions of the opioid stewardship initiatives to replicate the interventions in other practices and settings, as well as rigorously synthesize the evidence across studies.
- Improve the quality of future studies with control groups to account for secular trends, given the attention on the opioid epidemic and changing external environment, policies, regulations, and evidence.
- Examine the effect of coprescribing naloxone for patients on long-term opioid therapy on outcomes of interest.
- Study the effectiveness or benefits of different implementation strategies for changing practice in opioid stewardship efforts and in different settings.

- While the studies included in this review were not only in primary care settings, but also health system-wide, in EDs, and in an urgent care center, there is still a need to further understand the uniqueness and effectiveness of opioid stewardship efforts in different settings.
- Given that the latest waves in the epidemic's rise in overdoses are largely attributable to heroin and synthetic opioids, consider how best to identify and treat or refer patients using illicit opioids.

It should be noted that while most opioid stewardship efforts are aimed at preventing or reducing harms due to opioids with appropriate prescribing, the stewardship efforts could also result in unintended negative consequences, such as patients having poorly controlled pain, experiencing the negative consequences of forced tapers, or turning to illicit opioids.

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10.2 Patient Safety Practice 2: Initiation of Medication-Assisted Treatment in Healthcare Settings

10.2.1 Practice Description

Medication-assisted treatment (MAT) is a proven method to treat OUDs. Effective MAT includes a combination of behavioral therapy and medications approved by the Food and Drug Administration (methadone, buprenorphine, and naltrexone). Individuals with OUD can safely take medications used in MAT as part of a long-term recovery plan.

This review focuses on initiation of MAT, as MAT's effectiveness in reducing illicit opioid use and overdose deaths has already been demonstrated in multiple randomized clinical trials.[1] The review's key findings are located in the box to the right.

Key Findings:

- MAT can be initiated and provided safely in a variety of healthcare settings.
- It has been most studied in primary care settings, hospitals, EDs, and community-based centers and clinics—for example, HIV/AIDS clinics.
- Initiation of MAT in the ED, primary care setting, or outpatient clinics may result in faster access to care and longer retention in or adherence to treatment.
- The majority of the studies found through the searches of the literature had sample sizes too small to detect differences between treatment groups—for example, RCTs with limited power to detect differences. Additionally, many of the studies' followup periods were relatively short—for example, less than 6 months.

Initiation of MAT can occur in primary care offices, EDs, hospitals, and community-based centers and clinics. The setting of MAT initiation might impact process and clinical outcomes, including engagement in and adherence to the patient's treatment and recovery plan. Initiation usually refers to the first prescription of a medication, as the psychosocial aspects of the treatment are not available in every setting (e.g., hospital) in which the prescriptions can be given. Therefore, this review focuses primarily on the medication component of MAT, as studies focused on treatment initiation are more limited in scope, with relatively short followup periods.

Several studies evaluated outcomes related to the maintenance phase of treatment. The maintenance phase occurs when a patient is doing well on a stable dose of MAT medication, without side effects, cravings, or problematic use.[2] Patients achieve the maintenance phase at different lengths of time following medication initiation. A patient may remain in the maintenance phase on the same dose of medication indefinitely or may choose to taper off of the medication.

10.2.2 Methods

The review is intended to answer two primary questions:

1. Where can initiation of the pharmacotherapy component of MAT occur?
2. Which outcomes of MAT initiation have been measured in various settings?

Two databases (CINAHL® and MEDLINE®) were searched for articles published in the past 10 years using terms for opioids, the outcomes of interest (opioid abuse, overdose, death), and several terms for MAT strategies. Detailed search terms are provided in the Appendix.

The initial search yielded 469 unique abstracts. All 469 citations were screened, from which 47 studies were reviewed for full text. Twenty-six individual studies met the inclusion criteria shown in the PRISMA flow diagram.

Studies were included if they used experimental or quasi-experimental designs with pre/post, with or without a control group. Most studies had small sample sizes and many were observational in nature.

Studies were excluded if the outcomes were not relevant to this review (e.g., focused only on clinician outcomes such as knowledge or perceptions), if the article was out of scope, or if the report did not describe an intervention.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report A through C appendixes.

10.2.3 Review of Evidence

Reviewed and included studies examined initiation in a range of settings and combined with different psychosocial interventions provided in combination with MAT.

Nine of the included studies examined the feasibility, safety, and/or effectiveness of MAT initiated in primary care settings. One systematic review was included among these nine studies, which comprised 10 RCTs and 25 quasi-experimental designs.[3]

Ten studies explored outcomes associated with initiation of MAT in other outpatient settings. These included treatment programs specifically for substance abuse, a clinic to provide healthcare for homeless people, an HIV clinic, obstetric clinics, and FQHCs. One study examined outcomes among individuals introduced to buprenorphine while incarcerated.

Three studies, all originating from the same initiative at one facility, examined outcomes associated with initiation of buprenorphine and naloxone in the ED followed by 10-week followup in primary care. An additional four included studies were conducted in inpatient hospital settings.

Six studies examined the impact of the specific form of counseling or psychotherapy, as an independent variable, in various practice settings.

Three studies examined the use of shared medical appointments to provide MAT, in which several individuals who have OUD attend a longer medical appointment rather than a one-on-one appointment with a provider. The format includes all aspects of care that are covered in an individual appointment but allows more time for patient education and peer support.

A systematic review of 10 RCTs and 25 quasi-experimental designs in the primary care setting found that the most successful MAT programs involved clinical care managers—nurses or pharmacists—on the treatment team, used agreements that outlined conditions that the patient must meet to ensure continued treatment, or offered treatment induction in the patient's home.[3]

10.2.3.1 Clinical Outcome: Illicit Use of Opioids

Evidence suggests advantages to maintenance therapy as opposed to tapering MAT medications. Specifically, maintenance treatment was associated with less use of illicit opioids, as measured by urine drug tests (UDTs), as opposed to tapering off the medication after stabilization was achieved.

In an RCT of 113 patients at an urban primary care clinic, patients receiving a 3-week taper of buprenorphine reported more days per week of illicit opioid use (1.27 days) compared with those on

maintenance buprenorphine therapy (0.47 days). Patients being tapered also had fewer consecutive weeks of opioid abstinence, on average, compared with those on buprenorphine maintenance (2.70 vs 5.20 weeks). Participants in the taper groups were also less likely to complete the trial, and 16 of the 57 patients in the taper group reinitiated treatment after the trial due to relapse.[4]

Liebschutz et al. (2014) conducted an RCT of 139 hospitalized opioid-dependent patients in the general medical units of one urban safety-net hospital between 2009 and 2012. Patients were randomized to receive either transition to hospital-based outpatient buprenorphine treatment upon discharge or to receive a 5-day buprenorphine taper, which was continued at home if discharge occurred before finishing the taper. At 6-month followup, participants who received linkage to outpatient treatment were more likely to enter outpatient buprenorphine treatment (52 [72.2%] vs. 8 [11.9%]; p<0.001); were more likely to remain in treatment (12 [16.7%] vs. 2 [3.0%]; p=0.007); and were less likely to report illicit opioid use in the past month (IRR, 0.60; 95% CI, 0.46 to 0.73; p<0.01).[5]

In another RCT with three study groups, patients were randomized to receive either initiation of MAT in the ED; screening for OUD and referral to treatment; or screening, brief intervention, and referral.[6,7] Patients receiving MAT reported fewer days of illicit opioid use at 30 days and 2 months. However, no significant differences were found between the groups at 6-month followup.

A fourth RCT conducted at one outpatient substance use disorder treatment center found that clonidine as an adjunct to buprenorphine appeared to reduce craving, as evidenced by longer periods of abstinence during unstructured time—when cravings are more likely to arise—as compared with a placebo.[8]

In a hospital-based outpatient opioid treatment program, patients who received buprenorphine maintenance treatment had lower rates of positive UDTs for opioids at 20-month followup than patients who did not participate in the buprenorphine program.[9]

Results were generally mixed regarding the benefit to clinical outcomes of adding psychosocial interventions to MAT, which generally involved some form of individual or group psychotherapy using a modality such as cognitive behavioral therapy (CBT), Acceptance and Commitment Therapy (ACT), or motivational interviewing. In an RCT in which 141 patients receiving buprenorphine were randomized to receive physician management plus CBT versus physician management alone, both groups had a significant reduction in opioid use with treatment, with no additional advantage from adding CBT.[10] An RCT of 300 African-American participants receiving buprenorphine found that greater exposure to counseling was associated with negative outcomes in the form of greater days of heroin use, days of cocaine use, and days of criminal activity.[11] In an RCT of people seeking buprenorphine treatment, 49 participants were randomized to receive either standard-of-care health education or a distress tolerance intervention based on ACT, which aimed to reduce cravings. There was no statistically significant difference in the two groups' rates of opioid use at any of the three monthly followup points.[12]

10.2.3.2 Clinical Outcome: Retention in Treatment

Many studies used retention in treatment as a clinical outcome to assess MAT's effectiveness. Available evidence indicates that long-term buprenorphine maintenance in primary care may be feasible. In an observational study of 53 patients who initiated MAT in primary care, 38 percent continued to take buprenorphine after 2 years.[13]

Evidence further indicates that outcomes may be better when MAT is initiated upon first contact with the patient, as opposed to screening for OUD and providing a referral to MAT. In an RCT with three study groups, patients were randomized to receive either initiation of MAT in the ED; screening for OUD and referral to treatment; or screening, brief intervention, and referral. Patients who initiated MAT in the ED were more likely to be engaged in treatment at 30-day and 2-month followup than those in the other two groups.[6,7]

Like the evidence above indicating that initiation of MAT in the ED may be better than a referral, one RCT at an outpatient HIV clinic found that initiation of buprenorphine in the clinic resulted in faster access to care compared with referral to treatment.[14] Additionally, patients initiating MAT in the HIV clinic had fewer UDTs positive for opioids or cocaine and more visits with their primary care providers.

One included study examined 252 individuals being released from jail who had been treated with buprenorphine and naloxone while imprisoned. The outcome of interest was whether patients who continued MAT in a primary care setting were more likely to remain in treatment and abstinent from illicit opioids than those who received a referral for treatment in the community. No statistically significant differences were found between the two groups. This study did not support the hypothesis that direct linkage to care, as opposed to referral, offers a better chance of retention in care, yet it was observational with a relatively small sample size.[15]

A closely related outcome concerns whether patients who initiate MAT in the hospital are able to transition to longer term care following discharge. In a case series of 47 patients hospitalized for reasons other than treatment of opioid dependence at an urban medical center, patients were provided buprenorphine during their hospitalization if they met criteria for OUD in addition to the medical reason for the hospitalization. Twenty-two patients (46.8%) had initiated outpatient treatment between discharge and 2-month followup.[16] In another case series of 29 patients hospitalized at the same urban medical center with infective endocarditis related to intravenous drug use, patients were again provided buprenorphine during hospitalization.[17] Nine of these patients (31%) successfully initiated buprenorphine during their hospitalization, and nine patients (31%) accepted a referral to methadone maintenance following discharge. These studies did not show benefit from a followup with patients following referral.[17]

An RCT of 94 participants found that those who participated in a group-counseling CBT program were more likely to continue buprenorphine treatment than those receiving individual counseling.[18] Ober et al. (2018) found that, at an FQHC, having one session of behavioral therapy incorporating motivational interviewing and CBT improved the likelihood of engaging in MAT. However, the same study found that participants receiving the behavioral therapy intervention were more likely to report that they endorsed negative attitudes about themselves related to their substance use.[19] In a retrospective chart review of 356 patients, attending counseling was associated with completion of 6 months of buprenorphine treatment.[20]

Doorley et al. (2017) conducted a retrospective chart review of 77 opioid-dependent patients, over 60 percent of whom were currently homeless. Ninety-five percent of patients attended at least one shared medical appointment, and treatment retention at 12- and 24-week followup was 86 percent and 70 percent, respectively.[21]

10.2.3.3 Other Clinical Outcomes

Three included studies examined clinical outcomes other than those reviewed above—HIV risk behaviors, adverse events, and patient-reported outcomes. In an observational study of 166 patients receiving treatment with buprenorphine/naloxone in primary care, treatment was associated with a statistically significant reduction in overall HIV risk behaviors and drug-related behaviors in particular.[22]

Pade et al. (2012) assessed 143 patients with co-occurring chronic pain and opioid dependence at a clinic specifically for this population and found that the combination of buprenorphine and naloxone improved pain scores.[23]

Lee et al. (2009) assessed the safety and feasibility of induction to buprenorphine/naloxone at home, following assessment and education at the primary care provider's office. Of 103 patients in this observational study, no cases of severe precipitated withdrawal or adverse events were observed.[24] In a case series of 228 patients treated by two primary care providers over 4 years, only one patient experienced a rapid onset of withdrawal symptoms during buprenorphine induction.[25]

10.2.3.4 Cost Outcomes

Two cost-effectiveness studies suggest that maintenance therapy is a viable alternative to tapering from a cost perspective when quality-adjusted-life-years (QALYs) are considered. Schackman et al. (2011) examined the cost of providing long-term buprenorphine and naloxone for patients who had achieved stability on the regimen, with stability defined as 6 months in treatment. Their analysis was conducted using simulated data from hypothetical patients and concluded that the long-term use of these medications may be a cost-effective alternative to no maintenance but that further research is needed.[26] Additionally, Polsky et al. (2010) examined cost-effectiveness of detoxification using a 14-day taper of buprenorphine and naloxone, as compared with maintenance therapy, across six community outpatient treatment programs. Although treatment and medical costs for maintenance treatment were slightly higher than for detox, when analyzed at a threshold of $100,000 QALY, maintenance treatment was found to be a cost-effective alternative to detox when QALYs were taken into consideration, as the treatment resulted in better long-term health outcomes.[27]

In an RCT with three study groups, patients were randomized to receive either initiation of MAT in the ED; screening for OUD and referral to treatment; or screening, brief intervention, and referral. This RCT included a cost-effectiveness study using a subset of patients involved in the trial. Busch et al. (2017) found that the ED-initiated buprenorphine treatment was more cost-effective than either screening and referral or screening, brief intervention, and referral.[28]

10.2.4 Gaps and Future Directions

The majority of the studies found through the literature searches had sample sizes too small to detect differences between treatment groups, for example, RCTs with limited power to detect differences. Additionally, many of the studies' followup periods were relatively short, for example, less than 6 months.

Additionally, the majority of studies were focused on one component of MAT—the initiation of medications—in a few specific settings. Limited research exists on providing the initiation of MAT within the full definition of MAT and research that ties MAT to clinical outcomes. There is variance in the reported cost, clinical, and process outcomes, which makes it difficult to compare across studies.

Additionally, several studies within a specific setting were single-site studies, so there was limited variation of studies within a setting. More research is needed on the outcomes associated with the use of mobile technology, such as text messages, in delivering the psychosocial components of MAT.[3]

Research on initiating MAT in a variety of settings is critical for understanding the opportunity, capability, and outcomes associated with PSPs designed to reduce the impact and treat OUDs. As much of the previous research is limited in size and scope, future studies should incorporate defined, consistent outcomes in an expanded number of settings and with large sample sizes. Such studies would provide further insight into appropriate settings for initiating and sustaining MAT.

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Conclusion and Comment

The two PSPs addressed in this chapter—opioid stewardship and initiation of MAT in healthcare settings—aim to mitigate the potential harms of opioids, especially OUD, overdose, and death. Opioid stewardship can consist of a range of risk-reduction interventions or strategies (e.g., check PDMP, UDS, treatment agreement), often used in combination. The overall strength of the evidence on opioid stewardship varied from low to moderate by outcome. The evidence is moderately strong that opioid stewardship interventions can reduce opioid dosages (MMEs), which is an important intermediate outcome given high MMEs are associated with an increased risk of overdose.[1] The two studies that examined overdose did not find significant reductions.

MAT can be initiated and provided safely in a variety of healthcare settings. Initiation of MAT in the ED, primary care setting, or outpatient clinics may result in faster access to care and longer retention in or adherence to treatment. The majority of the studies in the review of MAT initiation had sample sizes too small to detect differences between treatment groups, and followup periods were relatively short (e.g., less than 6 months), limiting the strength of the evidence. MAT's effectiveness in reducing illicit opioid use and overdose deaths has already been demonstrated in multiple randomized clinical trials,[2] and effective MAT includes a combination of behavioral therapy and medications approved by the Food and Drug Administration (methadone, buprenorphine, and naltrexone). Research on initiating MAT in a variety is settings is critical for understanding the opportunity, capability, and outcomes associated with PSPs designed to reduce the impact of and treat OUDs. Such studies would provide further insight into appropriate settings for initiating and sustaining MAT.

References for Conclusion and Comment

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11. Patient Identification Errors in the Operating Room

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Introduction

In the first Making Health Care Safer report, authors reviewed two types of patient safety practices (PSPs) to prevent misidentifications—bar coding and strategies to avoid wrong-site surgery. While scant literature existed documenting evidence regarding healthcare applications of bar coding, that report documented four areas in which bar coding showed promise for improving patient safety: patient identification, medication dispensing and administration, specimen handling, and medical recordkeeping. For strategies to avoid wrong-site surgery, the report reviewed evidence regarding the PSP of marking the operative site and involving the patient in the process, and found that signing the site had no evidence but was a low-tech solution with high face validity. In 2004, based on expert consensus, the Joint Commission (JC) developed the Universal Protocol principles and steps for preventing wrong-site, wrong-procedure, and wrong-person surgery. In the Preoperative Checklist and Anesthesia Checklists chapter of the second Making Health Care Safer report, authors found "no literature to substantiate the effectiveness of the current Joint Commission Universal Protocol in decreasing the rate of wrong site, wrong-level surgery." Authors noted that combining signing the site and verification protocols for operating team members might be effective but resource intensive to implement.

Key Findings:

- Drawing meaningful statistical comparisons is difficult because wrong-site surgeries are rare.
- Protocols should be implemented with activities to convince and educate providers of their necessity and effectiveness.

After convening its Partnership for Health Information Technology Patient Safety workgroup and related Patient Identification workgroup, the ECRI Institute performed a literature review to better understand how to address patient identification errors in clinical care.[1] The review included 106 articles, and found that 0.9 percent to 1.86 percent involved wrong-patient procedures. During surgery, communication errors and problems during diagnostic processes were the primary causes for wrong-site/wrong-patient surgery. Wristband errors (wristbands removed during surgery and not replaced) also contributed to the wrong-patient errors. Interventions included improving design for physical, electronic, and assigned patient identifiers (e.g., through using 2 wristbands on patients undergoing procedures), and new technology and automated systems-level safety checks (e.g., bar coding technology systems for transfusions, 2-sample confirmations for blood typing).

JC has continued to emphasize the importance of patient identification, including naming it as the most important National Patient Safety Goal starting in 2014 and releasing a *Quick Safety* issue in October 2018 focused on "People, processes, health IT and accurate patient identification." The issue discusses how health information technology is one component of successful patient identification in a cross-section of healthcare settings, including the operating theater. A successful approach to patient identification must also be patient-centric, collaborative, comprehensive, and systematic, and include people in development and implementation of patient identification processes.

This review's key findings are presented in the box above.

References for Introduction

1. ECRI Institute. Patient Identification Errors. 2016. https://www.ecri.org/Resources/HIT/Patient%20ID/Patient_Identification_Evidence_Based_Literature_final.pdf.

11.1 Practice Description

Operating room processes, systems, and culture impact patient care and safety of surgical procedures. Patient identification, one component of patient safety, requires that patients, caregivers, clinicians, and providers work together to ensure accuracy and consistency, and awareness of the intent of the healthcare procedure. Patient identification errors can impact anyone and cause irreparable damage—wrong treatment to the right individual, wrong treatment to the wrong individual, delays in treatment, or serious harm or death—and errors are preventable. The estimated rate of wrong-site surgery varies from 0.0 to 4.5 per 10,000 surgeries performed.[1] Contributing factors to wrong-site surgery include incorrectly documented patient consent or lack of patient consent, failure to use site-markings, multiple surgeons, multiple procedures on the same patient, overall poor communication, and patient or family providing incorrect information.[1]

PSPs related to patient identification can help healthcare providers quickly identify the patient, the site of surgery, or correct medication to administer. This review focuses on PSPs related to patient identification errors in surgery or the operating room, specifically analyzing marking techniques and verification protocols related to performing the correct surgery for the right people. Research examining outcomes focuses primarily on compliance with protocols and procedures, as reported wrong-site events are limited in number.

11.1.1 Methods

The review intended to answer one primary question, "What PSPs can assist in decreasing patient identification error before surgery or entering the operating room?"

Two databases, CINAHL® and MEDLINE®, were searched for articles published from the past 10 years, using terms for patient identification errors specifically for healthcare provided in the operating room, the outcomes of interest (wrong patient, wrong site), and several terms for related strategies.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes C.

The initial search yielded 381 unique abstracts. All 381 citations were screened, from which 22 studies were reviewed for full text. Five evidence reviews and four systematic reviews met the inclusion criteria.

The review included observational studies and prospective audits. The search found no randomized controlled trials, studies with control groups, or experimental studies. Most studies had small sample sizes, with few having enough power to conduct significance testing. The strength of the evidence is low due to the observational and prospective nature of studies reviewed.

Studies were excluded if the outcomes were not relevant to this review (e.g., focused only on clinician outcomes such as knowledge, perceptions, or culture), if the article was out of scope, or if the report did not describe an intervention.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

11.1.2 Review of Evidence

11.1.2.1 Study Settings and Interventions

Four of the five evidence reviews and all four of the systematic reviews focused on patient identification errors in operating rooms. One evidence review examined errors in intensive care units.

Examined interventions included implementation protocols and checklists, site-marking (patient participation in site-marking and surgical site-marking by providers), and use of verification protocols and forms by healthcare providers.

11.1.2.1.1 Implementation Protocols and Checklists

Three systematic reviews and one retrospective study examined the JC Checklist Universal Protocol for Preventing Wrong Site, Wrong Procedure, Wrong Person Surgery and the World Health Organization's Safe Surgery Checklist. All found no evidence that application of checklists decreased wrong-site surgery, but both noted the difficulty in determining this, based on the low rate of wrong-site surgery and the need for a large study size to demonstrate a statistically significant decrease in wrong-site surgery.

Devine et al. (2010) found no evidence to support the effectiveness of the JC Checklist or other preventive measures in preventing a wrong-site surgery.[1] Ragusa et al. (2016) reported that the literature shows an effect of the checklists on improving patient safety and likely on preventing wrong-site surgery, but the authors noted that no systematic research knowledge supports using the checklists to prevent wrong-site surgery.[2] Hempel et al. (2015 found five studies that analyzed the effect of the Universal Protocol as a patient safety intervention.[3] One study was based on a time series of events reported to the American Board of Orthopedic Surgery database, and although it found a reduced incidence of wrong-site skin incision, wrong-site surgical exposure, incomplete operation, and wrong procedure 6 years after the implementation of the JC Universal Protocol, the trend was statistically significant.[3] Another study found a trend of reduced surgical confusion 14 months after Universal Protocol implementation, but the trend was not statistically significant. Hempel et al. also identified 25 studies that evaluated various methods of operationalizing components and alternatives to the Universal Protocol, and none of the studies reported a statistically significant effect on wrong-site surgery events. In a retrospective study, Moshtaghi et al. (2017) examined 142 cases of wrong-site surgery to evaluate the prevalence and causation of wrong-site surgery.[4] The study identified the three most common causes of wrong-site surgery as leadership (30.9%), human factors (23.4%), and miscommunication (10%), also cited by the JC as the most common causes of wrong-site surgery. Overall, the study did not demonstrate a reduction in wrong-site surgery prevalence since the implementation of the JC Universal Protocol.

11.1.2.1.2 Site-Marking

Two prospective audit studies by Masud et al. and Bergal et al. explored the use of surgical markings to limit patient identification errors.[5,6] Both studies showed high rates of compliance with the practice of using surgical markings as a tool to decrease patient identification errors and no incidence of wrong-site surgery.

In these two studies, health providers marked the surgical site with arrows drawn directly on the patient's body and signed the location using an indelible pen. A prospective audit of 500 surgical markings for a range of elective surgery sites found extremely high compliance with the process: 99.4 percent of operating surgeons marked the correct location (Masud et al., 2010).[1] The researchers also found that an indelible marker pen was used for 88 percent of correct marking cases and an arrow was used for 64 percent of correct marking cases.

Bergal et al. (2010) examined patient involvement in independently marking the surgical site in addition to the activities conducted by healthcare providers. Their study found that 68 percent of the 200 enrolled patients were compliant with marking before surgery, in all instances patients marked the correct side, and no wrong-site surgery occurred during the study.[2]

11.1.2.1.3 Use of Verification Protocols and Forms

Two studies—one qualitative survey and one observational study—examined the use of different verification protocols to limit patient identification errors. Neither study examined causation between protocols and wrong-site surgery.

The anatomic marking form (AMF) was developed in response to a 2001 JC review of the Sentinel Event Database, which found 150 cases of wrong-site, wrong-person, or wrong-procedure surgery.[7] Of these, 76 percent, or 126 cases, were related to surgery on the wrong body part or site. The JC partnered with key organizations to research the issue and, in response, developed the AMF.

The AMF has been used in more than 112,500 surgical procedures at the University of Illinois College of Medicine.[7] Key activities of this practice included:

- Hospital staff submitted an AMF, which engaged the patient in confirming the surgical site.
- JC and hospital staff established an administrative policy to guide the use of the form as an alternative process for site-marking by the surgeon.

Since the implementation of the AMF and overarching process at the College of Medicine, only one case of documented wrong-site surgery has occurred. Knight and Aucar surveyed surgeons and nursing staff regarding their use of and satisfaction with the AMF process, and found that 65 percent of 66 survey respondents indicated they used the AMF for "most or all" procedures, and 23 percent indicated they regularly followed standard site-marking practices (not including the AMF). Seventy-seven percent of respondents indicated they were very satisfied with the AMF, 16 percent were satisfied or neutral, and 7 percent were very dissatisfied and preferred traditional site-marking.[7]

In a study examining the use of a protocol to prevent wrong-site, wrong-procedure, and wrong-person surgery, researchers examined the use of a verification protocol involving the patient, and examined performance audits conducted to measure compliance and provide feedback to providers.[8] The verification protocol included the following:

1. The anesthetist or nurse anesthetist in charge of a patient performed checks on identity and site of surgery before administering the anesthetic.
    a. If the patient participated in the verification process, the patient was asked to provide his or her first and last names, date of birth, and, when applicable, the site of the surgery.
2. Following the patient identity verification, the identity data were compared with three other pieces of information:
    a. Information on the patient's wristband.
    b. Data provided in the operating theater schedule.
    c. Patient's medical record.
3. After the surgery, the site of surgery was compared with:
    a. Surgeon's mark.
    b. Information provided in the operating theater schedule.
    c. Patient's medical record.

Audits were conducted throughout the 9-month period of the intervention. Audits consisted of direct observations of the first contact between a patient and the anesthetist or nurse anesthetist, during which identity and site of surgery checks had to take place. The observational study examined compliance with the verification protocol in 1,000 interactions between patients and anesthetists or nurse anesthetists. Researchers recorded the percentage of observations that satisfied each audit criterion. Inclusion of patients in the compliance process was high (98.5% of the 1,000 interactions). With one exception, compliance with all audit criteria in the verification protocol improved significantly over time: for example, full compliance with the protocol when performing the patient identification check was at 9.7 percent in the fourth quarter of 2003 and rose to 58.7 percent in the follow-up period. The percentage of cases in which all identity data were obtained went from 19.4 percent in the fourth quarter of 2003 to 70.9 percent in the follow-up period. The one exception was the surgical site being signed by the surgeon: this was at 75.8 percent in the fourth quarter of 2003 and rose only to 83.5 percent in the follow-up period. During the follow-up period, over 90 percent compliance was reported for the two audit criteria: patient wearing wristband and check of surgical site performed.[8]

11.1.3 Implementation Findings

In a systematic review of surgery safety practices, Kim et al. (2015) concluded that the patient safety guidelines in surgery are too general and that more standardization is needed for effective and consistent implementation.[9] Kim et al. found that, when developing guidelines, the following phases and activities should be implemented:

- Receive all surgery requests in writing.
- When scheduling, verify patient documentation.
- During the preoperative visit, obtain patient's informed consent and mark the procedure site with patient involvement.
- Prior to the procedure, use a safety checklist such as the Universal Protocol.
- In post-surgery, discuss the discharge plan with the patient and caregivers before leaving the facility.

Kim et al. also found that some interventions cannot be implemented in isolation—protocols should correspond with appropriate information technology, processes should be implemented with activities to convince and educate providers of the necessity and effective use of the protocol or checklist, and checklists should be used with participatory planning. While a single change to the patient identification procedures could improve discrete processes and likely decrease the incidence of patient identification errors, a single change is not sufficient to eliminate errors.[9]

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Gaps and Future Directions

The prevalence of reported wrong-site surgeries is currently low, and patient identification errors are preventable. The studies found that health professionals use checklists, verification protocols, forms, and site-marking, and that these interventions limit the incidence of patient identification errors. Studies reviewed were observational in nature, and strength of evidence is low compared with in randomized controlled studies; therefore, future randomized controlled studies are needed to determine effectiveness. Most studies to date have had small sample sizes, limiting the ability to determine the statistical significance of observed outcomes. Interventions focused on provider and patient use of site-marking, and implementation checklists and verification protocols. The rarity of wrong-site events, one form of patient identification error, requires studies to be extremely large to demonstrate statistically significant results. Future studies should examine combining the use of checklists and protocols with supplemental interventions, correct information being shared by the patient or family member, and processes to provide multiple procedures on patient outcomes and team communication.

12. Infusion Pumps

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Introduction

In this chapter, we discuss two system-level patient safety practices that aim to reduce medication errors associated with infusion pumps, including smart pumps. One practice focuses on implementing structured process changes and redesigning workflows in order to improve efficiencies with pump use. The other focuses on investing in initial and ongoing staff training on the correct use, maintenance, and monitoring of infusion pumps.

Use of infusion pumps, and increasingly smart pumps, has become standard practice in hospitals to administer critical fluids to patients. However, there is still limited research on best practices for reducing errors and improving infusion pump use through workflow and process changes as well as education and training.

Background

Infusion pumps, common medical devices, are used to administer fluids such as nutrients or medications to patients. In comparison to manual administration of fluids, infusion pumps provide the advantage of controlled administration—the ability to deliver fluids in small volumes or at precisely programmed rates or intervals. Many newer infusion pumps are equipped with predetermined clinical guidelines, dose error reduction systems (DERSs), and drug libraries that provide a comprehensive list of medicines and fluids with dose, volume, and flow rate details. These "smart pumps" are designed to address the programming errors that traditional pumps are susceptible to by notifying a user when there is a risk of an adverse drug interaction or when the pump's parameters are set outside of specified safety limits for the medication being administered. Alerts generated by smart pumps include clinical advisories, soft stops, and hard stops. Clinical advisories provide information about medications within the administering facility's drug library, including prompts for correct administration, which are programmed into the pump by the facility or larger organization. Soft stops notify users that a selected dose is outside of the anticipated range for a specific medication. These alerts can be overridden without changing the pump's settings. Hard stops alert users that a dose is out of the institution's determined range and prohibit the infusion from being administered unless the pump is reprogrammed.[1]

As infusion pump technology continues to evolve, use of smart pumps in hospitals has increased. A report by the American Society of Health-System Pharmacists found that in 2013, 72.9 percent of all U.S. hospitals were using smart infusion pumps, compared with just 44 percent in 2007.[2] Along with this increase, many national organizations have identified implementing smart pumps as a key patient safety tool. The Institute for Safe Medication Practices (ISMP) strongly supports the use of smart pump safety features, and in 2006, the Institute of Medicine identified adoption of smart pumps as a strategy hospitals can use to help reduce the frequency and severity of medication errors.[3]

Despite the growing support for the use of smart pumps as a safety strategy, however, the literature shows varying results for the effect they have on reducing medication errors. User error, inadequate use

of safety technology, incorrect programming, and equipment failures can still occur, significantly impacting patient safety.

Importance of Harm Area

The infusion pump, along with its failures and user errors, can have significant implications for patient safety because of its ubiquitous nature and frequent use to administer critical fluids. Infusion-associated medication errors are mistakes related to ordering, transcribing, dispensing, administering, or monitoring drugs.[4] From 2005 to 2009, the U.S. Food and Drug Administration (FDA) received approximately 56,000 reports of adverse events related to the use of infusion pumps, and manufacturers conducted 87 infusion pump recalls.[5] Fourteen of these recalls were categorized as Class I, in which there is a reasonable probability that use of the recalled device will cause serious adverse health consequences or death. Although many of the events reported to the FDA were related to deficiencies in device design and engineering, user errors also occurred. One study found that almost half of all infusion-associated medication errors were attributed to deviations in following procedures and documentation requirements.[4]

Intravenous (IV) infusions in particular pose risks to patient safety due to their complexity and the multiple steps required in their administration. Studies have found that IV infusion is associated with 54 percent of all adverse drug events, 56 percent of medication errors, and 61 percent of serious and life-threatening errors.[6] In addition, IV medications are twice as likely to be involved in errors that cause harms when compared to medications delivered via other routes.[7]

Smart infusion pumps have been implemented to avert possible medication errors; however, the risk of programming errors and equipment failures has not been eliminated. For example, one study found that despite use of smart pumps, 67 percent of the infusions evaluated involved one or more discrepancies.

Methods for Selecting Patient Safety Practices

Initial literature searches for patient safety practices (PSPs) in the infusion pump harm area were focused on systematic reviews and guidelines. Results of these searches were reviewed by harm-area task leads to identify PSPs, iterate on searches as needed, and refine lists of potential PSPs on which to focus this chapter of the report. Then the project Technical Expert Panel and Advisory Group were engaged via a survey to prioritize PSPs for inclusion in the report. These survey results, along with refined recommendations for PSP inclusion, were submitted to the Agency for Healthcare Research and Quality (AHRQ) for review. After several rounds of review with AHRQ, two infusion pump PSPs were selected.

What's New/Different Since the Last Report

The infusion pump was included as a new topic in the 2013 Making Health Care Safer II report. The brief review focused on implementation of smart pumps, including integrated implementation with larger safety systems such as computerized provider order entry (CPOE) and electronic medication administration records (eMARs). The report concluded that the evidence supporting efficacy of smart pumps for prevention of medical errors is limited, and successful implementation of smart pumps requires extensive planning and usually involves multidisciplinary teams.

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12.1 PSP 1: Structured Process Change and Workflow Redesign

12.1.1 Practice Description

Established workflows are often used in clinical practice to accomplish patient care goals. In the context of infusion pumps, workflow may include having a staff hand-off procedure for shift changes or requiring two nurses to validate orders, doses, and pump programming for high-alert medications.

Studies have shown that infusion pumps can contribute to inefficiencies and lead to errors. This is largely due to time-consuming, indirect patient care tasks associated with infusion pumps, such as searching for available pumps, priming tubing, manual pump programming, responding to false or unnecessary pump alarms, and managing tangled tubing.[1] Inadequate workflows for these tasks can impede communication and cause unnecessary rework, delays, or gaps in care, all which impact patient safety.[2] Organizations must also consider how new technology, such as smart pumps, affects workflow and is best implemented in order to drive toward safer use processes. Successful implementation often requires organizational commitment, a shared vision, an understanding of the risks and strengths of current processes, and a unified design that includes all systems and stakeholders.[3] In this chapter, we review current practices related to the uses of the infusion pump in clinical settings, including designing workflows, measuring clinical outcomes associated with pump use, and barriers and facilitators to implementation.

12.1.2 Methods

Two databases (CINAHL® and PubMed/MEDLINE®) were searched for "infusion pumps," "smart pumps," and related synonyms, as well as "workflow," "workflow redesign," "process change," "product recalls and withdrawals," and other similar terms, using Boolean operators. Articles included were published from 2008 to 2018. The initial search yielded 168 results. Once duplicates were removed and additional relevant articles from selected other sources were added, a total of 163 articles were screened for inclusion, and full-text articles were retrieved. Of those, nine were selected for inclusion in this review. Articles were excluded if the outcomes were not directly relevant to the PSP addressed in this review.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

Key Findings:

Outcomes

- Four studies reported medication administration errors, procedural errors, or deviations from hospital policy as clinical outcomes of workflow or process changes.
- Two studies looked at process outcomes related to pump handling; however, mixed results were found.

Implementation

- Four studies identified streamlining and standardization of process and workflows as facilitators.
- Integrating technology and workflow was found to be a facilitator, and three studies demonstrated barriers that occur when implemented infusion pump technology and processes do not align.

12.1.3 Review of Evidence

Of the nine studies included in this review, four were observational studies, two were case studies, one consisted of semi-structured interviews, one was a perspective point prevalence study, and one was an online survey. The majority of the studies took place in a hospital setting; four took place outside of the United States.

The included studies primarily examined medication errors and deviations from hospital policy as outcomes of process changes. However, because nearly half of the studies were observational, it is difficult to draw conclusions about the impact of implemented process changes. A summary of key findings related to process changes and workflow redesign for infusion pump use are located in the Key Findings box above. The following section reviews outcomes associated with practice changes, followed by the barriers and facilitators to implementation.

12.1.3.1 Clinical Outcomes

Four of the nine studies reported clinical outcomes, including medication administration errors, procedural errors, or deviations from hospital policy, as outcomes of workflow or process changes. Deviations from hospital policy may indicate that the established processes do not align with the natural workflow of the clinic and that a workflow change is needed to better align current practice with new infusion pump technology.

Russell et al. observed a pediatric intensive care unit (PICU) before and after workflow changes as a result of expansion and implementation of a bidirectional interface between CPOE and the pharmacy system. The researchers compared the discrepancies between medication orders and infusion pump settings, and found that the overall discrepancy rate for medications did not significantly change but the type of discrepancy did. For example, they reported that the proportion of unauthorized medications decreased from 60 percent to 4 percent, but the rate of omitted medications and errors associated with dosage significantly increased.[4] In addition, Wiseman et al. conducted a pre/post observational study in Australia and found that, as a result of implementing a requirement for clinical pharmacist annotation on medication charts, medication administration errors dropped from 16.6 percent to 8.1 percent. Subsequent adoption of smart pump technology led the error rate to further decrease to 3.9 percent.[5]

Two observational studies did not measure the impact of a process change or workflow redesign on errors but reported types and frequency of errors related to an existing medication administration process. Schnock et al. measured policy violations to assess the IV medication administration process and found that the most frequent types of infusion errors were IV labeling (60%) and tubing change policies (35%).[6] Similarly, Lyons et al. observed 16 National Health Service trusts in England and found that 47.9 percent of all infusions had at least one procedural or documentation error, of which non-compliance with hospital labeling requirements was the most common.[7]

12.1.3.2 Process Outcomes

Two studies looked at process outcomes related to pump handling. DeGraff reported that in response to a shortage of IV pumps and staff members hoarding pumps, a hospital implemented a new procedure for cleaning and restocking pumps. This process change resulted in decreasing the steps for pump handling from 26 to 8.[8] The results of process change were more mixed in a study by Chaturvedi et al., in which a hospital integrated its electronic health records (EHRs), CPOE, smart pumps, and barcode-assisted medication administration (BCMA) systems, and engaged in multiple efforts to standardize workflows. The integrated system significantly reduced the amount of time required by nurses to program medications; however, nurses reported that their overall workload did not decrease and that there was an increase in the number of computer steps required to administer medications.[9]

12.1.3.3 Economic Outcomes

Biltoft and Finneman measured cost savings of integrating smart pumps with electronic medical records (EMRs) after determining the study hospital was losing revenue due to a lack of sufficient documentation to support the billed charges or missing documentation, specifically stop times, in the medication administration record for outpatient infusions. The researchers found that implementation of the integrated smart pump-EMR provided accurate start and stop times which reduced both mean lost charges for infusions (from 11.9% to 7.4%) and lost revenue (from $980,000 to $610,000).[10]

12.1.4 Implementation

12.1.4.1 Summary of Evidence on Implementation

Changing processes or redesigning workflows for infusion pumps can be a complex undertaking that includes a variety of interventions. The studies included in this review implemented or analyzed process changes that were specific to the needs of the hospital or infusion pump system and may not be generalizable. This section reviews some of the common facilitators and barriers that emerged in relation to implementing process changes or redesigning workflows to improve infusion pump use.

12.1.4.2 Facilitators and Barriers

12.1.4.2.1 Facilitators

Standardization and streamlining of processes and workflows were identified as main facilitators of optimal infusion pump use across multiple studies. For example, DeGraff found that a hospital was able to significantly improve utilization of IV infusion pumps by streamlining its workflow for cleaning and restocking pumps.[8] Biltoft and Finneman streamlined nursing workflows by reconfiguring rooms so that infusion pumps and EHR computers could be accessed at the same time, which led to more accurate infusion documentation.[10] In addition, Schnock et al. note that by reviewing existing policies, the study team recognized the benefits of using standardized tubing labels to indicate when a nurse should change tubing.[6] Finally Chaturvedi et al. found that hospital leaders viewed standardization of nursing workflow as extremely beneficial because it was perceived to reduce the frequency of nursing workarounds that could cause patient harm.[9]

The included studies also highlighted the importance of integrating technology and workflows. Pinkney et al. noted that implementation of smart pumps should be viewed as part of a larger safety initiative rather than just a technology upgrade and that in order to be successful, implementation should focus on design of workflows. For example, they found that implementing design-oriented solutions that constrain users to follow the preferred workflow, such as defaulting users into using the drug library, helps ensure users employ the safety features.[11] Similarly, Chaturvedi et al. concluded that implementation of an IV clinical integration system is not only a technology intervention but requires workflow changes to be successful.[9]

In addition, engaging multiple members of the care team in workflow redesign is an important facilitator. For example, Wiseman et al. found that clinical pharmacists play a key role in reducing error rates and should be consulted when configuring workflows.[5] Russell et al. found that after the PICU was relocated and expanded, pharmacist and dietician presence on rounds increased, resulting in greater collaboration between them and those responsible for ordering medications. This collaboration helped reduce the number of reorders.[4]

12.1.4.2.2 Barriers

Lyons et al. noted that in some cases procedural deviations are not representative of inadequate care practices but rather demonstrate a poor fit between hospital policy and everyday practice. If workflows do not align with new technology or policies are implemented that are not compatible with natural workflows, then errors or workarounds can occur that impact patient safety. For example, they found that staff reported deliberate deviations that would benefit patients but conflicted with official rules and formal procedures, such as giving patients fluids that had not yet been prescribed because a doctor was unavailable.[7] Schnock et al. found that information such as infusion start time, which was necessary to document on paper labels, was no longer needed after implementation of CPOE, eMAR, and BCMA, since it was automatically entered into the system. This example illustrates that when new technology is implemented, processes such as documentation workflows must be reevaluated for relevance.[6] Furthermore, Russell et al. noted that prior to implementation of a bidirectional interface between CPOE and the pharmacy system, if a provider requested a new urgent medication, the pharmacist could deliver the medication but would be unable to reconcile the order so it appeared as an unauthorized medication. In this case, implementing the new system rectified the misalignment between technology and the established workflow by allowing pharmacists to immediately reconcile verbal orders from physicians.[4]

Staff buy-in and hospital resources were also identified as barriers to process changes. Chaturvedi et al. reported challenges gaining buy-in from nurses to adopt workflow changes and noted that frontline staff often expressed concerns regarding the patient safety implications of workflow changes.[9] Iacovides et al. also noted that when implementing infusion pump technology, organizations need to ensure that adequate infrastructure and resources are available, and that the affected staff believe that the change is worth the time and money required.[12]

12.1.4.3 Resources To Assist with Implementation

As a result of a 2008 summit, the ISMP published Proceedings from The ISMP Summit on the Use of Smart Infusion Pumps: Guidelines for Safe Implementation and Use. A second summit was held in 2018, and the guidelines are currently being updated. The revised and expanded guidelines are designed to support optimization of smart pump technology and assist organizations in transition to smart pump interoperability. In 2010, the FDA undertook the Infusion Pump Improvement Initiative to support benefits of infusion pumps while minimizing risks. The FDA also has a list of infusion pump risk reduction strategies organized by type of user.

12.1.4.4 Gaps and Future Directions

There is strong evidence describing the frequency and type of medication and procedural errors associated with infusion pump use, however, there is limited research on workflow and process changes that can be implemented to address those errors. More implementation studies are needed to understand best practices for reducing errors and improving infusion pump use through workflow and process changes.

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12.2 PSP 2: Staff Education and Training

12.2.1 Practice Description

The literature shows that inadequate training is often associated with knowledge and rule-based mistakes when using infusion pumps.[1] These medication errors can occur when staff are inexperienced, including being unfamiliar with the medication, environment, procedure, or equipment. In addition, lack of training can lead to overriding of smart pump safety features erroneously. Although smart pumps can be a beneficial tool to reduce medication errors attributed to manual programming, using the embedded drug libraries and DERSs is not mandatory. The literature shows that nurses commonly bypass the safety features because the drug library parameters are not customized for their patient population, it takes too much time to program the pumps, and there are too many alarms.[2] To prevent overriding safety features and programming errors, some hospitals invest in initial and ongoing staff training on the correct use, maintenance, and monitoring of smart pumps. Hospitals may also implement standard procedures for pump management and provide education on the use of the standardized protocols.

The FDA recommends providing training and educational activities for all employees designed to promote the safe use of infusion pumps, including drug library usage, as a risk-reduction strategy for facility administrators and managers.[3] In addition, the ISMP, in its draft guidelines from the ISMP National Smart Infusion Pump Summit in 2018, states that organizations should establish a standard approach for staff training and ensure that the education provided emphasizes the intended safety benefits.

This section reviews studies of education and training programs implemented to address infusion pump errors by examining clinical and process outcome measures, as well as barriers and facilitators to implementation.

12.2.2 Methods

Two databases (CINAHL® and PubMed/MEDLINE®) were searched for "infusion pumps," "smart pumps," and related synonyms, as well as "in-service," "staff education," "staff training," and other similar terms, using Boolean operators. Articles included were published from 2008 to 2018. The initial search yielded 104 results. Once duplicates were removed and additional relevant articles from selected other sources were added, a total of 107 articles were screened for inclusion and full-text articles were retrieved. Of those, 12 were selected for inclusion in this review. Articles were excluded if the outcomes were not directly relevant to the PSP addressed in this review, the article was out of scope, or study design was insufficiently described.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

12.2.3 Review of Evidence

A summary of key findings related to staff education and training is located in the call-out box. The following section reviews the studies in more depth. Of the 12 studies included in this review, 5 were performance or quality improvement initiatives. Other study designs included a longitudinal study,

observational study, snapshot audit, and randomized controlled trial. Ten of the 12 studies took place in a hospital setting, two of which were pediatric hospitals. Two studies took place in a simulation laboratory used for training. Three of the studies took place outside the United States.

To evaluate the impact of implementing staff education and training on the correct use, maintenance, and monitoring of infusion pumps, the studies measured clinical outcomes as well as process outcomes related to compliance and use of safety features. The review's key findings are located in the box to the right.

Key Findings:

Outcomes

- Four studies measured clinical outcomes for the impact of investing in education on the correct use, maintenance, and monitoring of smart pumps, including three that reported a decrease in medication errors and one that reported a decrease in the number of adverse drug events.
- Two studies found an increase in nurses' adherence to using the medication safety software library as a result of education.

Implementation

- Five studies identified the type and content of education provided as facilitators.
- One of the studies noted that time and energy constraints on nurse educators can be barriers to implementing large hospital-wide education programs.

12.2.3.1 Clinical Outcomes

Of the 12 studies, 4 reported clinical outcomes for the impact of investing in education on the correct use, maintenance, and monitoring of smart pumps. Measured clinical outcomes included the number of medication errors, severe harms adverted, and adverse drug events.

A study by Ferguson et al. examined implementation of mandatory training over 4 months on the proper usage of patient-controlled analgesia pumps for all registered nurses (RNs) who use the pumps. The study found that the number of pump errors reported over 3 months significantly decreased from eight prior to the intervention to one after the intervention, addressing the primary cause of medication errors in the 22-unit hospital.[4] Van der Sluijs et al. used a Lean approach based on feedback and training to implement a fixed, dedicated moment of time to double-check medications and a standard operating procedure for changing syringe pumps. The Lean philosophy is a quality improvement method that aims to improve processes and reduce errors by paying attention to little problems. The implementation was communicated to clinical staff through lessons and instructions, and the authors found that over 18 months, the overall percentage of medication errors (the percentage of syringes used with a medication error) dropped from 17.7 percent to 2.3 percent.[5] In addition, Giuliano measured the impact of user training in a simulation lab on the frequency of programming use error for three IV smart pumps and found that use errors decreased from 30 percent to 7 percent, 17 percent to 3 percent, and 8 percent to 1 percent. Giuliano also found that programming time was significantly shorter after user training.[6]

One study measured different clinical outcomes of proper infusion pump usage: the number of severe harms adverted and adverse drug events. Orto et al. sought to increase compliance with use of the smart pump specifications by assigning nurse champions to conduct monthly educational sessions with RN staff, both individually and in groups, to ensure that they were using the smart pumps and their drug library parameters. The authors found that the aggregate number of severe harms averted (defined as high risk drugs being programmed by the nurse 2.5 times or greater than recommended) per 1,000 infusion starts over 6 months decreased from 0.68 pre-intervention to 0.44 post-intervention, indicating there were fewer episodes of severe infusion harms. In addition, the number of adverse drug events more severe than level 2—defined as events that reach the patient and require intervention and monitoring—decreased from four to one from pre-implementation to post-intervention.[7]

12.2.3.2 Process Outcomes

Studies examining the impact of implementing education and training on proper usage of infusion pumps measure compliance with pump technology protocols and adherence to using safety software. In a study by Gavriloff, researchers implemented staff education focusing on the correct use of the safety software and the benefits of preventing medication errors as part of a multicomponent intervention. The goal of the education program was to improve nurses' adherence to using the medication safety software drug library created by the healthcare organization. Just 1 month after it was implemented, the adherence rate had increased from 25 percent at baseline to 68 percent. The adherence rate further increased to 85 percent after the Chief Nursing Office sent a follow-up communication encouraging nurses to use the medication safety software.[8] In addition, Orto et al. measured compliance with use of the drug library in smart pumps in a hospital where not using the drug library constituted noncompliance with hospital policy. They found that, after implementation of a nurse-led smart pump champions program, compliance among RNs significantly increased from 85 percent to 92 percent. These gains were sustained post-intervention with a compliance of 92.9 percent and 93.3 percent at 3 and 6 months, respectively.[7]

One study examined the impact of an education intervention on the use of smart pump safety features. In a pre-intervention survey of nurses, Herring et al. found that 88.6 percent of respondents reported agreeing or strongly agreeing that training and education were adequate, and 82.8 percent agreed or strongly agreed that they knew how to use the drug library. However, 44 percent of the open-response comments requested additional training on the safety features. After implementing an education program that included a mandatory active-learning practical-skills laboratory and an optional education presentation that reviewed evidence of improved patient safety when smart pump safety features are fully used, the authors found that use of the pump mode with all safety features enabled increased from 5.5 percent to 30.5 percent.[9]

12.2.3.3 Economic Outcomes

Of the 12 studies, only 1 study measured cost outcomes. Orto et al. calculated potential cost avoidance, defined as costs that would have been incurred if the severe harms had not been averted. The study found the costs avoided because severe harms were averted came to $367,500 at the end of the intervention period compared to $612,500 6 months before the intervention. The lower cost is associated with lower numbers for severe harms averted due to the use of smart pumps.[7]

12.2.4 Implementation

12.2.4.1 Summary of Evidence on Implementation

Although limited evidence is provided in this review, common themes regarding implementation of an education intervention emerged. This section reviews some of the facilitators and barriers to implementing staff training on the correct use, maintenance, and monitoring of smart pumps.

12.2.4.2 Facilitators and Barriers

12.2.4.2.1 Facilitators

The type and content of education provided were identified as important facilitators to successful implementation. For example, Herring et al. found that education from the device manufacturer alone may be insufficient and that implementing a hands-on training targeting identified obstacles was essential to increasing use of safety features.[9] Similarly, Nemeth et al. found that in order to be most

successful, the training program should include opportunities for participants to apply learning through discussing case examples. They also found that training should provide information about the most relevant smart pump functions and the potential challenges nurses may encounter in using them. Virtual training systems have also been shown to facilitate learning, although the results are mixed.[10] In a study by Luctkar-Flude et al., participants who completed an online virtual IV pump learning module reported that the module enhanced their knowledge of programming; however, most students did not feel it increased their ability to program certain types of infusions.[11] Quattromani et al. compared use of a traditional training method with a faculty member to use of an interactive smart pump training app and found no significant difference in outcomes related to medical knowledge, performance, or learner confidence.[12]

In addition to the type of training, the choice of trainer can be a facilitator. For example, Orto el al. implemented a nurse champion-led group to improve smart pump compliance due to the success their hospital had in the past with this type of intervention.[7] Finally, Gavriloff found that training that focuses on "why" smart pumps are used instead of just "how" to use smart pumps is important to increase adherence. By understanding the safety software, nurses are able to provide ongoing evaluation on needed revisions and refinements.[8]

12.2.4.2.2 Barriers

Limited knowledge transfer and constrained hospital and staff resources were reported as potential barriers to implementation. For example, Lee found that when nurses move to different wards, they are often exposed to new devices on which they have not been trained.[13] In addition, Ferguson et al. note that after nurses are trained, they may not retain competency on use of a particular type of smart pump if they commonly use multiple types of pumps or if they infrequently use any pumps. Furthermore, Ferguson et al. note that establishing hospital-wide education programs can be a significant undertaking for staff development departments, and that the time and energy constraints on nurse educators should be carefully considered and planned.[4] Carayon et al. highlight the importance of planning by noting that a lack of attention devoted to the implementation planning process resulted in nurses reporting more negative perceptions of usefulness of information and clarity of training materials 6 weeks and 1 year after the time of the initial training.[14]

Resistance to culture change was also identified as a potential barrier. Subramanyam et al. found that, despite being educated on the use of standardized pump programming, nurses were resistant to a culture change from the old processes to a new two-person verification process.[15] Orto et al. noted that they implemented a nurse-led program focusing on promoting compliance, partnering with pharmacists, and supporting manual audits to help create a culture of safety.[7]

12.2.4.3 Gaps and Future Directions

Although the use of smart pump technology has increasingly become standard practice in hospitals, there is limited evidence on best practices for education and training on the proper usage of smart pumps. More research is needed to understand why clinicians commonly bypass smart pump safety technology and what type of training should be implemented to limit medical errors.

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Conclusion and Comment

The two patient safety practices reviewed in this chapter aim to reduce medication errors by implementing initiatives to improve the use, maintenance, and monitoring of infusion pumps. The review of evidence shows that protocols and workflows are integral to proper technology use and therefore should be carefully considered when implementing new infusion pump technology. The studies included in this review provide support for streamlining and standardizing workflows. However, more implementation studies are needed to better understand the impact of workflow changes and best practices for effective integration of processes and infusion pump use. The evidence also shows support for providing education and training on infusion pumps to promote safe use. In these studies, the type and content of education provided were highlighted as facilitators, while limited knowledge transfer and resistance to culture changes were identified as barriers.

13. Alarm Fatigue

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Introduction

Alarm fatigue occurs when clinicians experience high exposure to medical device alarms, causing alarm desensitization and leading to missed alarms or delayed response. As the frequency of alarms used in healthcare rises, alarm fatigue has been increasingly recognized as an important patient safety issue. Although the problem of alarm fatigue has been well documented, alarm-related events are often underreported, and there is still limited research examining interventions to address the issue.[1] In this chapter, we discuss two system-level patient safety practices (PSPs) that aim to address alarm fatigue: safety culture and risk assessment.

Addressing alarm fatigue through improving safety culture involves system-wide interventions, such as leadership ensuring that there are clear processes in place for safe alarm management and establishing practices to share information about alarm-related incidents and prevention strategies. The studies included in this summary provide moderate evidence for reduction in total alarms and noise level following the implementation of features of safety culture. Surveys assessing nurses' perceptions of alarm fatigue and behavior changes regarding alarm management showed mixed results; however, two studies reported perceived reduction in alarm fatigue. More high-quality studies are needed to test the effects of safety culture elements on process and outcome measures related to alarm fatigue.

Performing baseline alarm risk assessments is an important step in order to understand current needs and conditions contributing to alarm fatigue. Conducting an alarm risk assessment can include evaluating medical devices and computer systems, analyzing data from clinical event reporting systems, and assessing patient satisfaction and the physical environment. There is currently limited research studying the impact of conducting alarm risk assessments on reducing alarm fatigue. The studies in this review examined alarm risk assessments as a component of larger quality improvement (QI) projects or system-wide initiatives; still, they provide moderately strong evidence supporting the use of multidisciplinary teams to conduct these assessments.

Background

Healthcare continues to become increasingly computerized, and clinicians use an assortment of equipment and technology to monitor patient conditions. Most healthcare devices provide auditory or visual warnings intended to alert clinicians when a patient's condition deviates from a predetermined normal range. Many device alarms emit different sounds, tones, and/or pitches depending on the level of severity (i.e., advisory vs. warning vs. crisis alarms) to help clinicians determine how to respond. System status or non-clinical alarms can also occur and are caused by mechanical or electrical problems, such as a device needing new batteries.[2] Device alarms can be an important tool to assist in clinical decision making; however, alarms can become hazardous to patient safety if excessive alarm frequency coupled with high prevalence of false alarms leads to alarm fatigue.

Alarm fatigue occurs when clinicians, especially nurses, become desensitized to safety alarms due to the sheer number of alarm signals,[3] which in turn can lead to missed alarms or delayed response.[1] Alarm desensitization is compounded by the fact that false or nonactionable alarms occur frequently. False

alarms are those that occur in the absence of an intended valid event,[4] and nonactionable alarms occur when an alarm system works as designed but signifies an event that is not clinically significant and/or requires no additional intervention.[5] The high volume of these nuisance alarms is not only disruptive, but also creates a situation where staff doubt the reliability of alarms and as a result turn down the volume, ignore, or deactivate the alarms.[5] This adversely affects patient safety because clinicians are not only ignoring the nuisance alarms, but also ignoring or missing many clinically significant and actionable alarms.[3]

Importance of Harm Area

Alarm fatigue is increasingly recognized as a critical safety issue, and alarm management has become a priority for improvement in hospitals. From 2005 to 2008, the U.S. Food and Drug Administration (FDA) Manufacturer and User Facility Device Experience (MAUDE) reporting system received 566 reports of patient deaths related to monitoring device alarms.[6] Alarm fatigue was a major contributor to these events due to the excessive number of alarms and high percentage of false alarms.[6] A study at a major academic medical center found a total of more than 59,000 alarms over a 12-day period,[1] while another study found 16,953 total alarms over an 18-day period on a single medical unit.[7] Studies have shown that the percentage of false alarms can range from 72 percent to 99 percent.[1]

In growing awareness of this issue, a number of national organizations have established alarm management guidelines and prioritize addressing alarm fatigue. Since initiating its annual list of top 10 health technology hazards in 2011, the ECRI Institute has consistently identified alarm hazards as a top issue.[8] In 2011, the Association for the Advancement of Medical Instrumentation (AAMI) convened a summit with FDA, the Joint Commission, the American College of Clinical Engineers, and the ECRI Institute to address the issue of alarm safety, and published a report outlining recommendations, challenges, and priority actions.[9] In 2013, the Joint Commission published a Sentinel Event Alert on medical device alarm safety, which identified alarm fatigue as a main contributing factor to patient deaths.[1] Later that year, the Joint Commission released its 2014 National Patient Safety Goal on Alarm Management in two phases of implementation. Beginning in 2014, hospitals were required to establish alarms as an organization-wide priority and identify the most important alarms to manage based on their own internal situations. Beginning in 2016, hospitals were expected to establish policies for managing alarms and educate staff about alarm management.[10]

Methods for Selecting PSPs

Initial literature searches for PSPs in the alarm fatigue harm area were conducted, focusing on systematic reviews and guidelines. Results of these searches were reviewed by harm-area task leads to identify PSPs, iterate on searches as needed, and refine lists of potential alarm fatigue PSPs on which to focus for the report. Then the project Technical Expert Panel and Advisory Group were engaged via a survey to prioritize PSPs for inclusion in the report. These survey results, along with refined recommendations for PSP inclusion, were submitted to the Agency for Healthcare Research and Quality (AHRQ) for review. After several rounds of review with AHRQ, two alarm fatigue PSPs were selected.

What's New/Different Since the Last Report?

The potential for harm due to alarms' high frequency and low specificity was briefly discussed in the report Making Health Care Safer I, and alarm fatigue was mentioned in Making Health Care Safer II in respect to computerized provider order entry with clinical decision support systems. This is the first

Making Health Care Safer report to include an evidence review of alarm fatigue as a harm area and look at interventions specifically related to addressing alarm fatigue.

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13.1 Patient Safety Practice 1: Safety Culture

13.1.1 Practice Description

Establishing a culture of safety is essential to improving overall healthcare quality. Broadly, key features of safety culture include: acknowledgment of the high-risk nature of an organization's activities; a blame-free environment where individuals are able to report errors without fear of punishment; encouragement of collaboration across staff levels and disciplines to seek solutions to patient safety problems; and an organizational commitment of resources to address safety concerns.[1] Addressing alarm fatigue through improving safety culture can involve a variety of interventions that are often implemented as a system-wide or unit-wide initiative. Examples of these elements include the following: leadership ensures there are clear processes in place for safe alarm management and response; leadership establishes priorities for the adoption of alarm technology; and at all staffing levels, practices are established to share information about alarm-related incidents, prevention strategies, and lessons learned. This section reviews efforts to address alarm fatigue through improving safety culture; clinical outcome measures and provider perceptions, as well as barriers and facilitators to implementation, are examined.

13.1.2 Methods

Two databases (CINAHL® and MEDLINE®) were searched for articles published from 2008 to 2019 using the terms "alarm fatigue," "alarm management," and related synonyms, as well as "safety culture," "protocol," "leadership," and other similar terms. The initial database search yielded 117 results. Once duplicates were removed and 8 additional relevant articles from selected other sources were added, a total of 114 articles were screened for inclusion. Five of the eight additional articles from other sources were identified through a manual search of the Joint Commission, ECRI Institute, and AAMI websites for relevant case studies. Due to the overlap between Safety Culture and Risk Assessment for this topic, three additional articles from other sources were identified from the Risk Assessment literature search that were also relevant for this patient safety practice (PSP), and they were reviewed. After screening the 114 articles, 63 full-text articles were retrieved, of which 17 in total were selected for inclusion in this review. Articles were excluded if the outcomes were not relevant to this review, the article was out of scope, or the article did not describe an intervention.

Finally, after reviewing the initial set of full-text articles retrieved, we ran one additional search with the term "alarm desensitization" and related synonyms, which did not yield any relevant results.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report A through C appendixes.

13.1.3 Review of Evidence

A summary of key findings related to alarm management safety culture is located in the Key Findings box. The following section reviews the applicable studies in more depth by measure type. Of the 17 studies included in this review, 10 were QI initiatives, 5 were case studies, 1 was a quasi-experimental study, and 1 was an observational study. All took place in the hospital setting, with 4 of the 17 studies examining the establishment of safety culture to address alarm fatigue hospital-wide. The remaining 13 studies examined the implementation of this PSP in a specific unit, including the intensive care unit (ICU), progressive care unit (PCU), neonatal intensive care unit (NICU), and telemetry, step-down, transplant, cardiology, surgical, and surgical orthopedic units.

Key Findings:

Clinical Outcomes

- Eight studies found a decrease in the total number of alarms, including three studies that reported a decrease in the number of false alarms.
- Two studies found an overall reduction in noise level post-intervention in the study units.

Facilitators

- Securing buy-in from staff at all levels is key to achieving culture change.
- Cultural change was necessary throughout the unit to transition from alarm management being considered a nursing concern to everyone taking responsibility for alarm management.
- Changing the culture to recognize that patient safety is everyone's responsibility and each staff member has the duty to address alarms was an important step in improving care.

To evaluate the impact of implementing safety culture elements on alarm fatigue, the studies included in this review measured both clinical outcomes that are indicators of alarm fatigue as well as behavioral outcomes related to providers' perceptions of culture change.

13.1.3.1 Clinical Outcomes

Clinical outcome measures for alarm fatigue were reported in eight studies. Outcomes in these studies included total number of alarms, alarm rate, number of false alarms, and noise level. Clinical alarms are intended to provide a quick patient assessment; however, a high abundance of alarms, the majority of which are often false alarms, diminishes their efficacy. To address this abundance, the studies included in this review primarily sought to decrease overall alarm burden. The authors of the included studies note that they first identified which types of alarms were the greatest contributors to alarm fatigue and targeted those, so a decrease in overall number of alarms is consider a positive outcome.

De Vaux et al. observed 23–26 patients in a step-down unit over a 2-week period pre-implementation of the American Association of Critical-Care Nurses' (AACN) clinical toolkit to improve safety of alarm management and at three points post-intervention. The authors found that the total number of alarms decreased from 251 pre-intervention to 12 at 6 months post-intervention. They also found a decrease in the number of false alarms from 201 to 12 and a decrease in nonactionable alarms from 122 to 6 over the same time period.[2] Dandoy et al. reported that during implementation of a standardized cardiac monitor care process, which included daily electrode changes, daily evaluation of monitor parameters, and timely discontinuation of monitor use, the median number of cardiac alarms per monitored patient day decreased from 180 to 40 over 11 months, and the median number of false alarms decreased from 95 percent to 50 percent.[3] Rayo et al. found that after implementing a new continuous cardiac monitoring policy, the percentage of false alarms decreased from 18.8 percent to 9.6 percent, but the percentage of unnecessary alarms remained consistent.[4]

Five additional studies examined the change in total number of alarms, but did not measure the number of false or nonactionable alarms. A study by Epstein et al. showed that over 4 months the pilot

telemetry unit successfully lowered its total number of alarm signals by 69 percent.[5] In addition, Graham and Cvach found a 43-percent reduction in physiological monitor alarms,[6] Vockley found a 30-percent decrease in alarm signals,[7] and Whalen et al. found an 89-percent reduction in total number of audible alarms per week.[8] Finally, Srinivasa et al. reported a 54-percent reduction in the total alarm rate (alarms per bed per day).[9] Many of the interventions included in these studies were multifaceted so it is difficult to conclude which elements contributed to the changes in alarm frequency. Some of the facilitators, however, included small tests of change, educating staff on better alarm management, and empowering nursing staff to change default alarm settings. Additional facilitators are summarized below.[9]

In addition to number of alarms, alarm volume was used as a clinical outcome measure of alarm fatigue. Excessive alarm noise creates an unpleasant work environment and contributes to alarm fatigue as staff become desensitized to the white noise. Two studies measured noise level before and after an alarm-reduction patient safety intervention, and both found overall reductions in noise level in the study units. Srinivasa et al. reported that average noise in decibels (dB) for the left wing and main hallway of a surgical telemetry unit dropped from 58.94dB to 57.84dB and from 58.04dB to 54.43dB, respectively, pre- to post-intervention.[9] Whalen et al. found that the decibel level narrowed from a range of 54–90dB to 60–72dB after implementing a pilot QI project in a medical cardiology unit.[8]

13.1.3.2 Behavioral Outcomes

Safety culture is typically measured by surveying clinicians.[1] In this review, eight studies included surveys measuring physician and clinical staff perceptions, satisfaction, and understanding of procedures and factors related to implementation of the PSP.

Two studies included surveys exploring alarm fatigue. Results of a survey by Alsaad et al., before and after implementing guidelines and protocols for reducing alarms in cardiac telemetry, found a 27-percent reduction in a score of perceived alarm fatigue.[10] In a survey by Ketko et al., most respondents reported they felt that alarm fatigue was being addressed and alarm frequency decreased as a result of the implementation of processes for safe alarm management and response.[11]

Two studies asked nurses about their perception of alarm noise. Graham and Cvach found that nurses perceived the unit's overall noise level as lower after implementing changes to reduce alarms.[6] Whalen et al. found that the percentage of nurses who assessed the noise level on the unit as acceptable increased from 0 percent to 64 percent post-intervention.[8]

Three studies included surveys that asked clinicians about their perceptions and behaviors related to alarm management processes. The results from these surveys were mixed. For example, in a survey by Cameron and Little, 66 percent of nurses agreed or strongly agreed that they had improved their alarm management practices as a result of the new alarm policy, and there was a significant improvement in nurses selecting the appropriate intervention to manage an alarm. The same study, however, also reported that nurses' perceptions about alarms were more negative after the initiative in terms of reducing attention to patients, feeling overwhelmed by alarms, alarms contributing to stress levels, and situations requiring alarm disabling.[12]

Petersen and Costanzo, surveyed nurses about their knowledge of their hospital's initiatives to reduce alarm fatigue, and found that 58 percent of responding nurses felt that clinical policies and procedures were effectively used to manage alarms. However, only 15 percent of responding nurses recognized that a new alarm management team had been implemented to assess current needs, edit policies, decrease

alarm numbers, and change the culture of alarm management. In addition, only 19 percent of responding nurses recognized that new technology had been implemented to improve clinical alarm safety. Overall, the authors concluded that these survey results showed a lack of education in alarm management and therefore incorporated training into future hospital improvement intiatives[13]

Clinicians' confidence in addressing alarms may improve after implementation of an alarm management PSP. For example, after hospital-wide alarm management competency training, Allen et al. surveyed nurses and found a 13-percent decrease in the number of nurses who rated themselves as not confident in one or more aspects of monitor functionality, such as customizing patient alarms or reviewing alarm settings.[14]

13.1.3.3 Economic Outcomes

Only one included study measured outcomes of safety culture alarm management initiatives related to cost. Alsaad et al. calculated changes in cost (measured in dollars) for patients who were originally monitored by cardiac telemetry but were downgraded to being non-monitored after implementing new protocols. In accordance with the protocols, patients who were monitored with no clinical indications for cardiac telemetry were discontinued from monitoring and downgraded to a different inpatient status, resulting in a 42-percent cost reduction.[10]

13.1.3.4 Unintended Consequences

13.1.3.4.1 Negative

Authors of the studies we reviewed did not indicate many unintended negative consequences of implementing elements of safety culture to address alarm fatigue. McGrath et al. hypothesized that implementing wireless sensors would decrease the alarms caused by staff removing sensors to allow patients to move around; however, results showed a greater than expected increase in non-clinical alarms, which are associated with system status and device operation. Despite this increase, there was not a significant increase in clinical alarm rates per hour monitored, and overall alarm rates were still below a level where the authors judged that alarm fatigue would be a concern. In addition, the authors note that an increase in total number of alarms was expected in their study, because patients were monitored for a more continuous period as a result of the intervention.[15]

13.1.3.4.2 Positive

Positive unintended consequences were mentioned by a few authors. De Vaux et al. reported an incidental finding that default-setting parameters were more often customized to match a patient's clinical condition after the intervention. Pre-intervention, 39.0 percent of alarms were customized to diverge from the preset default settings (e.g., using a higher threshold to trigger the alarm), and after implementing guidelines for alarm management, 87.5 percent of alarms were customized.[2]

Vockley and Kloewer noted that introducing a new technology into a healthcare setting typically increases alarm burden, but the researchers observed that after introducing a continuous surveillance monitoring system, there were fewer and more meaningful alarms, and staff expressed higher trust that the system would relay clinically significant alarm signals, therefore easing the burden.[16]

13.1.4 Implementation

13.1.4.1 Summary of Evidence on Implementation

Improving the culture of safety in a unit or hospital can be difficult, and this PSP includes a variety of interventions involving commitment to a culture of safety by all staff at all levels, as well as changes to processes, workflows, and policies that embody this commitment. The studies we reviewed implemented a variety of changes that were specific to the unique needs of the hospital, unit, or type of monitor/alarm. Across these varied initiatives, some common themes of facilitators and barriers emerged.

13.1.4.2 Facilitators and Barriers

13.1.4.2.1 Facilitators

Buy-in, especially from leadership, can greatly facilitate an effective change in safety culture. Eight of the 17 studies directly mentioned that leadership was involved in developing and implementing the safety culture alarm fatigue PSP. For example, Jahrsdoerfer noted that hospital leaders decided to update existing alarm management processes to maximize use of modern technology.[17] Cameron et al., Rayo et al., and Whalen et al. also highlighted that strong leadership support was a key factor in successful implementation.[4,8,12] In addition to leadership commitment, securing buy-in from staff at all levels facilitates culture change. Whalen et al. noted that nurses became strong advocates of the project, which resulted in sustained change,[8] and Graham and Cvach attributed achieving true culture change in alarm management to having complete buy-in from staff.[6] AAMI also noted that a key to success was that technology matched the culture of change, and there was strong support from all stakeholders involved.[18] A survey respondent in a study by Petersen and Costanzo stated that an important step in improving care is changing the culture to recognize that patient safety is everyone's responsibility and each staff member has the duty to address alarms.[13] Echoing this, Ketko et al. noted that cultural change was necessary throughout the unit to transition from alarm management being considered a nursing concern, to everyone taking responsibility for alarm management.[11]

Another common theme identified as an implementation facilitator was the effort to standardize procedures. For example, Allen et al. stated that the health system's leaders, after recognizing a lack of standardized protocols, established a new protocol and adopted an evaluation tool across all departments in the system.[14] In addition, Graham and Cvach noted that the hospital did not have standards for alarm response before the QI project began, but as a result of the initiative, standardized education and a hospital-wide monitor protocol were implemented to improve alarm management.[6] Finally, Dandoy et al. noted that the aim of their project was to implement a standardized, team-centered process for cardiac monitoring to decrease nuisance alarms.[3]

13.1.4.4.2 Barriers

If a newly implemented alarm management process is not clearly defined or training is incomplete, adherence by clinical staff can be suboptimal. For example, Dandoy et al. found that when the cardiac monitor care process was first implemented, compliance was 33–43 percent. After roles and responsibilities were clearly defined, however, compliance increased to 73–98 percent.[3] In addition, Cameron and Little, Epstein et al., and Vockley and Kloewer noted the importance of ongoing training to educate providers about alarm management.[5,7,12]

13.1.4.3 Resources To Assist With Implementation

The AAMI Foundation National Coalition for Alarm Management Safety brings together stakeholders to discuss strategies to improve alarm management, and provides resources and toolkits for healthcare organizations to begin work in this area. The ECRI Institute developed The Alarm Safety Handbook and Workbook, which outline the measures healthcare facilities should take to effectively manage alarms. The National Association of Clinical Nurse Specialists Alarm Fatigue Toolkit provides recommendations and resources to help clinical nurse specialists effectively manage alarms and combat alarm fatigue.

13.1.5 Gaps and Future Directions

The current literature on this PSP primarily concerns QI initiatives and case studies; higher quality studies could help to better understand the impact of implementing elements of safety culture to address alarm fatigue. In addition, because efforts to improve safety culture typically involve multiple elements and are often part of a larger hospital-wide initiative, it is difficult to know which intervention(s) are most responsible for reducing alarm fatigue. The studies we reviewed had small sample sizes and focused on one hospital or specific unit, and often one type of monitor/alarm, and may have limited generalizability.

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13.2 Patient Safety Practice 2: Risk Assessment

13.2.1 Practice Description

Risk management is crucial to promoting safer healthcare and proactively identifying, prioritizing, and mitigating patient safety risk. Many national organizations recognize that conducting a baseline alarm assessment to understand current needs and conditions contributing to alarm fatigue is an important step in alarm management. For example, the AAMI Foundation recommends, as one of its Ten Ideas for Safe Alarm Management, engaging a multidisciplinary team to prepare an alarm inventory risk analysis and gap analysis that identifies patient safety vulnerabilities that could be amenable to change.[1] In addition, an element of performance for the Joint Commission's National Patient Safety Goal on Alarm Management is to "identify the most important alarm signals to manage based on: input from the medical staff and clinical departments; risk to patients if the alarm signal is not attended to or if it malfunctions; whether specific alarm signals are needed or unnecessarily contribute to alarm noise and alarm fatigue; potential for patient harm based on internal incident history; and published best practices and guidelines."[2] Conducting an alarm risk assessment can include evaluating medical devices and computer systems, including the default alarm settings; assessing patient satisfaction (e.g., sleep interruption from nuisance alarms); and assessing the physical environment to determine whether clinically significant alarm signals are audible to staff. In addition, healthcare settings may use data from event reporting systems to identify actual or near-miss harm reported by staff as a method of risk assessment. This section briefly reviews studies in healthcare facilities that engaged multidisciplinary alarm management teams to conduct alarm risk assessments.

13.2.2 Methods

Two databases (CINAHL® and MEDLINE®) were searched for articles published from 2008 to 2019 using the terms "alarm fatigue," "alarm management," and related synonyms, as well as "management," "risk assessment," "interdisciplinary," "committee," and other similar terms. The initial database search yielded 186 results. Once duplicates were removed and seven additional relevant articles from selected other sources were added, a total of 167 articles were screened for inclusion and 47 full-text articles were retrieved. Of those, 13 were selected for inclusion in this review. Articles were excluded if the outcomes were not relevant to this review, the article was out of scope, or the article did not describe an intervention.

To identify additional articles from other sources, we conducted a manual search of the Joint Commission, ECRI Institute, and AAMI websites for relevant case studies. This yielded three articles that we included. In addition, due to the overlap between Safety Culture and Risk Assessment for this topic, we identified three articles from the Safety Culture literature search that are also relevant for this PSP and were reviewed. Finally, we scanned the reference sections of all full-text articles retrieved and, as a result, identified one additional article for inclusion. These seven articles brought the total number of articles included in this review to 13.

Finally, after reviewing the initial set of full-text articles retrieved, we ran one additional search with the term "alarm desensitization" and related synonyms, which did not yield any relevant results.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report A through C appendixes.

13.2.3 Review of Evidence

Of the 13 studies included in this review, 10 were QI initiatives and 3 were case studies. All took place in the hospital setting, with 3 of the 13 studies examining the implementation of this PSP hospital-wide. The remaining 10 studies examined establishing a multidisciplinary alarm management committee to conduct ongoing alarm risk assessment in a specific unit, such as the ICU, PCU, NICU, or step-down, transplant, cardiology, surgical, or surgical orthopedic units.

All the articles included in the review of this PSP are also included in Chapter 17, Section 17.2, Safety Culture. After reviewing the literature, we found that in all the relevant studies, hospitals engaged teams to conduct an alarm fatigue risk assessment as a component of a larger QI project or system-wide initiative. In fact, for many of the studies, the team's assessment informed the creation and implementation of the safety culture initiative. Due to this overlap, many of the clinical and behavioral outcome measures for alarm fatigue detailed in the previous section are the same for this review. Highlights from these findings are briefly summarized in the Key Findings box. In addition to the outcomes measuring indicators of alarm fatigue, these studies also included outcomes from the alarm risk assessments. They are briefly described below.

13.2.3.1 Multidisciplinary Risk Assessment

The multidisciplinary teams assembled for these initiatives conducted risk assessments to understand the current state of alarm management and identify which alarms contributed most to alarm fatigue. Three studies mentioned specific methods used to conduct the analysis. In a study by Vockley, a multidisciplinary team evaluated the use of cardiac alarm technology using Failure Mode and Effects Analysis, which is a step-by-step approach for identifying errors and studying their potential consequences.[3] Similarly, a team in a study by AAMI conducted a Failure Mode and Effects Analysis, and Cameron and Little studied a team using Failure Mode Effects and Critical Analysis to assess alarm risk.[4, 5] In a study by De Vaux et al., an alarm management team used a gap analysis assessment tool from the American Association of Critical-Care Nurses to assess alarm safety.[6]

Key Findings:

Clinical Outcomes

- Five studies found a decrease in the total number of alarms.
- Three studies reported a decrease in the number of false alarms.
- Two studies found an overall reduction in noise level post-intervention in the study units.

The results from these multidisciplinary assessments varied due to the diverse range of hospital units and monitors that were studied. For example, a QI team, in a study by Cameron and Little, conducted a hospital-wide analysis and found that telemetry, pulse oximetry, intravenous pumps, and the fire alarm system were the most troublesome for nursing staff.[5] In a study by Whalen et al., a telemetry task force learned from clinicians that two types of arrhythmia alarms often created unnecessary noise because they occurred frequently but were rarely clinically significant.[7] De Vaux et al. reported that as a result of an alarm management team's assessment, audible alarms from bedside physiologic monitors were identified as the largest contributor to noise level in the medical ICUs.[6]

In addition to assessing the types of monitor that contribute to alarm fatigue, some studies focused on a specific type of alarm, and multidisciplinary teams assessed the current practices for managing those

alarms. For example, Dandoy et al. noted that a team reviewed the cardiac monitor care process to identify gaps in practice and areas for improvement.[8] Vockley reported that a team found that 40 percent to 50 percent of patients in the general medical and surgical units were monitored on cardiac telemetry, but there were no consistent criteria about which patients should be placed on cardiac telemetry monitoring.[3]

13.2.4 Implementation

13.2.4.1 Summary of Evidence on Implementation

Many of the barriers and facilitators to engaging a multidisciplinary team to conduct an alarm risk assessment are similar to those for implementing elements of safety culture to address alarm fatigue—most importantly, support from leadership and staff. This section reviews additional implementation facilitators that are specific to alarm risk assessment.

13.2.4.2 Facilitators

Engaging a team that includes stakeholders from different disciplines is an important facilitator of effectively assessing alarm fatigue risk. All the studies included in this review specifically mentioned that the multidisciplinary assessment team included representatives beyond just clinical staff, and several noted the important contributions of these additional stakeholders. For example, AAMI noted the importance of including biomedical, human factors, and cognitive systems engineers on the team to ensure that changes in a surveillance system caused no undue burden for patients and clinicians.[4] Epstein et al. found that a vendor representative on the alarm management committee helped ensure that the hospital was compliant with the alarm management goal, provided current best practice recommendations, and assisted with analysis of device integration.[9] Rayo et al. found that human factors engineers, clinicians, and IT professionals working together led to solutions that optimized usability and mitigated risks. In addition, guidance from human factors engineers led the team to measure true, false, and unnecessary alarms, which are reliable predictors of alarm response.[10] In addition, Ketko et al. noted that acknowledging alarm management as a collaborative effort was an important first step in the initiative.[11]

The decision to engage a team and conduct a risk assessment was often in response to a specific adverse patient event or external influence. For example, Vockley notes that after two sentinel events involving alarm signals at the studied hospital, a team was formed to investigate the incidents and conduct a larger assessment of the current alarm use practices.[3] Whalen et al. stated that leadership convened a telemetry task force to explore the issue of alarm fatigue after reports of sentinel events at other institutions.[7] Four studies (Cameron and Little, De Vaux et al., Epstein et al., and Rayo et al.) noted that alarm management teams were formed in response to and with the goal of meeting the Joint Commission's National Patient Safety Goal on Alarm Management.[5,6,9,10]

13.2.5 Gaps and Future Directions

As with safety culture, the studies we reviewed focused on one hospital or specific unit, so may have limited generalizability. Despite this, the research presents moderately strong evidence demonstrating the value of conducting a multidisciplinary risk assessment to address alarm fatigue.

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Conclusion and Comment

The two PSPs reviewed in this chapter aim to address alarm fatigue by implementing hospital- or unit-wide initiatives to target nonactionable, nuisance alarms and decrease overall alarm burden. The review of evidence shows that implementing elements of safety culture can lead to a decrease in the total number of alarms, number of false alarms, and overall alarm noise level; however, since these initiatives often involve multiple components, it is difficult to know which intervention(s) have the greatest impact. The evidence also shows moderately strong support for conducting risk assessments to understand the current state of alarm management and identify which alarms are the greatest contributors to alarm fatigue. The results of these risk assessments should be used to inform the implementation of processes for safe alarm management and priorities for adoption of alarm technology. Investing in training and education for care providers on new technology as well as ensuring buy-in at all levels and engaging multidisciplinary teams are key to effectively implementing these strategies to reduce alarm fatigue.

14. Delirium

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Introduction

Patient safety research and quality improvement efforts have been underway in the delirium harm area for many years, but clear and consistent recommendations regarding best practices have proven elusive. Studies have been conducted, including rigorously designed systematic reviews, but they have reached conclusions that have been contradictory and difficult to apply across settings.

One example of ongoing work to clarify practices that should be recommended is a planned Cochrane systematic review of nonpharmacological interventions for preventing delirium in hospitalized non-intensive care unit (ICU) patients.[1] A 2019 systematic review that focused on the effectiveness of nonpharmacological interventions in reducing the incidence and duration of delirium in critically ill patients concluded that "current evidence does not support the use of non-pharmacological interventions in reducing incidence and duration of delirium in critically ill patients" and recommended further research with clearly defined outcomes.[2] A 2019 Cochrane systematic review that targeted older adults in institutional long-term care (LTC) found only limited evidence on interventions for preventing delirium in the LTC setting.[3] However, a 2016 Cochrane systematic review including hospitalized non-ICU patients found moderate to strong evidence that "multicomponent interventions can prevent delirium in both medical and surgical settings and less robust evidence that they reduce the severity of delirium."[4] Hshieh and colleagues (2015) performed a meta-analysis to evaluate effectiveness of multicomponent nonpharmacological interventions in the acute care setting and found that such interventions could reduce delirium by 53 percent.[5]

Importantly, too, another recent Cochrane systematic review, which focused on pharmacological interventions for the treatment of delirium in critically ill adults, did not reach conclusions supporting the prescription of any medications to seek to avoid delirium-associated harms.[6] In recent systematic reviews examining antipsychotics for treating and preventing delirium in hospitalized adults, researchers found that current evidence does not support routine use of haloperidol or second-generation antipsychotics for prevention or treatment of delirium.[7,8] There is limited evidence that second-generation antipsychotics may lower the incidence of delirium in postoperative patients, but more research is needed. Future trials should use standardized outcome measures.

This chapter discusses three patient safety practices (PSPs) focused on delirium: use of screening and assessment tools for recognition of patients with delirium; training and education of staff to recognize signs and symptoms of delirium; and nonpharmacological interventions aimed at prevention or reduction of delirium among critically ill patients in intensive care.

Background

Delirium is the term used to refer to an acute decline in attention and cognition that constitutes a serious problem for older hospitalized patients and many residents in LTC facilities. Precipitating risk factors for delirium include acute illness, surgery, pain, dehydration, sepsis, electrolyte disturbance, urinary retention, fecal impaction, and exposure to high-risk medications. It is the most common complication among hospitalized individuals 65 years and over. Delirium in older hospitalized patients

ranges from 14 to 56 percent, with hospital mortality rates ranging from 25 to 33 percent.[9,10] Adults over 65 years of age account for 48 percent of all delirium-associated hospital days. Delirium is associated with increased mortality, postoperative complications, longer lengths of stay, functional decline, and significant financial costs.[11]

One study estimated that delirium is unrecognized in about 60 percent of all cases.[12] This statistic is particularly troubling, as early detection of delirium has been demonstrated to improve health outcomes. However, to recognize delirium, it is necessary to know the older adult's baseline health status so that any changes—which can occur within hours—can be quickly identified. Therefore, older adults should be assessed frequently using standardized tools so that up-to-date baseline information is readily available. Further, appropriate training and education for staff in recognizing and treating delirium should be provided.

Importance of Harm Area

With a longstanding and still-growing body of evidence pointing to significant health and financial impacts of delirium on hospitalization and other healthcare costs,[9-11] it is clear that individuals at risk for delirium should be identified as quickly as possible and preventive strategies should be implemented early in an encounter with the healthcare system. Affected individuals should be followed after discharge to mitigate any long-term effects of delirium after a hospital stay or other medical treatment.

Focusing patient safety efforts on delirium is appropriate, given that the problem is common and associated with serious complications, and is increasing in magnitude as the population ages. Delirium may be preventable in certain circumstances—with some estimates finding delirium preventable in 30 to 40 percent of cases[13]—thereby increasing quality and safety of care, as well as reducing costs to the healthcare system. Awareness of these costs can drive improvement in screening and assessment of individuals at risk for onset of delirium, and in further study of treatment strategies that both reduce costs of care and improve quality of life. Healthcare professionals need adequate training and education to be vigilant and effective in assessing their patients for delirium in all healthcare settings.[12,13]

Methods for Selecting Patient Safety Practices

Initial literature searches for PSPs in the delirium harm area were conducted, focusing on systematic reviews and guidelines. Results of these searches were reviewed by harm-area task leads to identify PSPs, iterate on searches as needed, and refine lists of potential PSPs on which to focus this chapter of the report. Afterward, the project Technical Expert Panel and Advisory Group were engaged via a survey to prioritize PSPs for inclusion in the report. These survey results, along with refined recommendations for PSP inclusion, were submitted to the Agency for Healthcare Research and Quality (AHRQ) for review. After several rounds of review with AHRQ, three delirium PSPs were selected.

What's New/Different Since the Last Report

The previous Making Healthcare Safer reports focused on the prevention of delirium in older hospitalized patients and the effectiveness and safety of in-facility multicomponent delirium prevention programs. This review focuses on evidence regarding the use of delirium screening tools to aid in the identification of individuals at risk for the development of delirium, and on education and training of staff in the identification of individuals at risk for developing delirium. In addition, this review looks at the contributing factors to delirium in a variety of care settings and strategies to appropriately manage

delirium as well, as nonpharmacological interventions aimed at prevention or reduction of delirium among critically ill patients in intensive care.

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14.1 PSP 1: Delirium Screening and Assessment

14.1.1 Practice Description

Key Findings:

- The tools most frequently used and evaluated in this review were the Confusion Assessment Method (CAM) and the Confusion Assessment Method-Intensive Care Unit (CAM-ICU).
- These tools have been tested singly and in comparison with other tools to determine concordance.

Delirium, a clinical diagnosis, is often unrecognized and easily overlooked.[1] Recognition requires brief cognitive screening and astute clinical observation. Key diagnostic features include an acute onset and fluctuating course of symptoms, inattention, impaired level of consciousness, and disturbance of cognition (e.g., disorientation, memory impairment, alteration in language).[2] Supportive features include disturbance in sleep-wake cycle, perceptual disturbances (hallucinations or illusions), delusions, psychomotor disturbance (hypo- or hyper-activity), inappropriate behavior, and emotional lability.

There is no widely accepted pharmacological means of preventing delirium in the at-risk population over 65 years of age. Consequently, multicomponent approaches for primary prevention of delirium have gained widespread acceptance as the most effective strategies for addressing delirium.

While a single factor may put a patient at high risk for developing delirium, it is more likely that a combination of risk factors, including multimorbidity, dementia, certain medications, and isolation, place an individual at a much higher risk, especially if he or she is over 65 years of age. The leading risk factors of delirium consistently reported at hospital admission are dementia or cognitive impairment, functional impairment, vision impairment, history of alcohol abuse, and advanced age (> 70 years). Comorbidity burden or presence of specific comorbidities (e.g., stroke, depression) are associated with an increased risk of delirium in all patient populations.

14.1.2 Methods

This review sought to identify evidence regarding performance properties of screening and assessment tests for delirium. Two databases (CINAHL® and PubMed/MEDLINE®) were searched using Boolean operators for terms including “delirium/prevention AND control,” “delirium/diagnosis,” “diagnostic techniques and procedures,” “structured approach,” “screening,” “assessment,” and “confusion assessment model.” The search was restricted to articles published from 2008 to 2018. The initial search yielded 331 results. Once duplicates were removed and relevant articles from reference lists returned in the search were added, a total of 274 articles were screened for inclusion, and a subset of full-text articles were retrieved and reviewed. Of those, 28 were selected for inclusion in this review. Articles were excluded if the outcomes were not directly relevant to the PSP addressed in this review. The search was designed to exclude literature related to alcohol-withdrawal delirium.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

14.1.3 Review of Evidence

Key findings are highlighted in the Key Findings box above.

The tools most frequently used and evaluated in this review were the Confusion Assessment Method (CAM)[3] and the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). In the studies reviewed, these are tested singly and in comparison with other tools to determine concordance.

Other tools tested include the emergency department (ED) screening form,[4] selected International Classification of Diseases-Clinical Modification (ICD-CM) Version 9 tools, Memorial Delirium Assessment Scale (MDAS),[5,6] short- and long-delirium severity forms, Richmond Agitation Sedation Scale (RASS),[7] three-minute diagnostic interview (3D)-CAM,[8,9] Delirium Rating Scale (DRS)-R98,[10-12] Diagnostic and Statistical Manual of Mental Disorders (DSM) tools, Nursing Delirium Screening Checklist/Scale (NuDESC),[13-15] Intensive Care Delirium Screening Checklist (ICDSC),[16-18] Delirium Detection Score (DDS),[13] Mini-Mental State Examination (MMSE),[19] Delirium Early Monitoring System (DEMS),[20] the Sour Seven Questionnaire,[21] the Neelon and Champagne (NEECHAM),[5] and the family version of the CAM (Family-CAM).[22,23] In the majority of the studies, the CAM tool was evaluated as the most useful.

In their review, Adamis and colleagues (2010) found that the evidence-based screening tools CAM, DRS, MDAS, and NEECHAM were all sufficiently validated "robust and useable."[5]

The following studies examined performance properties of available tools, typically comparing CAM to another tool: Adamis et al., 2010, Adamis et al., 2015, De and Wand, 2015, Gelinas et al., 2018, and Kuczmarska et al., 2016.[5,9,10,13,24]

Most of the other studies reviewed involved assessment of performance at the bedside in various settings:

- In acute care: Khan et al., 2012, Kuczmarska et al., 2016, Adamis et al., 2016, Neufeld et al., 2013, Radtke et al., 2008, Neufeld et al., 2011, Ringdal et al., 2011, Rippon et al., 2016, Shulman et al., 2016, O'Regan et al., 2014, and Rice et al., 2011.[7,9,11,14,15,18-21,25,26]
- In ICU: Khan et al., 2012, Boettger et al., 2017, van Eijk et al., 2009, Mistarz et al., 2011, Moon et al., 2018, and Vasilevskis et al., 2011.[7,16,17,27-29]
- In palliative care: Rainsford et al., 2014, and Ryan et al., 2009.[12, 30]
- In the ED: Arendts et al., 2017, and Frisch et al., 2013.[4,31]
- With family/caregivers: Bull et al., 2017, Steis et al., 2012, and Flanagan et al., 2016.[22,23,32]

Marcantonio (2014) used the 3D-CAM to evaluate 201 patients aged 75 and older, who had been admitted to general medicine or geriatric medicine services. Compared with the reference standard delirium diagnosis, the 3D-CAM had a sensitivity of 95 percent (confidence interval [CI], 90 to 97%) resulting in a positive likelihood ratio of 16.8 (95% CI, 8.9 to 31.9) and a negative likelihood ratio of 0.05 (CI, 0.01 to .20). In followup analyses, the sensitivity of the 3D-CAM improved to 96 percent and specificity to 98 percent.[8]

The CAM has also expanded into communities with its FAM-CAM version. Steis (2012) did an exploratory analysis of agreement between two primary studies: the eCare for Eldercare pilot study and the Hospital to Home: Cognitively Impaired Elders/Caregivers study. Researchers found that overall agreement between the CAM and FAM-CAM was 96 percent. Compared with the original CAM, the FAM-CAM had a sensitivity of 88 percent (95% CI, 47 to 99) and specificity of 98 percent (95% CI, 86 to 100).[23]

As part of its "Try This" series, the Hartford Institute for Geriatric Nursing has produced a two-page fact sheet on the CAM tool. It can be accessed at https://consultgeri.org/try-this/general-assessment/issue-13.pdf.

In the intensive-care setting, van Eijk (2009) compared a variety of screening tools and found that the CAM-ICU showed superior sensitivity and negative predictive value (64% and 83%, respectively) compared with the ICDSC (43% and 75%, respectively). The ICDSC showed higher specificity and positive predictive value (95% and 92% vs. 88% and 72%).[17] Neufeld (2013) compared the CAM-ICU with the NuDESC tool. The CAM-ICU had a sensitivity of 28 percent and a specificity of 98 percent. The NuDESC (using a threshold of >/- 2) had similarly high specificity of 92 percent and low sensitivity of 32 percent. If the threshold was >/-1, the sensitivity improved but the specificity was reduced.[14]

Arendts (2017) developed an ED delirium screening form and tested it in two tertiary hospitals. There was an absolute increase in delirium diagnosis of 2 percent across the study phases, but it was statistically insignificant (Pearson chi-square = 2.49, p=0.29).[4]

Mistarz and colleagues (2011) demonstrated the importance of using a structured assessment tool in the ICU rather than relying on routine nurse-patient interactions. The presence of delirium was identified by nurses in routine care in only 27 percent of CAM-ICU delirium-positive assessments in this study.[27] In their small, convenience-sample hospital study, Rice et al. (2011) documented a significant rate of nurse under-recognition of delirium in using the CAM in comparison with researcher results, pointing to a need for more research into clinical decision-making processes that nurses use in assessing acute cognitive changes and in identifying strategies to improve delirium recognition.[26] Vasilevskis and colleagues (2011) made similar observations in their ICU-focused study.[29]

Most of the studies reviewed found that the CAM or one of its variations and associated tools was reliable in identifying delirium patients. More studies comparing CAM tools to others available, such as the NuDESC, are needed in real-world practice and in a wide variety of settings other than hospitals and the ICU. New tools need to be evaluated and compared to the CAM as they are developed, especially in settings other than acute care. Attention will have to be paid to how long it takes to assess patients using these tools and the ability of clinicians to accurately use them.

14.1.4 Resources

There are many resources available on how to implement assessment and screening on all patients who are deemed at risk for developing delirium while hospitalized, including the following:

- Hartford Institute for Geriatric Nursing: https://consultgeri.org/try-this/general-assessment/issue-13.pdf
- Hospital Elder Life Program (HELP): https://www.hospitalelderlifeprogram.org/
- American Nurses Association: https://www.nursingworld.org/practice-policy/work-environment/health-safety/delirium/
- American Academy of Family Physicians: https://www.aafp.org/afp/2014/0801/p150.html
- Fong TG, Tulebaev SR, Inouye SK. Delirium in elderly adults: Diagnosis, prevention and treatment. Nat Rev Neurol. 2009;5(4):210-20. doi: 10.1038/nrneurol.2009.24.[33]

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14.2 PSP 2: Staff Education and Training

14.2.1 Practice Description

Given the significant impact of delirium on the well-being, safety, and morbidity/mortality of impacted individuals, it is of increasing importance for clinicians to be better educated and trained on how to perform delirium assessments and develop plans of care for those with delirium that focus on maintaining their safety and quality of care after discharge.

Key Findings:

- Studies find a need for more education and training to identify individuals at risk for developing delirium, the contributing factors for delirium in a variety of care settings, and strategies to appropriately manage delirium.
- Consideration should be given to implementing the Acute Care for the Elderly (ACE) model.
- Education and training using a variety of modalities—e-learning, partnering ACE units with non-ACE units, combining didactic course work with simulation or supervised clinical practice with feedback from experts—has shown promise.

14.2.2 Methods

This review sought to identify evidence regarding education and training of staff in the identification of individuals at risk for delirium and in appropriate delirium management. Two databases (CINAHL® and PubMed/MEDLINE®) were searched using Boolean operators for combinations of terms, including "delirium," "education," "in-service," "staff training," "physician," "nurse," "physical therapist," "social worker," and similar words. Selected articles were published from 2008 to 2018, and the initial search yielded 436 results. Once duplicates were removed and relevant articles from reference lists returned in the search were added, a total of 384 articles were screened for inclusion, and a subset of full-text articles were retrieved and reviewed. Of those, 27 were selected for inclusion in this review. Articles were excluded if the outcomes were not directly relevant to the PSP addressed in this review. The search excluded literature related to alcohol-withdrawal delirium.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

14.2.3 Review of Evidence

Key findings are highlighted in the Key Findings box above.

Reviewed studies identified a need for more education and training in the identification of individuals at risk for developing delirium, the contributing factors to delirium in a variety of care settings, and strategies to appropriately manage delirium. Healthcare providers and institutions should evaluate their training requirements in this area, and their specific patient populations, to plan appropriate education and training for their staff. Consideration should also be given to identifying a nursing unit where the Acute Care for the Elderly (ACE) model can be implemented if patient volume is high enough to warrant this. Some hospitals are using ACE resource nurses to support staff on other units where patients at risk for delirium are receiving care.

14.2.3.1 Improving Providers' Use of Screening and Assessment Tools

Many reviewed studies focused on improving providers' use of delirium screening and assessment tools, such as the CAM and the ICDSC. Babine and colleagues (2018) used the CAM in their study of the impact of delirium education efforts on falls and length of stay in the acute care setting, and their results suggest that interprofessional education can improve both of these outcomes.[1] Sockalingam and colleagues performed a systematic review in 2014 that suggested that interprofessional education programs may positively influence team and patient outcomes in delirium care and noted that more studies are needed.[2] Sockalingam et al. (2016) implemented a novel "flipped classroom" and train-the-trainer approach to interprofessional education in hospitals and found that this improved participants' perceived delirium care skills and confidence, as well as delirium knowledge.[3] Gordon and colleagues (2013) used didactic sessions and expert coaching at the bedside to improve nurses' ability to correctly use evidence-based delirium assessment tools for patients in a neuroscience intermediate care unit.[4] In a 2018 study conducted by Wong et al. in two academic hospitals in Canada, orthopedic-unit nurses who used the CAM daily participated in one of eight focus group sessions. While this group had mixed feelings about the CAM itself, only 35 percent of participants recalled receiving training on the tool in the past.[5] Young et al. (2012) assessed hospitalists' knowledge of the CAM and found that 82 percent had never used or heard of it, and only three respondents in this study felt proficient in its use.[6]

In the ICU setting, Devlin et al. (2008) found that use of both didactic and clinical reasoning–based educational efforts significantly improved nurses' ability to identify delirium using standardized tools. After the educational intervention in this study, the number of nurses able to evaluate delirium using any scale improved from 12 percent to 82 percent. Compliance with performing at least one delirium assessment every shift improved from 85 percent to 99 percent during the post-intervention period in this study.[7] DiLibero and colleagues (2016) made similar observations in their study in the ICU and a cardiac care unit, and they used a feedback loop, real-time auditing, and just-in-time learning techniques in their work.[8] Using the ICDSC and a multifaceted education program in the ICU setting, Gesin and colleagues (2012) found that these efforts resulted in the ability of nurses to evaluate delirium correctly.[9] Marino et al. (2015) found an increase in nurses' awareness and knowledge of ICU delirium following a formal didactic training program in the use of the ICDSC and better staff preparation for how to properly screen and manage patients.[10] In an effort to teach ICU nursing staff how to use the CAM-ICU to best effect, Nelson (2009) observed that assisting nurses with embracing the tool as part of their routine assessment activities, rather than as something added on, is essential to making improvements in this important screening and assessment step in the care of their patients.[11]

In 2017, in a Scottish study Baird and Spiller compared the CAM to the Four As Test (4AT) for assessing cognition in admitted hospice patients, with staff preferring the 4AT and the perception generally being that this tool can easily be incorporated into the admission process.[12]

Horvath and colleagues (2011) found that a low-tech, easy-to-use pocket card and assessment guide to evaluate delirium received favorable reception from an interdisciplinary group of clinical providers. This effort was disseminated systemwide in the U.S. Veterans Health Administration (VHA) primary care system.[13]

14.2.3.2 Improving Education and Training for Providers

Several researchers have examined how to better educate nurses and physicians on the care of the patient with delirium, utilizing a variety of modalities, including e-learning and partnering ACE units with non-ACE units. Detroyer (2018) developed an e-learning tool and found it to be a relatively easy and cost-effective way to educate nurses on delirium screening and management. However, no significant difference was found between the intervention cohort and the non-intervention cohort for in-hospital prevalence and duration of delirium in this study.[14]

In their study focusing on a narrative-based educational intervention for nurses in hospital units with a high incidence of delirium, Belanger and Ducharme (2015) found the intervention promising upon an initial qualitative assessment.[15] DiLibero et al. (2018) found that a nurse-led multifaceted intervention at a hospital trauma center was effective, with demonstrated improvement in delirium assessment accuracy, from 56.82 percent to 95.07 percent for all patients and 29.79 percent to 92.98 percent for sedated or agitated patients. This team called for more research of this intervention in other institutions and settings.[16] In an inpatient medical-surgical oncology unit, LaFever and colleagues (2015) implemented a delirium education program and found that it increased the nursing staff's delirium knowledge from 69 percent to 86 percent, and their overall confidence about managing delirium patients from 47 percent to 66 percent.[17] Meako et al. (2011) used a curriculum based on the Hartford Institute for Geriatric Nursing's resources and observed that a 1-hour educational intervention improved nurses knowledge; their baseline assessment had confirmed these orthopedic nurses' lack of understanding of delirium best practices.[18]

Focusing on a trauma intensive care unit (TICU), Johnson and colleagues concluded that education provided on causes of delirium, risk factors, strategies to prevent delirium, and routine screening can improve identifying and correctly treating delirium in a critical care setting. Further, their educational program had concrete results in respondents' knowledge about delirium. Changes in staff understanding that ''delirium is largely preventable'' were statistically significant ($p = 0.035$).[19]

Brooke et al. (2018) conducted a phenomenological study of cardiology, elderly care, renal, and respiratory hospital nurses using semi-structured interviews. Themes identified were that sometimes delirium is confusing, there is difficulty distinguishing between delirium and dementia, there is a need for collaborative working among providers, and patient aggression is a significant challenge. These researchers concluded there was a need for education across specialties with a combination of classroom and simulation activities.[20]

Coyle et al. (2017) explored current practices in assessing and identifying delirium in hospitalized older adults with nurses to inform educational initiatives. Themes that emerged in this work showed mixed opinions: assessing and identifying delirium is not my job; assessing and identifying delirium is my job; and assessing and identifying delirium is [too] complex.[21]

With colleagues, Godfrey (2013) developed an educational intervention implementation process aimed at embedding practice change that took a "participatory action research approach" (page 3). As part of this work, they explored knowledge and practices on delirium and delirium prevention, and found that awareness of delirium was variable, with no attention being given to prevention at any staffing level. Delirium prevention was "typically neither understood nor perceived as meaningful" (page 1).[22]

14.2.3.3 Surveying Providers About Educational Needs

Surveys and questionnaires of providers in various settings and types of units indicate that nurses and physicians feel they need more information and education about delirium.

Kennelly et al. (2013) surveyed medical, surgical, and emergency room physicians caring for older patients in the emergency room. This survey was completed by 76/97 (78%) of eligible respondents. About one-third felt they lacked the relevant expertise to perform cognitive screening; those with training in geriatrics were less likely to cite lack of experience as a factor. Seventy-eight percent of respondents felt that screening is important but identified limiting factors, including the following: lack of appropriate screening tools, lack of privacy, too much noise, and time constraints. No consensus emerged on who, ideally, should perform delirium screening.[23]

Nydahl et al. (2018) surveyed critical care nurses and physicians about delirium management in ICUs in Germany. More nurses than physicians reported screening for delirium. A majority reported screening when delirium was suspected, and more than 50 percent used validated instruments. Half of the clinicians surveyed had structures in place, such as a delirium-related process of care. This study's authors concluded that both nurses and physicians need more knowledge and training on when and how to use validated assessment instruments for identifying and managing delirium to improve safety and quality of care.[24]

In 2010, Forsgren and Erikkson conducted a survey of head nurses in Swedish ICUs. They found that assessment of delirium was performed by just 62 percent of these ICUs—commonly by observing symptoms versus using standardized tools. These authors concluded that educational efforts, including use of standardized tools, is necessary.[25]

Some researchers have reported on the provision of delirium training programs, but outcomes about participants' confidence, knowledge, and attitudes and/or clinical outcomes are not measured. Kubota et al. (2016) delivered a 16-hour program (including role-play exercises, group work, and didactic lectures) in a randomized trial for oncology nurses, with content focused on four issues: normal reactions, clinically significant distress, suicidal thoughts, and delirium. Confidence and knowledge (but not attitudes) were significantly improved in the intervention versus the control group. No significant intervention effects were found for job-related stress or burnout. Ninety-eight percent of participants considered this program useful in clinical practice.[26]

Many acute care hospitals have implemented ACE units over the past 20 years.[27] The primary purpose of the ACE model is to reduce adverse outcomes in older adults with frequent interdisciplinary team rounds. During these rounds, geriatric syndromes are recognized and managed, while transition planning is initiated from the day of admission. In previous studies, ACE units have been shown to improve processes of care, prescribing practices, physical functioning, and patient and provider satisfaction. These analyses have also suggested that ACE units help reduce rates of restraint use and institutionalization.

Booth et al. (2019) described a "Virtual ACE intervention" on two medical/surgical units in an academic medical center setting. The Virtual ACE Intervention standardizes care processes for cognition and function without daily geriatrician oversight on two non-ACE units. The Virtual ACE Intervention includes staff training on geriatric assessments for cognition and function and on nurse-driven care algorithms.

Post-intervention, the completion of the assessments for current functional status and delirium had improved from before the intervention (62.5% vs. 88.5%, p .001; 4.2% vs. 96.5%, p 001).[28]

14.2.4 Gaps and Future Directions

The studies reviewed indicated gaps in the education and training of healthcare professionals in the identification and management of individuals with delirium in all care settings. This is important because these patients are a growing population at significant risk for adverse safety events, such as falls. While no particular educational strategy was identified as a best practice, in general the reviewed articles found that a combination of didactic course work combined with either simulation or supervised clinical practice with feedback from experts improved both identification of patients and the ability of staff to implement appropriate strategies to minimize patient harms.

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14.3 PSP3: Nonpharmacological Interventions To Prevent Intensive Care Unit Delirium

14.3.1 Practice Description

The focus of this review is nonpharmacological interventions aimed at prevention or reduction of delirium among critically ill patients in intensive care. Nonpharmacological interventions aimed at prevention or reduction of delirium fall into several domains, including mobility (early mobilization, physical, occupational therapy), environmental (noise reduction, music, light adjustment, ear plugs, eye shades, avoidance of physical restraints), cognitive (reorientation, cognitive activities), and therapeutic (sleep promotion, attention to hearing or vision deficits, nutrition and hydration, minimization of indwelling urinary catheter use).

Key Findings:

- Studies have shown multicomponent nonpharmacological interventions to be effective for reduction of delirium among intensive care patients, although the quality of the evidence is low to moderate.
- Reproducibility and scalability are hindered by a lack of evidence regarding which components of many are required to achieve the desired effect.
- In addition, specific details of implementation required for replication and level of adherence to protocols are not often reported.

14.3.2 Methods

Two databases (CINAHL® and PubMed/MEDLINE®) were searched using Boolean operators for combinations of terms including "delirium/prevention AND control," "postoperative complications/prevention and control," "nonpharmacological," "intensive care unit(s)," "geriatrics," and "aged." Articles included were published from 2008 to 2018. The search aimed to retrieve intervention or patient safety practice papers related to nonpharmacological interventions to prevent or manage delirium among older adults in intensive care settings. The search excluded literature related to alcohol-withdrawal delirium, as this particular type of delirium substantively differs from postoperative or intensive care delirium.

A total of 409 records were identified with this strategy. Titles and abstracts were screened, and 76 full-text papers were acquired for more in-depth screening for eligibility for inclusion in this review. Sixty-three articles were excluded for the following reasons: out of scope (n=51); no delirium outcome measured (n=5); clinical, epidemiological, or commentary paper (n=3); only abstract available from conference presentation, with information too limited to summarize (n=3); and a dissertation, not peer-reviewed publication (n=1). Papers were deemed out of scope if the intervention or practice approach included a pharmacological component, such as administration of a medication to prevent or manage delirium, or discontinuation of medications that placed patients at higher risk for experiencing intensive care delirium (e.g., benzodiazepines). Any paper reporting an intervention conducted in a non-intensive care setting was also excluded. These two issues comprised a majority of exclusions since a combination of nonpharmacological and pharmacological interventions is the most common approach to prevention and management of delirium among older adults in intensive care; the incidence of delirium in regular medical or surgical hospital units is high; and research and quality improvement projects focused on prevention are common. This process resulted in inclusion of 13 articles in this review.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

14.3.3 Review of Evidence

Key findings are highlighted in the Key Findings box above.

Thirteen manuscripts were included in this review: eight research studies [1-8] and five reviews.[9-13] Of the research studies, four were randomized controlled trials,[1,5,6,8] one a controlled trial,[4] one a cohort study,[2] and two a pre/post quality improvement design study.[3,7] Four of the review papers were systematic reviews,[9,11-13] and one was a narrative review.[10] Studies were heterogeneous in terms of design, interventions, samples, measurement, and outcomes, limiting our ability to quantitatively summarize the evidence.

Nonpharmacological interventions are described in terms of domains, such as cognition, sensorium, function, sleep, or environment. The specific activities that comprise each domain are not consistently described across studies. For example, music therapy may be described as part of a sensory or sleep domain. As another example, light therapy is variously defined as an activity to promote sleep or an environmental intervention. For clarity in this review, specific activities or components of interventions are described to the extent possible.

In the reviewed articles, both single and multiple component interventions were tested, however, no studies examined exactly the same intervention. The setting, as mentioned in the Methods section, was intensive care. The interventions tested varied across studies, with most including multiple components. However, combinations of components differed across studies, further limiting comparability. Seven of the papers in this review reported on a single intervention: three in single studies [2,6,8] and four in systematic reviews.[9,11-13] Three studies reported interventions comprising four components.[1,3,7] Two studies tested interventions with more components, one with six[5] and the other with eight.[4]

Sleep is the focus of most interventions tested, including specific components, such as using eye masks and/or earplugs,[5,11,13] reducing light, reducing noise, clustering care,[4,5,7] and listening to patients.[3-5,7] Four studies provided sensory stimulation and ensured that patients who needed them used eyeglasses and hearing aids.[1,3,5,7] Reorientation activities and/or cognitive exercises were tested in three studies.[1,5,7] Mobility interventions, including early mobilization and other specific physical and occupational therapy activities, were tested in three studies.[1,2,8] Family involvement was mentioned in three studies,[1,2,4] although the exact type of involvement was not described in enough detail to determine the nature of the involvement. Only two studies[4,5] included pre-operative visits to the ICU as a component in their multicomponent interventions. Finally, four components identified in the reviewed papers were noted only once: social/emotional/informational support,[4] placing patients in a single room versus a group ward,[4] supportive nutrition, [5] and avoidance of physical restraints.[5]

14.3.3.1 Clinical Outcomes

The most common clinical outcomes reported were delirium incidence,[2,4,5,7,9,12,13] followed by duration of delirium.[5,7,8,9,12,13] Three papers reported relative risk for development of delirium.[1,6,11] One study reported delirium prevalence.[3] In another, outcomes were not clearly described;[10] the authors made recommendations for practice based on their analysis of the evidence reviewed.

Results related to effectiveness of nonpharmacological interventions are mixed. Nonpharmacological interventions significantly reduced delirium incidence in four trials,[4,5,7,12] while two reported nonsignificant results [2,12] and one a nonsignificant increase.[12] Statistically significant reduction in

duration of delirium was reported in four studies;[5,7-9] one study recorded a nonsignificant reduction. Significant reduction in prevalence of delirium was demonstrated in one study,[9] while a nonsignificant increase was reported in another.[3] Statistically significant reductions in risk of delirium were reported in three studies;[1,7,11] two studies demonstrated nonsignificant reduction.

14.3.3.2 Process Outcomes

As this review focused on the outcome of delirium, process outcomes were typically not considered in the reviewed studies. One study examined adherence to assessment for delirium pre- and post-intervention. Foster and Kelly reviewed 216 assessments pre-intervention, identifying missing data for delirium status in 52 records (24.07%), and reviewed 92 assessments post-intervention, finding missing data in only 8 records (8.69%). Statistical significance of the difference was not reported.[3]

14.3.3.3 Economic Outcomes

None of the research studies reviewed included any type of economic outcomes, although a cost benefit may be inferred from the report of decreased length of stay (LOS) associated with one intervention. Schweickert and colleagues' 2009 study of the effect of early mobility interventions among adult mechanically ventilated patients in the ICU setting demonstrated a decreased LOS in intervention compared with control group patients, which presumably is associated with lower overall hospital costs for the stays.[8]

14.3.3.4 Unintended Consequences

Only one study reported an adverse event. Schweickert and colleagues (2009) examined the effect of early physical and occupational therapy on delirium and functional outcomes among adult ICU patients. In 498 therapy sessions, desaturation (less than 80%) occurred in one patient, an adverse event characterized by the authors as severe. In the same study, 19 (4%) of the rehabilitation therapy sessions were discontinued because of patient instability.[8]

14.3.4 Implementation

Nonpharmacological intervention implementation was not fully described in the reviewed papers, particularly as pertains to details required for reproducibility. Details about adherence to intervention protocols were also lacking.

14.3.5 Gaps and Future Directions

14.3.5.1 Gaps

One or more nonpharmacological interventions are included in multicomponent trials, yet evidence about the relative effectiveness of each component is lacking. Providers interested in implementation of multicomponent nonpharmacological interventions in their own setting to prevent or reduce occurrence of ICU delirium have little guidance about how many and which specific components to include.

As mentioned above, the studies also lack details about specific prescriptions or protocols, guidelines, or clinical pathways that lay out how an intervention is to be carried out. There is currently no widely accepted, standardized approach to implementing nonpharmacological interventions. Finally, despite the general trend of evidence supporting the effectiveness of multicomponent nonpharmacological strategies for prevention and reduction of delirium in intensive care, large-scale methodologically rigorous studies are lacking. The level and quality of available evidence are mixed, ranging from low to

moderate. Given the importance of ICU delirium as a harm area and its implications for short- and long-term outcomes in critically ill patients, further research is warranted.

14.3.5.2 Future Directions

Although reorientation and interaction are hallmarks of multicomponent nonpharmacological programs, emerging research is exploring more specific cognitive training exercises that may prevent or reduce severity or duration of delirium in the ICU. Wassenaar and colleagues (2018) conducted a two-phase pilot study with ICU adult delirious and non-delirious patients to determine the feasibility of selected cognitive training exercises. Feasibility was assessed via surveys of patients and ICU nurses in multiple dimensions: difficulty, burden, exhaustion, clarity, fun factor, and general appreciation. Exercises that patients scored as more difficult or burdensome, not easy to understand, not fun, and/or very tiring were deleted following phase 1 of the pilot test. The remaining exercises tested in phase 2 of the study were found to be feasible among cooperative delirious and non-delirious patients.[14] Among several nonpharmacological interventions for prevention of delirium, future research may investigate the effect of these exercises on delirium and other outcomes.

Multidisciplinary team-based approaches have shown promise in preventing or improving management of delirium, involving collaboration among physicians, nurses, social workers, and engaged families and caregivers. The American Nurses Association (ANA) 2016 publication "Delirium: A Nurse's Primer" is an important resource in this harm area. A 2016 ANA Delirium Workgroup also published a set of prevention strategies that is a valuable resource.

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Conclusion and Comment

Large-scale, methodologically rigorous studies are lacking, despite a general trend of evidence supporting the effectiveness of multicomponent nonpharmacological strategies for prevention and reduction of delirium. Given the importance of delirium as a harm area in many healthcare settings, additional research appears necessary. The results of this review highlight the need for evidence-based tools that can be readily used by frontline caregivers to reliably assess and re-assess patients for signs/symptoms of delirium, whether they are in acute care or in a variety of post-acute care settings.

Early identification of delirium and the application of best practices to reduce harm with these populations at risk for delirium are crucial to maintaining patients' functional capabilities and improving their safety in the healthcare system. The literature is clear that unrecognized, untreated delirium leads to adverse events such as falls, polypharmacy, restraints, and readmissions. Studies reviewed found that the CAM or one of its variations and associated tools was reliable in identifying delirium patients. More studies should compare the CAM to other instruments available, such as the NuDESC, and in settings other than the hospital and intensive care environments. New tools should also be evaluated as they are developed, again especially in settings other than acute care. Attention will have to be given to how long it takes to assess patients using these tools and the ability of clinicians to accurately use them. Additional time may be needed for ongoing training and evaluation of competence in using methods and tools specific to a particular institution.

There is clearly an ongoing need for inclusion of delirium as an important patient safety topic in the education and training of clinicians and other providers including nurses, physicians, pharmacists, and social workers, especially as our population continues to rapidly age. Education and training utilizing a variety of modalities—including e-learning, partnering ACE units with non-ACE units, and combining didactic course work with either simulation or supervised clinical practice with feedback from experts—have shown promise.

15. Care Transitions

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Introduction

Importance of Harm Area

As patients prepare to move from the hospital to other settings, failing to make adequate discharge arrangements can lead to costly and unnecessary hospital readmissions, preventable adverse events, and drug-related errors.[1-12] For example, in 2008 nearly one-fifth of Medicare beneficiaries had an unplanned hospital readmission within 30 days of discharge, which together totaled nearly $15 billion; more than 75 percent of those readmissions (costing about $12 billion) were potentially preventable.[13]

Ensuring safe and seamless transitions starts well before hospital discharge.[14] Successful transitioning of patients from the hospital to other care settings is a dynamic, multifaceted process in which healthcare systems, hospitals, providers, patients, and their families share responsibility. Models or interventions such as Better Outcomes for Older Adults (BOOST), the Care Transitions Intervention (CTI), and the Transitional Care Model (TCM) were developed with the intention of improving transitions across the continuum of care. These models appear to be especially beneficial for high-risk and older adult populations, who are often hospitalized; move frequently across care settings; and experience high rates of post-discharge complications, readmissions, or morbidity and mortality.[10,15-18]

Methods for Selecting Patient Safety Practices

Initial literature searches for patient safety practices (PSPs) in the harm area of care transitions were focused on systematic reviews and guidelines. Results of these searches were reviewed by task leads for the harm areas to identify PSPs, iterate on searches as needed, and refine lists of PSPs to concentrate on. Next, the project Technical Expert Panel and Advisory Group were engaged via a survey to prioritize PSPs for inclusion in the report. These survey results, along with refined recommendations for PSP inclusion, were submitted to the Agency for Healthcare Research and Quality (AHRQ) for review. After several rounds of review with AHRQ, one care transition PSP was selected for this harm area: use of multi-element models to improve care transitions.

PSP: Use of Multi-Element Models To Improve Care Transitions

This review includes articles published from 2004 to 2017 that focus on transitional care and patient safety. It highlights three evidence-based multi-element care transition models that were developed to reduce harm and improve transitions as patients move from one setting to another, specifically from hospital to home. The three models are Better Outcomes for Older adults through Safe Transitions (BOOST), the Care Transitions Intervention (CTI), and the Transitional Care Model (TCM). The definition of this practice area, along with key elements recommended by the National Transitions of Care Coalition (NTCC), are to help shape the thinking about how best to improve transitional care practices. An overview of each of the three models and a discussion of the current evidence are presented in this chapter. The review concludes by identifying potential gaps or challenges and future directions.

Practice Description

Transitioning patients from one setting to another is a particularly vulnerable time. Safety lapses can result in negative clinical outcomes,[1-4] preventable adverse events,[5-9] and avoidable hospital readmissions.[10,12] The Joint Commission defines transitions of care as "the movement of patients between health care practitioners, settings, and home, as their conditions and care needs change."[19] In light of consequences that hospitals can face when patients return within 30 to 60 days of discharge,[20,21] this review focuses specifically on evidence related to transitions from hospitals to ambulatory care settings, by highlighting three multi-element models as indicated in the Key Findings box.

Key Findings:

BOOST
- Implementing BOOST contributes to reductions of 30-day re-hospitalization rates, and using the assessment tool accurately predicts 90 percent of readmissions.

CTI
- Implementing CTI contributes to significant reductions in healthcare costs.
- Studies show reductions in hospital readmissions at 30, 60, and 180 days.

TCM
- This model effectively reduces rates of readmissions and reduces costs for healthcare systems.

The NTCC considers the following seven key elements as essential for safe and seamless transitions, and we use this framework to present the evidence in this review:

- **Medication Management:** Ensuring the safe use of medications by patients and their families based on patients' plans of care.
- **Transition Planning:** Creating a plan/process that facilitates the safe transition of patients from one level of care to another, including home or from one practitioner to another.
- **Patient/Family Engagement and Education:** Educating and counseling patients and families to enhance their active participation in their own care, including informed decision making.
- **Communicating and Transferring Information:** Sharing of important care information among patient, family, caregiver, and healthcare providers in a timely and effective manner.
- **Follow-Up Care:** Facilitating the safe transition of patients from one level of care or provider to another through effective follow-up care activities.
- **Healthcare Provider Engagement:** Demonstrating ownership, responsibility, and accountability for the care of the patient and family/caregiver at all times.
- **Shared Accountability Across Providers and Organizations:** Enhancing the transition of care process through accountability for care of the patient by both the healthcare provider (or organization) transitioning, and the one receiving the patient.

Essential Elements of Safe and Seamless Care Transitions

Table 15.1 describes how the essential elements for safe and seamless transitions are represented across the three models.

Table 15.1: Essential Elements of Safe and Seamless Care Transitions for Three Multi-Element Models

Essential Elements	Description	Better Outcomes for Older Adults Through Safe Transitions (BOOST)	Care Transitions Intervention (CTI)	Transitional Care Management (TCM)
Medication Management	Ensuring the safe use of medications by patients and their families based on patients' plans of care.	Using the BOOST Assessment Tool, providers can screen patients for one of eight risk factors for readmissions, two of those being problem medications and polypharmacy (patients who are taking more than 5 medications). Risk-specific interventions are then performed using components of the BOOST Toolkit.	CTI promotes medication self-management as one of its four pillars, with the goal of ensuring that the patient is knowledgeable about medication and has a medication management system.	Medication management is a key element of TCM. Led by advanced practice nurses (APNs), medication reviews are done to identify discrepancies and inappropriate prescriptions.
Transition Planning	Creating a plan/ process that facilitates the safe transition of patients from one level of care to another, including home or from one practitioner to another.	The BOOST Toolkit provides a universal patient discharge checklist for all patients being discharged from the hospital to home, a general assessment of patient preparedness to be discharged, and patient transition record and discharge patient education tool to assist the care team with transition planning.	CTI formalizes the transition planning process with the implementation of a transitions care coach. The transitions care coach assists with transition planning by encouraging self-management and direct communication between patients/caregivers and primary care providers.	The TCM model facilitates transition for older patients from the hospital to the home setting. An APN meets with patients within 48 hours of discharge and then coordinates follow-up visits for them with their providers. When possible, the APN attends the follow-up visits.
Patient/Family Engagement and Education	Educating and counseling of patients and families to enhance their active participation in their own care, including informed decision making.	BOOST promotes patient education through the use of the teach-back technique. BOOST provides a video and 60–90 minute curriculum to educate the care team about the teach-back technique. BOOST also encourages the use of a DPET (Discharge Patient Education Tool) to help patients understand the discharge instructions given to them.	The transitions coach works directly with the patient/caregiver to increase self-management through a hospital visit, home visit, and three follow-up phone calls. The transitions coach assists patients in asserting a more active role through care transitions by educating them on their condition, medications, patient-centered health record, follow-up care, and any indications that their condition is worsening.	A primary role of the APN care coordinator is to educate patients and caregivers on their care. The APN discusses the care plan with patients and their family caregivers, and ensures that they understand the diagnoses, how to identify symptoms, and when to seek follow-up care.

Essential Elements	Description	Better Outcomes for Older Adults Through Safe Transitions (BOOST)	Care Transitions Intervention (CTI)	Transitional Care Management (TCM)
Communicating and Transferring Information	Sharing of important care information among patient, family, caregiver, and healthcare providers in a timely and effective manner.	The BOOST Model stresses the importance of communicating with patients using the teach-back technique and encourages information transfer from provider to patient through the use of the PASS Tool (Patient Preparation to Address Situations After Discharge Successfully). The tool is a transition record that patients leave the hospital with. Providers are encouraged to use large print, avoid medical jargon, and keep sentences short to address literacy issues.	One of the four pillars of the CTI intervention is a patient-centered record owned and maintained by the patient to facilitate cross-site information transfer. The transitions coach uses the patients' health records/portal to facilitate communication between them and their providers.	Communication is a key element of TCM. APNs develop a relationship with patients and family caregivers to ensure continuity across care. The APN also fosters communication between other members of the patient's care team, including primary care providers and specialists.
Followup Care	Facilitating the safe transition of patients from one level of care or provider to another through effective follow-up care activities.	The BOOST model stresses the importance of a post-hospitalization touchpoint to decrease hospital readmissions. The implementation guide recommends follow-up phone calls within 72 hours of discharge to identify many of the new issues and barriers patients may face after discharge.	The third of the four pillars of the CTI intervention is timely follow-up care. The transitions coach works with patients to schedule and complete follow-up visits with primary care providers or specialists.	TCM emphasizes robust follow-up care. An APN care coordinator follows up with patients in person within 48 hours of discharge from acute care. Additionally, the APN follows up with phone calls and can conduct additional in-person visits through 2–6 months post-discharge.
Healthcare Provider Engagement	Demonstrating ownership, responsibility, and accountability for the care of the patient and family/caregiver at all times.	The model encourages provider engagement by having front-line personnel involved with the process of providing safe, effective care transitions in the hospital.	Health systems involved in CTI designate a care transitions coach, typically an APN, to assist patients in the transition process and encourage self-management.	TCM designates an APN care coordinator, who coordinates both with the patient's care team within the hospital setting and with the patient's primary and specialist providers to follow up post-discharge.
Shared Accountability Across Providers and Organizations	Enhancing the transition of care process through accountability for care of the patient by both the healthcare provider (or organization) transitioning and the one receiving the patient.	The BOOST Model encourages shared accountability by recommending the creation of a care transition improvement team to oversee the implementation of BOOST. The collaboration also includes a year of individual physician mentoring and access to an online resource center to facilitate implementation.	Not provided	The APN acting as care coordinator in TCM primarily takes responsibility for the patient's care by facilitating follow-up visits post-discharge for the patient and promoting communication between inpatient and outpatient providers caring for the patient.

Methods

The general methodology used across the project is available in the Methods chapter of this report. Below, is a summary of the approach that was used to search for literature and the review methods specific to the practice area.

Two databases (CINAHL® and MEDLINE®) were scanned for literature specific to the three models by using "BOOST," "Better Outcomes for Older Adults Through Safe Transitions," "CTI," "Care Transitions Intervention Model," "Transitional Care Model," and "TCM." Then we expanded the search by including "care transitions," "transitional care," "patient safety," "follow up," and "health." MeSH terms included "patient discharge," "patient transfer," "transfer," "discharge," "patient handoff," "discharge planning," "teach back models," "health," "ambulatory," and terms related to the seven essential elements previously discussed. The search string also included different healthcare settings, such as "hospitals," "inpatient," "long-term care," "nursing home," and "skilled nursing facility." To make sure we identified the most relevant articles, reference lists of selected articles were screened and additional articles were reviewed. A developer of each model was consulted to confirm that all known model-specific publications were identified.

In all, 157 de-duplicated publications were identified, and 115 full-text articles were considered eligible for further review based on whether they were published in English, explicitly focused on a transition from one care setting to another, included one of the three care transition models, and addressed ways to improve patient safety. Priority was given to intervention studies that centered on one of the three models, foundational or seminal reports, and research studies with quantitative and/or qualitative methods. Records were excluded if the focus was on children/pediatric care and/or if the publication was more of a commentary or editorial than a research study. Upon closer review, full-text articles were disqualified if they were deemed incomplete, insufficient, or "out of scope" by the review team. Out-of-scope articles referenced the care models but were primarily comprised of topics such as handoffs between providers, not from one care setting to another, or teach-back methods. As a result, 16 studies were selected for this review.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in report appendixes A through C.

Review of Evidence

The next sections of this chapter present evidence from the 16 studies that we reviewed. These studies describe implementation activities that examined how implementing BOOST, CTI, and TCM have impacted the care transition process and influenced hospital readmission rates. The evidence in this section highlights intervention, prevalence, observational, and incidence studies that will inform the reader about key outcomes, and implementation strategies and resources for the three care transition models.

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15.1 BOOST: Better Outcomes by Optimizing Safe Transitions

15.1.1 Overview

Project BOOST is a multicentered quality improvement (QI) transitional care program created in 2008 by the Society of Hospital Medicine to improve care for patients as they transition from the hospital to home.[1] The objective is to reduce 30-day readmission rates, improve provider workflow, and reduce medication-related errors. The model involves tools and resources to identify and manage patients who are at high risk for readmissions, with a particular focus on older adults. The contents of the BOOST Toolkit are shown in the box on this page.

BOOST Toolkit:

- Participant Implementation Guidance
- Patient Risk Assessment—8Ps
- Universal Patient Discharge Checklist
- General Assessment of Preparedness
- The Patient Preparation to Address Situations Successfully (Patient PASS)
- Discharge Patient Education (DPET)
- Teach Back Curriculum
- Discharge Instructions for Providers
- Guidance for a 72-Hour Post-Discharge Follow-Up Call and Appointment
- General Guidance for Medication Reconciliation

When hospitals adopt this model they can tailor components to align with their unique needs, priorities, available resources, and culture. There is a toolkit that includes resources to address areas of the discharge process that are predisposed to result in adverse events.[2] Implementation outcomes (e.g., organizational change, reduced hospital readmissions) are estimated for 12 and 24 months post-discharge.[3] After the model is adopted, the hospital becomes part of a QI collaborative network through which they can communicate with and learn from other BOOST members around the country. Additionally, a BOOST Data Center allows users to store and benchmark data against control units and other providers.

BOOST is intended for use by all clinicians involved in the hospital discharge process (physicians, nurses, case managers, social workers), with a core team consisting of a team leader (nurse, case manager, social worker, or physician), QI facilitator, project manager, process owners (frontline staff involved in providing safe, effective care transitions in the hospital, including pharmacy, nursing, and case management staff), and information technology experts.

15.1.2 Key Components

- **Comprehensive Intervention**—The BOOST toolkit, which is used by hospitals to identify patients at high risk for readmissions, contains material for comprehensive intervention.
- **BOOST Implementation Guide**—Provides detailed implementation guidance for hospitals.
- **Individual Physician Mentoring**—One year of mentorship by external physicians to provide implementation technical assistance to implementation teams at each participating hospital.
- **BOOST Collaborative**—A peer-to-peer network of hospitals that are able to share resources via a listserv, regularly scheduled and ad hoc teleconferences, and other web-based platforms.

15.1.3 Clinical Outcomes

The Centers for Medicare & Medicaid Services (CMS) Hospital Readmission Reduction Program (HRRP) reduces payments to hospitals that have excessive 30-day readmissions for six diagnoses. This program applied initially to Medicare beneficiaries and, as of 2019, applies to Medicaid beneficiaries as well. The HRRP has increased attention on readmissions and length of hospital stay. In 2013, Hansen et al.

evaluated the effect of BOOST on Medicare beneficiaries' readmission rates and length of stay in a sample of 11 hospitals of varying size, academic affiliation, and location.[1] They found that BOOST was associated with a 3 percent decrease in 30-day readmissions (p=.010) after 12 months of implementation. The length of stay did not change significantly.

15.1.4 Process Outcomes

A qualitative study by Williams et al. (2014) sought to identify factors that contributed to how programs could be implemented to enhance collaboration across care settings, reduce hospital readmissions, and achieve optimal implementation of Project BOOST. The design involved an initial cohort of 6 pilot hospitals and a subsequent cohort of 24 hospitals of various academic affiliations, locations, and bed sizes. Based on qualitative findings from the first cohort, investigators added interactive exercise sessions in kickoff trainings, continued education via webinars, and increased mentoring calls, which they anticipated would lead to more complete implementation of BOOST in the second cohort. The individual mentoring component of BOOST was also refined for the second cohort. Qualitative analysis of the first cohort of hospitals included examining BOOST enrollment applications, examining the project listserv, and scripted telephone interviews with each site. Evaluation of BOOST implementation in the second cohort of hospitals occurred via mid-year and end-year surveys. By looking across the two cohorts, the investigators reported being able to better understand how the model can be implemented to enhance collaboration, as well as identifying important facilitators and barriers to implementation. Implementation facilitators included having individual physician mentoring sessions; establishing goals, objectives, and expectations that were small in scale but realistically attainable; teamwork exercises; and active patient engagement practices. Barriers included inadequate understanding of the BOOST implementation process, lack of administrative support, lack of protected time or resources dedicated to BOOST, and insufficient front staff buy-in.[2] When Lee et al. (2016) looked at the BOOST patient risk assessment tool via retrospective chart reviews, their findings indicated that the tool successfully predicted 90 percent of readmissions for patients 65 years of age and over when they assessed for two or more risk factors for readmission, but the tool was 99-percent effective in assessing risk when one factor was used. Although the tool shows promise in predicting readmissions, the authors cautioned against the use of multiple risk factors, as it could decrease the predictive power of the tool.[4]

15.1.5 Economic Outcomes

To date, no studies have intentionally studied the costs or economic outcomes related to implementing BOOST to reduce readmissions.

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15.2 CTI: Care Transitions Intervention

15.2.1 Overview

Dr. Eric Coleman developed the Care Transitions Intervention in 2002 to improve continuity of care across care settings and providers. CTI is a patient-centered, multi-component program that has since been implemented in hospitals across the country.[1] Developed based on input from patients and their caregivers, CTI aims to improve the efficiency and quality of care in the transition from hospital to home by providing patients with tools and support to navigate the healthcare system and effectively manage their health conditions.[1]

CTI's Four Pillars of Care

- **Medication Self-Management**: Patient/caregiver is knowledgeable about prescribed medication(s) and establishes a medication management process.
- **Dynamic Patient-Centered Health Record**: Patient (with assistance from caregiver, if necessary) uses the Personal Health Record (PHR) to communicate with and consult about continuity-of-care providers from across different settings.
- **Primary Care and Specialist Follow-Up**: Patient schedules and completes follow-up visits with the providers (i.e., primary care provider or specialist) and is empowered to actively participant throughout
- **Knowledge of Red Flags**: Patients understand indicators for when their condition is worsening and know how to respond.

CTI is a 4-week, low-cost, low-intensity self-management program designed to provide patients discharged from an acute care setting with skills, tools, and the support of a transition coach to ensure that their health and self-management needs are met. The intervention targets patients age 65 years and older, who often have acute or chronic health conditions such as congestive heart failure, chronic pulmonary disease, diabetes, stroke, hip fractures, pulmonary embolism, and deep vein thrombosis.[2]

CTI begins when the patient is in the hospital. A Transitions Coach sets up a meeting to discuss the patient's concerns and to engage the patient and family to begin participating in the program. Next, the Transitions Coach conducts a follow-up home visit and a series of three phone calls in order to help the patient increase self-management skills and attain personal goals, and to provide the patient and his or her family continuity across the transition. Transition coaches can be advanced practice nurses (APNs), registered nurses, social workers, student nurses, community workers, or trained volunteers. Since CTI is designed to help patients manage their care once they transition out of the hospital, no studies reported long-term participation.

15.2.2 Key Components

CTI's four pillars of care are shown in the box on this page. CTI relies on personal health records (PHRs), which document the patient's medical history, medications and allergies, any red flags or warning signs; provide a structured checklist of critical activities that take place prior to discharge (instructions and dates of follow-up appointments); and provide space for the patient to record questions and concerns.

First, a CTI transitions coach meets with a patient in the hospital prior to discharge to establish rapport, introduce the PHR, and arrange a home visit within 72 hours after discharge. One of the main goals of the home visit is to reconcile all of the patient's medications using the Medication Discrepancy Tool. During this time, the transitions coach also helps the patient understand the purpose, instructions for use, and potential side effects of each medication. If medication discrepancies are identified, the coach encourages the patient/caregiver to call the physician's office or make an appointment in person. Next, the transitions coach and patient role-play effective communication strategies to teach the patient to

clearly articulate his or her needs with providers. Another goal of the home visit is to help the patient recognize red flags or warning signs that the health condition may be worsening. The intervention is implemented in a short timeframe, only 4 weeks. The home visit takes place during the first week. For the next 3 weeks, the transitions coach continues to support the patient and his or her ability to effectively manage care. For instance, the coach calls once a week to help the patient continue to make and track progress. The coach asks patients if they received appropriate outpatient services, reminds them to share their PHR with their primary care provider or specialists, and supports their disease self-management activities.

15.2.3 Clinical Outcomes

CTI focuses on 30-, 90-, and 180-day readmissions. Readmission rates were reported in five reviewed studies about CTI, three clinical controlled trials and two randomized controlled trials. They addressed three different patient populations: Medicare Advantage beneficiaries, fee-for-service Medicare beneficiaries, and low-income patients. Intervention patients enrolled in Medicare Advantage plans who had 1 or more of 11 diagnoses (stroke, congestive heart failure, coronary artery disease, cardiac arrhythmias, chronic obstructive pulmonary disease, diabetes, spinal stenosis, hip fracture, peripheral vascular disease, deep vein thrombosis, and pulmonary embolism) had lower readmission rates than patients with these diagnoses for whom CTI was not applied in all three time periods: 30 days (8.3 vs. 11.9, p=.048), 90 days (16.7% vs. 22.5%, p=.04), and 180 days (8.6% vs. 13.9%, p=.046).[2,3] Among beneficiaries with original fee-for-service Medicare insurance and with the same conditions as the previous group, readmission rates were also lower for CTI patients than non-CTI patients at 30 days (6.8% vs. 16.7, p=.15%), 90 days (9.3% vs. 31%, p=.01), and 180 days (38.1% vs. 20.9%, p=.08).[4,5] Among low-income patients for whom CTI was implemented who had hypertension, stroke, diabetes, heart conditions, or dementia, and/or were taking four or more medications, readmission rates were generally lower than for those without CTI, but this difference was not statistically significant at 30 days (9.6% vs. 17.3%), 90 days (28.9% vs. 25%), and 180 days (32.7% vs. 36.5%).[6]

15.2.4 Process Outcomes

Parrish et al. (2009) worked with five hospitals and five community sites to identify key factors for sustaining CTI. Based on feedback from hospitals, they found that engaged leadership support, a strong project champion, adequate training of the transition coaches, and dedicated CTI staff were integral to sustaining CTI.[7] Coleman et al. (2015) adapted CTI to better serve the needs of family caregivers in one non-profit acute care hospital that had 253 beds through addition of a Family Caregiver Activation Assessment Tool (FCAA).[8] Family caregivers, who participated using the FCCA tool, experienced a mean improvement in activation of 6 points on a 1–10 scale in relation to the four intervention pillars than caregivers who did not use the tool (p<.0001), and became more involved in successful care transitions.

15.2.5 Economic Outcomes

Of the six CTI studies reviewed, four examined the cost or cost effectiveness of implementing CTI, which varies based on provider characteristics and benefits and salary structure. For instance, in 2002, for patients who resided in the same State, the annual cost for implementing CTI for patients receiving or eligible for Medicare Advantage was $74,310, compared to $68,830 for patients who were eligible for Medicare fee-for-service coverage.[2,4] The difference in implementation costs appear to be influenced by provider characteristics, benefits, and salary structure. For example, the salary of a transition coach could be $70,980 for an APN compared to $65,500 for a registered nurse. As part of their role, transition

coaches receive a cell phone and pager ($650), mileage reimbursement ($2,500), and other supplies such as PHR forms ($180). Coleman et al. (2006) observed that implementing CTI was significantly more cost efficient than usual care when treating patients eligible for Medicare Advantage. For example, hospital costs for those who received CTI were $2,058, as compared to $2,456 for those who received usual care (p=.049) at 180 days post-discharge.[2] In 2014, Gardner et al. observed similar patterns. Their study reports that among Medicare beneficiaries, those for whom CTI was used had significantly lower healthcare utilization during the 180 days after hospital discharge, lower total health costs ($14,729 vs. $18,779, p=.03), and an average cost avoidance of $3,762 compared to the controls.[9]

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15.3 TCM: Transitional Care Model

15.3.1 Overview

TCM's Core Components:

- Screening
- Staffing
- Maintaining Relationships
- Engaging Patients and Caregivers
- Assessing/Managing Risks and Symptoms
- Educating/Promoting Self-Management
- Collaborating
- Promoting Continuity
- Fostering Coordination

Developed in 1981 at the University of Pennsylvania's School of Nursing by a team led by Dr. Mary Naylor, the Transitional Care Model is a nurse-led intervention designed to improve the outcomes of chronically ill older adults who transition from hospital to home[1] and are at risk of readmission based on the following factors: one or more chronic illnesses, more than one hospital visit within the last 6 months, multiple prescribed medications to treat multiple conditions (i.e., polypharmacy), and living alone.[2,3] The model is implemented through the use of individualized, multidisciplinary, evidence-based clinical protocols that help to prevent declines in health and to reduce 30–60 day hospital readmissions.[2,3] In addition to reducing rates of readmissions, TCM also aims to enable patients and their family caregivers to manage their conditions themselves. Although originally designed for older adults at risk of readmission, the model has been recently adapted and tested with other populations, including individuals who are eligible for Medicaid and patients with psychiatric diagnoses in addition to chronic and other comorbidities.[4,5]

Patients who fit the criteria for the intervention meet with an advanced practice nurse either in the hospital prior to discharge or within 48 hours after discharge. The APN conducts home visits and telephone support, and is available 7 days a week through the length of the intervention (usually extending for 2 months after discharge). The APN uses the initial visit to assess the patient and develop a plan of care based on medical needs and patient values. Subsequently, the APN focuses on active engagement and education of patients and family caregivers. APNs educate patients about their health conditions and risks, including how to recognize and manage symptoms of worsening. They use home visits to monitor symptoms and do medication reconciliation. APNs serve as liaisons between patients/family caregivers and healthcare providers to ensure that followup visits are scheduled with primary or specialist providers after discharge from the hospital. APNs are available to accompany patients to these followup visits, if requested.

15.3.2 Key Components

Rigorous evaluation of interventions of TCM and detailed case summaries developed by participating APNs have led to continued refinement of the model's nine core components, shown in the box on this page.

15.3.3 Clinical Outcomes

A recent study compared TCM to augmented standard care (ASC) and resource nurse care in three hospitals that are part of a larger healthcare system. ASC included usual care plus cognitive screening within 24 hours of each patient's index hospitalization and delirium assessment continuously during the hospital stay. In resource nurse care, resource nurses coached hospital nurses and provided direct care. Resource nurses completed training on management and transition of hospitalized cognitively impaired older adults and attended seminars on cognitive impairment throughout the study period. The TCM

intervention group had lower hospital readmission rates at 30 days (6/66) than the ASC (15/66, p<0.001) and resource nurse care (14/71, p=0.06) groups.[2]

15.3.4 Process Outcomes

A pilot study by Solomon et al. (2014) found that adapting TCM for patients with psychiatric diagnoses added unique challenges. While the pilot used a psychiatric nurse practitioner and had a psychiatrist available for consult, patients had needs that could not be addressed in the existing program, primarily related to housing instability and relationship conflicts. The study team suggested adding a social worker and peer specialist as part of the care team in addition to the specialized nurse practitioner.[4]

15.3.5 Economic Outcomes

A study of TCM in Aetna's Medicare Advantage patient population found cumulative per-member cost savings of $2,170 over the 52-week period after utilizing TCM (p<0.037).[1] In another study, Naylor and colleagues (2014) compared post-acute care (i.e., skilled nursing facility) and readmission costs for hospitalized older adults with cognitive impairment for the three care management interventions (i.e., TCM, ASC, and resource nurse care).[2] ASC added cognitive screening within 24 hours of index hospitalization to usual care. Resource nurse care provided coaching to nurses by nurses specially trained in management and transition of cognitively impaired older adults. TCM had significantly lower costs than ASC at 30- and 180-day observations. Implementing TCM lead to significantly lower costs than implementing resource nurse care during the first 30 days. Overall, these findings suggest that implementing TCM can reduce both the amount of post-acute care (i.e., skilled nursing facility stays) and the total cost of care compared with alternative services with cognitively impaired older adults.[6]

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15.4 General Issues

15.4.1 Unintended Consequences

15.4.1.1 Negative

15.4.1.1.1 Related to Implementing BOOST

No unintended negative consequences were reported in this review of studies that examined the use of BOOST.

15.4.1.1.2 Related to Implementing CTI

No unintended negative consequences were reported in this review of studies that examined the use of CTI.

15.4.1.1.3 Related to Implementing TCM

Within a population of serious mental illness, there is a lack of patient receptivity to the intervention. Additionally, many participants lacked basic needs such as housing. Without stable housing, it is difficult to focus on managing medical conditions.[1]

The effect on re-hospitalizations dissipated after 90 days, which could potentially be attributed to the cognitive impairment many older adults face.[2]

There was no improvement in functional status, including basic activities of daily living.[2]

15.4.1.2 Positive

15.4.1.2.1 Related to Implementing BOOST

Length of hospital stay decreased in BOOST hospital units.[3]

15.4.1.2.2 Related to Implementing CTI

Primary care service utilization rates increased.[4]

15.4.1.2.3 Related to Implementing TCM

No unintended positive consequences were reported in this review of studies that examined the use of TCM.

15.4.2 Implementation

15.4.2.1 Summary of Evidence on Implementation

We reviewed 16 studies targeting three care transition models that, collectively, create a synergy for using multiple elements in order to more effectively impede preventable harm to patients as they transition across care settings. All three models were designed to target and improve care for adults age 65 and older.

15.4.2.2 Barriers and Facilitators

This section describes barriers to and facilitators of using the multi-element models BOOST, CTI, and TCM to improve care transitions.

15.4.2.2.1 Barriers Related to Implementing BOOST

Challenge of translating external QI content to a local setting[3]

Sites being encouraged to implement Project BOOT with no funds or dedicated time to support the implementation efforts.[3,5]

Limited data submission due to hospital implementation design (no geographic rollouts or simultaneous rollout on appropriate clinical floors due to limited resources).[3]

Inadequate staff understanding of hospital's current discharge process.[5]

Insufficient executive leadership support.[5]

Limited front-line staff buy-in.[5]

15.4.2.2.2 Barriers Related to Implementing CTI

Limited funding dedicated to the implementation of CTI.[6]

Lack of dedicated transition coaches.[6]

Insufficient executive leadership support.[6]

15.4.2.2.3 Barriers Related to Implementing TCM

Limited patient receptivity to TCM intervention.[1]

Insufficient communication between providers and service coordinators.[1]

Limited access to patient data due to lack of electronic health record interoperability between service facilities.[1]

15.4.2.2.4 Facilitators When Implementing BOOST

Intensive mentor engagement to assist with site accountability and implementation trouble-shooting.[3,5]

High level of institutional leadership support.[3]

Increased team engagement in reducing hospital admissions. [3]

Presence of an effective project champion to lead the implementation effort.[3]

Implementation of Project BOOST initially as a small project with specific goals.[5]

Use of interdisciplinary teams to facilitate teamwork and collaboration.[5]

Regular feedback from patients, physicians, and other involved in the project.[5]

15.4.2.2.5 Facilitators When Implementing CTI

Presence of executive leadership support for CTI or presence of a CTI champion.[6]

Dedicated transition coaches made available through specific funding allotment.[6]

Strong project management leadership.[6]

Frontline staff commitment to CTI.[6]

Continuity of transition coach relationships across care settings.[7]

15.4.2.2.6 Facilitators When Implementing TCM

Tailored care targeting specific patient populations.[1,2]

High level of institutional leadership support.[2]

High level of front-line staff buy-in.[2]

15.4.3 Resources To Assist With Implementation

The following resources were cited in our review of the evidence and can be used when implementing the three models.

BOOST

- Society of Hospital Medicine: Project BOOST Implementation Toolkit[4,3] provides a compilation of materials to help hospitals implement the intervention and optimize the discharge process at local institutions. Visit https://www.hospitalmedicine.org/clinical-topics/care-transitions to download the Project BOOST Implementation Toolkit.

CTI

- The Care Transition Measure–15[8,9] is a 15-question care transition measure questionnaire to assess the quality of care transitions and focus on patient-centeredness for the purpose of performance improvement. Visit https://caretransitions.org/wp-content/uploads/2019/09/CTM-15.pdf to access the CTM–15 questionnaire.
- The Care Transition Measure–3[8,9] is a 3-question care transition measure questionnaire to assess the quality of care transitions and focus on patient-centeredness for the purpose of performance improvement. Visit https://caretransitions.org/wp-content/uploads/2019/09/CTM-3.pdf to access the CTM–3 questionnaire.
- The Family Caregiver Activation in Transitions (FCAT) Tool[8,9] is a tool designed to facilitate productive conversations between healthcare professionals and family caregivers during the discharge process. The tool can be administered by a health professional or self-administered by the caregivers at any point of transition of care. Visit https://caretransitions.org/wp-content/uploads/2019/09/Family-Caregiver-Activation-in-Transitions-FCAT-tool.pdf to download the Family Caregiver Activation in Transitions (FCAT) tool.
- For instructions on how to implement the above tools, please visit The Care Transition Program website's Tool and Resources page at https://caretransitions.org/all-tools-and-resources/.

TCM

- TCM nurse-specific orientation and web-based modules[3,2] are available. The Foundations of Transitional Care seminar is an orientation designed for nurses and other team members reviewing evidence-based tools and strategies used for successful transitional care. There are also three TCM-specific modules, Understanding TCM Components and Tools, Applying TCM to Individual Patients, and Incorporating TCM in System Redesign, which focus on aspects of TCM implementation. For more information on these resources, please visit https://www.nursing.upenn.edu/ncth/resources/.

15.4.4 Gaps and Future Directions

15.4.4.1 Gaps

Across the three models, there are notable gaps with regard to implementation. For instance, while BOOST has been implemented in over 180 hospitals, more evidence is needed to determine its effectiveness, especially as it relates to implementing the model in care settings other than hospitals and to cost-related outcomes.[10] For CTI, although the evidence is rapidly advancing, given the prominent role of physicians, there is a need to assess their perspective and/or satisfaction regarding implemention.[8] More strategies are also needed to determine how best to incorporate patients and family caregivers voice and preferences into the CTI to further engage them[5] Since the majority of CTI studies have focused on Medicare fee-for-service or Medicare Advantage beneficiaries, the generalizability of the intervention beyond these populations should be explored. Despite advances in TCM research, gaps exist regarding the effectiveness of specific services that qualify under certain Current Procedural Terminology (CPT) codes.[11] TCM is an understudied approach, with only three studies identified that have utilized all the required elements for TCM service for Medicare's billing code.[11] Current studies often lack a focus on the organizational contexts of various health systems that promote a successful transitional care strategy; therefore, future research should focus on TCM effectiveness across a variety of different settings.

15.4.4.2 Future Directions

The evidence for each of the models is still evolving. In this section we highlight considerations for future work. The hospitals that have implemented BOOST were described as being big urban academic medical centers that often have the infrastructure and resources to run large quality improvement projects. Future implementation efforts of BOOST should focus on examining its impact in smaller or rural hospital settings, where additional financial support for QI and data collection may be required.[12] Researchers also recommended that future studies assess the influence of using BOOST's mentoring component as well as assessing the role of organizational content on the effectiveness of this model.[12] Researchers who studied CTI recommended more attention to factors such as medication management, patients with cardiovascular disease and diabetes, and patients older than 85 years who identified as African American or Latino, as the average profile of CTI patients was white women 76–85 years old.[6] Since researchers are starting to expand the use of TCM beyond older adults, examining the effectiveness of implementing this model for patients with lower socioeconomic status or lower incomes, and also patients with psychiatric conditions or disorders, would be beneficial to the field. Researchers should also consider examining the potential of implementing TCM to add value to emerging care delivery models, including patient-centered medical homes, accountable care organizations, community-based palliative care programs, and population health models.

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Conclusion and Comment

Moving patients from one care setting to another can pose significant risk. Implementing transitional care models such as BOOST, CTI, and TCM, which place an emphasis on medication management, transition planning, patient/family engagement and education, communication and transferring information, follow-up care, healthcare provider engagement, and shared accountability across providers and organizations, is a patient safety practice that appears to have great potential. Evidence shows that implementing these models results in standardization in discharge protocol, ultimately leading to a decrease in hospital readmissions and an increase in associated cost savings. However, more diverse studies using these models are needed to establish a firm evidence base in a variety of care settings.

Studies focusing on model implementation in a variety of care settings, including rural hospitals, patient-centered medical homes, accountable care organizations, and community-based palliative care programs, would lead to stronger clinical evidence and improved implementation. Existing studies primarily focus on Medicare populations in large urban academic medical centers. Future research on implementation of these models in a variety of settings with diverse patient populations is critical for understanding opportunities and outcomes associated with multi-element models designed to improve transitional care.

16. Venous Thromboembolism

Eleanor Fitall, M.P.H., and Kendall K. Hall, M.D., M.S.

Introduction

Background

Venous thromboembolism (VTE) is a disorder that includes deep vein thrombosis (DVT) and pulmonary embolism (PE). A DVT occurs when a blood clot forms in a deep vein, usually in the lower leg, thigh, or pelvis. A PE occurs when a clot breaks loose and travels through the bloodstream to the lungs.[1]

It is estimated that 300,000 to 600,000 Americans are affected each year by VTE, making it the third leading vascular diagnosis behind heart attack and stroke, and the leading cause of death due to major orthopedic surgery.[2,3] Common causes for VTE are surgery, cancer, immobilization, or hospitalization.[2,4] The risk of VTE is the highest for patients undergoing major orthopedic surgery, such as total knee arthroplasty (TKA), total hip arthroplasty (THA), or hip fracture surgery (HFS).[3,5,6] Without appropriate prophylaxis, rates of VTE among these patients have been estimated to be as high as 60 percent.[7] Given that major orthopedic surgeries typically occur among older adults, the Centers for Medicare & Medicaid Services (CMS) has made the prevention and treatment of VTE a priority among their quality improvement efforts, such as through programmatic measure inclusion and harm area prioritization in initiatives. Accreditation organizations have followed suit, with the Joint Commission and the National Committee for Quality Assurance including measures for VTE treatment and prevention in their hospital accreditation and certification programs.

Method for Selecting Patient Safety Practice

Agency for Healthcare Research and Quality (AHRQ) subject matter experts requested an update of the previous Making Healthcare Safer reports' coverage of the topic of VTE prophylaxis, with a specific focus on the use of aspirin.

What's New/Different Since the Last Report

The previous Making Healthcare Safer reports reviewed the effectiveness, safety, cost effectiveness, and indicators for VTE prophylaxis, as well as the most effective VTE prophylaxis regimens and interventions to improve adherence to prevention strategy guidelines. Whereas the last report discussed newer pharmacologic agents on the market and approaches to improve clinical decision making and guideline adherence, this review specifically focuses on the use of aspirin for prophylaxis. With the increase of pharmacologic agents on the market, research has focused primarily on the effectiveness of these agents and, to some degree, their safety. This current review provides an update on the state of the evidence specifically for the use of aspirin as a low-cost, widely available generic option.

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16.1 Patient Safety Practice: Use of Aspirin for VTE Prophylaxis

16.1.1 Practice Description

As VTE, in particular DVT, can be very difficult to diagnose, actively employing prevention techniques is critical to ensuring patient safety. Prevention methods include both mechanical and pharmacologic prophylaxis. Mechanical prophylaxis includes the use of compression devices, such as stockings and foot pumps. Pharmacologic prophylaxis is available via a number of different anticoagulant and antiplatelet drugs, including heparin derivatives, vitamin K antagonists, direct thrombin inhibitors, direct factor Xa inhibitors, and aspirin.

There are two different types of pharmacologic agents available for VTE prophylaxis—anticoagulants and antiplatelets. Aspirin is an antiplatelet, and while there are other antiplatelets used for other cardiovascular conditions, these are not recommended for use in VTE prophylaxis and are therefore not the focus of this review. There is slight variation in existing guidelines regarding the use of aspirin for pharmacologic prophylaxis. The American Society of Hematology (ASH)[1] the American College of Chest Physicians (ACCP),[2] and the American Academy of Orthopedic Surgeons (AAOS)[3] all recommend pharmacologic prophylaxis and/or mechanical prophylaxis for patients undergoing THA, TKA, or HFS. ASH and AAOS further recommend that patients receive both forms of prophylaxis, particularly patients who are at an increased risk for VTE. However, ASH and ACCP provide a list of recommended pharmacologic agents that specifically includes aspirin, whereas AAOS does not make recommendations regarding specific pharmacologic agents. Further, ACCP recommends low molecular weight heparin (LMWH) over other pharmacologic prophylaxis agents, whereas other guidelines have not made such a specific recommendation statement specifying the use of one type of pharmacologic prophylaxis agent over another.

Many hospitals include the use of aspirin in their surgical protocols for patients undergoing major orthopedic surgery. For prescribing surgeons, its use is at their discretion based on guideline recommendations, perceived patient risk, and the need to balance prevention with safety concerns, such as bleeding risk. This balance has become increasingly important as a growing number of studies have found that newer anticoagulant drugs are associated with a higher incidence of bleeding than prophylaxis agents.[4] The review's key findings are located in the box to the right.

Key Findings:

- Use of aspirin following major orthopedic surgery was generally found to be of similar effectiveness as other agents.
- An overwhelming majority of studies concluded that aspirin has a lower bleeding risk rate than other pharmacologic agents, which, combined with its lower cost, makes it an appealing option for VTE prophylaxis, particularly in low-risk patients.
- More prospective randomized controlled trials are needed to directly compare the effectiveness of aspirin with other prophylactic methods across patient risk levels.

16.1.2 Methods

To answer the question, "Is aspirin safe and effective for post-operative VTE prophylaxis in patients undergoing surgery?" two databases (CINAHL® and MEDLINE®) were searched for "Venous Thrombosis/Prevention & Control," "deep vein thrombosis," "pulmonary embolism," and related synonyms, as well as "Aspirin/therapeutic use," "Surgical Procedures, Operative," "Perioperative Care/methods," "Postoperative Complications/prevention & control," and other similar terms. Articles

included were published from 2008 to 2018. The initial search yielded 123 results. Once duplicates were removed and additional relevant articles from selected other sources were added, a total of 63 articles were screened for inclusion and full-text articles were retrieved. Of those, 33 were selected for inclusion in this review. Articles were excluded if the outcomes were not relevant to this review, the article was out of scope (including not quantitative), or study design was insufficiently described. As the results of this literature review were predominantly about major orthopedic surgery, relevance to this review included limiting articles to patients undergoing major orthopedic surgery.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

16.1.3 Review of Evidence

A box summarizing key findings related to the use of aspirin for the prevention of VTE in patients undergoing major orthopedic surgery is located in the Practice Description section. This section reviews applicable studies, organized by the scope of the intervention the patient received (aspirin alone, aspirin in combination with another pharmacologic prophylaxis agents, and aspirin in combination with mechanical prophylaxis) before discussing implementation considerations and any potential unintended consequences.

All included studies took place in the hospital setting and addressed patients undergoing total joint arthroplasty (TJA), THA, TKA, or HFS, with one notable exception of a study analyzing VTE outcomes in patients receiving surgery to remove cancerous tissue from a lower limb. Findings in this chapter can be best summarized by the conclusions reached in the six systematic reviews that met our inclusion criteria. Findings from these reviews varied in their determination of the efficacy of aspirin as a VTE prophylaxis and its benefits over other pharmacologic prophylaxis agents with regard to safety outcomes, predominant operative site, and other major bleeding.

One pooled analysis by Brown (2009) reviewed 14 randomized clinical trials to determine whether aspirin decreased the rate of operative site bleeding, without increasing the rate of thromboembolic events in patients undergoing THA, TKA, or HFS. The analysis found that the rates of VTE were not significantly different with aspirin when compared with vitamin K antagonists, LMWH, and pentasaccharides, but that the risk of bleeding was lower with aspirin.[5] Similarly, Mistry et al. (2017) reviewed eight articles published from 2014 to 2017 on the use of aspirin for VTE prophylaxis following TKA or THA. Five of the articles concluded that aspirin was effective, and the systematic review noted that aspirin had a lower rate of complications while also being more cost effective than other available anticoagulants.[6] Finally, a meta-analysis performed by Wang et al. (2017) sought to provide a comprehensive review of pharmacologic prophylaxis agents and reviewed 104 trials, 30 different drugs, and outcomes in 110,643 patients. Researchers found that aspirin, along with factor XI antisense oligonucleotide (FXI-ASO), ardeparin, and apixaban, were the most effective drugs at both preventing all-cause VTE and avoiding unintended bleeding events. While the meta-analysis findings were supportive of the use of aspirin, apixaban was found to have the most favorable outcomes.[4]

Conversely, Drescher et al. (2014) found in the eight clinical trials included in their review that, while overall the rate of DVT did not differ between aspirin and anticoagulants, aspirin may be associated with a higher risk of DVT following hip fracture repair when compared with anticoagulants, although it may

be associated with lower bleeding risk.[7] Similarly, Wilson et al. (2016) found in their analysis of 13 studies that, while there is evidence from one of their included studies that aspirin has similar rates of VTE following TKA when compared with LMWH, the majority of trials included were at a moderate to severe risk of bias and had insufficient evidence that aspirin was more or less effective than LMWH, warfarin, or dabigatran.[8] Finally, in their review of 14 studies to assess the appropriateness of aspirin as a prophylaxis in high-risk patients undergoing THA, TKA, or HFS, Stewart and Freshour (2013) determined that the evidence is inconsistent as to whether aspirin is effective at preventing VTE and whether there is a decreased risk of bleeding in comparison with other anticoagulants. This may indicate a need for patient risk stratification when determining the appropriateness of aspirin, as discussed later in this chapter.[9]

16.1.3.1 Aspirin as Sole Prophylaxis Treatment

Five studies included in our review discussed aspirin as the sole prophylaxis used in patients at risk for developing VTE following surgery. A number sought to directly compare its effectiveness as a sole approach with other pharmacologic approaches. Goel et al. (2018) found that, in patients undergoing simultaneous bilateral TKA, the risk for PE was significantly lower for patients prescribed aspirin (n=1528) versus warfarin (n=2157) after accounting for baseline VTE risk (p=0.005). Goel et al. also found that the risk for combined VTE, consisting of both PE and DVT, was nearly significantly lower for those on aspirin (p=0.052).[10]

In a more comprehensive analysis of available pharmacologic prophylaxis options, Agaba et al. (2017) conducted a retrospective review of patients undergoing THA using a nationwide private and Medicare insurance database. Patients studied received either aspirin alone or one of five anticoagulants. The analysis found that patients given aspirin alone had a significantly lower rate of both DVT and PE at 30 and 90 days following surgery, with an insignificant bleeding risk. Following a review of the effectiveness and safety side effects of each of the pharmacologic agents included in the study, Agaba et al. concluded that while rivaroxaban and fondaparinux have lower bleeding and thromboembolic events compared with other newer anticoagulants, aspirin also meets these criteria. In addition, aspirin is an easy-to-use, inexpensive option for prophylaxis following THA.[11] In a similar study reviewing TKAs over a 9-year period in a combined Humana and Medicare database, Bala et al. (2017) compared outcomes of patients receiving aspirin (n=1016) matched by age and sex with patients receiving enoxaparin (n=6096), warfarin (n=6096), and factor Xa inhibitors (n=5080). Factor Xa inhibitors were found to have the lowest incidence of DVT and PE (p<0.01) at 90 days, and there was no difference in bleeding-related complications between the agents (p=0.81). However, researchers concluded that aspirin had the lowest incidence of postoperative anemia (p<0.01) and blood transfusion (p<0.01) at 90 days, and provided VTE prophylaxis comparable to Xa inhibitors and more effective than enoxaparin and warfarin.[12]

Mendez et al. (2017) conducted a retrospective review of medical records for patients who underwent lower-limb surgery as a component of their oncology treatment. Patients either received 325 mg of aspirin twice daily (n=103) or were assigned to the non-aspirin group (n=39) (which included LMWH, unfractionated heparin, warfarin, and intermittent pneumatic compression device only). No patient in the aspirin group developed a VTE. Aspirin for VTE prophylaxis in patients undergoing orthopedic oncologic surgery appears to be effective, but more robust study may be necessary.[13]

16.1.3.2 Multimodal Prophylaxis

16.1.3.2.1 Aspirin in Combination With Other Pharmacologic Prophylaxis

Several of the studies reviewed addressed the use of aspirin in combination with other pharmacologic prophylactic agents. Anderson et al. (2013) conducted a randomized controlled trial at 12 tertiary care orthopedic referral centers in Canada. All patients undergoing elective THA surgery were prescribed a 10-day course of LMWH before being randomly assigned to either 28 days of continued LMWH (n=400) or 28 days of aspirin (n=386). Findings indicate that switching patients to aspirin following an initial course of LMWH was not worse ($p<0.001$) but not better than continued use of LMWH. Additionally, clinically significant bleeding occurred in five patients with a continued course of LMWH (1.3%), versus two (0.5%) who switched to aspirin ($p=0.45$).[14]

In a similar study, Anderson et al. (2018) conducted a double-blind randomized controlled trial at 15 university-affiliated health centers in Canada. Patients undergoing elective unilateral primary or revision hip or knee arthroplasty received once-daily oral rivaroxaban for the first 5 days following surgery, and then were randomized to either continue the course of rivaroxaban or switch to aspirin for the next 9 days after TKA, or 30 days after THA. Findings indicate that aspirin is not worse ($p<0.001$) but not better than continued use of rivaroxaban. Additionally, there was not a significant difference in bleeding between the two groups ($p=0.43$).[15]

Finally, Hamilton et al. (2012) conducted a retrospective review of patients receiving aspirin prophylaxis after primary hip and knee arthroplasties. Patients received a course of enoxaparin during their inpatient stay, followed by a course of aspirin for 28 days following discharge. Patients were compared with a control group that first received enoxaparin for 2 weeks following discharge before receiving a course of aspirin for a further 2 weeks. Researchers concluded that a protocol of only inpatient enoxaparin and then aspirin post discharge was both safe and effective in standard-risk patients.[16]

16.1.3.2.2 Aspirin in Combination With Mechanical Prophylaxis

The majority of articles reviewed (20) included the use of an anticoagulant or antiplatelet in combination with other mechanical prophylaxis methods. Seventeen of the articles reviewed concluded that aspirin was safe and effective when used in combination with mechanical prophylaxis methods. For example, Deirmengian et al. (2016) conducted a retrospective review of patients undergoing TJA. All patients received mechanical prophylaxis and then either warfarin (n=2463) or aspirin (n=534). The study found that the differences between the groups with regard to DVT or PE alone were not statistically significant ($p=0.15$; $p=0.06$, respectively). Fisher's exact test showed a significantly higher risk for any symptomatic VTE in patients receiving warfarin (43 events, 1.75%) compared with patients receiving aspirin (3 events, 0.56%; odds ratio [OR]: 3.2; 95% confidence interval [CI], 1.03 to 16.3; $p=0.03$).[17] Similarly, Raphael et al. (2014) conducted a retrospective analysis of patients undergoing TJA. Patients were treated with compression devices while at the same time receiving either aspirin (n=2,800) or warfarin (n=26,123) prophylaxis. The analysis found that the overall symptomatic PE rate was lower ($p<0.001$) in patients receiving aspirin (0.14%) than in the patients receiving warfarin (1.07%). The incidence of symptomatic DVT was significantly lower in the aspirin group (0.29%) than in the warfarin group (0.99%) (OR=3.50; 95% CI, 1.75 to 8.19; $p<0.001$) and the risk of symptomatic DVT remained lower in the aspirin group than in the warfarin group even after propensity score matching was performed.[18]

Only two studies among those reviewed assessed whether the effectiveness of aspirin was improved by the use of mechanical devices, with mixed findings. Daniel et al. (2008) performed a retrospective study comparing the incidence of VTE in patients undergoing THA and hip resurfacing among those who received aspirin for 30 days following surgery (n=258) and those who received aspirin and mechanical prophylaxis for 30 days (n=229). Results indicate a statistically significant difference in DVT prevalence, indicating aspirin in combination with mechanical prophylaxis is more effective than aspirin alone.[19] However, Hamilton et al. (2012), in their retrospective review of patients receiving primary hip and knee arthroplasties, compared patients receiving enoxaparin and mechanical compression prior to a 28-day course of aspirin post discharge, versus enoxaparin alone during the inpatient stay prior to an outpatient 2-week course of enoxaparin followed by a 2-week course of aspirin. There was a trend toward a lower rate of DVT among those who received mechanical compression compared with those who did not, but this difference did not near statistical significance until using a Fisher exact test (p=0.07). Additionally, there was no significant difference between the two groups in the number of patients with the following outcomes: pulmonary embolus, deep infection, superficial infection, readmission, or death.[16]

Three articles did not reach a conclusion as to whether aspirin in conjunction with mechanical prophylaxis was safe and effective for preventing VTE in orthopedic patients. In two studies, this was because either the incidence of VTE in the patient population was so low that it was too difficult to achieve statistical significance in the data analysis[20] or the incidence was so low that there were no DVTs or PEs identified in the patient population.[21] However, in one of the three studies, the authors concluded that antiplatelet agents were not effective in preventing symptomatic VTE in HFS patients after those who received an aspirin or other antiplatelet had a VTE incidence of 4.8 percent, compared with no antiplatelet use with an incidence of 4.3 percent (p=0.718).[22]

16.1.3.3 Aspirin Dosing Considerations

Several included studies examined the impact of different aspirin doses on clinical outcomes following surgery. In their retrospective analysis, Faour et al. (2018) analyzed the medical records of patients receiving aspirin twice daily for 4 to 6 weeks following TKA. Patients received low-dose, 81 mg, aspirin (n=1,327) or standard-dose, 325 mg (n=2,903). Analysis concluded that aspirin is safe and effective but that there was a significant difference in the incidence of VTE and DVT between the two groups (p=0.02 and p<0.001, respectively), with those receiving a standard dose experiencing a higher incidence of VTE and DVT (1.5% vs. 0.7% and 1.4% vs. 0.3%). However, there was not a significant difference in the incidence of PE (p=0.13), and a regression analysis showed no correlation between aspirin doses and the incidence of VTE (both DVT and PE) or DVT alone (p=0.94 and 0.20). Further, there is no statistically significant difference in the incidence of gastrointestinal (GI) or wound bleeding (p=0.62). Faour et al. reached similar conclusions when conducting the same retrospective analysis for patients undergoing THA (2018),[23] but Feldstein et al. (2017) noted there may be more GI distress and nausea when patients are prescribed standard-dose aspirin versus low-dose aspirin following TJA.[24]

In their retrospective multi-institutional study, Goel et al. (2018) reviewed the outcomes for patients receiving either aspirin or warfarin following unilateral or bilateral TKA. Patients in the aspirin group received either regular-dose (325 mg) or low-dose aspirin (81 mg), at the surgeons' discretion. The results showed that regardless of the dosing, aspirin was more effective than warfarin and deemed an appropriate agent for VTE prophylaxis for patients in all risk categories.[10]

16.1.3.4 Economic Outcomes

When considering the use of aspirin for VTE prophylaxis in patients undergoing major orthopedic surgery, cost considerations are a factor noted in a number of the articles reviewed. While there were no cost-effectiveness analyses included in the identified articles, Hamilton et al. (2012) noted that limiting enoxaparin to the inpatient setting and prescribing only aspirin post discharge saved on average $400.30 per case in medication costs.[16] Further, Mendez et al. (2017) estimated that, in 2010 wholesale drug prices, 14 days of aspirin therapy is approximately $0.38, versus $730.50 for 14 days of twice-daily LMWH.[13] Similarly, Jiang et al. (2014) also found a cost savings in the use of aspirin when compared with rivaroxaban and LMWH.[25] Other study authors frequently noted that use of aspirin should be considered, particularly among low-risk patients, due to not only its similar efficacy but also its low cost—compared with both direct and indirect costs associated with other pharmacologic agents—as a "widely available generic agent." (Anderson et al., 2018). [11,14,15,17,23,26]

16.1.3.5 Unintended Consequences

16.1.3.5.1 Positive Unintended Consequences

There are a number of potential positive unintended consequences associated with the use of aspirin for VTE prophylaxis. As previously mentioned, generic aspirin is widely available and significantly cheaper than alternative medications. Additionally, administrative costs are lower than with some alternative pharmacologic prophylaxis agents that require intravenous delivery or ongoing laboratory monitoring, such as with warfarin. Ease of administration may in turn have a positive impact on patient quality of life during the treatment period and support medication adherence.

16.1.3.5.2 Negative Unintended Consequences

As with other pharmacologic prophylaxis agents, there is the potential risk that patients prescribed aspirin following major orthopedic surgery will experience operative site or major bleeding. The analysis of the incidence of these events was a priority for many of the articles included in this review. Twenty-three of the studies specifically addressed unintended patient safety outcomes in their analysis and conclusions. Of those, 22 concluded that overall aspirin was safer than other pharmacologic options, or had comparable risk. For example, Jiang et al. (2014) found that patients in the aspirin group had a lower blood loss index than patients who received LMWH or rivaroxaban following TKA (p=0.000), and Deirmengian et al. (2016) found a higher rate of bleeding events in patients prescribed warfarin versus aspirin (p=0.02) following TJA.[17,25] The identified systematic reviews reached similar conclusions, with two of the reviews determining that use of aspirin has a lower bleeding relative risk than other pharmacologic options.[5,6] Other studies found no difference in bleeding risk between aspirin and other therapies. For example, Anderson et al. (2018) found there was no statistical difference in major bleeding and clinically nonmajor bleeding between aspirin and rivaroxaban following THA or TKA (p=0.43).[15] Similarly, Zou et al. (2014) found no significant differences in hidden blood loss between patients receiving aspirin, rivaroxaban, or LMWH, and Huang et al. (2016) found no significant difference in GI complications between patients receiving warfarin or aspirin.[26,27]

16.1.4 Implementation

16.1.4.1 Patient Risk Stratification

An important consideration when establishing the appropriateness and potential efficacy of aspirin following major orthopedic surgery is the patient risk profile. While 24 of the 27 included studies

determined aspirin is safe and as effective, if not more effective, than other prophylaxis methods, a potential confounding or even misleading factor is the risk stratification of patients. In almost 50 percent of studies, some degree of patient risk stratification occurred. For example, Kaye et al. (2015) conducted a randomized prospective study comparing the use of standard-dose aspirin with no form of chemoprophylaxis among patients undergoing arthroscopic knee surgery (n=170). They found that there were no incidences of DVT or PE regardless of treatment status, and a logistical regression found that aspirin was not statistically significant for a decreased risk of complications following arthroscopic knee surgery. However, they conducted this study specifically in low-risk patients and no conclusions can be made for other risk groups.[21] Parvizi et al. (2017) similarly excluded patients at high risk from their prospective data collection protocol.[28] Among retrospective studies, Raphael et al. (2014) specifically removed patients considered at high risk for VTE from their retrospective data analysis and Deirmengian et al. (2016) indicated that treatment was based on the surgeons' discretion, which may imply some risk stratification in treatment determinations as part of normal practice.[17,18]

16.1.4.2 Resources To Assist With Implementation

Resources to help identify patient VTE risk are available from:

- AHRQ
  - Preventing Hospital-Associated Venous Thromboembolism: A Guide for Effective Quality Improvement: https://www.ahrq.gov/professionals/quality-patient-safety/patient-safety-resources/resources/vtguide/vtguide4.html[p]
    - This guide includes a chapter that provides an overview of the major categories and characteristics of VTE risk assessment models to support the development of a VTE prevention protocol within the facility.
- The Center for Outcomes Research at the University of Massachusetts Medical School: https://www.outcomes-umassmed.org/risk_models_improve_vte.aspx [q]
  - The IMPROVE VTE Risk Calculator is a clinical decision tool for VTE risk assessment and prophylaxis that can be accessed via computer, iPhone, and iPad.
- The University of Michigan: https://www.med.umich.edu/clinical/images/VTE-Risk-Assessment.pdf[r]
  - A thrombosis risk factor assessment checklist is available to be printed for manual use. This checklist is for elective general surgery but may be modified for patients undergoing major orthopedic surgery.

[p]Agency for Healthcare Research and Quality. Preventing Hospital-Associated Venous Thromboembolism: Chapter 4—Choose the Model to Assess VTE and Bleeding Risk. https://www.ahrq.gov/professionals/quality-patient-safety/patient-safety-resources/resources/vtguide/vtguide4.html.
[q]University of Massachusetts Medical School. Center for Outcomes Research: Risk Assessment Models—IMPROVE (VTE). https://www.outcomes-umassmed.org/risk_models_improve_vte.aspx.
[r]University of Michigan. Deep Vein Thrombosis Prophylaxis Orders: Thrombosis Risk Factor Assessment. https://www.med.umich.edu/clinical/images/VTE-Risk-Assessment.pdf.

16.1.5 Gaps and Future Directions

16.1.5.1 Gaps

There are a number of gaps in current literature highlighted by our review. First, only eight of the included studies were prospective and only six included patient randomization to an intervention. As previously mentioned, risk stratification of patients for treatment determination may play an important role in ultimate patient outcomes. So, while the overarching evidence from this review does indicate that aspirin is an effective and safe option for VTE prophylaxis following major orthopedic surgery, there may be limitations to the generalizability of these findings. There is a need for more prospective, randomized controlled trials directly comparing patient outcomes between those prescribed aspirin and those given other available prophylaxis options across risk levels. Second, there is a lack of studies providing direct comparison between aspirin in conjunction with mechanical prophylaxis versus aspirin alone. Given that the use of mechanical prophylaxis is pervasive in the studies identified, it would be useful to determine whether this makes a difference across different levels of patient risk. Finally, while researchers often note that aspirin is cheaper and more cost effective than other prophylaxis options, formal cost-effectiveness analyses are needed for both chemoprophylaxis and mechanical prophylaxis alternatives.

16.1.5.2 Future Directions

In addition to addressing the gaps noted above, a further area that may help better determine the efficacy of aspirin in different patient populations is research into best methods or approaches for diagnosing VTE, in particular DVT. Additionally, as noted in Stewart and Freshour (2013), individual studies may define “bleeding” differently, posing a challenge when making comparisons across multiple bodies of research. Therefore, a standardized definition may be helpful for researchers and providers alike.[9]

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Conclusion and Comment

The Patient Safety Practice reviewed in this chapter aims to reduce VTE by providing an effective, safe, and low-cost approach to pharmacologic prophylaxis in patients undergoing major orthopedic surgery. This review of the evidence generally finds that use of aspirin following these surgical procedures—either as the sole prophylaxis agent in combination with other pharmacologic agents or in conjunction with mechanical prophylaxis—is equivalent to other agents or has a better safety profile. Many studies were retrospective and/or included patient risk stratification either in the treatment allocation or in the exclusion of data for analysis. This indicates a need for prospective randomized controlled trials directly comparing the impact of different prophylaxis methods across patient risk categories. However, this review provides greater insight into the effectiveness of aspirin for preventing VTE in patients following major orthopedic surgery.

17. Cross-Cutting Patient Safety Topics/Practices

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Introduction

Over the last decade, there have been more quality and safety improvement efforts in healthcare than ever before, with programs funded by Federal grants, State agencies, and privately run organizations.[1] Despite these efforts, reliably safe healthcare has remained somewhat elusive as adverse events continue to occur. A more recent trend in healthcare quality improvement has been focused on building high reliability organizations (HROs). HROs are described as organizations that operate in complex environments while maintaining high levels of safety for extended periods of time.[2] HROs also have strong leaders who are committed to safety. Leaders are key to instilling a commitment to safety in all members of the organization to create a positive safety culture, where staff continually scan and monitor their environment to identify and correct even minor deviations that could lead to unsafe conditions. When a deviation in safety processes or practices is observed, staff speak up or take action to contain the problem and/or resolve the issue. In the event that an adverse event or near miss does occur, incidents are reported without fear of blame or punishment. In addition, HROs rely on process improvement tools to systematically solve safety issues, including reliable assessments of the problem's scope (e.g., isolated to a unit or organizationwide), identification of root causes associated with the problem, and application of the most appropriate solutions.

While a great deal can be learned through the study of HROs, it can be difficult to articulate the exact steps to achieve high reliability, as many different paths can be taken.[1] Moreover, what works in one organization does not always work in another, as demonstrated by the many conflicting results found within the healthcare quality and patient safety literature. To increase the reliability of healthcare quality, it is also necessary to understand the context in which improvement practices are applied. Any pre-existing norms, processes, resources, or quality improvement initiatives will influence how new practices are viewed and adopted, and the degree to which they achieve their intended result(s).

A wide range of contextual factors can impact performance. In considering five specific (yet diverse) patient safety practices, Taylor et al. (2011)[3] generated a total of 42 contextual factors that could influence their implementation and effectiveness. To identify the most important contextual factors, a panel of subject-matter experts were surveyed regarding the importance of each of the factors and then engaged in group discussions. Through an iterative process, the original list of 42 contextual features was reduced down to 4 factors that could influence successful implementation.

The current review followed a similar approach to that described by Taylor et al. (2011). Specifically, an initial scan of the literature was conducted related to the specific patient harms included in the current report (e.g., diagnostic errors) to better understand each problem/harm, the contributing factors, and the potential practices to address each. Members from the Technical Expert Panel and the Advisory Group were surveyed and their input was reviewed via conference calls. While the specific patient safety practices related to each harm has been detailed in the previous chapters, several factors were identified as contributing to, or as being root causes of, multiple harms. These factors included: (1) patient and family engagement, (2) safety culture, (3) clinical decision support, (4) cultural competency, (5) monitoring, auditing, and feedback(6) teamwork and team training, and (7) education and training through simulation. These contextual factors were thought to be among the most important ones with

respect to potentially influencing the success of the patient safety practices related to the specific harms discussed in the current report. For example, clinicians must monitor vital signs to accurately identify patient deterioration, but communication (a key aspect of teamwork) between clinicians and rapid-response teams was identified as a contributing factor in failure-to-rescue cases. In addition, the six cross-cutting contextual factors often represent broader organizational initiatives. For instance, efforts to improve teamwork represent a popular patient safety initiative that is expected to directly improve patient outcomes overall, not only those related to failure-to-rescue cases. These seven selected cross-cutting contextual factors are presented in the following sections.

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17.1 Patient and Family Engagement

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Introduction

Traditionally, patient safety management has been the sole responsibility of the healthcare provider, but in recent decades, new approaches to patient safety include actively engaging patients and/or patients' families and caregivers. While there is no standard definition, patient and family engagement (PFE) is commonly defined as "the desire and capability to actively choose to participate in care in a way that is uniquely appropriate to the individual, in cooperation with a healthcare provider or institution, for the purposes of maximizing outcomes or improving care experiences."[1]

17.1.1 Patient and Family Engagement as a Patient Safety Practice

The Agency for Healthcare Research and Quality (AHRQ) identified four overarching threats to primary care patient safety—communication breakdowns, medication issues, diagnosis and treatment issues, and fragmentation—in its *Guide to Improving Patient Safety in Primary Care Settings by Engaging Patients and Families: Environmental Scan Report* (2018).[2] One way to address these threats is by engaging patients and families in a patient's care and, as stated in recent systematic reviews by Park and Giap (2019) and Berger et al. (2014), including the patient in patient safety. This makes sense because patient-centeredness is a vital aspect of healthcare, and patients are uniquely positioned to provide information throughout an entire course of care.[1,3]

Patient and family engagement can be conceptualized in two primary ways: (1) as an overarching principle that is applicable to many patient safety practices and (2) as a specific component of another particular patient safety practice.[3] Some strategies to encourage adoption of patient and family engagement patient safety practices are highlighted in AHRQ's *Guide to Improving Patient Safety in Primary Care Settings by Engaging Patients and Families: Environmental Scan Report* and Web page.[2] They include:

- Patient and family advisory councils, boards, and committees.
- Team-based care.
- Interventions to support medication safety.
- Structured communication for patients, families, and primary care providers.
- Teach-back.
- Warm handoffs.

As patient and family engagement is still an emerging patient safety practice (PSP), there is little if any published research that provides comprehensive insight into its relationship to patient safety. Because such studies are limited, healthcare providers may find it difficult to apply appropriate guidelines and implement effective patient and family interventions in their current practice.

17.1.2 What's New/Different Since the Last Report?

Key Findings:

- Although four of the six studies related to adverse events resulted in statistically significant results, more studies are needed to measure the direct outcomes of patient and family engagement as a PSP.
- The studies included in the systematic reviews revealed a lack of understanding about the effects of PFE on patient safety among healthcare providers, patients, and families.
- PFE implemented through an educational intervention was linked to positive perceptions and attitudes about PFE among healthcare providers.

In Making Health Care Safer II (MHCS II), the authors noted that when compared with other PSPs, patient and family engagement did not lend itself to specific practices, in part because "engagement" is an umbrella term that does not refer to specific PSPs. In MHCS II, the case was made that this PSP involves patients being present for all treatment, providing important information that may not be available from other sources, and being highly motivated to decrease the risk of harm and ensure good outcomes. In MHCS II, only three studies were identified as relevant to patient and family engagement; they focused on medication management and hand washing, and were of low methodological rigor. Since the publication of MHCS II, there are still too few studies that empirically measure changes in patient and family engagement after implementation of practices focused on this topic.[4] Typically, patient and family engagement is not the primary target of overall PSP interventions reviewed; instead, it is treated as a contextual variable and is often not separately reported.[3]

In addition to the AHRQ material on patient and family engagement, the American Institutes for Research (AIR), along with the Gordon and Betty Moore Foundation, published *A Roadmap for Patient and Family Engagement in Healthcare* (2015),[5] which recommended eight strategies for change and improvement in patient and family engagement:

- Patient and family preparation.
- Clinician and leadership preparation.
- Care and system redesign.
- Organizational partnership.
- Measurement and research.
- Transparency and accountability.
- Legislation and regulation.
- Partnership in public policy.

17.1.3 Methods

Two databases (MEDLINE® and CINAHL®) were searched for articles published in English within the past 10 years using terms related to patient and family engagement and safety improvement. The search generated 220 citations. Duplicates were removed, and the remaining abstracts were reviewed for relevance, leading to the review of one full-text article. Since the individual study results yielded few results, we also included systematic reviews published in English within the past 10 years. This chapter is

based on two recent systematic reviews and the one individual study we found. Key findings are located in the box above.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

17.1.4 Review of Evidence

Since individual studies are limited, this chapter provides an overview of the current landscape of patient and family engagement as a PSP using two recent systematic reviews and one identified study.

17.1.4.1 Implementation of Patient and Family Engagement

One systematic review by Berger et al. (2014) evaluated how patient and family engagement is implemented. The authors used MEDLINE®, CINAHL®, Embase®, and Cochrane to find two types of studies: (1) standalone interventions meant to improve patient or family engagement and (2) patient and family engagement interventions implemented as part of an overarching PSP. The review identified six articles with standalone interventions, four of which focused on hand hygiene. All four studies used a pre-post methodology, and one study found that, post-intervention, patients asked their physicians about hand hygiene 40 percent of the time and asked nurses 95 percent of the time. Another study, by Davis et al., found that patients showed an increased willingness to ask healthcare providers about hand hygiene and expressed an increased appreciation of the importance of participating in safety-related behaviors post-intervention. The authors noted that, while appreciation of importance increased, patients' willingness to participate remained lower than their appreciation of importance.[2]

One randomized controlled study cited in the Berger et al. review (Weingart et al.) found no significant differences in adverse drug events (ADEs) or close calls between the control group and the patient and family engagement intervention group, which used a personalized medication list to reduce ADEs and close calls. In another study in the Berger et al. review, the authors cited limited evidence and poor quality of benefits for patient involvement in patient safety.[3]

Berger et al. identified 12 studies in which patient and family engagement was part of a broader PSP intervention. These studies focused on hand hygiene, rapid response systems, surgical checklists, prevention of falls, prevention of ventilator-associated pneumonia, and prevention of medical errors after discharge. Patients and families were encouraged to actively participate in ensuring their own safety, but engagement strategies varied across the studies.[3]

Four of these 12 studies encouraged patients and families to directly address healthcare providers to point out lapses or remind them of safety behaviors. As authors Weissman et al., Taylor et al., and Weingart et al. note, the effectiveness of the approach depended on the patient's willingness and ability to participate in reporting clinical errors to healthcare providers. The study by McGuckin et al. found that, while 80–90 percent of patients expressed willingness to ask their healthcare providers to wash their hands, only 60–70 percent of patients did.[3]

In addition to directly approaching healthcare providers, several studies in the Berger et al. review highlighted patients' engaging in "direct activation" of a patient safety intervention, such as patients and/or families calling a rapid response system.[3] One observational study by Eden et al. (2017)

examined the use of a patient- and family-initiated rapid response system called Condition Help.[5] This system was designed to prevent medical errors and communication problems by encouraging patients and families to call the Condition Help hotline if they believed there was a breakdown in care or if their health was in immediate danger. Outcomes of interest included activation of a traditional rapid response team or transfer to an intensive care unit, inpatient mortality, and discharge against medical advice. Patient and family engagement as an outcome was not measured; rather, it was a component of the overall intervention.[3]

Berger et al. cited one systematic review that summarized the patient factors most associated with patient willingness to encourage healthcare providers to engage in hand hygiene. These factors included an extroverted patient personality, patient belief that they could control the healthcare provider's behaviors, younger age, awareness of healthcare-associated infections, and an invitation by the healthcare provider to discuss hand hygiene.[3]

Overall, Berger et al. found strength of evidence on this topic to be low because of the limited number of studies and the lack of studies that assessed the effectiveness of the interventions, and whether the interventions actually improved patient and family engagement and safety outcomes.[3]

17.1.4.2 Effectiveness of Patient and Family Engagement Implementation

In another recent systematic review, the goal was to provide comprehensive insight into the impact of patient and family engagement interventions on patient safety and related issues. Forty-two studies published from 2009 through 2018 were included in this review. Park and Giap used an adapted patient and family engagement framework to classify the level of engagement found in the studies. The study interventions described in this systematic review are of two types: direct care and organizational. Direct care occurs when healthcare providers partner with the patient and/or family in the processes of shared decision making. An organizational engagement can be in the form of quality and safety improvement initiatives or advisory councils that contain patient and/or families/caregivers as members.[1]

Most of the reviewed studies were conducted in hospitals, including 6 randomized controlled trials, 8 non-randomized controlled trials, 12 qualitative studies, and 11 surveys. Other settings included the community, nursing homes, private clinics, academic medical centers, and primary healthcare centers. Study outcomes of interest included satisfaction; perception and awareness of patient safety and risks; perception, attitude, and concerns; length of stay; depression or anxiety; performance of safety-related behaviors; and clinical deterioration.[1]

Six studies in the Park and Giap review showed positive effects in relation to PFE interventions preventing or reducing adverse events related to healthcare-associated infections, falls, pressure ulcers, and medication errors. In one randomized controlled trial (Chaboyer et al., 2016), patients received educational materials, including DVDs, brochures, and posters, that encouraged them to ask questions of their providers with an aim of reducing the incidence of pressure ulcers.[1] While the intervention led to a large reduction in the potential harm or hazard of pressure ulcers, the results were not considered statistically significant. Another study, by Lawton et al. (2017), used two engagement interventions—a questionnaire and incident reporting tool—to reduce the incidence of adverse events, measured via harm-free care scores. The interventions led to greater but nonsignificant improvement in the harm-free care scores.[1] In a quasi-experimental intervention study by Schwappach et al. (2011), the intervention

group, which received an educational pamphlet about how to prevent medical errors, was less likely to experience any adverse events and unsafe situations (odds ratio=0.57, confidence interval [CI]=0.38–0.87, P=0.009).[1] In another randomized controlled trial, by Van Gaal et al. (2011), the SAFE or SORRY? Programme, also known as essential guidelines for preventing adverse events, was implemented through education, patient involvement, and feedback on process and outcomes indicators. The results showed a statistically significant reduction in the rate of adverse events in the intervention group (rate ratio=0.57, 95% CI=0.34–0.95).[1]

The same six studies also showed that patients and families were satisfied with interventions when they played a role as a partner in the healthcare process, as described in two studies (Pokrywka et al., 2017 and Pokrywka et al., 2014), which encouraged patient and family hand hygiene to reduce the spread of *Clostridium difficile*.[1] In Pokrywka et al. (2017), an educational intervention study focused on providing patients with opportunities to wash their hands saw a significant decrease (p=.05) in *C. difficile* infection 6 months after the intervention. In the other study by Pokrywka et al. (2014), a bundle strategy including patient hand hygiene significantly reduced the rate of *C. difficile* infection.[1] Regarding clinical outcomes such as length of stay, depression, anxiety, clinical deterioration, physical and mental health, and lifestyle changes, however, most studies found no statistically significant differences between study outcomes.

Although nine of the reviewed studies found that patients and families expressed willingness to engage in care processes, several studies (Longtin et al., 2010, Pittet et al., 2011, and McMurray et al., 2011) found that some patients and families were not comfortable with asking their healthcare providers questions about their medical care and preferred passive engagement rather than active engagement.[1]

Five studies implemented interventions with a positive effect on healthcare providers in terms of perception of and attitude toward the role of patient and family engagement in patient safety and the provider relationship with the patient and/or family. This was especially relevant in the studies in which patient feedback was used to develop an educational intervention (Langer et al., 2016, and Schwappach et al., 2011).[1] Only two studies (Lawton et al., 2017, and Jha et al., 2014) showed that healthcare providers' perception and attitude to PFE did not change after a PFE intervention.[1]

Park and Giap found that only 12.5 percent of the reviewed randomized controlled studies and 11.1 percent of non-randomized controlled studies were assessed as high quality, while 69.2 percent of the qualitative studies and 75 percent of the surveys were considered high quality. The authors concluded that obtaining insight into the impact of patient and family engagement on patient safety is difficult; less than half of the reviewed articles evaluated a patient and family engagement intervention, and less than a quarter of the studies measured direct outcomes related to patient safety events. Overall, the authors found that patients and families, along with healthcare providers, do not have a strong understanding of the effects of patient and family engagement on patient safety.[1] Therefore, strategies are needed to help foster a better understanding of potential benefits of patient and family engagement as it relates to patient safety among patients and families as well as providers.

17.1.4.3 Barriers

Both systematic reviews found barriers related to the patient-provider relationship. Although many patients were willing to participate in an intervention, some expressed fear that this might affect the care they receive from their providers. Lack of patient awareness about the severity of potential harms

also affected patients' willingness to participate in interventions aimed at improving patient and family engagement. The effectiveness of interventions was also limited if they did not receive sufficient support from hospital administration, physicians, and staff.

17.1.4.4 Facilitators

When patients received encouragement to participate in their healthcare at the direct invitation of a provider, they were more likely to participate in patient and family engagement practices. Healthcare providers were more likely to engage patients when hospital leadership strongly endorsed patient and family engagement interventions.

17.1.5 Resources To Assist Implementation

AHRQ developed *The Guide to Improving Patient Safety in Primary Care Settings by Engaging Patients and Families* (2018) to support collaboration among primary care practices, patients, and their families to improve patient safety: https://www.ahrq.gov/patient-safety/reports/engage.html.

AIR developed a unified vision, or roadmap, for improving patient and family engagement across the healthcare system. The roadmap is based on information from a diverse group of stakeholders, including patients, advocates, clinicians, researchers, payers, funders, and policymakers—*A Roadmap for Patient and Family Engagement in Healthcare Practice and Research*: https://www.air.org/project/roadmap-guides-patient-and-family-engagement-healthcare.

17.1.6 Gaps

The overall evidence for improving patient safety through patient and family engagement is suggestive and mostly case-based. The AHRQ environmental scan, *Guide to Improving Patient Safety in Primary Care Settings by Engaging Patients and Families* (2018), noted that few interventions are reviewed in the literature. The environmental scan found 33 peer-reviewed articles and 60 grey literature sources that described an evaluated intervention. Berger et al. (2014) found few individual studies that assessed the effectiveness of interventions, particularly whether or not an intervention actually improved patient and family engagement and safety outcomes.[2]

The review by Park and Giap revealed gaps between the healthcare provider and the healthcare system. as exemplified by healthcare providers who expressed a favorable view of patient and family engagement but a lack of knowledge about how to implement such practices. This may be due to inadequate training or limited knowledge and culture of healthcare systems that support the patient and family engagement strategy. Park and Giap also noted that more observational studies are needed to assess the effectiveness of patient and family engagement and any links to improvements in patient safety outcomes.[1]

17.1.7 Conclusion

Patient safety in primary care continues to evolve, and so do the practices used to engage patients and families in their care. Strategies are needed to help patients and families understand the role of PFE in their safety. Healthcare providers also need to understand the importance of engaging patients in their care. In order to accomplish this, Berger et al. and Park and Giap recommend that stakeholders become more involved in the process to address the following: (1) building consensus on the definition and guidelines for implementing patient and family engagement, whether it is through an independent intervention or as part of another intervention within an existing PSP; (2) widening the research scope

for patient and family engagement and patient safety; and (3) addressing priority areas for implementing patient and family engagement.[1, 2]

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17.2 Safety Culture

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17.2.1 Practice Description

As evidenced in the current review, many patient safety practices are available to reduce harms. However, these practices sometimes fail to achieve their intended results. Even when implemented properly, contextual factors and organizational characteristics can reduce their effectiveness. For example, the patient safety culture can affect the degree to which patient safety practices are adhered to, or not. Patient safety culture, which is part of the overall culture, has been described as "the beliefs, values, and norms that are shared by healthcare practitioners and other staff throughout the organization that influence their actions and behaviors."[1] Patient safety culture helps inform staff about the behaviors that are acceptable, are worthy of praise, or are punishable (formally and/or informally) by the organization. A positive patient safety culture can be characterized as one where:

Key Findings:

- Strategies for improving patient safety culture have been tested.
- Studies of patient safety culture strategies have demonstrated some improvements in perceptions of safety culture using validated measures.
- Studies of safety culture interventions are generally of low to moderate quality and rely on self-report measures.
- More robust studies are needed that demonstrate the usefulness of these practices on perceptions of safety culture, as well as on clinical outcomes and patient harms.

- Safety has been articulated as an organizational priority.
- Staff work as a team to accomplish their tasks and reduce error.
- There is open communication and transparency in discussing near-misses and adverse events.
- There is an emphasis on learning from mistakes.

Leaders in healthcare quality improvement, such as The Joint Commission, the National Quality Forum, and the Agency for Healthcare Research and Quality (AHRQ), have recognized the importance of safety culture and encouraged its measurement. Several safety culture survey instruments have been developed, and research has established their psychometric properties. For instance, AHRQ sponsored the development of Surveys on Patient Safety Culture™ (SOPS™) in multiple healthcare settings, such as hospital, medical office, nursing home, community pharmacy, and ambulatory surgery center. As part of this program, survey instruments and support materials are available, as are voluntary databases to which users of the Hospital, Nursing Home, Community Pharmacy, Medical Office, and Ambulatory Surgery Center SOPS™ can voluntarily submit data from patient safety culture surveys. (Please refer to Section 17.2.5, Resources, for more information on SOPS™.) These, as well as other safety culture surveys (e.g., Safety Attitudes Questionnaire)[2] reliably measure multiple dimensions of safety culture, including teamwork, safety climate, communication, and error reporting.

Using such measures, studies have demonstrated a relationship between safety culture and a variety of patient outcomes. For instance, evidence suggests that perceptions of safety culture are related to readmission rates of cardiac patients,[3] length of stay for intensive care unit patients,[3] postoperative complication rates,[4] medication errors,[5,6] patients' perceptions of care,[7] and safety incidents.[8,9] Further,

a positive safety culture may be a prerequisite for attaining safety goals, such that organizations with a favorable safety culture in place may be more likely to adopt new safety practices and have a better chance that those practices will take hold.[10,11] As such, there is increasing interest in identifying the practices that lead to improved safety culture and evaluating their effectiveness.

17.2.2 Methods

The question of interest for this review is, "What are the most effective methods to improve safety culture?"

To answer this question, two databases (i.e., CINAHL® and MEDLINE®) were searched to identify studies published between 2008 and 2018 that implemented practices to improve safety culture. Search terms included "patient safety culture," "organizational culture," and related synonyms, as well as terms such as "performance improvement." More specific terms such as "Leadership WalkRounds," "comprehensive unit-based safety program," and "team training" were also searched, since these practices were identified in the previous Making Healthcare Safer project and in initial scans of the safety culture literature. The initial search yielded 1,052 results. After duplicates were removed, 916 were screened for inclusion and 77 full-text articles were retrieved. Of those, 21 were selected for inclusion in this review; 19 of them are single studies and 2 are systematic reviews: 1 of safety culture[12] and 1 on teamwork, communication, and safety climate.[13] Articles were excluded if the article was out of scope (including not quantitative), the study design was insufficiently described, the study did not evaluate a practice/method to enhance safety culture, the primary goal was not on improving safety culture, the study did not report statistical analyses, or the study was conducted outside of the United States. Key findings are located in the box above.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

17.2.3 Review of Evidence

The practices used to improve safety culture fell into four main categories: Leadership WalkRounds, Team Training, Comprehensive Unit-based Safety Program (CUSP), and those that implemented multiple methods. Across these categories, the majority of the studies took place in a hospital setting (18 out of 19) and one study was conducted in a subacute rehabilitation unit of a long-term care facility. Safety culture was most frequently measured using AHRQ's 2004 Hospital Survey on Patient Safety Culture (HSOPS)[s] or Sexton et al.'s (2006) Safety Attitudes Questionnaire (SAQ),[2] which was cited as the most frequently used measure in Sacks et al.'s 2015 review.[13] (Refer to Table 17.1, where each column lists the safety culture measures used in the reviewed studies, their associated dimensions, and brief descriptions of each. Please note that this table is not meant to compare the dimensions of each scale against one another, nor is it an exhaustive list of the safety culture measures available. Additional measures have been included in the Resources section.) Moderate changes in safety culture, along with some mixed results, were reported following the implementation of safety culture practices.

[s] In October 2019, AHRQ published HSOPS 2.0. Please refer to the Resources section for the link to both versions of this survey.

Table 17.1: Safety Culture Survey Instruments—Dimensions and Descriptions

Hospital Survey on Patient Safety Culture (HSOPS)	Nursing Home Survey on Patient Safety Culture	Safety Attitudes Questionnaire (SAQ)	Teamwork and Safety Climate Questionnaire (TSCQ)	Safety, Communication, Operational Reliability, and Engagement (SCORE)
Communication Openness: Staff freely speak up if they see something that may negatively affect a patient and feel free to question those with more authority. **Feedback and Communication About Error:** Staff are informed about errors that happen, are given feedback about changes implemented, and discuss ways to prevent errors. **Frequency of Events Reported:** Mistakes of the following types are reported: (1) mistakes caught and corrected before affecting the patient, (2) mistakes with no potential to harm the patient, and (3) mistakes that could harm the patient but do not. **Handoffs and Transitions:** Important patient care information is transferred across hospital units and during shift changes. **Management Support for Patient Safety:** Hospital management provides a work climate that promotes patient safety and shows that patient safety is a top priority. **Non-Punitive Response to Error:** Staff feel that their mistakes and event reports are not held against them and that	**Communication Openness:** Staff speak up about problems, and their ideas and suggestions are valued. **Compliance With Procedures:** Staff follow standard procedures to care for residents and do not use shortcuts to get their work done faster. **Feedback and Communication About Incidents:** Staff discuss ways to keep residents safe, tell someone if they see something that might harm a resident, and talk about ways to keep incidents from happening again. **Handoffs:** Staff are told what they need to know before taking care of a resident or when a resident's care plan changes, and they have all the information they need when residents are transferred from the hospital. **Management Support for Resident Safety:** Nursing home management provides a work climate that promotes resident safety and shows that resident safety is a top priority. **Non-Punitive Response to Mistakes:** Staff are not blamed when a resident is harmed, are treated fairly when they make mistakes, and feel safe reporting their mistakes.	**Teamwork Climate:** Perceived quality of collaboration between personnel. **Job Satisfaction:** Positivity about the work experience. **Safety Climate:** Perceptions of strong and proactive organizational commitment to safety. **Working Conditions:** Perceived quality of the work environment and logistical support (staffing, equipment, etc.). **Stress Recognition:** Acknowledgement of how performance is influenced by stressors.	**Teamwork:** Perceived quality of collaboration between personnel. **Safety Climate:** Perceptions of strong and proactive organizational commitment to safety. **Perceptions of Management:** Approval of managerial action.	**Teamwork Climate:** Extent to which norms of local interaction are effective, such as speaking up, resolving conflicts, and asking questions to clarify ambiguities. **Safety Climate**: Extent to which local patient safety norms are proactive and positive, such as discussing, handling, and learning from errors. **Improvement Readiness**: Extent to which quality improvement is supported within a work setting through continuous learning through both strengths and deficits in quality. **Local Leadership:** Extent to which leaders communicate with and are available to healthcare workers. **Personal Burnout:** Extent to which a respondent personally experiences unhealthy or negative emotions related to his/her work, such as frustration. **Burnout culture:** Extent to which a group or multiple groups experience unhealthy or negative emotions related to their work, such as frustration.

Hospital Survey on Patient Safety Culture (HSOPS)	Nursing Home Survey on Patient Safety Culture	Safety Attitudes Questionnaire (SAQ)	Teamwork and Safety Climate Questionnaire (TSCQ)	Safety, Communication, Operational Reliability, and Engagement (SCORE)
mistakes are not kept in their personnel file. **Organizational Learning—Continuous Improvement:** Mistakes have led to positive changes, and changes are evaluated for effectiveness. **Overall Perceptions of Patient Safety:** Procedures and systems are good at preventing errors, and there is a lack of patient safety problems. **Staffing:** There are enough staff to handle the workload and work hours are appropriate to provide the best care for patients. **Supervisor/Manager Expectations and Action Promoting Patient Safety:** Supervisors/managers consider staff suggestions for improving patient safety, praise staff for following patient safety procedures, and do not overlook patient safety problems. **Teamwork Across Units:** Hospital units cooperate and coordinate with one another to provide the best care for patients. **Teamwork Within Units:** Staff support each other, treat each other with respect, and work together as a team.	**Organizational Learning:** There is a learning culture that facilitates making changes to improve resident safety and evaluates changes for effectiveness. **Overall Perceptions of Resident Safety:** Residents are well cared for and safe. **Staffing:** There are enough staff to handle the workload, meet residents' needs during shift changes, and keep residents safe, because there is not much staff turnover. **Supervisor Expectations and Actions Promoting Resident Safety:** Supervisors listen to staff ideas and suggestions about resident safety, praise staff who follow the right procedures, and pay attention to safety problems. **Teamwork:** Staff treat one another with respect, support one another, and feel that they are part of a team. **Training and Skills:** Staff get the training they need, have enough training on how to handle difficult residents, and understand the training they get in the nursing home.			

17.2.3.1 Practice: Leadership WalkRounds

Leadership WalkRounds is a tool that executives and leaders can use to: increase awareness of safety; demonstrate their commitment to (and the importance of) safety; reinforce safety behaviors and concepts such as speaking up and non-punitive reporting; and gather and help solve patient safety–related issues. As the term implies, this tool involves leaders "walking around" to engage in face to face, candid discussions with frontline staff about patient safety incidents or near-misses. Leadership WalkRounds vary in the way they are implemented, including the composition of the WalkRound team, the frequency with which WalkRounds are used, the degree of structure that each WalkRound follows (e.g., whether a standard set of questions is used), and the degree to which the WalkRound team communicates the issues raised and the potential solutions identified to the rest of the staff.

The systematic review conducted by Weaver et al. (2010), as well as four individual studies, examined the use of Leadership WalkRounds for enhancing patient safety culture. All four individual studies were conducted in a hospital setting, with three implementing WalkRounds in multiple units and one study focusing specifically on the neonatal intensive care unit (NICU).[14]

17.2.3.1.1 Process Measures

Eight studies reviewed by Weaver et al. (2010) reported that perceptions of safety culture improved (to varying degrees) following the use of WalkRounds, and three reported perceived improvements in care processes. All four studies of Leadership WalkRounds in the review collected process measures. Three studies evaluated the impact of Leadership WalkRounds by administering the SAQ or specific subscales of the SAQ. One study used the Safety, Communication, Operational Reliability, and Engagement (SCORE) survey (Table 17.1). All studies reported some improvement (and in some cases, significant improvement) on individual items, or on one or more dimensions of safety culture (e.g., teamwork climate, error reporting).[14]

Frankel et al. (2008) examined the impact of a weekly WalkRound project on the safety climate dimension of the SAQ. The project, conducted in two hospitals, yielded some positive improvements approximately 18 months following implementation. One hospital increased its "overall safety climate" score from 62 percent to 77 percent (p=0.03), while the other hospital had an increase from 46 percent to 56 percent (p=0.06).[15]

Another study found that greater exposure (i.e., where a minimum of 60% of the unit had been exposed to 1 WalkRound) was related to significantly higher SAQ dimension scores of "safety climate."[16] "Safety climate" scores were 73.5 percent for the high-exposure group, 64.1 percent for the moderate-exposure group, and 61.2 percent for the low-exposure group. Between-group comparisons indicated significant differences between high- and moderate-exposure groups (p=0.000) and between moderate- and low-exposure groups (p=0.149). Greater exposure to WalkRounds was also associated with significantly greater likelihood of reporting a reduction in patient safety risks (54.9% reduction for high-exposure group, 30.9% for moderate, and 13.3% for low; p=0.000 for all between-group comparisons) and significantly greater odds of reporting that they had more feedback about actions taken as a result of the Leadership WalkRounds (52.5% for high-exposure group, 27.4% for moderate, and 11.3% for low; p=0.000 for all between-group comparisons).[16]

Two additional studies conducted by Sexton and colleagues focused on the provision of feedback following the WalkRound process. Sexton et al. (2014) reported that NICU respondents in the high

WalkRound feedback quartile had significantly higher "safety climate" ($p<0.001$) and "teamwork climate" ($p=0.01$) scores on the SAQ than the low-feedback quartile. Respondents in the high WalkRound feedback quartile also reported less burnout than those in the low feedback quartile, although this difference was not statistically significant ($p=0.07$).[17]

Similarly, Sexton et al. (2018) found that staff who received more feedback (i.e., were told what problems were discussed during the WalkRounds and what actions were taken to address them) had more positive perceptions of all safety culture dimensions (improvement readiness, local leadership, teamwork climate, safety climate; $p<0.001$), higher engagement scores on four of six subscales (advancement, growth opportunities, job uncertainty, participation in decision making; $p<0.001$), and lower reports of burnout (personal burnout, burnout climate, $p<0.001$).[18]

17.2.3.1.2 Outcome Measures

In their systematic review, Weaver et al. (2013) reported on one study that examined WalkRounds and found an improvement in a patient outcome. Specifically, the frequency of serious adverse events significantly decreased after WalkRounds were introduced. None of the four studies in the review of Leadership WalkRounds collected patient outcome measures.[12] However, a more proximal outcome is the effectiveness of Leadership WalkRounds in resolving and/or correcting issues. Saladino et al. (2013) conducted structured, monthly WalkRounds within a critical care unit as part of a CUSP intervention. The WalkRounds focused on a set of three questions: consider which processes within the unit are cumbersome; discuss the delays that were experienced in care delivery; and identify any communication issues that occurred between team members. Using this approach, 77 safety issues were identified during the study period, with 44 (57.1%) being resolved and communicated back to the staff.[19]

Building on the work of Sexton et al. (2014, 2018),[17,18] data could also be gathered regarding how well the issues uncovered and resolved are communicated back to the staff (e.g., what percentage of staff are aware of safety issues discussed during WalkRounds and specific solutions). Finally, in terms of patient-oriented outcomes, data related to delays in care, length of stay, and re-admission rates could be examined within the unit or across units participating in Leadership WalkRounds. However, selection of the most appropriate outcome(s) to be measured should be informed by the specific problems and issues identified in each department/unit through the WalkRounds process.

17.2.3.2 Practice: Team Training

Team training is another strategy that has been used to build a culture of safety. Team training programs focus on enhancing teamwork skills and communication between healthcare providers in order to foster a more positive work environment and safety culture. Most often, these programs include the delivery of a training workshop followed by the selection of specific tools that will be implemented to increase teamwork on the job.

In their systematic review, Sacks et al. (2015) reported that the majority of the included studies employed some form of team training or team building (23 out of 47, 49.9%) in their safety culture efforts. However, it should be noted that the inclusion criteria in their study differed from the criteria employed in the current review. They also included studies in which safety culture was measured but was not the primary focus, while in this review it is. Eight studies in the current review examined the use of team training for enhancing patient safety culture. Studies were conducted in a variety of settings including five hospitals, two Department of Veterans Affairs (VA) medical facilities, and one subacute

rehabilitation unit in a long-term care facility.[13] A total of 20 studies in Weaver et al.'s (2013) systematic review studied team training to improve safety culture.[12]

17.2.3.2.1 Process Measures

Weaver et al. (2013) included 20 studies that implemented team training or tools to enhance teamwork in an effort to improve safety culture. The majority (16 out of 20, 80%) reported significant improvement in staff perceptions of safety culture, and five reported improved care processes. All of the individual studies included in the review collected data on perceptions of safety culture. Four studies evaluated the effectiveness of their team training effort by administering the HSOPS, three used the SAQ, two used the Teamwork and Safety Climate Questionnaire (TSCQ), and one used the Nursing Home Survey on Patient Safety Culture (Table 17.1). All studies found some pre to post improvement on individual items, or on one or more dimensions of safety culture (e.g., teamwork climate, error reporting) after implementing their team training program.[12]

Three studies incorporated Crew Resource Management (CRM) training into their safety culture efforts, all of which specifically examined differences in safety culture perceptions by role types. For instance, Budin et al. (2014) examined the differential impact of CRM training on nurses and physicians working in a labor and delivery unit. Perceptions of "teamwork climate" and "safety climate" subscales of the SAQ significantly improved for all respondents following the training, with physicians having more positive perceptions than nurses on both the baseline and follow-up assessments (physician teamwork climate scores: T1=66.49 vs. T2=85.44, p=0.000; physician safety climate scores: T1=60.48 vs. T2=77.70, p=0.000; nurse teamwork climate scores: T1=55.60 vs. T2=102.86, p=0.000; nurse safety climate scores: T1=56.64 vs. T2=76.68, p=0.000).[20]

Similarly, Hefner et al. (2017) reported a statistically significant increase on 10 of 12 HSOPS dimensions across all respondents and eight departments within a medical center ($p<0.05$), with no changes observed for 2 dimensions, "supervisor promotes patient safety" and "staffing," which were not the emphasis of the training program. As noted in this study, practitioners (which included physicians and advanced-practice registered nurses) responded more favorably than other staff on all 12 HSOPS dimensions both prior to and after the CRM training.[21]

In contrast, only minor improvements on the SAQ following CRM training were documented in a study conducted by Gore et al. (2010). The most notable improvement in this study was observed for nurses' perceptions of "teamwork climate," with statistically significant improvements related to 3 of 4 items on this subscale, 3 of 11 items on the "safety climate" subscale, and only 1 of 13 items on the "error reporting" subscale. However, no significant improvements were reported for faculty physicians, and significant improvement was found on only one item (related to error reporting) for resident physicians.[22]

Two studies in the review researched team training programs within the VA. The first, conducted by Carney et al. (2011), studied the use of the Medical Team Training program applied in operating rooms of high- and medium-complexity VA facilities. They found that respondents had improved perceptions of all seven SAQ safety climate domain items measured following training.[23]

In the second study, Schwartz et al. (2018 examined the VA's Clinical Team Training program and measured changes in safety culture perceptions over time. At an 8-month follow-up, statistically significant improvement was found on 8 of 27 items (29.6%) on the TSCQ ($p<0.05$). Five of these items

related to teamwork and three items related to safety climate. A total of 11 of the 27 items (40.7%) showed statistically significant improvement at the 12-month follow-up (6 items related to teamwork, 4 items related to safety climate, and 1 item related to perceptions of management, $p<0.05$).[24]

One study included in the review evaluated AHRQ's Team Strategies and Tools to Enhance Performance and Patient Safety (TeamSTEPPS®) program. Using a static group for comparison, Jones et al. (2013) reported that the TeamSTEPPS® training was associated with more positive perceptions of three HSOPS dimensions: "organizational learning" (76% vs. 71% for static group), "teamwork between departments" (82% vs. 80% for static group), and "teamwork across hospital departments" (67% vs. 62% for static group). Moreover, they examined differences across adopter categories (early, early/late majority, and laggard) and concluded that early adopters had significantly more positive scores than early/late majority adopters, followed by "laggard" hospitals, on three of the HSOPS dimensions: "frequency of events reported" (71% vs. 65% vs. 56%), "staffing" (76% vs. 70% vs. 64%), and "hospital management support for patient safety" (89% vs. 83% vs. 75%).[25] The Sacks et al. (2015) review reported one study, in which TeamSTEPPS® training was associated with a significant increase on the "communication" dimension of the HSOPS.[13]

Lastly, two additional studies tested the effectiveness of their own team training effort. Using a unit-based, multidisciplinary team training program, Blegen et al. (2010) found statistically significant improvements in two hospitals on 10 out of 11 HSOPS survey dimensions (tests of mean scores, $p<0.05$). No significant change was observed on the "frequency of error reporting" dimension. Interestingly, in contrast to other studies of safety culture, nurses in this sample consistently provided *more* favorable responses on the post-training safety culture items than did the physicians and pharmacists.[26]

Finally, a study conducted by Berkowitz et al. (2012) evaluated biweekly patient safety conferences for frontline staff over the course of a year in a nursing home facility. In these conferences, cases involving a near-miss or adverse event were discussed within 2 weeks of their occurrence and the team identified solutions for avoiding similar situations in the future. Overall mean scores of patient safety culture significantly increased over time (mean=3.3 at baseline, mean=3.5 at 6 months, mean=3.9 at 1 year, $p<0.005$). An examination of dimension scores confirmed that positive improvements were made in all areas.[27]

17.2.3.2.2 Outcome Measures

Five team training studies included in Weaver et al.'s (2013) systematic review reported improvement in patient outcomes such as reduced errors resulting in harm and decreased safety events.[12] None of the individual studies reviewed on team training interventions used to improve safety culture measured outcomes. Future research should examine the degree to which such interventions enhance perceptions of safety culture while also improving patient outcomes, such as the frequency of mistakes caught and corrected, frequency of undetected errors, length of procedures, or rates of readmission.

17.2.3.3 Practice: Comprehensive Unit-Based Program

A final practice used in safety culture improvement efforts to address unit-related issues is CUSP. While there is flexibility in tailoring the CUSP method, the original work of Pronovost and colleagues[28] included eight steps: (1) A baseline assessment of safety culture, (2) educating staff on the "science of safety," (3) identifying safety concerns within the unit, (4) identifying a champion for the unit, (5) implementing improvements, (6) sharing stories, (7) documenting results, and (8) reassessing the unit's safety culture.

The systematic review conducted by Weaver et al. (2013) included eight studies that examined the impact of CUSP on safety culture. In addition, six individual studies were identified that used CUSP in their safety culture efforts, and all were conducted in a hospital setting.[12]

17.2.3.3.1 Process and Outcome Measures

Six of the eight CUSP studies reviewed by Weaver et al. (2013) reported significant improvements in safety culture perceptions. Two of the eight studies reported improved care processes (care during second stage of labor, timely resolution of safety concerns), and two reported improvements in patient outcomes (reduced length of stay, reduction in infection rates). All six individual studies in the review collected process measures to evaluate the effect of CUSP on safety culture. Five measured the impact on safety culture by administering the SAQ, and one study collected data via the HSOPS (Table 17.1). Additionally, data on care processes were collected in one study, and three studies collected outcome data in the form of infection rates. [12]

CUSP can be implemented within a unit/department, as well as on a larger scale. A study conducted by Hsu and Marsteller (2016) evaluated the changes in safety culture perceptions for intensive care units (ICUs) adopting CUSP against a non-CUSP comparison group. ICUs in the CUSP group significantly improved their SAQ scores on four dimensions ("teamwork climate" T1=45.2, T2=52.5; "safety climate" T1 41.7, T2=52.5; "job satisfaction" T1=52.8, T2=60.2; "working conditions" T1=29.7, T2=37.4; all $p<0.05$) from the baseline to the follow-up administration of the SAQ, whereas no significant difference was found in SAQ scores in the non-CUSP ICUs. While this study also collected data on central line-associated blood stream infection (CLASBI) rates, no significant between-group differences were found.[29]

However, another study in a critical care unit with a Magnet-designated community hospital found somewhat different results. Examination of pre- to post-implementation SAQ data indicated safety culture perceptions did not significantly change following the CUSP implementation. In fact, the only improvement was the "stress recognition" dimension (T1=61.50, T2=65.60). Scores on the other six dimensions decreased on the post-intervention assessment. The authors speculated that the 6-month period between the pre and post SAQ measurement was not sufficient to measure "real" or meaningful change.[19]

A study in an obstetrics unit found increased scores on several SAQ dimensions following the introduction of CUSP. The most pronounced improvements were related to "job satisfaction" (65% vs. 75%), "working conditions" (48% vs. 69%), and "perceptions of hospital management" (36% vs. 54%). No changes were observed for the "teamwork climate" or "safety climate" dimensions. This study did, however, demonstrate significant improvements on all six care processes ($p<0.05$).[30]

A slightly different approach was taken by Vigorito et al. (2011), in which the CUSP program encouraged units to develop an action plan based on their SAQ baseline measurement. Those that submitted a SAQ action plan bettered their scores on all SAQ dimensions except for "working conditions" by 4.5 percent to 25.9 percent. In comparison, the scores for units without a SAQ action increased by 3.4 percent and declined by as much as -6.6 percent across dimensions. Units with a SAQ action plan also decreased their CLASBI rates by 10.2% (compared with 2.2% for units without a SAQ action plan, $p=0.59$) and ventilator-associated pneumonia rates by 15.2%, as compared with 4.8% for units without a SAQ action plan ($p=0.39$).[31]

In a broader implementation, Paine et al. (2010) applied CUSP throughout the Johns Hopkins Hospital and measured changes in attitudes toward safety over a 2-year period. They reported significant improvement on all dimensions of the SAQ except for "stress recognition." Mean score increases on the safety culture dimensions ranged from 5.60 for "job satisfaction" (p=0.000) to 8.36 for the "safety climate" (p=0.000).[32]

Lastly, a recent study found positive results in a statewide implementation of CUSP throughout hospitals in Hawaii. First, pre- to post-intervention scores on 10 of the 12 HSOPS dimensions increased significantly, ranging from 4 percent on "handoff/transitions" ($p<0.05$) to 11 percent on "organizational learning and continuous improvement" ($p<0.001$). Moreover, they found that surgical site infection rates decreased from 12.08 percent to 4.63 percent ($p<0.01$).[33]

17.2.3.4 Multiple Practices

One study in the review implemented multiple practices to improve safety culture in two pediatric hospitals. After receiving baseline HSOPS results (Table 17.1), a series of interventions were chosen to address the low scores on "non-punitive response to error" and "handoffs and transitions." The interventions included: safety rounds, an enhanced self-reporting system, situation background assessment recommendation (SBAR), transfer or care check sheets, and a staged implementation of an electronic medical record system. Post-intervention scores significantly increased on 6 of the 12 HSOPS dimensions, including "non-punitive error," which had been a focus. However, perceptions of "teamwork across hospital units" decreased (3.28 to 3.23 percent) and perceptions of "handoffs and transitions" decreased significantly (3.29 to 3.09 percent, $p<0.001$) over the course of the study, which was discouraging. Further analyses revealed that perceptions of both these HSOPS dimensions decreased slightly at the academic hospital, while scores at the participating community hospital remained stable for "handoffs and transitions" and slightly improved on "teamwork across units." Follow-up discussion pointed to some unintended consequences of the new electronic medical record system, which seemed to impede handoffs.[34]

17.2.4 Conclusion and Comment

17.2.4.1 Implementation

A great deal of variation was found in the studies aimed at improving safety culture. Some studies targeted a smaller group and were applied at a department or unit level (e.g., operating room, NICU, ICU), while others sought to introduce a practice throughout the organization. Generally, the studies compared baseline and post-intervention measures of safety culture. Evaluation periods ranged from 6 months to 2 years across studies and practices, with the majority allowing a year for the intervention to take effect. Consistent with quality improvement efforts, leadership support and project champions were often cited as critical to achieving results. Reluctance to participate was frequently noted as a barrier and also contributed to the fluctuations in response rates observed across studies. Finally, implementing any of the practices reviewed here is an ongoing process. If efforts lose momentum or importance priorities shift, improvements in safety culture may begin regressing toward the mean.

17.2.4.2 Gaps and Future Directions

Although the most frequently used measures of safety culture (i.e., SAQ, HSOPS) incorporate a 5-point Likert-type scale, there is a disparity in how these data are reported across studies. For instance, some studies reported mean scores, while others reported the percentage of favorable responses

(i.e., percentage of respondents who "agree" or "strongly agree"). Some studies reported dimension scores, as well as item-level scores, while others included bar graphs with no specific data points labeled. There were also studies that failed to report the results of their statistical analyses and only indicated which scores were significant. These inconsistencies make it more difficult to judge results obtained from single studies, interpret trends across studies, and identify where further effort is needed.

The changes in safety culture dimension scores reported varied from study to study. For instance, Carney et al. (2011) reported significant increases on all SAQ dimensions following CRM training,[23] whereas Gore et al.'s (2010) study of CRM failed to produce significant changes in dimension scores.[22] Rather, statistical improvements were found only at the item level and only for nurses. These mixed results are consistent with those reported in the Sacks et al. (2015) review, in which 30 out of the 47 studies (63.8%) reported improvements on one dimension of safety culture, but no improvements on any other dimensions measured. Sacks et al. also noted that significant improvements occurred in some groups of providers, but not in others.[13] Future research is needed to identify why these disparities exist. Perhaps organizations need to tailor these broader, more widely implemented interventions such as CRM more to their own specific environment. Or perhaps they are measuring too much and should focus only on elements that the intervention "should" improve versus "might" improve. Furthermore, since post-intervention data were collected 6 months to 2 years following safety culture interventions, it is difficult to draw firm conclusions about whether it is the intervention that is resulting in changes in safety climate or whether other factors (e.g., personnel changes, other quality improvement efforts) are having an impact as well.

Small sample sizes, lack of study details, reliance on correlational data comparisons, and lack of outcome measures also affect the quality of studies in this area, with more robust studies clearly needed. While all of the studies included in the review collected process measures, additional outcome data are needed to determine the degree to which safety culture practices add any value above and beyond more specific clinical practices. The CUSP was the only practice for which clinical outcome measures were reported.

17.2.5 Resources

AHRQ's Surveys on Patient Safety Culture:
https://www.ahrq.gov/sops/index.html

AHRQ's Hospital Survey on Patient Safety (version 1.0 from 2004 and 2.0 from 2019):
https://www.ahrq.gov/sops/surveys/hospital/index.html

AHRQ's Medical Office Survey on Patient Safety:
https://www.ahrq.gov/sops/surveys/medical-office/index.html

AHRQ's Nursing Home Survey on Patient Safety:
https://www.ahrq.gov/sops/surveys/nursing-home/index.html

AHRQ's Community Pharmacy Survey on Patient Safety:
https://www.ahrq.gov/sops/surveys/pharmacy/index.html

AHRQ's Ambulatory Surgery Center Survey on Patient Safety:
https://www.ahrq.gov/sops/surveys/asc/index.html

CUSP Tools and Resources from Johns Hopkins Medicine Center for Innovation in Quality Patient Care: https://www.hopkinsmedicine.org/armstrong_institute/training_services/workshops/cusp_implementation_training/cusp_guidance.html

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17.3 Clinical Decision Support

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This review provides a summary of evidence published from 2008 to 2018 on clinical decision support (CDS) as a cross-cutting factor in efforts to improve patient safety. First, we provide a brief practice description. The review then explores evidence for employing CDS to improve patient safety. Key findings are highlighted in the text box at right.

Key Findings:

- CDS is widely believed to have the potential to positively impact patient safety; this belief has face validity.
- The most consistent impact of CDS in the literature reviewed was on improving medication safety.
- While some results are promising, more evidence is needed to clearly establish the significant role CDS could play in increasing patient safety.

17.3.1 Practice Description

HealthIT.gov, the website for the Office of the National Coordinator for Health Information Technology (ONC), describes CDS as follows:

> CDS provides clinicians, staff, patients or other individuals with knowledge and person-specific information, intelligently filtered or presented at appropriate times, to enhance health and healthcare. CDS encompasses a variety of tools to enhance decision-making in the clinical workflow. These tools include computerized alerts and reminders to care providers and patients; clinical guidelines; condition-specific order sets; focused patient data reports and summaries; documentation templates; diagnostic support, and contextually relevant reference information.[1]

ONC also asserts that CDS "promotes patient safety," contributing to "increased quality of care and enhanced health outcomes" and "avoidance of errors and adverse events."[1]

To achieve these patient-safety goals across clinical conditions and healthcare settings, it is essential that CDS be well designed and successfully implemented. Osheroff et al.'s "Five Rights" are near-universally cited as a necessary framework for any CDS tools to succeed: getting the *right information* to the *right people* in the *right intervention formats* through the *right channels* at the *right times* in workflows.[2]

In its 2016 Final Report, *Identification and Prioritization of Health IT Patient Safety Measures*, the National Quality Forum (NQF) points to the potentially significant and positive patient-safety impacts of CDS:

> CDS can help guide clinicians in diagnosis and decision making by providing access to information at the point of care, including evidence-based best practices, guidance for treatment or preventive care (e.g., immunizations and routine screening visits), and information on potential allergies and medication interactions.[3]

Experts consulting with NQF prioritized key health information technology (HIT) patient safety measurement areas, and CDS was selected as the highest priority, as "one of the most promising functionalities of HIT."[3]

17.3.1.1 Methods

The question of interest for this review is, "What evidence exists regarding the employment of CDS to improve patient safety?"

To answer this question we searched the CINAHL® and MEDLINE® databases from 2008 to 2018 for "clinical decision support," "decision support systems, clinical," "decision making, computer-assisted," and related MeSH terms and synonyms, combined with "patient safety," "quality assurance, health care," and related terms. After duplicates were removed, the initial search yielded 763 results, all of which were screened for inclusion, and 107 full-text articles were retrieved. Of the total retrieved articles, 26 were selected for inclusion in this review. We also report on CDS-related effects on patient outcomes cited in a 2016 systematic review, "Effects of Health Information Technology on Patient Outcomes: A Systematic Review."[4]

Articles from the searches were excluded if the outcomes were not relevant or precisely reported and/or if the study design was insufficient.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

17.3.2 Review of the Evidence

The Committee on Patient Safety and Health Information Technology of the Institute of Medicine (now the National Academy of Medicine) published a 2011 report on health information technology and patient safety.[5] The report authors concluded that, while many studies suggested that CDS has a positive impact on patient safety, the evidence base at that time was not strong and study results were inconsistent. This Institute of Medicine (IOM) Committee recommended further research. In general, the evidence cited in the report was strongest for the relationship between CDS and medication safety. In the present review, we examine CDS and patient safety as broadly as possible. Consistent with the IOM report, however, a majority of the relevant primary research we review concerns CDS related to medication safety.

Brenner et al. (2016) systematically reviewed 40 studies about CDS: 15 studies had positive results in terms of CDS's impact on patient outcomes (e.g., reductions in adverse drug events or readmission rates), and 25 had non-significant or mixed results. None of the CDS studies reviewed showed negative results of CDS on patient safety. Findings from this systematic review are included in the sections below by subcategory.[4]

The sections that follow describe the literature in several categories of CDS impact: drug ordering and adverse drug events, prevention of deep vein thrombosis, antibiotic prescribing/stewardship, blood glucose control, reducing uninformative CDS alerts (reducing alert fatigue), and other potential patient-safety effects of CDS.

17.3.2.1 Medication Prescribing and Adverse Drug Events

In their 2016 review, Brenner et al. assessed several studies about CDS and adverse drug events (ADEs), many of which found no impact of CDS.[4] For example, a 2008 randomized controlled trial (RCT) conducted in two long-term care facilities found that computerized provider order entry (CPOE) with

CDS did not reduce ADEs or preventable ADEs.[6] A 2009 prospective cohort study in two Dutch hospitals similarly found that CPOE with CDS did not have a significant effect on rates of preventable ADEs.[7] The Brenner et al. review also mentions that Fleming et al. (2009) studied the use of order sets (i.e., prescribing guidelines) in a large multi-hospital U.S. health system for patients admitted with community-acquired pneumonia and found no impact on in-hospital mortality or 30-day mortality when order sets were used.[8] In contrast, a large ambulatory care–based prospective observational U.S. study (including adult primary care, pediatrics, psychiatry, and other specialties) found that CDS with alerts reduced preventable ADEs, hospitalizations, emergency department visits, and office visits.[9]

In a retrospective study with no baseline or comparison group, Abramson et al. (2013) studied e-prescriptions written by 20 community-based primary care providers in the United States after they all adopted a commercial electronic health record (EHR) with CDS to aid in prescribing. Errors were identified by chart review. Overall rates of prescribing errors were low at 3 months post-implementation (6.0 errors per 100 prescriptions), and this was sustained after 1 year (4.5 errors per 100 prescriptions). There is no indication of what the error rate would have been in the absence of the new EHR and CDS.[10]

Ahuja et al. (2018) studied the use of CDS tools to enhance patient safety related to direct oral anticoagulant (DOAC) ordering. These researchers retrospectively reviewed the records of 121 patients who received at least two doses of a DOAC and determined whether DOAC dosing was consistent with the CDS provided upon order entry. Adherence to the CDS-recommended dosing ranged from 75 to 87 percent for different DOACs. Most non-adherence was related to under-dosing of DOACs. The absence of any baseline or comparison group, however, makes it difficult to conclude whether DOAC dosing was better than it would have been without CDS.[11]

A cluster RCT was conducted in a U.S. academic medical center to assess the effects of an EHR CDS tool designed to improve appropriate prescribing of medications for patients with renal insufficiency.[12] The authors examined scenarios in which drug discontinuation or dosage adjustment was recommended by the CDS for adult patients with impaired renal function in the ambulatory and acute settings, both at the time of the initial prescription ("prospective" alerts) and by monitoring changes in renal function for patients already receiving one of the study medications ("look-back" alerts). These researchers found that appropriate discontinuation or dosage adjustments occurred in 17 percent of intervention patients (with CDS) versus 5.7 percent of the control group (with no CDS). Findings of this RCT suggest that clinicians responded more frequently to drug dose adjustment alerts than to alerts about contraindicated drugs. Further, prospective alerts appeared to have more impact on appropriate medication adjustments than look-back alerts did.[12]

A Canadian RCT (Field et al., 2009) examined CDS that provided specific dose recommendations for patients with renal insufficiency living in a long-term care facility. Medication alerts were displayed to prescribers in intervention units and hidden but tracked in control units. Overall, final drug orders were appropriate significantly more often in the intervention group, and CDS was also associated with reduced risk of prescribing drugs that should be avoided in the elderly.[13]

Chaparro and colleagues (2017) evaluated medication ordering in 21 U.S. pediatric hospitals to identify drug-drug interactions, dosing errors, and other ordering errors. They found that the CPOE systems with embedded CDS were able to identify and intercept (prevent) 62 percent of potential medication errors in test scenarios, but this ranged widely, from 23 to 91 percent, in the institutions tested. The highest

scoring categories included drug-allergy interactions, dosing limits (both daily and cumulative), and inappropriate routes of administration.[14]

Prewitt et al. (2013) evaluated patient-controlled analgesia (PCA) safety events in intermediate and step-down units before and after implementing CPOE/CDS with PCA smart pump technology for adults with acute pain. The researchers reviewed both voluntary reports of ADEs and ADEs identified via hospital surveillance systems. After implementation of the CPOE/CDS with smart pump technology, there were fewer PCA events per 1,000 PCA days, whether measured by surveillance (22% reduction) or voluntary reporting (72% reduction).[15]

At four U.S. Department of Veterans Affairs (VA) emergency departments, Stevens and colleagues (2017) conducted a pre-post study to assess the effectiveness of a multicomponent quality improvement initiative that combined provider education, CDS, and individual provider feedback to reduce the use of potentially inappropriate medications and improve medication safety for older adults. All four sites showed a significant and sustained reduction in use of inappropriate medications, and this was sustained over the course of the year-long study.[16]

Finally, Gill et al. (2011) conducted a large RCT in 27 primary care offices in 14 U.S. States. The intervention group received an EHR-based CDS coupled with clinician education about guidelines for reducing gastrointestinal risk for patients taking non-steroidal anti-inflammatory drugs. Results were mixed. Intervention patients (for whom CDS was employed during ordering) were more likely than usual-care patients to receive guideline-concordant care (25.4% vs. 22.4%, adjusted odds ratio = 1.19). Patients taking low-dose aspirin were more likely to receive guideline-concordant care with the intervention than with usual care (25.0% vs. 20.8%, adjusted odds ratio = 1.30). There was no significant difference, however, for patients in other high-risk groups.[17]

17.3.2.2 Preventing Venous Thromboembolism/Deep Vein Thrombosis

A subset of studies on medication ordering addressed the specific issue of preventing deep vein thrombosis (DVT) through CDS-enhanced medication ordering.

As described in Brenner et al.'s 2016 systematic review, Fiumara et al. (2010) found that a CDS effort to encourage DVT prophylaxis in a U.S. hospital had no significant impact on rates of venous thromboembolism (VTE).[18] Similarly, in a 2010 prospective observational study conducted in the surgical wards of a U.S. hospital after implementation of a VTE-prophylaxis CDS, rates of VTE at 30, 60, and 90 days declined, but not significantly, although DVT prophylaxis ordering increased.[19]

A few other studies in the 2016 systematic review found mixed or inconsistent impacts of CDS on VTE. Researchers in Spain found that alerts to physicians had no impact on hospital VTE rates; however, a sub-analysis of surgical patients found a significant reduction in VTE events.[20] Maynard et al. (2010) found that the rate of hospital-acquired VTE was reduced after implementation of CPOE with CDS.[21] Further, Parente and McCullough (2009) found that rates of hospital-associated infections significantly decreased, but neither post-operative VTE nor post-operative hemorrhage rates were reduced with a CDS intervention.[22]

A large retrospective study at three U.S. academic medical centers tested the impact of a message-based CPOE with CDS to improve VTE prophylaxis. The CPOE-CDS intervention significantly increased the use of "recommended" and "any" prophylaxis at all three hospitals.[23]

17.3.2.3 Antibiotic Prescribing/Stewardship

Three articles included in the systematic review by Brenner et al. (2016) examined the impact of CDS on antibiotic prescribing and antibiotic stewardship.[4] In a prospective study conducted in an Australian hospital, Buising et al. (2008) examined the impact of CDS on appropriate antibiotic prescribing for gram-negative bacteremia. They found no impact of CDS on in-hospital mortality or length of stay.[24] Linares et al. (2011) conducted a prospective study in a U.S. hospital focused on computerized-alert CDS and found decreased complications associated with asymptomatic bacteriuria and culture-negative pyuria.[25] In a retrospective observational U.S. hospital study based on chart review, implementation of an EHR with CDS had no effect on rates of nosocomial *C. difficile* infection, but rates of nosocomial Methicillin-resistant *Staphylococcus aureus* (MRSA) infections decreased significantly.[26]

In a more recent article on this topic, not covered in the 2016 systematic review, Burgess et al. (2016) compared initial antibiotic regimens prescribed for patients with lower extremity cellulitis with the regimens prescribed for similar patients after implementation of a CDS prescribing tool. When the optional CDS prescribing tool was used, these researchers found improved adherence to antibiotic prescribing guidelines.[27]

17.3.2.4 Blood Glucose Control

CDS to improve blood glucose control was addressed in two studies we reviewed.

Bode et al. (2017) conducted a small pre-post study to improve blood glucose control for patients for whom insulin therapy was not effective. These researchers assessed an intervention with Bluetooth-capable blood glucose meters and insulin dose titration guided by CDS. After an initial 3-day titration, the CDS recommended new insulin doses, as well as a new dose titration at intervals of 3, 7, 14, or 28 days based on a patient's glucose control. The authors found that the intervention helped high-risk patients achieve and maintain glucose targets over a 1-year follow-up period.[28]

In the intensive care units of two U.S. hospitals, Flanders and colleagues (2009) prospectively tested a CDS tool for intravenous insulin dosing, with automated calculation of intravenous insulin drip rates. After 3 years, ICU patients were more than twice as likely to have safe blood glucose levels of less than 150 mg/dL (odds ratio = 2.28; 95% confidence interval = 2.25-2.30; $P < .001$) compared with the baseline period.[29]

17.3.2.5 Inconsequential Alerts

Genco et al. (2016) conducted a large retrospective chart review in a U.S. academic medical center focused on clinically inconsequential alerts related to opioid prescriptions. They found that CDS prevented some ADEs, but at the expense of generating a large volume of inconsequential alerts. To prevent one ADE, providers dealt with more than 123 unnecessary alerts. When providers ignored or over-rode the unnecessary CDS opioid alerts, there was no impact on ADEs. The authors concluded that refining CDS alert systems to eliminate inconsequential alerts is essential for preventing alert fatigue and maintaining patient safety.[30]

A Dutch pre-post study in an academic medical center sought to determine whether adding CDS to CPOE could improve compliance with Dutch guidelines for prophylaxis for patients at increased risk of gastrointestinal bleeding in both inpatient and outpatient settings. Before CDS implementation, gastrointestinal prophylaxis was co-prescribed in 84.0 percent of prescriptions. After implementation,

this percentage increased to 94.5 percent ($p < 0.001$). The CDS also improved the appropriateness of drug safety alerts. The total number of drug safety alerts decreased by 78.2 percent. The authors concluded that CDS for gastrointestinal prophylaxis improved adherence to Dutch guidelines, most likely due to a reduction in the number of irrelevant drug safety alerts.[31]

Harinstein et al. (2012) studied whether CDS could detect drug-induced thrombocytopenia in critically ill ICU patients. The CDS used information from both laboratory values and drug ordering systems, alerts were generated when the patient had a low platelet count and was ordered a potentially causal drug, and patients were evaluated in real time for ADEs. The CDS was not used to prevent these events, but in this study it was tested to determine its accuracy in detecting the ADEs. Sixty-four patients met the inclusion criteria, for whom 350 alerts were generated by the CDS. There were 137 ADEs identified in the 350 alerts, with heparin, vancomycin, and famotidine as the three most common potential causes. The authors concluded that, compared with previous studies, the drug–laboratory combination alert performed better than alerts based exclusively on laboratory values and should be considered to reduce alert fatigue.[32]

17.3.2.6 Other Patient-Safety Impacts

A variety of studies addressed other uses of CDS, beyond those described above.

Brenner et al. addressed other potential benefits of CDS in their 2016 systematic review and generally found little or no improvement in patient safety. For example, in an RCT in four U.S. hospitals, use of a CDS fall-prevention tool was associated with decreased falls, with the greatest reduction among patients over age 65, but no impact of CDS was observed in falls resulting in patient harm.[33]

Boustani and colleagues (2012) conducted an RCT in a U.S. academic medical center to evaluate the efficacy of a screening program with CDS aimed at improving several aspects of hospital care for older adults with cognitive impairment. They found that CDS did not change physician prescribing behavior and did not increase physicians' orders for Acute Care for Elders (ACE)—a continuous quality improvement program of care—consultation, discontinuation of Foley catheters, or discontinuation of physical restraints. CDS also had no significant impact on patient outcomes such as mortality.[34]

A Canadian prospective cohort study in two academic medical centers cited in the 2016 systematic review reported that a real-time laboratory alerting system with concurrent CDS had no significant impact on rates of adverse events.[35]

The systematic review also identified several studies with mixed results. For example, investigators in a U.S. hospital found that CPOE with CDS was associated with a reduction in in-hospital bleeding among patients with chronic kidney disease admitted with acute coronary syndromes, but there were no effects on length of stay or 90-day mortality.[36] In a prospective observational study in a U.S. hospital, CDS with CPOE decreased the length of stay for patients with diabetes but had no effect on patient-days of hypoglycemia.[37]

In a small cluster RCT conducted in the United States, Abdel-Kader et al. (2011) studied whether an educational intervention coupled with CDS versus an educational intervention alone could enhance care for patients with chronic kidney disease. Approximately 10 percent of patients in the intervention group were referred to a nephrologist versus 17 percent in the control group (P=0.1). Just over 39 percent of patients in the intervention group had a proteinuria assessment versus 30 percent in the control group

(P=0.1). Chronic kidney disease was documented in the EHR in 37 percent of patients in the intervention group versus 21 percent in the control group (P=0.008). Despite the improvement in these process measures, there were no significant differences in angiotensin-converting enzyme (ACE) inhibitor/angiotensin-receptor blocker (ARB) use, optimal blood pressure management, or limiting use of non-steroidal anti-inflammatory drugs to protect renal function.[38]

In an RCT, Schnipper et al. (2010) assigned primary care physicians (PCPs) in 10 ambulatory practices to usual care or to CDS for their patients with coronary artery disease and diabetes, and measured the proportion of deficiencies in care that were addressed within 30 days after a patient visit. The CDS they tested required substantial additional documentation on the part of physicians ("smart forms") to trigger elements of the CDS. Patients of PCPs assigned to the intervention arm were more likely to have care deficiencies addressed in their next visit, and the measures that improved included documentation of smoking status and prescription of antiplatelet agents when appropriate. However, rates of voluntary completion of the documentation underlying the CDS were very low.[39]

Milani et al. (2011) studied patients admitted to a major U.S. academic medical center cardiac service. On admission (73% through the emergency department), the admitting physician had the choice of using pre-printed paper orders with check boxes that followed national guidelines for standard orders or CPOE-CDS software that generated printed/paper orders. The CDS also included drug dosing based on clinical risk, weight, calculated creatinine clearance, and guidelines. Numerous performance measures were combined to assess attainment of "perfect" care. The authors concluded that use of CPOE with CDS markedly increased the likelihood of achieving perfect care.[36]

Felcher and colleagues (2017) studied whether CDS implemented in the EHR of a large U.S. integrated group-model health system could decrease unnecessary vitamin D testing. The CDS included a new vitamin D screening guideline, an alert that required clinician acknowledgment of current guidelines to continue ordering the test (a "hard stop"), and removing the test from standard order sets so that a physician would need to separately/explicitly order the vitamin D test. This three-part CDS led to significantly reduced rates of vitamin D testing, a significant increase in the proportion of vitamin D screening that was appropriate, and substantial cost savings for the health system.[40]

Fitzgerald et al. (2011) conducted an RCT at a U.S. Level 1 trauma center to test whether CDS implemented during the first 30 minutes of trauma resuscitation could reduce errors. They found that CDS increased protocol compliance and error-free resuscitations, and reduced morbidity from avoided shock management, blood use, and aspiration pneumonia.[41]

Kharbanda et al. (2016) examined the effects of EHR-linked CDS in reducing costly imaging for pediatric patients admitted to two U.S. academic medical centers with suspected appendicitis. The electronic CDS included three components: a standardized abdominal pain order set, a risk stratification tool, and a "time of ordering alert." The order set specified options for pain medications and laboratory tests. For high-risk patients, surgical consultation was recommended before diagnostic imaging; imaging was ordered at the discretion of the surgeon (not the admitting emergency department physician). Low-risk patients were recommended for discharge without imaging but with outpatient or emergency department follow-up in 12 to 24 hours. A focused abdominal ultrasound was recommended for medium-risk patients, and computed tomography (CT) imaging was to be considered only if the ultrasound was equivocal or at the request of the surgeon. The authors found a significant decrease in

CT imaging with equivalent patient outcomes (and no difference in rates of negative appendectomies or missed appendicitis).[42]

In New Zealand, Lavin and Ranta (2014) assessed a transient ischemic attack (TIA)/stroke CDS tool in primary care settings to aid general practitioners in the timely management of TIAs. They retrospectively reviewed all patients managed with the help of the CDS tool and any subsequent morbidity and mortality. They found no evidence of serious preventable harm due to misdiagnosis, inappropriate triage, or over/undermedication prompted by the CDS.[43] Using the same tool, Ranta and colleagues (2014) conducted a prospective observational study focused on diagnostic accuracy by PCPs, limiting emergency department referrals, and improving secondary prevention of TIAs/strokes. The authors concluded that the availability of TIA/stroke CDS support in the primary care setting was associated with reductions in TIA treatment delays without compromising patient safety.[44]

Mishuris et al. (2014) retrospectively analyzed data from the National Ambulatory and National Hospital Ambulatory Medical Care Surveys for adult primary visits to understand the association between the use of CDS (problem lists, preventive care reminders, lab results, lab range notifications, and drug-drug interaction warnings) and quality measures (blood pressure control, cancer screening, health education, influenza vaccination, and visits related to ADEs). The survey databases contained an estimated 900 million adult outpatient primary care visits to clinics with EHRs from 2006 to 2009. The presence of CDS was associated with improved blood pressure control (86% vs. 82%; odds ratio 1.3) and more visits not related to ADEs (99.9% vs. 99.8%; odds ratio 3.0); these associations were also present when comparing practices with CDS against practices that had disabled their CDS. The authors concluded that the use of CDS was associated with improvement in several primary care quality indicators.[45]

Olsho and colleagues (2014) conducted a small interrupted time series study assessing impact of the On-Time Quality Improvement for Long-term Care tool in U.S. nursing homes selected because they used team-based care and had leadership support for quality improvement. On-Time is a CDS intervention for pressure ulcers that uses risk reports embedded in nursing home health information technology systems to identify recent changes in patient risk status and integrate these reports into routine care. The authors found large and statistically significant reductions in pressure ulcer incidence associated with implementation of On-Time, amounting to approximately 2.6 pressure ulcers avoided per 100 nursing home residents per month, with substantial associated cost savings.[46]

17.3.3 Gaps and Future Directions

Our results, almost a decade later, are quite similar to those cited in the IOM's 2011 report on HIT and patient safety: the evidence is not very strong, and results are inconsistent.

CDS was defined differently in almost every study we reviewed and applied to many different care processes and settings, from laboratory testing to medication prescribing, and from emergency department admission protocols to nursing home fall prevention. The range of problems and settings studied and the diversity of CDS interventions make it impossible to draw broad conclusions about the impact of CDS on patient safety, other than to observe that it has been most thoroughly evaluated as a tool to improve medication safety.

Additionally, it is very challenging to link patient safety outcomes or improvements directly to the use of CDS. To support the often-cited assertion and widely held belief that "clinical decision support promotes patient safety," more high-quality data regarding "increased quality of care and enhanced health

outcomes" and "avoidance of errors and adverse events" achieved through the use of CDS are needed.[1] Furthermore, it remains a challenge to tie process outcomes (CDS use and adherence) to patient outcomes. There may be useful outcomes measures—outside of mortality and length of stay—that would be more proximal in timing and more specific to CDS guidance.

The Five Rights of CDS—delivering the right information to the right people using the right formats via the right channels at the right times in the workflow—discussed previously highlight the need for CDS interventions to meet specific criteria as a critical element to improve case processes and outcomes. Despite an emphasis on EHR usability, little progress has been made to protect end-users from inadequately designed workflows and unnecessary interruptions. The potential solution that CDS represents may be limited by problems associated with improper design, implementation, and local customization. This contributes, in part, to low acceptance rates for some forms of CDS, with alerts being overridden or ignored by clinicians because of time constraints, perceived misleading alerts, or believing that patients did not meet certain criteria for use of CDS (such as age or condition). By identifying factors that predict clinically insignificant alerts and inappropriate responses, informatics personnel can improve alert logic to account for factors such as workflow and patient complexity, increasing the specificity of alerts.

In a three-meeting series convened by the National Academy of Medicine (2017), U.S. experts met to discuss realizing the untapped potential of CDS. A common theme that emerged from these efforts was: "Current CDS lacks measurement practices and standards. Evaluation of current and future CDS should assess whether it measurably improves quality, health outcomes, safety, cost, and physician productivity."[47]

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17.4 Cultural Competency

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This review includes a summary of evidence published from 2008 onward on cultural competency as a patient safety practice. We start by defining cultural competency and discussing standards, measures, and related practices. We then provide background on the links between safety and cultural competency, and major policy impacts. We review the evidence for the estimated impact of cultural competency interventions on patient safety, touch briefly on cultural competency implementation considerations, and finally discuss research gaps and future directions for cultural competency as a safety practice.

Key Findings:

- Existing evidence supports the use of language services to improve patient safety.
- With the exception of studies on language services and community health workers, there is limited research on cultural competency initiatives to improve patient safety.
- Prompt access to language assistance has shown promise in the areas of preventable hospital readmissions, medication adherence, length of stay, advance care planning, and informed consent.

It should be noted that our focus is not on cultural competency and healthcare *quality* (e.g., patient satisfaction, health, and access), but rather on healthcare safety as the prevention of patient harm (or potential harm) as a result of error or negligence in medical care.[1] In the review of studies, we focus on research that examines patient safety and safety-related process and outcome measures. Outcomes in the reviewed studies include patients' use of emergency services, medication adherence, comprehension of medication instructions, advance care planning, and informed consent. In cases in which there are gaps in the literature with regard to safety, we look more broadly at the literature on cultural competency. Specifically, given that we found no systematic reviews *exclusively* devoted to cultural competence and patient safety, we instead provide an overview of several reviews that examine cultural competency to improve a range of healthcare outcomes—highlighting safety-related findings (e.g., provider communication) when possible. We take a similar approach for the section on implementation. Key findings are located in the box above.

17.4.1 Practice Definition and Standards

While there is not a single definition of cultural competency,[2] a frequently cited definition, referenced by the Agency for Healthcare Research and Quality (AHRQ),[3] U.S. Department of Health and Human Services (2016),[4] and others, comes from an early article by Cross et al. (1989),[5] who described the practice as, "A set of congruent behaviors, attitudes, and policies that come together in a system or agency or among professionals that enables effective interaction in a cross-cultural framework."

To operationalize cultural competency at the organizational and provider level, there are a number of guidelines and recommended practices, some of the most recent of which are provided as resources later in this section. Cultural competency includes linguistic competency and, in part, centers on effective communication and language services. At the healthcare professional level, cultural competency can be defined as the ability to communicate with, and effectively provide high-quality care to, patients from diverse sociocultural backgrounds.[6,7] Historically, cultural competency consisted of teaching providers about different cultural groups.[8] More recent pedagogy takes into account the dynamic nature of culture, in addition to intragroup variability, and social determinants of health such as

socioeconomic status. Rather than categorizing and learning about different cultural groups, a more effective strategy is to teach providers skills that can be applied in any cross-cultural situation.[8] Additionally, in recent years, there is greater focus on provider and organizational self-reflection, current and historical racism (and other forms of oppression), as well as structures of power and privilege, and how biases impact care [9-11]

A number of tools have been developed to measure aspects of clinician cultural competency.[12,13] AHRQ's Consumer Assessment of Healthcare Providers and Systems (CAHPS®) is made up of a number of validated survey instruments measuring patient experience of care in different healthcare settings, with providers, and with health plans. It includes optional supplemental items on interpreter services. These optional items can be used in conjunction with both the adult and pediatric versions of the CAHPS Clinician & Group Survey and the CAHPS Health Plan Survey, as well as the CAHPS Hospital Survey (adult only). Patients are asked about their experiences with using interpreters in these settings and in communications with their health plan.[14] Additional measures in the literature that are safety specific include patient comprehension and adherence.[11] There are also a number of self-assessments available online for providers in different settings and different fields;[15] these assessments can be used to help measure a provider's understanding, acceptance of, and respect for other cultures, as well as the provider's communication skills and styles.

Lie et al. (2011), in their review, note that provider training alone may not be adequate to create change without system changes to reduce errors, improve efficiency, and include language services.[16] While early understanding of cultural competency was limited to the provider/interpersonal level, the scope of cultural competency now includes the organizational and systems domains. [17] For example, the U.S. Department of Health and Human Services established a framework for cultural and linguistic competency: The National Standards for Culturally and Linguistically Appropriate Services (CLAS) standards. According to the CLAS standards, organizations that are culturally competent provide "effective, equitable, understandable, and respectful quality care and services that are responsive to diverse cultural health beliefs and practices, preferred languages, health literacy, and other communication needs."[18]

This principal standard is followed by additional standards in three areas: Governance Leadership and Workforce; Communication and Language Assistance; and Engagement, Continuous Improvement, and Accountability. The full list of standards can be found on the Office of Minority Health website.[18] To paraphrase, the Governance Leadership and Workforce standards include: promoting CLAS and health equity through policy, practices, and allocated resources to recruit, promote, and support a diverse leadership and workforce, and to regularly educate and train leadership on culturally and linguistically appropriate policies. The standards for Communication and Language Assistance consist of offering limited English proficient (LEP) patients professional or qualified language assistance and providing easy-to-understand print and multimedia materials and signage in the languages commonly used by the populations in the service area. For Engagement, Continuous Improvement, and Accountability, the standards are to: establish culturally and linguistically appropriate goals; conduct ongoing assessment and improvement of CLAS activities; collect accurate demographic data; conduct community needs assessments to inform services and service delivery; partner with the community to design and evaluate practices; **c**reate conflict- and grievance-resolution processes that are culturally and linguistically appropriate; and communicate the organization's progress in implementing and sustaining CLAS to all stakeholders.

It is important to note that the studies we review in this section (as well as some of the measures of cultural competency discussed above) include similar and analogous practices, including patient-centeredness and efforts to address health literacy. For example, an intervention to provide language-concordant medication labels for LEP patients is described as "patient centered."[19] The links between patient-centeredness and cultural competency are evident—both focus on building rapport, seeing the patient as a unique person, exploring patient beliefs, and finding common ground regarding treatment plans.[9] In providing patient-centered care, "an individual's specific health needs and desired health outcomes are the driving force behind all healthcare decisions and quality measurements."[20] "Health literacy" is an important concept, as it indicates the degree to which a patient has the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions.[21] The American healthcare system can be confusing, and contains many cultural assumptions.[22] Disparities in patient health literacy are recognized as contributing to racial/ethnic health disparities[23] and patient safety disparities.[24] Two of the interventions evaluated in the studies included in this section involve efforts to improve patient "health literacy" as part of cultural competency interventions.

17.4.2 Cultural Competency as a Patient Safety Practice

Cultural competency is often framed as a best practice and as an achievable response to health and healthcare disparities in minority populations; it is also deemed an important practice in the context of increasing diversity in the U.S. population.[18,25-27] The literature on cultural competency as a patient safety practice is limited; however, evidence suggests a link between provider and organizational cultural competency and patient safety. As with many healthcare quality outcomes, studies have found disparities in adverse safety events between cultural and racial/ethnic groups in the United States. Safety outcomes in which certain groups experience disproportionately high adverse events include: healthcare-associated infections, diagnostic errors, adverse birth outcomes, medication errors (e.g., polypharmacy and adverse medication events), inappropriate care transitions; and failure to obtain patient directives.[28-35] One study found that 49.1 percent of adverse events for LEP patients resulted in physical harm, whereas 29.5 percent of adverse events for patients who speak English resulted in harm.[36] Patient–provider communication challenges and cross-cultural issues are at the root of many adverse events.[11,37,38] Conversely, patients of physicians reporting greater cultural competency were more satisfied, and reported seeking and sharing more information during the medical visit.[39,40] In one study, provider cultural competency was linked to higher prescribing of antiretroviral medications, patient medication adherence, and viral suppression in non-white HIV patients.[41] Tools specifically developed to mitigate potential adverse events, such as patient suicide, may be more effective when tailored to a patient's culture,[42] and language services and language concordance between providers and patients have been associated with improved patient outcomes.[2,43]

External drivers related to cultural competency date back to the Civil Rights Act of 1964, which outlawed discrimination in federally assisted programs. Other significant legislation includes the Americans with Disabilities Act in 1990, which prohibits discrimination based on disability, and Executive Order 13166 in 2000, which requires Federal agencies to examine the services they provide and identify any need for services to those with LEP. Additional drivers for cultural competency to specifically improve patient safety are financial, including the threat of malpractice suits as well as penalties for adverse safety events.[44,45] Mandates and standards for culturally competent care include requirements for training and CLAS-related services at the State level in many States; incorporation of cultural competency into

medical curriculums; and cultural competency guidelines from several national accreditation agencies (e.g., the Joint Commission).[t] [6,18] Most recently, the Affordable Care Act of 2010 was implemented in part to reduce healthcare disparities. It includes provisions for workforce diversity and funding for demonstration projects for cultural competency training in healthcare.[6,46] Between 2013 and 2017, health insurance coverage for minority groups increased due to the Affordable Care Act. For example, the proportion of Hispanics who were uninsured dropped from 30 percent to 19 percent.[47] It has been noted that, as the diversity in the insured population increases utilization, there is a need for continued efforts for culturally competent care.[47]

17.4.3 Methods

The question of interest for this review is, "Is culturally competent care effective in improving patient safety?"

To answer this question, we searched the databases CINAHL® and MEDLINE® from 2008 to 2019 for "patient safety" and related medical subject headings, terms, and synonyms; "cultural competency;" and related terms, including, "transcultural nursing," "cultural diversity," "cultural intelligence," "cultural proficiency," "cultural competencies," "cultural sensitivity," "cultural humility," "limited English proficiency," "multicultural health," "linguistically appropriate approach," and "cultural safety." After duplicates were removed, the initial search yielded 552 results, all of which were screened for inclusion, and 80 full-text articles were retrieved. We included papers that discussed cultural competency and patient safety outcomes (or safety-related process measures) and excluded studies whose outcomes were exclusively provider attitudes or knowledge. Studies were excluded from the evidence summary if outcomes were not precisely reported, if outcomes were qualitative, or if the methods were not clearly described. Nonsystematic reviews were not included in the evidence summary but are used to provide background and context. To ensure thoroughness, reference lists of included articles were also screened, as well as articles and reference lists from articles found while researching background information for the introductory sections. An additional 25 papers were reviewed. A cursory search using Google Scholar was conducted, yielding three additional systematic reviews. Experts were also consulted and an additional seven, previously undiscovered studies were provided. Of the total retrieved articles, four reviews and eight studies were selected for inclusion in this review.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

17.4.4 Review of the Evidence

In this evidence summary, we examine four systematic reviews on cultural competency studies in healthcare and highlight findings related to patient safety. We then review eight studies on cultural competency and patient safety. Reviews and studies examined a variety of healthcare settings and contexts, including hospitals and outpatient settings. When describing the target population in the studies and reviews, we use the same terminology as the authors of the articles.

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[t]The Joint Commission: Advancing Effective Communication, Cultural Competence, and Patient- and Family-Centered Care: A Roadmap for Hospitals— https://www.jointcommission.org/assets/1/6/ARoadmapforHospitalsfinalversion727.pdf.

17.4.4.1 Reviews

A vast number of reviews examine cultural competency and patient/provider outcomes, although we found none that addressed safety specifically. Due to this gap, we choose here to include a brief overview of systematic reviews of studies on cultural competency interventions at the systems, organizational, and provider levels, addressing a variety of outcomes. Two of the reviews[2,48] take a broad approach, looking at interventions at the provider, facility, and policy levels, and two articles focus specifically on provider training.[16,49]

In a systematic review of reviews on interventions to improve provider, organizational, or system cultural competency, Truong et al. (2014) examined 19 reviews published between January 2000 and June 2012.[2] The reviews focused on provider education, as well as on policy and practice modifications. The majority of them found moderate evidence of improvement in provider outcomes (e.g., cultural competency knowledge, skills, and attitudes). Healthcare access and utilization outcomes improved following cultural competency interventions. The evidence was not as strong for improvements in patient outcomes: satisfaction and trust, decision making and communication, and physiological outcomes (e.g., measures of diabetes management). Interventions that showed promise included the use of patient navigators and community health workers (CHWs), appropriate and competent linguistic services, culturally adapted patient education, and intercultural staff trainings. Forsetlund et al. (2011), in their review of studies to improve healthcare services for racial/ethnic minority groups, found 19 studies going back to the 1990s.[48] Interventions included education for health personnel and/or patients, treatment and screening reminders for providers, remote professional interpreter services, ethnic matching between provider and patient, and additional follow-up support for patients. Overall study quality was low. Five of the six studies that examined computerized reminders showed statistically significant positive effects for the selected outcome. The reminders were for mammography or Pap smears and diabetes care for racial/ethnic minority populations. Studies of professional remote interpreters had positive findings. Followup support interventions and patient–therapist ethnic matching had mixed results.

Two reviews looked specifically at provider training and found that, while provider knowledge and patient satisfaction improved, there was sparse evidence on other outcomes. Horvat et al. (2014) examined randomized controlled trials, cluster randomized controlled trials, and controlled clinical trials published up to 2014[49] and include five studies. They found that patient involvement in care and use of services improved, while care quality was mixed. The quality and paucity of evidence was such that the reviewers were unable to draw generalizable conclusions. Lie et al. (2011) conducted a review of studies published between 1990 and 2010 on cultural competency educational interventions and patient outcomes; seven studies met their inclusion criteria.[16] The studies were of low to moderate quality, and many studies lacked important information on patient and provider variables (e.g., race, language concordance). In general, the studies showed that, following provider training, patient satisfaction and sense of provider concern improved, whereas clinical outcomes were mixed. The authors found it was difficult to draw conclusions about cultural competency trainings given the lack of robust and consistent evidence.[16]

17.4.4.2 Studies

We found eight studies that measured associations between cultural competency and patient safety outcomes or safety-related process measures. Most were intervention studies and one was a

measurement study. The studies were all at single sites and primarily observational. The studies are organized by outcome type: medication adherence and healthcare utilization, advanced care planning and informed consent, and patient comprehension. Studies were observational, before and after, randomized/controlled, or cross-sectional.

17.4.4.2.1 Language Services: Medication Compliance, Length of Stay, Emergency Services Utilization

Four studies examined the impact of additional language services, culturally-competent education, and/or lay health worker support on medication adherence and/or service utilization in LEP patients.[50-52] The studies indicate that professional or qualified interpretation and cultural and language concordance improve patient medication adherence and decrease preventable hospital admissions. These four studies are summarized below and outcomes are provided in Table 17.2.

In a retrospective study of a 3-year period, Lindholm et al. (2012) found that hospital length of stay and the percentage of patients readmitted within 30 days were lower for those who received a professional interpreter than for those who did not receive professional interpretation at admission and/or discharge ($p<0.001$).[50] In another study on interpreter services, Karliner et al (2017) examined hospital outcomes, including 30-day readmission rates, length of stay, and hospital expenditures before and after implementation of highly accessible professional interpreter services.[51] The study took place on a medicine floor of an academic medical center where interpreter services at baseline consisted of in-person staff interpreters who had to be scheduled during business hours and were not always available. The intervention consisted of a dual-handset interpreter telephone at the bedside of every patient with LEP. These 66 telephones had a programmed button that allowed 24-hour access to a professional (trained and tested) medical interpreter for more than 100 languages. During the 8-month intervention period, the number of interpreter encounters went from less than one per patient to over four per patient. As shown in Table 17.2, during the intervention there was a decrease in the number of 30-day readmissions for LEP patients; there was no change in length of stay. The intervention was found to be cost-effective in terms of preventing the cost of readmissions.[51]

Woerner et al. (2009) examined a multi-pronged intervention that aimed at reducing hospitalizations and use of emergency services, and increasing medication adherence among Hispanic home care patients served by a home care agency in Rochester, New York.[52] Despite the use of interpreters and Spanish-speaking providers at baseline, compared with the non-Hispanic patients, the Hispanic participants in the study had higher numbers of diagnoses (e.g., hypertension, diabetes mellitus, depressive disorder, gait abnormality), medications, emergency department visits, and hospitalizations. The intervention evaluated in this study involved several components, including recruiting Hispanic home health aides, conducting trainings in Spanish for LEP workers, allowing aides to share their personal cell phone numbers with patients, and creating educational materials for patients in a telenovela (soap opera) video format. Aides wrote down patients' questions to ask during physician visits. Local foods were incorporated into diabetic nutrition education. Data from a year prior to the intervention and post-intervention were compared for 125 Hispanic patients. As shown in Table 17.2, after a year the acute hospitalization rate and emergency department visit rate dropped for Hispanic patients. Oral medication adherence rates increased. Data were collected on patient characteristics and all non-Hispanic patients also received the intervention but p-values were not calculated. A follow-up inquiry on barriers to medication adherence found a number of discrepancies between what the patient

was taking and what had been prescribed and/or discontinued by a physician. This led to development of a communication notebook, kept by patients and their aides, with notes from providers to improve communication between providers.[52]

Finally, Cardarelli et al. (2018) examined the use of lay health workers to help reduce 30-day readmissions in high-risk patients at an Appalachian hospital. Lay health workers such as CHWs are members of the patients' community and intended to provide culturally sensitive community-based services. Most of the participating patients were Caucasian with only a high school education. In this case, the lay health workers served a rural Appalachian population, a population with unique psychosocial needs and stressors. The intervention began with the patient and lay health worker, working together to develop an individualized post-discharge plan prior to hospital discharge. The plan was provided to the patient upon discharge along with the lay health worker's contact information. The lay health worker conducted a follow-up call 24–48 hours after discharge to review any issues during the interim post-discharge period, assess patient follow-through in engaging with identified community resources, and review plans for appropriate follow-up visits. Compared to pre-intervention outcomes, the program was associated with an insignificant decrease in 30-day readmission rates but significant decrease in odds of being readmitted within 30 days when adjusted for education, transportation cost, and a positive anxiety screen. The authors assert that the lay health worker model may be a cost-effective way to prevent hospital readmissions in rural settings.[53]

Table 17.2: Studies of Cultural Competency: Language Services and Clinical Safety

Article	Setting	Intervention/ Exposure	Outcome
Cardarelli et al., 2018[53]	A hospital in Northeast Appalachia Kentucky	Use of lay health workers for post-discharge follow-up calls for high-need patients.	Thirty-day readmission rates decreased from 28.3 to 14.8% (p = 0.09) between the baseline and intervention phases. When adjusted for education, transportation cost, and a positive anxiety screen, the odds of being readmitted within 30 days further decreased to 77% (odds ratio [OR] 0.33; 90% confidence interval [CI] 0.14–0.81; p=0.04) among those exposed to the lay health worker program.
Karliner et al., 2017[51]	A medicine floor of an academic medical center	Increased access to professional interpreters by providing a dual-handset telephone with a direct connection to interpreter services at each hospital bedside	There was a significant decrease in observed 30-day readmission rates for the limited English proficiency (LEP) group during the 8-month intervention period compared with the 18 months pre-intervention (17.8% vs. 13.4%). At the same time, English-proficient patients' readmission rates increased (16.7% vs. 19.7%). Results remained significant in adjusted analyses (pre-intervention OR=1.07; 95% CI, 0.85 to 1.35; intervention CI=0.64; 95% CI, 0.43 to 0.95). There was no significant change in length of stay. After accounting for interpreter services costs, the estimated 119 readmissions were associated with estimated monthly savings of $161,404.

Article	Setting	Intervention/ Exposure	Outcome
Lindholm et al., 2012[50]	A tertiary care, university hospital, MA	Professional language interpretation for LEP patients at admission and discharge	Of the 3,071 patients included in the study, 39% received language interpretation on both admission and discharge date. Patients who did not receive professional interpretation at admission or both admission/discharge had higher length of stay of between 0.75 and 1.47 days compared with patients who had an interpreter on both day of admission and of discharge ($p<0.02$). Of the patient admissions who did not have an interpreter present at admission or admission/discharge, 24.3% were readmitted within 30 days, compared with 16.9% of patients with an interpreter at admission only, 17.6% of those with an interpreter at discharge only, and 14.9% with an interpreter at both admission and discharge (Chi square=19.5, degrees of freedom=3, $p<0.001$).
Woerner et al., 2009[52]	Home nursing care for 125 Hispanic patients, NY	Delivery of home nursing care using a culturally congruent approach; hiring of Hispanic nurses; staff education; culturally competent patient education	Acute hospitalization for Hispanic patients/all patients pre-intervention: 43%/30%; post-intervention: 24%/17%. Emergency department rate pre-intervention: 23%/24%; post-intervention: 21%/26%; oral medication adherence pre-intervention: 22%/42%; post-intervention: 28%/42%. (no p-values provided).

17.4.4.2.2 Language Services: Informed Consent and Advance Care Planning

Two studies showed that increasing language services for LEP patients was associated with improvements in patient participation in advance care directives.[54,55] To mitigate literacy, cultural, and language barriers to advance care planning, Sudore et al. (2018) studied an online tool for creating advance directives available to English- and Spanish-speaking patients at four safety-net primary care clinics.[54] Among the 986 participants (603 women and 383 men), the mean age was 63.3 years, 387 of 975 (39.7 percent) had limited health literacy, and 45 percent were Spanish speaking. The intervention materials were written at a fifth-grade level and designed for patients to use without needing assistance. As outlined in Table 17.3, compared with the advance directive alone, the tool resulted in a higher rate of advance care planning documentation. The researchers report the results were significant among both English and Spanish speakers.[54]

Lee et al. (2017) examined the impact of having 24 dual-handset interpreter phones at patient bedside on several surgery floors of a hospital.[55] Subjects included Chinese- and Spanish-speaking patients with LEP who were undergoing invasive procedures. Informed consent understanding was measured by patient-reported understanding of the reasons for and risks of the procedure and having had all questions answered. Understanding was measured before and during the 6 months after the phones were installed, with post-implementation patients more likely to demonstrate adequate informed consent. While disparities in comprehension between English-speaking and LEP patients still existed after the installation of the headsets, compared with pre-implementation, patients with LEP were more likely to meet criteria for adequate informed consent. Outcomes are provided in Table 17.3.[55]

Table 17.3: Studies of Advance Care Planning and Informed Consent

Article	Setting	Intervention/ Population	Outcome
Lee et al., 2017[55]	Cardiovascular, general surgery, orthopedic surgery floors of a hospital	Installation of dual-handset interpreter phones at every bedside enabling 24-hour immediate access to professional interpreters	During post-implementation (vs. pre-implementation) patients with limited English proficiency (LEP) were more likely to meet criteria for adequately informed consent (54% vs. 29%, p=0.001) and, after propensity score adjustment, had significantly higher odds of adequate informed consent (adjusted odds ratio [OR] 2.56; 95% confidence interval [CI], 1.15 to 5.72) as well as of each consent element individually. However, compared with post-implementation English speakers, post-implementation patients with LEP still had significantly lower adjusted odds of adequately informed consent (adjusted OR 0.38; 95% CI, 0.16 to 0.91).
Sudore et al., 2018[54]	Four safety-net, primary-care clinics, San Francisco	Easy-to-read advance directives and a patient-directed, online advance care planning program called PREPARE For Your Care (PREPARE) were created in English and Spanish	Compared with the advance directive alone, PREPARE resulted in a higher rate of advance care planning documentation (unadjusted: 43.0% [207 of 481] vs. 33.1% [167 of 505]; p<0.001; adjusted: 43.0% vs. 32.0%; p<0.001) and higher self-reported advance care planning engagement scores (98.1% vs. 89.5%; p<0.001). Results were significant among English speakers and Spanish speakers.

17.4.4.2.3 Process Outcomes: Language Services—Patient Comprehension, Translation Accuracy

Two additional process studies illustrate the importance of language interpretation, both in helping patients to comprehend written medication instructions[19] and in using professional interpreters (vs. ad hoc or no interpretation) to maximize accuracy of oral translation.[56] Quantitative outcomes are presented in Table 17.4.

Bailey et al. (2012) examined the efficacy of multilingual prescription drug label instructions on 202 LEP adults who spoke five non-English languages (Chinese, Korean, Russian, Spanish, and Vietnamese).[19] Participants were recruited from nine clinics and community organizations in San Francisco and Chicago. As shown in Table 17.4, participants who received the language-concordant instructions showed greater understanding and medication adherence compared with patients who received standard English prescription instructions.[19] Flores et al. (2012) conducted a cross-sectional error analysis of pediatric emergency department visits over 30 months.[56] Participants were Spanish-speaking LEP patients and their care-givers who received services with a professional interpreter, ad hoc interpreter, or no interpreter. Professional interpreters had a lower percentage of errors with potential clinical consequence than ad hoc interpreters and no interpreters. The number of errors by professional interpreters with more training was significantly lower than the number of errors by professional interpreters with less training.[56]

Table 17.4: Studies of Language Services: Patient Comprehension and Professional Translation Accuracy

Article	Setting	Intervention/ Population	Outcome
Bailey et al., 2012[19]	Nine clinics and community organizations in San Francisco and Chicago	Multilingual prescription instructions	Subjects receiving the ConcordantRx instructions demonstrated significantly greater understanding of their prescription (Rx), regimen dosing, and regimen consolidation than those receiving standard instructions (incidence rate ratio [IRR]: 1.25; 95% confidence interval [CI], 1.06 to 1.48; p=0.007 for Rx understanding, IRR: 1.19; 95% CI, 1.03 to 1.39; p=0.02 for regimen dosing, and IRR: 0.76; 95% CI, 0.64 to 0.90; p=0.001 for regimen consolidation).
Flores et al., 2012[56]	Two largest pediatric emergency departments in MA	Comparison of professional interpreter, ad hoc interpreter, or no interpreter	Fifty-seven encounters included 20 with professional interpreters, 27 with ad hoc interpreters, and 10 with no interpreters; 1,884 interpreter errors were noted, and 18% had potential clinical consequences. The proportion of errors of potential consequence was significantly lower for professional (12%) versus ad hoc (22%) versus no interpreters (20%) (p<0.01). The median number of errors by professional interpreters with at least 100 hours of training was significantly lower, at 12, versus 33 for those with fewer than 100 hours of training.

17.4.5 Implementation

Certain recommendations and challenges are repeatedly discussed in the literature for cultural competency in healthcare. In this section, we highlight these recommendations and challenges, drawing from a range of sources, including reviews and studies on healthcare quality, as well as safety articles and initiatives. We discuss organization-, provider-, and patient-level considerations.

17.4.5.1 Implementation: Facilitators and Recommendations

At the facility level, multiple reviews discussed the importance of self-assessment, data collection,[2] and root-cause analyses to identify factors, gaps, and systems in the organizational context that impact healthcare disparities and safety of patients from minority culture and language backgrounds.[11,57] Implementation efforts may benefit from analyses of the "organizational culture," biases, and readiness to change, as well as how the organization is embedded in policy frameworks, organizational arrangements, and physical settings.[2,17] Successful efforts also require commitment by leadership, allocation of resources, and performance indicators to improve accountability.[2,17,58] Experts recommend consultation/collaboration with the communities they serve on implementation (and development) of cultural competency initiatives.[17,59-61] For cultural competency efforts in general, any additional services should be fully integrated into existing systems of care.[59,60]

A number of studies and reviews from the quality literature discuss creating roles for and use of culturally similar CHWs as facilitators of implementation, in addition to their being a crucial component of an intervention for working with LEP or certain racial/ethnic groups.[52,60,61] McElmurry et al. (2009) suggest thoughtful recruitment of CHWs, ensuring that they are appropriately trained and that other staff are aware of the CHWs' roles and level of knowledge.[62] Henderson et al. (2011) note it is important to appropriately match CHWs with patients—taking into account gender norms and customs of culturally and linguistically diverse communities.[63] Further, McElmurry et al. and Henderson et al. recommend efforts to support and improve retention of CHWs.[62,63]

Intercultural communication is not just an exchange of words, but an exchange of shared meanings.[56] Clinicians, bilingual staff, and interpreters should verify understanding of meaning across cultures and language.[57] Providers should be trained in how to work with interpreters. When using professional interpreters, experts have found that interpreting accuracy decreased when clinicians use long sentences, medical jargon, or terms that are unfamiliar to the interpreter. It is suggested that interpretation is best when the message is short, simple, and clear. Additionally, interpreters perform best when, at the onset of the encounter, introductions are made that set up a collaborative relationship among the clinician, the interpreter, and the patient and family.[64] Suggestions for implementing interpreter services (e.g., augmenting in-house interpreters with phone interpreters, incorporating interpreters into rounding protocols, developing visual cues to remind hospital staff to attend to language and cultural needs) can be found in AHRQ's Improving Patient Safety Systems for Patients With Limited English Proficiency: A Guide for Hospitals.[65]

17.4.5.2 Implementation: Challenges

Several barriers to implementing cultural competency practices have been identified, including translating training into practice[16] and understanding the best methods for providing performance feedback to physicians.[66] Another challenge is identifying patients' language needs. One small study found that nurses misclassified 27 percent of self-identified Spanish-speaking patients as being English proficient in the triage process.[67] To assist in this process, protocols exist for helping to identify LEP patients.[68]

A specific implementation issue is the underuse of professional interpreters in the clinical setting. This is despite the fact that language services are legally mandated and that providers have reported a preference for working with professional interpreters over ad hoc interpreters (family, friends, or untrained staff).[69] One study found that use of professional interpreters by physicians was less than 20 percent at admission and since admission. In this study, LEP Spanish- and Chinese-speaking patients reported they either "got by" without an interpreter or were less frequently spoken to by physicians and nurses.[70] Another study found that 65.8 percent of LEP patients never had a documented interpreter visit.[71]

There are structural and provider-level reasons for underuse of interpreters, such as the fact that not all States provide reimbursement.[72] For example, pediatricians in States with reimbursement had twice the odds of using a formal interpreter versus those in nonreimbursing States (odds ratio [OR] 2.34; 95% confidence interval [CI], 1.24 to 4.40).[73] Barriers to interpreter use at the clinician level include lack of convenience and time pressures,[74] as well as concerns about the quality of interpretation and resource constraints.[75] While physicians have expressed a preference for in-person interpreters,[76] use of telephone and video conferencing increases efficiency and may help to increase use of interpreters.[73,77] To improve utilization, some have called for organizational resources and guidelines that are consistent with institutional policies and professional norms.[75] Additionally, educational campaigns could help shift clinician culture away from ad hoc interpreters.[55] Despite the cost of interpreter services, studies show that, ultimately, providing the service is cost-effective in terms of improved care[77,78] Sharing of resources across organizations has helped some facilities to overcome cost barriers.[78] Finally, to address need, more effort could be made to recruit bilingual clinicians with appropriate training and certification.[55]

17.4.6 Resources

A number of resources provide practice guidance for working with diverse populations, such as LEP patients, patients from different racial/ethnic backgrounds, immigrants, people with disabilities, people with HIV, and sexual and gender minorities. Below is a sample of resources from Federal agencies.

AHRQ: Improving Patient Safety Systems for Patients With Limited English Proficiency: A Guide for Hospitals:
https://www.ahrq.gov/health-literacy/systems/hospital/lepguide/index.html

AHRQ: Re-Engineered Discharge (RED) Toolkit. Tool 4: How To Deliver the Re-Engineered Discharge to Diverse Populations:
https://www.ahrq.gov/hai/red/toolkit/redtool4.html

AHRQ Team STEPPS®: Patients With Limited English Proficiency:
https://www.ahrq.gov/teamstepps/lep/index.html

Centers for Disease Control and Prevention (CDC): Culture & Health Literacy:
https://www.cdc.gov/healthliteracy/culture.html

CDC Effective Communication for Healthcare Teams: Addressing Health Literacy, Limited English Proficiency and Cultural Differences:
https://www.train.org/main/training_plan/3985

CDC, National Prevention Information Network: Cultural Competence:
https://npin.cdc.gov/pages/cultural-competence#1

CDC: Practical Strategies for Culturally Competent Evaluation:
https://www.cdc.gov/dhdsp/docs/cultural_competence_guide.pdf

Centers for Medicare & Medicaid Services: A Practical Guide to Implementing the National CLAS Standards:
https://www.cms.gov/About-CMS/Agency-Information/OMH/Downloads/CLAS-Toolkit-12-7-16.pdf

Georgetown University National Center for Cultural Competence:
https://nccc.georgetown.edu/

Health Resources & Services Administration: Culture, Language, and Health Literacy Resources:
https://www.hrsa.gov/cultural-competence/gender.html

Office of Minority Health: A Blueprint for Advancing and Sustaining CLAS Policy and Practice:
https://www.thinkculturalhealth.hhs.gov/clas/blueprint

Office of Minority Health: Multi-Cultural Resources for Health Information:
https://sis.nlm.nih.gov/outreach/multicultural.html

Office of Minority Health: The Guide to Providing Effective Communication and Language Assistance Services:
https://www.thinkculturalhealth.hhs.gov/education/communication-guide

The Joint Commission: Advancing Effective Communication, Cultural Competence, and Patient- and Family-Centered Care: A Roadmap for Hospitals: https://www.jointcommission.org/assets/1/6/ARoadmapforHospitalsfinalversion727.pdf

17.4.7 Gaps and Future Directions

Based on the research presented in this review, there is promise for cultural competency as a way to reduce adverse safety events in target populations. However, limiting our focus exclusively to patient safety outcomes resulted in a small number of studies from which to draw conclusions. Additionally, our search terms did not include certain key terms, such as *language assistance, bilingual, bicultural, interpretation, language concordance*, and *cultural brokers*. Still, there is a clear need for studies that are robust and that look specifically at associations between race and culture in the study of patient safety.[28,79] Since most of the small group of studies on safety were limited to language services and LEP populations (studies in the category were still minimal—perhaps due to standardization of these practices), there is a need for studies that examine the link between patient safety and other elements of organizational and provider cultural competency. There also is a need for studies that examine cultural competency interventions to improve safety for a wider range of populations (e.g., Native Americans, transgender patients) and patients who belong to more than one priority population. As the body of research grows, it will be important to see interventions that address a broader range of safety issues, such as birth outcomes, pressure ulcers, and adverse events in mental and behavioral health. Future cultural competency research should include more detailed information about patient populations and subpopulations, comorbidities, geographic and hospital-level variations, provider demographics, cost-effectiveness, links between provider knowledge and behavior, and the content and presentation of cultural competency trainings.[8,16,17,25,28] Longitudinal studies and studies that incorporate patient participation in research development could be considered.[49]

Given the paucity of research on cultural competency and patient safety, there are many opportunities for future research—for example, in-depth research on the association between CLAS and diagnostic errors. Proposed approaches to improving patient safety could also be studied. For example, Mattox (2010) recommends identifying patients at heightened risk for medical error, including patients with low health literacy, LEP, and certain racial/ethnic minority groups (e.g., African Americans).[80] Errors may be avoided with these patient groups by proactively ensuring meaningful communication, use of interpreters, and/or carefully evaluating latent and overt health risks. Other practices that address safety and could inform cultural competency include patient and family engagement, which has shown some promise, although study quality is low.[81]

Some outcomes and practices have been studied that are provider based and conceptually related to safety, and could help inform future safety research. These practices include quality patient–provider communication and trust in culturally discordant encounters.[82] As noted in our discussion of systematic reviews, studies have shown a link between provider cultural competency and communication skills, and patient trust and adherence. Other outcomes that are related to safety include provider initiation of routine screenings for minority populations. This outcome is similar to provision of appropriate medications, as it addresses whether providers are consistently following recommended practices. For example, two studies have shown that combining physician training and patient education has helped to increase colorectal cancer screening among high-risk racial/ethnic minority patients.[83,84] Finally, more could be done to explore the link between adverse safety events and provider bias and/or racism.

Several studies show a link between providers' implicit bias and patient communication challenges, as well as healthcare and health outcomes.[85,86] Given structural changes, population changes, shifting priorities, and increased understanding, in the future the meaning/framework of cultural competency will continue to shift focus and evolve. [87]

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17.5 Monitoring, Auditing, and Feedback

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17.5.1 Practice Description

Audit and feedback methods provide information to clinicians and others about performance to motivate and measure change, and are broadly defined as "any summary of clinical performance over a specified period of time."[1]

Audit and feedback interventions can be targeted to physicians, other clinicians, or entire care teams. Audits rely on chart review, direct observation, analysis of electronic data, or other clinical and non-clinical sources. Feedback can be delivered during meetings, or via email or other modes of communication. Feedback often includes a dashboard to visually show performance over time or against a benchmark, and may include an indicator of underachieving, reaching, or exceeding a predetermined threshold or benchmark. Feedback is often combined with education about the intended practice improvement and suggestions about workflow or other care process redesign.

17.5.2 Methods

Two databases (CINAHL® and MEDLINE®) were searched to identify studies published from 2008 to 2018 describing audit and feedback interventions. We included search terms for "feedback," "clinical audit," "medical audit," "quality assurance, health care," and "benchmarking." In total, 2,472 studies were identified. Abstracts from 2,335 studies were assessed and 127 full-text articles were reviewed. Thirty-one articles are included in this review, including three systematic reviews and one nonsystematic review. Studies were included if they were in English, and had an audit and feedback intervention directed at clinicians, whether individuals or clinical groups/units within a setting. We focused on research conducted in the United States and Canada, but studies conducted in the United Kingdom and the Netherlands were also reviewed. We selected studies that focused on improving patient safety and had measurable outcomes. All clinical settings and patient populations were included. Studies were excluded if the intervention was focused only on administrators or top-level executives and did not reach clinicians, or if the focus was on quality improvement without a patient safety benefit, was not health focused, or was a government-run initiative. Uncertainties were discussed with authors of other cross-cutting topics.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

17.5.3 Review of Evidence

Key findings are highlighted in a text box below.

17.5.3.1 Clinical Outcomes

Few of the reviewed articles studied the association between audit and feedback methods and clinical outcomes, and even fewer of those found significant impacts. An example of the association includes a study by Mahant and colleagues (2008). They conducted a pre/post observational study at a tertiary care pediatric hospital in Canada to audit the appropriateness of hospital days for all admissions and to provide feedback to attending physicians. A nurse used a utilization review tool to rate hospital days as

"qualified" or "nonqualified" on the basis of the nature of the inpatient services. The intervention consisted of (1) weekly feedback to attending physicians about which patients had nonqualified hospital day, and (2) dissemination of summary reports to attending physicians. The intervention was associated with a significant reduction in inappropriate hospital days (33% versus 47% in the baseline; p=0.0001). The authors calculated that 7.35 hospital days would have to be reviewed, combined with weekly feedback, to prevent 1 nonqualified hospital day. There was no significant impact on the hospital readmission rate.[2]

Key Findings:

- Audit and feedback is a somewhat common strategy for improving compliance with patient safety processes.
- Audit and feedback appears to be most effective when it employs both written and oral feedback.
- Studies show more significant improvements when performance was lower at baseline.
- Research on audit and feedback predominantly focuses on process improvement, and more research is needed to measure the impact of audit and feedback on patient outcomes.

In another study with significant patient outcomes, Hubner et al. (2017) evaluated the impact of standardized postresuscitation feedback on quality of advanced life support (ALS) for patients experiencing an out-of-hospital cardiac arrest and whether such feedback could improve patient outcomes. Feedback delivered to the emergency medical services teams included detailed process information about ALS performance, such as ventilation rate, chest compression during defibrillator loading phase, and post-arrest oxygen saturation, and outcomes such as survival and neurological outcomes for survivors. ALS performance was evaluated by trained personnel and the feedback highlighted both good performance/guideline conformity (green) and poor performance (red). Over the course of the 2-year intervention period, the standardized postresuscitation feedback protocol was associated with significant improvements in the quality of ALS, and there was a strong linear increase in both survival until hospital discharge (+6.3%) and favorable neurological outcome in survivors (+16.0%).[3]

Several other studies measured patient outcomes without finding any statistically significant impacts of audit and feedback. For example, Boet and colleagues (2018) studied the incidence of inadvertent perioperative hypothermia in a Canadian hospital. They compared benchmarked feedback (individual performance outcomes and a reminder of the target temperature) with ranked feedback (individual performance and ranking within the anesthesiology department); they also included a control group that received no feedback. They found no evidence that benchmarked or ranked feedback was more effective than no feedback in influencing anesthesiologists' performance related to patient temperature.[4] For another example of a study that found no impact of audit and feedback, van der Veer et al. (2013) studied a multifactorial quality improvement program in Dutch hospitals that included educational sessions, monthly reports to monitor performance over time, and quarterly benchmark reports. They found no significant impact on hospital length of stay, duration of mechanical ventilation, or in-hospital mortality.[5]

17.5.3.2 Care Processes Outcomes

Seventeen of the 31 reviewed studies measured whether the audit and feedback approach improves compliance with patient safety care processes. Ivers et al. (2012) conducted a systematic review of articles published from 1950 to 2010 about the impact of audit and feedback on patient outcomes, and factors that explain variation in effectiveness of audit and feedback. In their meta-analysis of 49 studies with dichotomous outcomes, in which audit and feedback was compared with usual care, they found an

average 4.3-percent absolute increase in healthcare professionals' compliance with the desired practice (interquartile range [IQR] 0.5% to 16%), and for 5 studies with continuous patient outcomes, the average percent change was 17% (IQR 1.5% to 17%). For 6 studies with dichotomous patient outcomes compared with controls, the average difference was -0.4%, and in 21 other studies with continuous outcomes, they found that the average percent change relative to controls was 1.3% (IQR 1.3% to 28.9%). Ivers and colleagues concluded that audit and feedback generally leads to small but potentially important improvements in professional practice, and that improvement is greatest when baseline performance was low.[6]

Tuti et al. (2017) conducted a systematic review of nine studies of electronic audit and feedback, ranging from antibiotic prescribing to cholesterol measurement, and completeness of records regarding lifestyle factors. Of these studies, three showed a positive impact of audit and feedback on quality of care. Five of the studies were similar enough in the outcomes studied to conduct a meta-analysis; the weighted pooled odds ratio (OR) of compliance with desired practice was 1.93 (95% confidence interval [CI], 1.36 to 2.73) when comparing audit and feedback with usual care. However, the authors considered this average effect to be unreliable, due to likely biases in this small selection of studies.[7]

Coleman et al. (2013) studied several interventions to reduce missed antibiotic doses among hospitalized patients, including: (1) the ability of doctors to pause medication doses; (2) clinical dashboards; (3) visual indicators for overdue doses; and (4) root cause analysis meetings to investigate overdue/delayed doses. Rates of both missed antibiotics and missed non-antibiotic doses decreased significantly after the introduction of clinical dashboards (0.60, p=0.001), as well as following instigation of executive-led root causes analysis meetings. However, a visual indicator for overdue doses was not associated with significant decreases in the rates of missed antibiotic or non-antibiotic doses.[8]

Diamantouros et al. (2017) studied a multifactorial, multihospital intervention to improve prescribing for venous thromboembolism (VTE) prophylaxis. Chart audits were used to identify VTE prophylaxis, and feedback included written summary reports presented at group meetings with each clinical team. The authors found a significant improvement in the rate of appropriate thromboprophylaxis for a patient subgroup with moderate risk of VTE (67% vs. 62% at baseline; p=0.048). Scales et al. (2011) randomized intensive care units in Canadian hospitals and tested audit and feedback (versus usual care) to improve six specific care processes. Overall, adoption of the targeted practices was greater in intervention intensive care units than in controls (2.79 OR; 95% CI, 1.00 to 7.74); it was greatest for semi-recumbent positioning to prevent ventilator-associated pneumonia (90.0% of patient-days in last month vs. 50.0% in first month; OR 6.35; 95% CI, 1.85 to 21.79) and for precautions to prevent catheter-related bloodstream infection (70.0% of patients receiving central lines vs. 10.6%; OR 30.06; 95% CI, 11.00 to 82.17). Adoption of other practices, many that started with high baseline adherence, changed little.[9]

Several other studies found mixed results. Langston (2011) evaluated a peer-monitoring and feedback intervention that all clinical staff could use to observe the hand hygiene practices of other health care professionals, and when hand hygiene was not performed appropriately, provide feedback to that staff member. The intervention significantly improved hand hygiene compliance among nurses after nonpatient contact in a patient's room (16.9% improvement over baseline; p=0.003) but had no impact on physicians, nursing assistants, or ancillary staff.[10]

Timing of feedback may affect its impact on compliance with patient care best practices. Zoutman and Ford (2012) randomly assigned physicians to receive monthly versus "delayed" feedback about their

antibiotic prescribing. Monthly feedback did not influence the rate of prescribing antibiotics when compared with baseline prescribing or delayed feedback; however, monthly feedback increased the appropriateness of first-line antibiotic choices when compared with baseline prescribing or delayed feedback. In addition, physicians receiving monthly feedback prescribed fewer broad spectrum antibiotics compared with baseline prescribing and the delayed feedback group, when these drugs were not the first-line choices.[11]

Some audit and feedback studies address completeness of documentation in medical records. Gilkes et al. (2017) enlisted medical students to audit the case notes completed by their supervisors (general practitioners) to identify whether the notes documented 11 specific preventive care practices for every patient encounter. Supervisors agreed to this audit and received feedback about the completeness of their case note documentation. The audit and feedback led to significant improvements in documentation of patients' alcohol consumption (24% to 36%; OR 1.19; 95% CI, 1.10 to 1.29) but did not improve documentation of patients' smoking status.[12] As another example, Dinescu et al. (2011) studied completeness of discharge summaries, which can influence the receipt of appropriate post-acute care. They found that discharge summaries were more likely to be thorough and complete following the audit and feedback intervention (91% vs. 71%, $p<0.001$).[13]

17.5.3.3 Economic Outcomes

One study (Johri et al., 2017) addressed economic impacts of audit and feedback. Researchers randomly assigned 32 Canadian hospitals to intervention or control; in the intervention group, hospital audit committees assessed the appropriateness of caesarean childbirth deliveries and provided feedback to clinicians about best practices. The authors found a significant average cost reduction of $190 (per patient); this was associated with less frequent neonatal complications in the intervention group (95% CI, -$255 to -$125, $p<0.001$).[14]

17.5.3.4 Unintended Consequences

The 31 reviewed studies mentioned no unintended consequences of audit and feedback on patient outcomes or care processes.

17.5.3.5 Summary of Evidence on Implementation

The 31 studies varied in terms of the format of the audit and feedback intervention, who provided feedback, and the frequency and timing of feedback. It has been noticed that, for the most part, studies reviewed focus on feedback as opposed to audit; audit is typically mentioned only as the first part of an audit and feedback intervention.

Colquhoun and colleagues (2017) conducted a nonsystematic review to identify audit and feedback design elements. They reviewed 17 audit and feedback interventions and found that feedback was primarily given to individuals only (51%), rather than to groups (18%) or a combination of both individual and group (16%). Feedback was rarely given on patient outcomes (14%); instead, feedback was mostly about care processes (79%). The most common comparison in the feedback was to peers' performance or "others''' previous performance (49%). Fifteen percent included a standardized guideline as a comparator, and 4% measured change against the person's own previous performance. Lag time (the time between the collection of data for audit and the resulting feedback) was most commonly a few to several months (33%), and rarely a fast turnaround such as days or weeks. Feedback was given in person

in less than half of the studies (44%). Feedback was delivered just once in 24 percent of the studies, twice in 15 percent, three times in 9 percent, and more in 28 percent.[1]

Le Grand Rogers et al. (2015) reviewed 24 studies published from 1994 to 2014 related to audit and feedback of physicians in hospital emergency departments. In 5 of the 24 studies, electronic feedback was provided, and the remaining 19 studies used a combination of oral, written, and electronic feedback. Twenty of the 24 (83%) provided feedback with explicit, measurable instructions and with a plan for change. Seventeen gave feedback in intervals greater than 1 week, four gave feedback at intervals ranging from 1 day to 1 week, and three gave feedback less than 24 hours after the audit.[15] Zoutman and Ford (2012) surveyed 40 physicians who completed an audit and feedback intervention related to antibiotic prescribing, and the preferred frequency for feedback was quarterly (53% of respondents).[11]

In their large systematic review, Ivers et al. (2012) found that feedback is most effective when provided by a supervisor or colleague, when feedback is provided more than once, and when feedback is delivered in both oral and written formats.[6] Many studies were structured with a supervisor, peer, or independent researcher providing feedback, but there were exceptions. For example, Gilkes et al. (2017) used medical students to audit their general practitioner physician supervisors.[12] Langston (2011) had all nurses, nursing assistants, and unit coordinators complete audits and give feedback to other clinicians on the unit about hand hygiene.[10]

17.5.3.6 Barriers and Facilitators

Dawson et al. interviewed 30 healthcare professionals involved in a hand hygiene audit and feedback study about perceptions of the usefulness of the feedback. Interviewees raised concerns about how data generated by the audit process were used to engender change, and found it hard to perceive any change stemming from the audit process. Interviewees also felt unable to relate the feedback data they received to the training program for hand hygiene, or to understand how the results of the audit could inform strategies to improve hand hygiene.[16] Ivers et al. (2014) tested whether audit and feedback could improve the proportion of patients meeting quality targets for chronic disease management. They found that family physicians did not readily act upon the feedback reports they received for a number of reasons, including competing organizational level priorities, difficulty with patient-level (and personal) priority setting, and concern about potential flaws in the data or targets used in the feedback.[17]

Locus of control can affect the perceived credibility of and reactions to feedback. Redwood et al. (2013) studied whether a weekly dashboard providing feedback on prescription warning information and laboratory alerting acceptance rates was effective in changing the prescribing behavior of junior physicians. Nineteen of the junior physicians participated in follow-up interviews. While interviewees confirmed that the dashboard was helpful in stimulating reflection on their clinical behaviors and responsibilities, they felt the feedback did not reflect their own clinical practice because actions that generated alarms, alerts, and warnings were often ordered by senior physicians. They felt that the feedback could better motivate behavior change if directed to the ordering physician, not to the junior physician carrying out the order.[18]

Several studies interviewed or surveyed clinicians about their attitudes regarding the audit and feedback intervention. Jeffs and colleagues (2014) interviewed 56 nurses and unit managers about the feedback dashboards used in six hospital units. The majority of interviewees found the visual cues in the

dashboard to be useful, understandable, and motivating, and valued seeing feedback about the performance of the individual unit where they work.[19] In the Zoutman and Ford antibiotic study (2012), 40 physicians responded to a survey about the audit and feedback intervention and reported that feedback on antibiotic use was interesting (3.4 out of 4), useful (3.4), and influential (3.2).[11] The systematic review by Ivers et al. (2012) found that feedback was most effective when it included both explicit targets and an action plan.[6]

Two studies noted that effects of audit and feedback are greater when baseline performance is low. In the meta-analysis by Ivers et al. (2012), lower baseline performance was associated with greater improvement following audit and feedback intervention (p=0.007). Specifically, their regression model predicted that participants who were at 25 percent of desired practice at baseline would have an expected improvement of 9 percent, while those who were at 75 percent of desired practice at baseline would have an expected improvement of only 5 percent.[6] Similarly, Scales et al. (2011) found little improvement for care processes when baseline adherence to best practices was high.[20]

17.5.3.7 Resources To Assist With Implementation

Short descriptions of resources for implementing patient safety practices discussed in this review (e.g., tools/toolkits from the U.S. Centers for Disease Control and Prevention [CDC] and Agency for Healthcare Research and Quality) can be found in the following locations:

CDC presentation on giving infection prevention feedback:
https://www.cdc.gov/infectioncontrol/pdf/strive/CBT103-508.pdf

Patient Safety Network Patient Safety Toolkit for General Practice, which includes significant event audit:
https://psnet.ahrq.gov/resources/resource/30259/Patient-Safety-Toolkit-for-General-Practice?q=audit+and+feedback

Clinical Audit Tool from Royal College of Physicians and Surgeons of Canada:
http://www.royalcollege.ca/rcsite/documents/continuing-professional-development/clinical-audit-tool-e.pdf

17.5.4 Gaps and Future Directions

17.5.4.1 Gaps

Few of the 31 articles addressed the impact of audit and feedback on patient outcomes. Most studies compared performance on specific care processes with performance at baseline or to a control group, and some assessed performance against benchmarks or standards/guidelines, rather than measuring impact on patient outcomes. In the studies reviewed, many authors appear to assume that compliance with guidelines, or achieving care process targets, will yield better (unmeasured) patient outcomes.

There is some evidence[6, 15-18] that audit and feedback is most effective when clinicians understand and trust the data on which feedback is based, when feedback is actionable, and when there is a clear plan clinicians can follow to improve. There is also some evidence that it is important to select performance measures that are meaningful to clinicians and on which there is substantial room to improve (i.e., when baseline performance is low).

17.5.4.2 Future Directions

Based on this review, some evidence indicates that audit and feedback can yield small improvements in care processes, but more information is needed about whether this in turn improves patient outcomes. Future research should focus, ideally, on clinical outcomes, and also on care processes that are meaningful in the eyes of clinicians, where baseline performance is poor, where data are unambiguous and trusted by clinicians, and where it is possible to clearly connect feedback with action plans for improvement.

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17.6 Teamwork and Team Training

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17.6.1 Practice Description

Key Findings:

- The majority of studies conducted to improve teamwork and communication occurred in a hospital setting.
- CRM and TeamSTEPPS® were the most frequently studied team training programs. They led to immediate improvements in learning; longer term transfer of knowledge, skills, and attitudes (KSAs) to the job; and some patient outcomes.
- Psychological fidelity is more important than physical fidelity when using simulation to improve non-technical skills such as teamwork.
- Performance support tools (e.g., briefings, checklists, and handoffs) have been implemented to enhance team performance, resulting in a variety of improved processes and some improved outcomes for patients.

Failures in communication and teamwork have been identified as contributing factors in approximately 68 percent of adverse events.[1] Considerable effort has been made to improve teamwork within healthcare settings through the use of team training programs and performance support tools. According to Weaver et al. (2014), "team-training is defined as a constellation of content (i.e., specific knowledge, skills, and attitudes (KSAs) that underlie targeted teamwork competencies), tools (i.e., team task analysis, performance measures) and delivery methods (i.e., information, demonstration and practice-based learning methods) that together form an instruction strategy."[2] Some of the earliest healthcare team training programs were based on Crew Resource Management (CRM), an established and validated strategy within the aviation community. Subsequently, the Veterans Health Administration introduced its own team training program, called Medical Team Training (MTT). Similarly, the Agency for Healthcare Research and Quality (AHRQ) partnered with the Department of Defense to develop a team training program specifically designed for healthcare providers called Team Strategies and Tools to Enhance Performance and Patient Safety (TeamSTEPPS®). Introduced in 2006, TeamSTEPPS aims to improve a common set of team KSAs that providers can apply when working in any healthcare team. Four specific, trainable skills are highlighted in the program: leadership, situation monitoring, mutual support, and communication.

Since its inception, TeamSTEPPS has become the national standard for team training in healthcare.[3] In 2015, it was estimated that over 1.5 million individuals had been trained in TeamSTEPPS.[4] In sharing their insights of 10 years of TeamSTEPPS work, Baker et al. (2017) recognized the immense spread of TeamSTEPPS, not only in the United States, where it is estimated that approximately 35 percent of all healthcare workers have been exposed to TeamSTEPPS in some form, but also around the world. One reason for this uptake is that TeamSTEPPS concepts are applicable across healthcare environments and the training (and associated support tools) are easily adaptable.[5] Moreover, evaluation data collected on TeamSTEPPS and other team training programs have demonstrated positive results.[6, 7]

Most studies have incorporated into their evaluation efforts Kirkpatrick's (1956; 1996) multi-level framework, which suggests that learning interventions be assessed on four criteria: reactions, learning, transfer, and results (Table 17.5).[8, 9] Studies that assess multiple criteria, collect measures at multiple levels (e.g., individual and team, team and organization), and/or incorporate multiple measurement methods (e.g., surveys and observations) provide the most meaningful evaluations and insights regarding an intervention's effectiveness.[10]

Table 17.5: Kirkpatrick's Evaluation of Learning

	Level	Criteria
Weakest to Strongest Indicators of Learning	1	Reactions: The degree to which participants like the training and feel it is relevant to their work.
	2	Learning: The extent to which knowledge or skill has changed as a result of the intervention.
	3	Transfer: The application of knowledge and skills gained during training back in the actual work environment.
	4	Results: The greater impact that the training has on important organizational outcomes.

Team training programs such as TeamSTEPPS also include a variety of tools to help ensure that teamwork skills are transferred from the training environment and integrated into daily practices. Toward that end, performance support tools such as checklists, briefings, and huddles have been implemented to increase communication and teamwork in a variety of healthcare environments. This review summarizes the practices used to improve teamwork in healthcare and presents evidence of their effectiveness based on Kirkpatrick's four criteria of learning.

17.6.2 Methods

The question of interest for this review is: "What are the most effective practices to improve teamwork?" To answer this question, two databases (i.e., CINAHL® and MEDLINE®) were searched to identify studies published from 2008 to 2018 that implemented practices to improve teamwork. Search terms included "teamwork," "team processes," "collaboration," "communication," "team performance," "team training," "team effectiveness," and related synonyms, as well as terms such as "training intervention" and "quality improvement." Based on previous reviews, specific team training programs such as "TeamSTEPPS," "VA Medical Team Training," "Crew Resource Management," and "MedTeams" were also searched. The initial search yielded 1,760 results. After duplicates had been removed, 1,231 were screened for inclusion, and 126 full-text articles were retrieved. Of those, 33 were selected for inclusion in this review, of which 29 are single studies, 3 are systematic reviews,[2,11,12] and 1 is a meta-analysis.[13] Articles were excluded if the article was out of scope (including not quantitative), the study design was insufficiently described, the primary goal was not improving teamwork, the study did not evaluate a practice/method to enhance teamwork, the study was conducted with medical or nursing students, or the study was conducted outside of the United States. Key findings are located in the box on the previous page.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

17.6.3 Review of Evidence

The practices used to improve teamwork fell into seven categories: CRM, TeamSTEPPS, MTT, Simulation (either standalone or coupled with team training), briefings, checklists, and handoffs. Across these categories, the majority of the studies took place in a hospital setting (including academic teaching hospitals, community-based hospitals, and military hospitals), and one study was conducted in a psychiatric hospital. A variety of survey and observational data were gathered as indicators of effectiveness. These data are evaluated using Kirkpatrick's model of learning. For the purposes of this

review, we follow the criteria included in Table 17.5, noting that we consider learning as immediate changes in knowledge, skills (teamwork or clinical processes), or KSAs, whereas transfer refers to the longer term changes in KSAs demonstrated on the job. Measurements taken in the work environment at least 30 days following training will be treated as indicators of transfer. Also, organizational outcomes as well as patient outcomes are treated as results criteria.

Both the systematic reviews and meta-analysis provide data related to the four criteria in Kirkpatrick's evaluation framework (although not every study collected data on all 4 criteria), and findings are presented where applicable. Out of the 29 individual studies in the review, 6 reported data on participant reactions. Nineteen studies (66%) collected data immediately following the intervention to demonstrate participant learning. Fifteen of the 29 studies (52%) collected evidence of transfer of training, as most post-intervention measures of teamwork and clinical processes were collected approximately 3 months following the intervention. Results, in the form of clinical or patient outcomes, were reported in 11 studies. Measures of learning, transfer, and results were selected based on the environment where the intervention had been introduced. A wide variety of measures were incorporated and few studies used the same measures.

The following subsections summarize the evidence related to the seven practices identified for improving teamwork. Next, a summary of how these practices have been implemented is presented. Finally, areas for future research are proposed.

17.6.3.1 Practice: CRM

CRM Training was originally developed to improve teamwork within the aviation community. CRM programs focus on improving attitudes toward and knowledge about teamwork, as well as increasing the use of teamwork skills. CRM programs generally follow a workshop format (i.e., classroom training) that includes a didactic lecture, demonstration of both positive and negative examples of teamwork, hands-on practice using teamwork skills (e.g., in role play exercises or simulation exercises), and feedback regarding the effectiveness of teamwork skills demonstrated by participants. A considerable amount of research on improving teamwork and communication within healthcare has applied CRM as an instructional strategy.[2]

17.6.3.2 Process Measures

Studies included in Weaver et al.'s (2014) systematic review and Hughes et al.'s (2016) meta-analysis of team training collected process measures related to reactions, learning, and transfer. Additionally, the five individual studies of CRM collected process measures of three criteria included in Kirkpatrick's framework. One study collected reaction criteria as part of their evaluation. Three studies collected data immediately following the training to assess participant learning. All five studies collected pre- and post-training measures of team behaviors (e.g., perceptions of teamwork, communication) a few months after the training, which represent Kirkpatrick's transfer criteria. Clinical processes relevant to the setting (emergency department, an obstetrics/neonatal unit, and operating room) provide additional data on transfer criteria in two of the studies.

17.6.3.2.1 Process Measures: Reactions Criteria

Six of the nine CRM studies reviewed by Weaver et al. (2014) measured participant reactions as part of their evaluation efforts. Only 5 of the 126 studies included in the meta-analysis conducted by Hughes et al. (2016) reported reactions to team training. Overall, the studies that used CRM report positive

reactions to the training. Similarly, Hughes et al. reported that healthcare team training programs result in positive participant reactions (corrected standardized mean difference in a repeated measures metric=.53 and the 95% confidence interval [CI] excluded zero: 95% CI, .33 to .73).[13]

Of the individual CRM studies identified, Halverson et al. (2009) demonstrated positive reactions to preoperative briefings that were introduced as part of CRM training. Survey data indicated that respondents had positive reactions toward the preoperative briefings and felt that they were useful in setting the stage for good communication (approximately 75% favorable), understanding the plan for care (approximately 70% favorable), and teamwork (approximately 75% favorable).[14]

17.6.3.2.2 Process Measures: Learning Criteria

Four of the CRM studies reviewed by Weaver et al. (2014) collected measures of learning. All studies reported that participants were more confident in using teamwork skills and dealing with critical events following the CRM training. In addition, one study also demonstrated increased knowledge of teamwork as a result of the training. Further evidence of learning was provided by the meta-analysis published by Hughes et al., which found that healthcare team training increased learning (affective, cognitive, and skill-based learning) from pre- to post-training (corrected standardized mean difference in a repeated measures metric=.89, *k* =79, 95% CI, .66 to 1.11).[13]

In an individual study conducted by Levy et al. (2014), CRM training was delivered in the emergency departments at three different hospitals to improve acute coronary syndrome (ACS)-centered care. Positive results were reported in participant learning. Specifically, immediately following the training, participants were significantly more confident in their ability to identify processes that could lead to errors (pre-training=12% reported being extremely confident vs. post-training=32%, p<0.001); apply CRM techniques (pre-training=4% reported being extremely confident vs. post-training=35%, p<0.001); and implement recommended treatment strategies for ACS (pre-training=18% reported being extremely confident vs. post-training=38%, p=0.002). Additionally, scores on a knowledge test significantly improved from the pre- to post-test (pre-training=61% correct vs. post-training=73%, p=0.003).[15]

Measures of participants' confidence and knowledge were also used as an indicator of learning in a study conducted by Tapson et al. (2011). They delivered CRM training to 160 surgical staff and surgeons with privileges at the participating hospital in an effort to increase teamwork and decrease venous thromboembolism (VTE). Following training, participants were significantly more confident in their ability to identify processes that could lead to errors (pre-training=35% reported being extremely confident vs. post-training=68%, p<0.001); use CRM techniques (pre-training=16% reported being extremely confident vs. post-training=62%, p<0.001); and identify surgical patients who should receive VTE prophylaxis (pre-training=20% reported being extremely confident vs. post-training=55%, p<0.001). In addition, substantial improvement was found in knowledge, as participants answered 43 percent of the questions correctly prior to the training and 72 percent immediately following the CRM training. Finally, significant improvements were also reported in three clinical processes. Specifically, a review of patient charts showed that significantly more cases met American College of Chest Physicians guidelines for standards in care for timing (pre-intervention=81% vs. post-intervention=94%, p=.024); inpatient duration (pre-intervention=89% vs. post-intervention=94%, p=.022);, and prophylaxis use beyond hospital discharge (pre-intervention=84% vs. post-intervention=96%, p=.0264). These findings suggest that the training had a positive impact on participant learning.[16]

Sax et al. (2009) also found positive results in learning following CRM training. Pre to post data indicated that participants felt significantly more empowered to speak up immediately after the CRM course. For example, they reported being significantly more comfortable communicating that an error was about to occur (pre-training mean=3.0 vs. post-training mean=3.4, p<.05); confronting mistakes made by a technician (pre-training mean=2.8. vs. post-training mean=3.7, p<.05); confronting mistakes made by a nurse (pre-training mean=2.8. vs. post-training mean=3.3, p<.05); and confronting mistakes made by a physician (pre-training mean=2.8. vs. post-training mean=3.2, p<.05). These findings suggest that trainees learned the importance of communication, which had been emphasized during the training.[17]

17.6.3.2.3 Process Measures: Transfer Criteria

The systematic review conducted by Weaver et al. (2014) included four studies that measured transfer of training on to the job. Collectively, the studies reported continued levels of confidence using CRM skills (sustained up to a 12-month followup), improvements in team skills on the job, and improvements in safety culture.[2] Similarly, the Hughes et al. (2016) meta-analysis found that team training resulted in a significant increase of KSAs demonstrated on the job (corrected standardized mean difference in a repeated measures metric=.67, *k*=63, 95% CI, .52 to .82).[13]

The individual CRM study conducted by Levy et al. (2014), which found improvements in learning, also found slightly longer term effects that support transfer. At a 30-day post-training check-in, the levels of increased confidence that participants had reported immediately after training had been sustained. Participants were significantly more confident in their ability to identify processes that could lead to errors as compared with in the pre-intervention period (pre=12% reported being extremely confident vs. follow-up=36%, p<0.001); apply CRM techniques (pre=4% reported being extremely confident vs. follow-up=37%, p<0.001); and implement recommended treatment strategies for ACS (pre=18% reported being extremely confident vs. follow-up=35%, p=0.002). Improvements in knowledge of CRM were also sustained at the 30-day post-intervention follow-up (61% vs. 66%, p=0.026). These data suggest that the CRM training resulted in positive transfer to the job.[15]

In their CRM effort, Mancuso et al. (2016) focused on improving communication surrounding cesarean births. CRM training and a pre-brief/debrief checklist for cesarean births were introduced to increase information shared by team members. Observational data collected during the pre-briefings and debriefings indicated that communication increased for both obstetric and neonatal teams. The number of team members who were fully engaged during the pre-brief in both teams increased following training, and was significant for the obstetrics team (number of obstetrics team members engaged before training=2.13, number after training=4.46, p<.001; number of neonatal team members engaged before training=2.78, number after training=3.18, p=.178). The amount of communication increased significantly for the obstetrics team during their within-team pre-brief (pre=31 vs. post=50, p<0.001); when they debriefed with the neonatal team (pre=10 vs. post=33, p<0.001); and during their within-team debriefings (pre=15 vs. post=36, p<0.001). Communication significantly increased for the neonatal team when they debriefed with the obstetrics team (pre=37, vs. post=48, p<0.001).Thus, this study provides partial evidence that CRM training resulted in increased participation and information sharing during briefings that occurred on the job.[18]

The study of CRM training conducted by Tapson et al. (2011) also collected data on Kirkpatrick's transfer criteria. Participants' confidence in their ability to use CRM techniques remained significantly higher at 30-day follow-up than at baseline (pre-training=21% reported being extremely confident vs. 30-day

post-training=55%, p<0.001). They also remained significantly more confident in their ability to identify which patients were appropriate candidates for VTE at the 30-day follow-up (pre-training=24% reported being extremely confident vs. 30-day post-training=48%, p=0.003). These findings suggest some longer term retention and transfer of training, although 30-day follow-up data were available only for a sample of 29 participants.[16]

Finally, Halverson and colleagues conducted two studies of a team-training program based on CRM principles and delivered to operating room staff. Both studies collected survey and observational data to assess whether the CRM training improved teamwork on the job. In the first study, Halverson et al. (2009) reported that perceptions of teamwork significantly improved on 14 of the 19 items measured 6 months following the training (p<.05); that is, respondents indicated that teamwork behaviors had increased following the CRM training. Some of the largest improvements were related to speaking up with persistence in the operating room (48% to 70%, p<.001) and leader communication/updates, especially during non-routine situations (46% to 63%, p<.001). However, results were mixed when evaluating transfer of training on clinical processes. Following the training, a substantial increase was observed in compliance with all required elements in time-outs (pre=47%, post=86%), indicating that the teams began conducting a more thorough pre-procedural verification process of the patient, surgical site, and planned procedure. However, there were no significant improvements in the timely administration of prophylactic antibiotics, nor in turnover times between surgical patients at the 6-month followup.[19] Together, these data (along with the positive participant reaction data reported) lend partial support for CRM training effectiveness, as improvements were observed in teamwork and in the one clinical process measured.

In their second study, also concerning the operating room, Halverson et al. (2011) examined the impact of CRM training on communication errors. Significantly fewer communication errors were observed in the post-training period, which occurred 6 to 9 months following the training, suggesting that participants applied what they had learned about communication from the CRM training (pre-training communication errors per hour=0.737, post-training communication errors per hour=0.270, p<0.001). Results concerning the consequences of the communication errors were mixed. On a positive note, errors were more frequently evaluated as having “no consequences” following the training (pre-training=12%, post-training=25%), as well as resulting in fewer inefficiencies (pre-training=24%, post-training=13%). However, the post-training period was associated with higher levels of tension due to the communication errors committed (pre-training=12%, post-training=17%), perhaps due to changes in expectations following the training.[14]

17.6.3.3 Clinical Outcomes: Results Criteria

The systematic review of team training conducted by Weaver et al. (2014) included nine studies of CRM. Four CRM studies in that review measured results through the collection of various clinical process and outcome measures. They reported that CRM was associated with improvements in clinical management scores, decreases in adverse outcome index (i.e., composite score of clinical outcomes), increases in standards in care (e.g., speed and completeness of resuscitations in the emergency department), and increased patient satisfaction.[2]

A meta-analysis conducted by Hughes et al. (2016) specifically examined the impact of healthcare team training on organizational results, such as safety climate and length of stay, and on patient outcomes, including patient satisfaction and mortality. Although they did not differentiate between specific team

training programs (such as CRM), they reported that team training had a positive impact on results (corrected standardized mean difference in a repeated measures metric=.37, k=47, 95% CI, .21 to .52) such as organizational outcomes (corrected standardized mean=.34, *k*=31, 95% CI, .19 to .49) and safety climate (corrected standardized mean difference in a repeated measures metric=.31, *k*=24, 95% CI, .14 to .48). Team training was also shown to improve patient outcomes (corrected standardized mean difference in a repeated measures metric=.38, *k*=20, 95% CI, .10 to .66).[13]

Overall, results from the systematic review, the meta-analysis, and individual studies demonstrated positive results on process measures. Specifically, trainees reacted positively to the CRM training across studies, improved their knowledge of teamwork, and reported greater confidence in using teamwork skills. Importantly, data also indicated that trainees increased their use of team KSAs back on the job. Finally, evidence that CRM resulted in improved patient safety (e.g., reduced length of stay, reduced mortality) was provided by one systematic review of CRM and one meta-analysis on team training programs in general.

17.6.3.4 Practice: TeamSTEPPS® Training

TeamSTEPPS is a team training program developed specifically for healthcare providers by the U.S. Department of Defense in collaboration with AHRQ. TeamSTEPPS training focuses on four trainable teamwork behaviors: communication, leadership, situation monitoring, and mutual support. The training imparts information on these behaviors, incorporates videos demonstrating positive and negative examples of the skills being used, and provides multiple tools that can be used to increase teamwork behaviors in healthcare settings. Although the TeamSTEPPS program has evolved over the years to include multiple settings (e.g., office-based care, long-term care), as well as online training modules, the studies in the current review followed the traditional TeamSTEPPS program for hospital settings.

17.6.3.5 Process Measures

Both the systematic review conducted by Weaver et al. (2014) and the meta-analysis conducted by Hughes et al. (2016) collected process measures related to reactions, learning, and transfer.[2,13] However, only the work of Weaver et al. reported findings by specific team training program/curriculum (e.g., TeamSTEPPS). The findings are presented in the following subsections. Additionally, six individual TeamSTEPPS studies were identified, which were conducted in an emergency department, a psychiatric unit, an obstetric unit, a pediatric intensive care unit (ICU), a surgical ICU, and among respiratory therapist staff. All of the studies reviewed collected process measures relevant to their setting. Two of the individual studies reported data on participant reactions and three collected measures of participant learning immediately following the training. Four studies collected post-training data at least 45 days following TeamSTEPPS training and are reported as indicators of Kirkpatrick's transfer criteria.

17.6.3.5.1 Process Measures: Reactions

One out of the seven TeamSTEPPS studies reviewed by Weaver et al. (2014) measured participant reactions as part of their training evaluations, with the majority of participants providing favorable reactions and indicating that the TeamSTEPPS training was useful to their work.[2] Likewise, Hughes et al. (2016) also reported that participants had positive reactions to team training efforts in healthcare (which included studies that used TeamSTEPPS).[13]

Evidence of reaction criteria was also provided by two individual TeamSTEPPS studies. Sonesh et al. (2015) delivered a condensed version of TeamSTEPPS training to obstetric (OB) clinicians. Overall, participants had positive feelings toward the training, with 85 percent indicating that they had enjoyed the training and 90 percent agreeing that they would likely apply the tools presented during the training on the job.[20]

Similarly, participants responded favorably when TeamSTEPPS training was delivered to operating room teams. For example, 94 percent of respondents indicated that the training content was appropriate and 81 percent believed that the training would help their organization improve patient safety.[21]

17.6.3.5.2 Process Measures: Learning

Two of the TeamSTEPPS studies reviewed by Weaver et al. (2014) collected measures of learning. The results were mixed: one of the studies found no changes in teamwork knowledge (i.e., no changes in cognitive-based learning) following the training, while the other study reported increased confidence in leadership and clinical management skills (i.e., increase in affective-based learning).[2] However, results from Hughes et al.'s (2016) meta-analysis provided full support for the hypothesis that team training in healthcare resulted in increased learning.[13]

In terms of individual studies reviewed, Sawyer et al. (2013) provided support of learning immediately following TeamSTEPPS training. They reported that immediately following the training, newborn intensive care unit personnel had significantly more positive attitudes toward teamwork (pre-training mean=4.4 vs. post-training mean=4.7, p<.001) and significantly greater knowledge of teamwork (pre-training mean=86.6% vs. post-training mean=92.6%, p<.001). In addition, significant improvements were noted in all five teamwork dimensions: team structure (pre-training mean=2.5 vs. post-training mean=4.2, p <.001); leadership (pre-training mean=2.6 vs. post-training mean=4.4, p<.001); situation monitoring (pre-training mean=2.5 vs. post-training mean=4.3 p<.001); mutual support (pre-training mean=2.9 vs. post-training mean=4.3, p<.001); and communication (pre-training mean=3.0 vs. post-training mean=4.4 p<.001).[22]

The effort by Sonesh et al. (2015), which delivered TeamSTEPPS training to OB clinicians, examined participants' knowledge of situation awareness and teamwork before and after the training as an indicator of learning. No significant improvements were reported in learning in this study (p>.05).[20]

Based on behavioral observations in the operating room (OR), Weaver et al. (2010) reported some improvements in learning in their TeamSTEPPS study. They reported that trained teams engaged in significantly more pre-briefings than the control group (p<.001) and that significantly more team members participated in the pre-briefings (i.e., shared information) compared with control teams (p<.001). Additionally, observations made during surgery indicated that trained teams significantly improved on two teamwork behaviors following the training: communication (p<.05) and mutual support (p<.01). Taken together, these studies provide some evidence of participant learning as result of TeamSTEPPS.[21]

17.6.3.5.3 Process Measures: Transfer

Weaver et al.'s (2014) systematic review included six studies that measured transfer of TeamSTEPPS training onto the job. Overall, the studies reported a variety of positive results related to transfer, including satisfaction with process improvements (maintained for up to 2 months), sustained use of performance tools to increase teamwork (at a 3-month followup), improved perceptions of teamwork

(some of which were sustained for up to 12 months), and some improvements in participants' perceptions of safety.[2] Further support of transfer of team training was provided by Hughes et al. (2016). Results of their meta-analysis, which included TeamSTEPPS studies, indicated a significant increase in KSAs on the job following healthcare team training programs.[13]

Four individual studies also collected measures to assess transfer of TeamSTEPPS training. The first study provided TeamSTEPPS training in an emergency department of an academic medical center.[23] Repeated measures of communication climate and knowledge of teamwork were taken prior to training and at two points (45 days and 90 days) following training. The communication climate subscale of AHRQ's Hospital Survey on Patient Safety demonstrated significant improvements on all subscale items at both 45 and 90 days after training (p=.05). Scores on the TeamSTEPPS Knowledge Test also significantly improved on 15 of the 21 items at the 45-day followup, and were sustained on 13 of the 21 items at the 90-day follow-up. Huddles and the CUS script ("I am Concerned," "I am Uncomfortable," "This is a Safety issue") were chosen as TeamSTEPPS strategies to implement following the training to improve communication. Huddles occurred 64 percent of the time, and 47 percent of survey respondents indicated that they had used the CUS technique at least once. Collectively, these data provide moderate evidence that KSAs had been applied on the job as a result of the TeamSTEPPS training.[23]

In their study of a psychiatric unit, Mahoney et al. (2012) reported significant improvement on five out of seven dimensions measured by the Team Assessment Questionnaire 12 months following TeamSTEPPS training. Significant improvements were found related to: team foundation (pre-training=3.76, post-training=4.10, p=.001); team functioning (pre-training=3.88, post-training=4.16, p=.003); team performance (pre-training=3.78, post-training=4.10, p=.001); team skills (pre-training=3.76, post-training=4.08, p=.001); and climate and atmosphere (pre-training=3.68, post-training=3.97, p=.004). While no significant change was found on team leadership (pre-training=4.07, post-training=4.23, p=.122) or team identity dimensions (pre-training=4.09, post-training=4.22, p=.156), the mean scores for these two dimensions were high prior to the training and increased over time. Given that the post-training measure was collected 12 months after the training, this study demonstrates sustained improvement in teamwork.[24]

A study of a customized 2.5-hour version of TeamSTEPPS training (delivered to all pediatric ICU, surgical ICU, and respiratory therapist staff) conducted by Mayer et al. (2011) also examined participant learning. They found significant improvements in observed teamwork skills, a clinical process, and safety climate. Using the Teamwork Evaluation of Non-Technical Skills observation tool, scores on all six teamwork dimensions significantly improved from baseline to 1 month after the training (p<.01). Moreover, scores on five of the six teamwork dimensions were significant (p<.01) at a 12-month assessment (with the exception of situation monitoring), indicating long-term behavioral change. Data gathered on clinical processes revealed improvement as a result of the TeamSTEPPS training as well. Specifically, the average time to place patients on an extracorporeal membrane oxygenation life support machine was significantly lower after training (pre-training=23.00 minutes, post-training=13.96 minutes, p=0.02). Mayer et al. reported that pre- to post-scores on the Hospital Survey on Patient Safety Culture significantly increased on two subscales (i.e., "overall perceptions of safety" and "communication openness") for participants in both units.[25]

Finally, Sonesh et al. (2015) also examined whether TeamSTEPPS training resulted in improved teamwork on the job. Data collected using the Teamwork Perceptions Questionnaire showed that self-

reported perceptions of teamwork had improved on all four TeamSTEPPS behaviors, but these increases were not statistically significant ($p > .05$). However, additional data from behavioral observations of patient-related decisions indicated that more-accurate decisions were made 1 to 3 months following the training (pre-training accuracy=61.54% vs. post-training=82.9%, $p<.05$).[20] Therefore, this study provides some evidence of improved performance on the job.

17.6.3.6 Clinical Outcomes: Results Criteria

Four studies in the Weaver et al. (2014) review used TeamSTEPPS and reported improved clinical outcomes such as reductions in surgical morbidity, lower infection rates, and decreases in adverse events reported. Hughes et al.'s (2016) meta-analysis found support that healthcare team training (including TeamSTEPPS) improves results. including organizational outcomes, safety climate, and patient outcomes.

Three of the individual studies of TeamSTEPPS in the review gathered outcome measures that align with results criteria from Kirkpatrick's evaluation framework. Mayer et al. (2011) delivered a customized, 2.5-hour version of TeamSTEPPS training to minimize the time that staff were away from clinical work. The training, delivered to all pediatric ICU, surgical ICU, and respiratory therapist staff, had a positive impact on the clinical outcome variable collected. Following the training, the rate of nosocomial infections was consistently lower in the pediatric ICU (i.e., in 7 out of 8 post-intervention months) and intermittently lower in the surgical care unit (i.e., in 4 out of 8 post-invention months).[25]

As part of their TeamSTEPPS study of OB clinicians, Sonesh et al. (2015) examined several patient outcomes in their study, including length of stay for infants, length of stay for mothers, transfer to the newborn intensive care unit, and morbidity of infants. The only outcome that approached statistical significance was length of stay for infants, which decreased from 3.85 days to 2.83 days ($p=.07$) over the course of the study.[20]

Weaver et al. (2010) measured the impact of TeamSTEPPS training on safety culture to demonstrate larger organizational results criteria. Pre- to post-comparisons on the Hospital Survey on Patient Safety Culture showed that the teams trained in TeamSTEPPS significantly increased their percentage of positive responses following the training. However, safety culture scores also increased over the pre- and post-assessment for the teams in the control group. The authors noted that their results should be interpreted cautiously, especially given that a total of only three teams had been trained (approximately 29 individuals).[21]

Taken together, the TeamSTEPPS studies reviewed provided positive support for this practice on process measures such as trainee reactions. Although the studies provided partial support for the idea that the TeamSTEPPS training increased participant learning, each study that collected data on longer term transfer of training provided moderate evidence that team KSAs were applied on the job. Likewise, moderate improvements in patient outcomes were associated with the TeamSTEPPS training.

17.6.3.7 Practice: MTT

In 2007, the Veterans Health Administration (VA) introduced its own team training program, MTT. MTT focuses on improving communication through a training workshop, as well as on the job through the implementation of team briefings before and after surgical cases.

17.6.3.8 Process Measures

In their systematic review, Weaver et al. (2014) included three studies of MTT that collected process measures, while Hughes et al. (2016) provided evidence on these criteria for healthcare team training programs in general.[2,13] In addition, the current review identified two individual studies of MTT. None of the individual studies identified reported data on participant reactions, nor did they collect measures of learning immediately following the training. One study collected process measures as an indicator of transfer of training.

17.6.3.8.1 Process Measures: Transfer

One study included in Weaver et al.'s (2014) systematic review measured transfer of training following the VA's MTT; significant improvements in teamwork climate items were reported for physicians and nurses.[2] Further support of transfer of team training was provided by Hughes et al. (2016), who reported significant increases of KSAs on the job following team training.[13]

In an individual study conducted by Wolf et al. (2010), MTT was delivered to OR personnel, and a standard briefing/debriefing protocol was developed. Based on follow-up data collected 12 to 17 months after the training, improvements were reported on all Safety Attitudes Questionnaire domains, with significant improvements noted on two domains: perceptions of management (p=0.003) and working conditions (p=0.004). In addition, case delays due to staffing issues, equipment problems, or patients not being fully prepped for surgery decreased significantly over the study period, signifying improved workflow and use of resources. At the 12-month follow-up, delays had dropped from 23 percent to 10 percent (p<0.0001); they were at 8 percent at the 24-month follow-up (p=0.09).[26] These data suggest the longer term impact that the team training program had on participants' attitudes and clinical processes.

17.6.3.9 Clinical Outcomes: Results Criteria

Two studies included in Weaver et al.'s (2014) systematic review measured patient outcomes as part of their evaluation of the VA's MTT program. One study, conducted by Young-Xu et al. (2011), was also identified in the current review and will be reported as an individual study. Since the meta-analysis conducted by Hughes et al. (2016) grouped all team training programs together, we remind the reader that they found that team training resulted in improved outcomes.

In the individual study conducted by Young-Xu et al. (2011), data collected on annual surgical morbidity rates after MTT were compared with the rates 1 year prior to the training. They showed a significant decrease (17%) in the observed annual morbidity rate for the facilities that had participated in MTT (rate ratio, 0.83; 95% CI, 0.79 to 0.88; p=.01), whereas the facilities that had not participated in MTT observed a decrease of 6 percent, which was not statistically significant (rate ratio, 0.94; 95% CI, 0.86 to 1.05; p=.11).[27] The second study of MTT included in Weaver et al.'s review found a reduction in risk-adjusted surgical mortality for the group that had participated in MTT, but this was not statistically significant.[2]

Unlike the CRM and TeamSTEPPS studies, none of the studies of MTT measured participant reactions or learning. Results from the few studies that evaluated MTT provide evidence that team KSAs learned during the training were later applied on the job and resulted in improved patient outcomes (i.e., decreased morbidity rates, reduced surgical mortality).

17.6.3.10 Practice: Team Simulation

Simulation is another method used to improve teamwork skills. Simulation provides teams with realistic scenarios that they may face, either routinely or in emergencies. These scenarios allow participants to practice critical teamwork behaviors and receive feedback. As noted in the review by Weaver et al. (2014), simulation is commonly used to train healthcare teams and can have high or low fidelity.[2] High-fidelity simulations refer to those that strongly mimic real life scenarios, the actions that should be taken by the participant(s), and the actual work environment, including equipment and patients. Low-fidelity simulations present realistic scenarios and require participants to react as they would in the real world but do not replicate all aspects of the environment (e.g., a doll could be used in place of a mannequin).

17.6.3.11 Process Measures

One systematic review[12] presented evidence that team simulation improves team processes such as communication and situational awareness. None of the individual studies in the current review reported participant reactions to simulation team training. Seven of the studies assessed participant learning immediately following the simulation intervention and reported improvements. One study of simulation team training reported data on transfer criteria.[12] The meta-analysis conducted by Hughes et al. (2016) also provided evidence that simulation improves processes.[13]

17.6.3.11.1 Process Measures: Learning

In their systematic review, Dietz et al. (2014) reported that five studies used simulation-based team training as a strategy to improve teamwork in the ICU. All five studies used high-fidelity simulators and reported positive impacts on learning such as improvement in teamwork skills.[12] Hughes et al. (2016) reported that high-fidelity simulation was not more effective than low-fidelity simulation when examining participant learning (high-fidelity: corrected standardized mean=.66, *k*=10, 95% CI, .23 to 1.08; low-fidelity: corrected standardized mean=2.76, *k* =4, 95% CI, .53 to 6.06).[13]

Lutgendorf et al. (2017) investigated the use of multidisciplinary obstetrics simulation to manage postpartum hemorrhage cases and collected measures of participant learning. For example, they examined the use of established protocols, as well as teamwork and communication during postpartum hemorrhage cases. After 16 simulations and corresponding debriefings following TeamSTEPPS principles, participants reported significantly higher comfort levels (1=very uncomfortable, 5=very comfortable) in dealing with hypertensive emergencies (pre-intervention mean=3.88, post-intervention mean=4.14, p=0.01); shoulder dystocia (pre-intervention mean=3.66, post-intervention mean=4.29, p=0.001); and postpartum hemorrhage (pre-intervention mean=3.86, post-intervention mean=4.35, p=0.001). Findings from this study suggest that the simulation exercises increased learning of and confidence in applying CRM material, and the participants were better prepared to address issues that occurred in postpartum hemorrhage cases.[28]

Paull et al. (2013) measured pre to post change following simulation-based CRM training. Following the training, participants from 12 VA facilities completed two simulated scenarios and were debriefed immediately afterward. Participants' confidence in their ability to engage in teamwork was measured before and after the training using the Self-Efficacy of Teamwork Competencies Scale (e.g., "All team members are committed to performing as a highly effective team," "The team has a shared understanding of its plan of action"). Significant changes in mean scores were reported for all eight items in the post-intervention period. Improvement on individual items ranged from 13 percent to 26

percent (p<.05). Significant improvement was also observed in the participants' use of the targeted teamwork skills from the first to second simulated scenario (improvement on teamwork skills ranged from 15% to 23%, p<.05). The only skill for which no significant change was noted was "resource allocation," a specific behavior under the situational awareness dimension.[29]

Another study delivered a team training workshop to two groups of 41 first-year interns working in a trauma department.[30] Following the didactic instruction, all interns completed four high-fidelity simulations and received feedback on their performance. Half of the interns completed the simulations on the first day (Group 1), while the other half completed the scenarios on the second day (Group 2). Pre- and post- Situational Judgement Tests indicated that participants in both groups increased their scores on the test following the training, suggesting that their decisions became closer to that of a subject matter expert. However, only the participants in Group 2 showed significant improvement (Group 1 pre-mean=15.63, post-mean=17.29, p<0.10; Group 2 pre-mean=13.77, post-mean=16.55, p<0.01). This study provides limited evidence that team training with simulation significantly increases participant learning.[30]

Similarly, Riley et al. (2011) tested the impact of using team training alone (i.e., didactic training only) or using team training with simulation (i.e., didactic training plus simulation) on neonatal outcomes and culture of safety within three small community hospitals. However, their findings did not support participant learning. There were no changes in safety culture scores (as measured by the Safety Attitudes Questionnaire) after either of the interventions.[31]

A slightly different approach was taken by Thomas et al. (2010). They examined the impact of low-fidelity skills stations (control group), team training with low-fidelity skills stations, and team training with high-fidelity skills stations on teamwork and the quality of resuscitation skills. The study was conducted with interns for pediatrics, combined pediatrics and internal medicine, family medicine, emergency medicine, and obstetrics and gynecology completing the Neonatal Resuscitation Program. Results suggested that the team training intervention had positive impacts on learning. Compared with the control group, interns in the station group with team training with high-fidelity skills exhibited significantly greater rates of teamwork behaviors (control group mean=9.0, team training with high-fidelity skills station=12.8, p <0.001). The groups that received team training and either form of simulation (i.e., high-fidelity or low-fidelity mannequins) handled workload management significantly better than participants in the control group (p<.001) and completed the resuscitation more quickly than the control group (control subjects=average of 10.6 minutes; team training with low-fidelity simulation=8.6 minutes, p<.040; team training with high-fidelity simulation=7.4 minutes, p<.001).[32]

One study in the review implemented stand-alone simulation training (i.e., without the use of team training) in acute-care medical units.[33] Participants completed 17 simulation exercises in which they responded to a cardiopulmonary arrest. Perceptions of only one of the five teamwork dimensions measured with the TeamSTEPPS Teamwork Perceptions Questionnaire (i.e., leadership) significantly improved following the simulation intervention (pre-training mean=2.167 vs. post-training mean=2.566, p=.003). However, as the authors noted, greater change might have resulted had the participants received TeamSTEPPS training prior to (or in conjunction with) the simulation training.[33]

17.6.3.11.2 Process Measures: Transfer

Four studies in Boet et al.'s (2014) systematic review of simulation team training collected data on transfer of training. Simulation team training was found to result in significantly greater transfer of KSAs on the job when compared with the group that had received only didactic team training or the no-intervention group.[11] Additionally, the use of high-fidelity simulation did not results in greater transfer of KSAs on the job than low-fidelity simulation in the Hughes et al. (2016) meta-analysis (high-fidelity: corrected standardized mean=.54, *k*=13, 95% CI, .27 to .80; low-fidelity: corrected standardized mean .71, *k*=8, 95% CI, .34 to 1.08).[13]

The individual study conducted by Thomas et al. (2010) collected data at a 6-month follow-up to assess whether longer term transfer of training had occurred. Participants who had received the team training with some form of simulation engaged in significantly more teamwork behaviors during neonatal resuscitation scenarios than participants in the control group (intervention group=11.8 teamwork behaviors/minute vs. control group=10 teamwork behaviors/minute). The significant improvements that had been achieved immediately following the intervention related to workload management and length of resuscitation were not sustained at the 6-month follow-up.[32]

17.6.3.12 Clinical Outcomes: Results Criteria

Several studies cited by Weaver et al. (2014) used simulation (both high- and low-fidelity) to improve knowledge, attitudes, and teamwork behaviors, as well as improve outcomes such as mortality and morbidity. In particular, two studies achieved significant improvements in clinical outcomes without the use of high-fidelity simulations.[2] A second systematic review of simulation team training (Boet et al., 2014) reported that five studies measured patient outcomes to provide evidence on results criteria. These studies found some improvements in efficiency of patient care and decreases in complication rates, and one demonstrated that simulation-based team training significantly improved patient mortality.[11]

Fifty (38.8%) of the 129 team training studies included in a meta-analysis conducted by Hughes et al. (2016) included simulation as part of their intervention (33 used high fidelity; 17 used low fidelity). They reported that high-fidelity simulation was not more effective than low-fidelity simulation (high-fidelity: corrected standardized mean=.80, *k*=30, 95% CI, .59 to 1.01; low-fidelity: corrected standardized mean=1.01, *k*=11, 95% CI, .09 to 2.10). As a result, the authors concluded that while high physical fidelity may be important in training technical skills, it is not necessary when attempting to improve non-technical skills such as communication. Thus, the authors suggested that greater emphasis should be placed on developing scenarios that have high psychological fidelity in team improvement efforts.[13]

Two of the five individual studies in the present review collected outcome measures to evaluate results in their simulation efforts. Riley et al. (2011) tested the impact of using team training alone (i.e., didactic training only) against using team training with simulation (i.e., didactic training plus simulation) on neonatal outcomes and culture of safety within three small community hospitals. They found that the group who received the full intervention (a condensed TeamSTEPPS didactic training course coupled with 11 simulation exercises over the course of 12 months) significantly decreased their Weighted Adverse Outcomes Score (WAOS) from 1.15 to 0.72 ($p<0.05$) over the study period. The WAOS for the group that received only the condensed TeamSTEPPS didactic training remained stable (pre-intervention mean=1.46, post-intervention mean=1.45, nonsignificant), and the WAOS for the control group

increased over the study period from 1.05 to 1.50. Thus, the simulation exercises seem to have been integral to the improvements observed in outcomes.[31]

Using a sample in which 92 percent of the participants had previously received TeamSTEPPS training, Lutgendorf et al. (2017) investigated the use of multidisciplinary obstetrics simulation to manage postpartum hemorrhage cases. Sixteen simulations were conducted over a 2-day period, each followed by a structured debriefing. The data suggested that simulation improves outcomes, as the length of time to prepare blood products decreased on the second day of exercises (6 minutes on the first day vs. 4 minutes on the second day). A downward trend was also observed in postpartum hemorrhage cases following the 2-day simulation intervention as compared with the baseline period.[28]

In summary, participant learning was the most commonly collected measure across the simulation studies reviewed. The majority of studies reported that participants had increased their confidence in using teamwork skills and demonstrated teamwork skills more frequently following the simulation intervention. The results on transfer of training were mixed, with some studies demonstrating that the use of team-related KSAs was sustained over time, while one study did not report sustained improvement. Lastly, the studies that measured results-level criteria reported some improvements in patient outcomes such as efficiency of patient care and decreased complication rates.

17.6.3.13 Practice: Briefings

Briefings have a long history of use in the field of aviation and have been included as a tool within healthcare CRM programs, as well as in the TeamSTEPPS training program. Prebriefings help set the stage for teamwork by reviewing tasks that need to be accomplished, identifying which team member(s) will be responsible for each task, and discussing any contingency plans. Debriefings then review (post-performance) what went well and what could have gone better, with the goal of improving performance in the future. As noted by Kessler et al. (2015), debriefings can cover a combination of individual and team performance as well as system issues.[34]

17.6.3.14 Process Measures

Two of the three studies that examined the effectiveness of briefings collected process measures. One study collected process measures immediately following the intervention, which are treated as measures of learning. In the second study, evaluation data were collected more than 30 days after the intervention had been introduced, and these data are treated as an indicator of transfer criteria.

17.6.3.14.1 Process Measures: Learning Criteria

A study of resuscitation teams examined the effectiveness of a debriefing program following pediatric cardiac arrest cases (Wolfe et al., 2014). Structured debriefings were conducted within 3 weeks of a chest compression event. During the debriefing intervention period, chest compressions were significantly more likely to meet quality targets associated with excellent cardiopulmonary resuscitation (95% CI, 2.9 to 10.6, $p<0.01$). Reviewing the cardiac arrest cases during the structured debriefings appeared to have led to increased learning and to the achievement of improved clinical processes.[35]

17.6.3.14.2 Process Measures: Transfer Criteria

One of the three studies of briefings collected process measures to assess transfer of KSAs on the job. Kleiner et al. (2014) introduced a coach to help improve communication during surgical briefings and debriefings. Observations of the frequency and quality of briefings and debriefings were collected. No

differences in the frequency of briefings and debriefings were observed in the OR prior to or after the coaching, as they occurred 100 percent of the time in both study periods. However, differences were reported in the quality of the briefings and debriefings. Following the coaching intervention, the average briefing score increased significantly, from 3.478 to 3.644 (p=.044), indicating increased use of a standardized checklist, and that team members were introduced more consistently, there was greater discussion about contingency plans, and team members were given the opportunity to ask questions. Similarly, the average debriefing score significantly increased from 2.377 to 2.991 (p<.0001). In the post-intervention period, a standard checklist was used more frequently, teams more often discussed what went well and what did not go well, and team members were thanked. Therefore, this study supports the idea that team communication can be improved during pre-briefings and debriefings and that changes were sustained on the job.[36]

17.6.3.15 Clinical Outcomes: Results Criteria

Two of the three studies of briefings assessed patient outcomes and provide evidence on Kirkpatrick's results criteria. First, the study of resuscitation teams conducted by Wolfe et al. (2014) examined the effectiveness of a debriefing program following pediatric cardiac arrest cases. A comparison of 60 historical control cases and 59 interventional cases showed improvement in survival to hospital discharge for cases in the debriefing intervention group (52% for debriefed cases vs. 33% for control cases, p=0.054). Survival with favorable neurological outcomes significantly increased for the cases in the debriefing intervention group as well (50% for debrief cases vs. 29% for control cases, p=0.036).[35]

Second, Murphy et al. (2015) assessed the effectiveness of roundtable debriefing on patient fall rates in the emergency department. Roundtable debriefings were held weekly to discuss patient falls that had occurred in the department over the previous week. They found that fall rates declined somewhat in the post-intervention period (14 months after the intervention had been introduced), but there were no statistically significant differences in the number of assisted falls (p=0.17) or unassisted falls (p=0.28) and the rate of falls per 1,000 patient encounters (p=0.28) as compared with the pre-intervention period. This finding was unexpected, since the authors had observed a decrease in falls in other inpatient acute areas as a result of using roundtable debriefings. They attributed the lack of consistent results to differences between the acute care and emergency department settings.[37]

Overall, the review included few studies of briefings. One study provided evidence that briefings led to increased participant learning, and another demonstrated that briefings led to transfer of team KSAs on the job. Two studies reported that briefings were associated with favorable patient outcomes; however, only one found significant improvements. Due to the limited number of studies, it is difficult to draw conclusions regarding the effectiveness of this practice.

17.6.3.16 Practice: Handoff Protocol

Handoff protocol is a tool that can be used to increase teamwork during patient transitions. Such transitions occur between shifts within a unit or when a patient is transferred from one unit to another (e.g., from the OR to the surgical ICU). During this time, critical information needs to be passed that, if missed, can affect the quality of care. A standardized handoff protocol can ensure that information is consistently exchanged between providers.

17.6.3.17 Process Measures

All three studies employing handoffs collected process measures as part of their evaluation. Two of the studies reported reaction criteria in the form of satisfaction with handoffs. Two of the studies collected measures of learning immediately following the introduction of their handoff protocol. Two studies reported data on the transfer of KSAs into the work environment following the handoff intervention.

17.6.3.17.1 Process Measures: Reactions Criteria

A study by Petrovic et al. (2015) provided training on a new handoff protocol in a perianesthesia care unit, and pocket-sized informational cards were distributed as job aids. The authors found that satisfaction with the new handoff protocol varied by team member role, with nurses in the unit reporting greater satisfaction than anesthesia providers. Nurses showed significant improvement on five of the nine satisfaction survey items, while satisfaction scores for anesthesia providers declined slightly (but not significantly) in the post-intervention period. Pre-intervention satisfaction data were not available for surgeons because they were not present at bedside handoff in the baseline period, but surgeons reported high levels of satisfaction with the new handoff protocol (ranging from 91% to 97% favorable on the post-satisfaction survey).[38]

Krimminger et al. (2018) studied a structured handover process between the OR and ICU to reduce information sharing errors. Data from this study indicated that satisfaction with handovers increased in the post period on all satisfaction survey items, with 8 out of the 12 items showing significantly greater satisfaction ($p<.05$).[39]

17.6.3.17.2 Process Measures: Learning Criteria

Mukhopadhyay et al. (2018) introduced a standardized handoff tool to improve communication during patient transfers from the OR to a surgical ICU. Key parts of the handoff included: presence of key caregivers, identifying the patient and members of the care team, a detailed surgical report, a detailed anesthesia report, and the duration or occurrence of key activities. Thirty-one handoffs were observed before and after the new protocol was introduced, with slight improvements in efficiency observed in the post-intervention period. Specifically, the average time for patients to be placed on the ventilator (pre-intervention mean=86 seconds, post-intervention mean=74 seconds) and time to complete transfer to ICU monitors slightly decreased (pre-intervention mean=133 seconds, post-intervention mean=106 seconds), but these changes were not statistically significant.[40] Therefore, the handoffs were associated with slight, but not significant, improvements in care processes.

Petrovic et al. (2015), in their study of a new handoff protocol introduced in a perianesthesia care unit, observed that surgery providers became significantly more involved in the handoff process 2 weeks following the handoff protocol (pre-intervention=21%, post-intervention=83%, $p<.01$). The total number of defects per handoff decreased following the handoff intervention (pre-intervention=9.92, post-intervention=3.68, $p<.01$), with a significant decrease in both communication errors and technical defects. Specifically, the average number of items missing dropped from 2.02 to 0.94 ($p<.01$) on the anesthesia reports and dropped from 7.75 to 2.64 on the surgery report ($p<.01$). These data suggest that the handoff protocol was effective in improving teamwork and information sharing. However, while the authors had expected that the handoff protocol would not increase transition times, the duration of the handoff did increase (pre-intervention period=9.0 minutes, post-intervention period=11.0 minutes, $p=.01$) due to the increase in items covered during the handoff process.[38]

17.6.3.17.3 Process Measures: Transfer Criteria

Two of the three studies employing handoffs collected process measures consistent with Kirkpatrick's transfer criteria. The study conducted by Mukhopadhyay et al. (2018) found that several elements of the handoff had demonstrated significant improvement 6 months after the handoff protocol implementation. First, the presence of a surgical team member at handoff significantly improved, from 32 percent to 84 percent of the time ($p<0.001$), and physician team member presence at handoff increased significantly, from 52 percent to 94 percent ($p<0.001$). Second, all information regarding the surgical procedure was relayed significantly more frequently in the post-intervention period, with the greatest increase observed on "further interventions" (4% to 81%, $p<.001$) and the smallest increase on "procedure performed" (29% to 84%, $p <.05$). Third, positive results were found on the anesthesia report, where all pieces of information increased from pre- to post-intervention, with 7 of the 15 elements increasing significantly.[40]

In the study of a structured handover process between the OR and ICU[39], data were collected to assess longer term changes related to the handover intervention. Observations made prior to and 6 months following the handover implementation showed a significant decrease in both the number of process errors (pre-intervention=6.1, post-intervention=2.8, $p<.001$) and information sharing errors in the post-intervention period (from 5.2 per handover to 2.3 per handover, $p<.001$). The duration of the handover increased from the pre- to post-intervention periods, from 13.2 minutes to 14.6 minutes, although this increase was not statistically significant. Therefore, the handover resulted in fewer information sharing and process errors.[39]

In sum, the small number of studies implementing handoff protocols provide limited evidence of their effectiveness. Two studies reported favorable reactions to the use of the handoff protocol. Evidence of participant learning was also provided by two studies, with the handoff protocol significantly improving the efficiency of care processes in one study, and resulting in greater information sharing and in fewer communication errors in the second study. Similarly, positive transfer of team KSAs on the job was reported for up to 6 months following the introduction of the handoff protocol. However, none of the studies that implemented handoff protocols collected data on patient outcomes.

17.6.3.18 Practice: Checklists

Checklists constitute another tool that has historically been used in the aviation industry, specifically during the pre-flight phase. Checklists are well suited for completing procedural tasks and have been implemented as a way to improve teamwork (especially to increase communication among team members) and to reduce technical errors.

17.6.3.19 Process Measures

Two of the three studies employing checklists collected process measures. One of the studies collected participant satisfaction with the checklist (i.e., reactions). Two studies incorporated measures of participant learning to evaluate the effectiveness of their checklist tool, and one study reported evidence of transfer.

17.6.3.19.1 Process Measures: Reactions

A study conducted by Fargen et al. (2013) introduced a checklist to improve communication in the neurointerventional suite. Opinion surveys gathered from 21 participants were positive, with 95 percent indicating that the use of the checklist should continue.[41]

17.6.3.19.2 Process Measures: Learning

A study conducted by Fargen et al. (2013) in the neurointerventional suite also collected a measure of learning over a 4-week period immediately following the introduction of the checklist. They reported that communication during procedures (as rated by staff) significantly improved in the cases where the checklist was used (baseline=38.8% were rated as excellent, 43% were rated as good; post-intervention=68.2% were rated as excellent, 28.8% were rated as good, $p<0.001$).[41]

Based on observations and audits of their OR, Porter et al. (2014) revised their preprocedural pause (PPP) checklist to increase participation and communication among all members of the operating team. The revised checklist (based on the World Health Organization surgical checklist) required that each team member be responsible for a specific section. Compliance with the PPP increased from an average of 78 percent of cases in the baseline period to 96 percent of cases in the period immediately following the revisions ($p<.0001$). Team member self-introductions also increased from an average of 44 percent in the baseline to 94 percent immediately following the intervention ($p<.0001$). The proportion of cases in which all checklist items were completed rose from 54 percent in the baseline to 97 percent of cases in the post-intervention period (no statistical analysis reported). These data suggest that participants learned the importance of using the checklist.[42]

17.6.3.19.3 Process Measures: Transfer

In addition to their measure of learning, Porter et al. (2014) also assessed transfer of KSAs to the job. Their finding that PPP compliance had significantly increased to 96 percent immediately following the introduction of the revised PPP checklist was sustained at an 18-month audit, in which compliance remained at 96 percent. Similarly, team member self-introductions, which were reported to occur 94 percent of the time immediately following the intervention, continued to increase slightly at the 18-month audit (97%, $p<.0001$). Thus, Porter et al. found support of sustained transfer of team KSAs as a result of the checklist intervention.[42]

Overall, very few studies in the review evaluated the effectiveness of checklists. The one study that collected participant reactions reported high satisfaction among users of the checklist. Improvement in participant learning was also reported in one study, in which greater compliance using the checklist was noted directly after the training, and sustained compliance with the checklist was reported up to 18 months following the intervention (i.e., positive transfer). While only two of the studies collected data on patient outcomes, both reported a decrease in adverse events in the post-intervention period.

17.6.3.20 Clinical Outcomes: Results Criteria

Two of the three studies reviewed tested the effectiveness of checklists by collecting data on Kirkpatrick's results criteria. Both studies provide evidence for the use of checklists for improving team performance. Fargen et al. (2013) introduced a checklist based on the World Health Organization surgical checklist to increase communication and reduce adverse events in their neurointerventional suite. The overall number of adverse events decreased after the implementation of the checklist as compared with in the baseline period (6 events with the checklist vs. 25 in the baseline/without the checklist, $p=0.001$). When examined individually, eight of the nine specific adverse events/near misses decreased after the checklist had been implemented (but these changes were not significant) and one adverse event/near miss remained the same (i.e., maximum contrast dose exceeded).[41]

Bliss et al. (2012) reported that cases in which a surgical safety checklist was used were associated with significantly lower adverse event rates. Data from three cohorts were evaluated: a historical control group; a cohort that had received team training but did not use a checklist; and a cohort that had received team training and used the checklist. Comparison of 30-day morbidity revealed that the adverse event rate was 23.6 percent for the historical control group, 15.9 percent for the team training only cohort, and 8.9 percent for the team training with checklist cohort (p=0.000). Thus, the cohort that received team training and used the checklist had the lowest rate of adverse events.[43]

17.6.4 Conclusion and Comment

17.6.4.1 Implementation

The majority of studies in the current review were conducted in a hospital setting and focused on improving teamwork among frontline staff. Studies varied in their approach, with some relying on team training programs to improve teamwork and some implementing tools aimed at enhancing teamwork directly in their work settings. In some instances, a teamwork intervention that had been successfully implemented in at least one unit or clinical area at a given institution was extended and tested in another.[18, 37] In other cases, the study reviewed served as a jumping-off point for the institution, with plans to introduce the training and/or tools in additional clinical areas in the future.[19,21]

In terms of team training programs, training was most often delivered in a 4- to 5-hour session and evaluated within a specific unit (e.g., obstetrics, ICU), although some studies conducted training at the hospital level.[15] Post-training measures were collected anywhere from 30 days to 18 months following the training. Interestingly, few studies reported reaction data, instead reporting measures of learning, transfer, and results, which are better indicators of training effectiveness.[8,9] Improvements were demonstrated on a variety of process measures (indicative of reaction, learning, and transfer criteria) and outcome measures (i.e., results criteria) relevant to the participants' settings.

Studies reviewed also used simulation and other performance support tools such as briefings, checklists, and handoff protocols to enhance teamwork. Consistent with Hughes et al. (2016) and Weaver et al. (2014), studies used simulation in conjunction with team training programs, and one study used simulation as a standalone strategy. Tools to foster teamwork and communication were introduced in a mixture of units/departments, including surgical units, ICUs, emergency departments, and perinatal units. Across studies, these low-cost tools demonstrated positive impacts on the processes and clinical outcomes measured, with sustained improvements reported 6 to 18 months following implementation.

As cautioned by Rosen et al. (2018), tools such as checklists and briefings may appear to require less time or fewer resources to implement than team training programs such as those described in the current review.[44] However, time and due diligence are needed to educate staff on why the selected tool is being implemented, how to use the tool, and how the tool fits into the established workflow. Once implemented, new protocols sometimes required greater time and participation by the entire team to ensure all elements were covered. For example, increases in the length of handoffs were reported by Krimminger et al. (2018) and Petrovic et al. (2015).[38,39] The protocol introduced by Porter et al. (2014) required that more members of the OR team take an active role in completing the PPP checklist.[42] While this can lead to resistance and dissatisfaction in some cases, the new protocols also led to more engaged teams, more information being exchanged, and fewer errors.

The importance of leadership involvement and project champions was stressed across studies regardless of the specific practice used to improve teamwork.[19,24,26,42] Leadership support is needed not only to help get a practice off the ground, but also to ensure compliance over time. For example, leaders may be involved in promoting or endorsing the training, as well as participating in (or being present during) team training workshops. In the case of implementing performance support tools on the job, leadership support can signal that the improvement tools are critical to quality and safety of care rather than merely an additional administrative task.[44] Additionally, leadership can provide reinforcement when staff use the tools as intended and help ensure that their use is sustained over time. As mentioned earlier, researchers suggest that studies that assess multiple criteria, measure KSAs at multiple levels, and/or incorporate multiple measurement methods provide the most meaningful evaluation data regarding an intervention's effectiveness. Additionally, the strength of evidence increases as the level of Kirkpatrick's framework moves from reaction data (the weakest) to learning, transfer, and then results (strongest). The majority of studies within the review assessed multiple levels of criteria. Transfer criteria were most often gathered, but some reaction, learning, and results-oriented data were reported as well. The studies reviewed used multiple methods of measurement, including surveys and observational data. Furthermore, these data were collected at the individual level (in the case of survey data) and at the team level (in the case of observational data). Collectively, the studies reviewed provide support for team training interventions and performance support tools for improving teamwork, sustaining those improvements on the job, and positively influencing clinical and patient outcomes.

17.6.4.2 Gaps and Future Directions

Both the systematic review conducted by Weaver et al. (2014) and the meta-analysis conducted by Hughes et al. (2016) focused on team training interventions. Weaver et al. provided evidence that programs such as TeamSTEPPS, CRM, and MTT can result in both improved processes (e.g., attitudes, knowledge, teamwork skills) and improved clinical outcomes. Based on a meta-analysis of 129 studies, Hughes et al. reported that medical team training programs can positively impact reactions, learning, and transfer of teamwork skills. Results from the individual studies reviewed in the current chapter provide evidence consistent with that reported by Weaver et al. and Hughes et al. Although specific settings were not included in the search strategy to identify articles, nearly all of the individual studies reviewed were conducted within hospital settings. However, efforts to improve teamwork have also been introduced in other healthcare settings, such as primary care, ambulatory settings, and long-term care. For example, AHRQ has developed tailored TeamSTEPPS programs for multiple nonhospital settings. (Please refer to the Resources section for more information.) While work may be under way in these settings, there is a lack of published studies to add to the evidence base (especially related to the impact on patient outcomes) and thus, this is an area requiring further research.

Neither the systematic review conducted by Weaver et al. (2014) nor the meta-analysis conducted by Hughes et al. (2016) examined the effectiveness of specific tools to sustain performance on the job (e.g., checklists). As evidenced by the individual studies in the current review, team training and support tools have been implemented in a variety of inpatient settings. The breadth of departments and specialty areas in which studies have been conducted helps demonstrate the importance of teamwork, as well as the applicability of team training and tools. However, this breadth also makes it more difficult to draw conclusions about what team intervention is most effective in specific settings. Additionally, some studies included small sample sizes. Further studies are needed to help understand which teamwork

interventions have the greatest impact in different healthcare environments including those outside of in-patient hospital settings.

Lastly, limitations to the current review should be noted, including the exclusion criteria followed in the search strategy. Specifically, the review focused on collecting evidence from studies that were conducted in the United States. However, numerous studies of teamwork and team training have been conducted abroad and provide additional evidence that team training programs such as CRM and TeamSTEPPS enhance team KSAs as well as patient outcomes. Additionally, studies in which improving teamwork was not the primary focus were excluded. While this made it easier to attribute desirable results to the teamwork intervention employed, in the future, researchers may wish to include studies in which improving teamwork was a secondary objective.

17.6.4.3 Resources

AHRQ's TeamSTEPPS® program:
https://www.ahrq.gov/teamstepps/index.html

AHRQ's TeamSTEPPS® 2.0 Online Master Training Course:
https://www.ahrq.gov/teamstepps/master-trainer-registration.html

AHRQ's TeamSTEPPS® for Office-Based Care:
https://www.ahrq.gov/teamstepps/officebasedcare/index.html

AHRQ's TeamSTEPPS® for Long-Term Care
https://www.ahrq.gov/teamstepps/longtermcare/index.html

VA MTT program:
https://www.patientsafety.va.gov/professionals/training/team.asp

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17.7 Education and Training Through Simulation

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17.7.1 Practice Description

Simulation is used in many high-stakes industries where it is too dangerous for individuals to practice and refine their skills on the job. According to Gaba (2004), simulation is a "technique, not a technology, to replace or amplify real experiences with guided experiences, often immersive in nature, that evoke or replicate substantial aspects of the real world in a fully interactive fashion" (p. 12).[1] Within healthcare, simulation has been used at multiple points in the education and training continuum to improve technical proficiency, as well as teamwork skills, while not endangering the lives of actual patients. (For further discussion on the use of simulation to enhance teamwork, please refer to Section 17.6, Teamwork and Team Training.)

With a greater emphasis being placed on patient safety than ever before, a growing number of medical and nursing programs are adopting a simulation-based education curriculum to mitigate risk and better prepare students to treat patients. Simulation provides structured opportunities to practice skills in a safe environment without harming actual patients. Using simulation, participants can make mistakes, reflect upon them and receive feedback, and learn from their mistakes until mastery has been achieved. As a result of this deliberate practice and feedback, participants are better prepared to perform procedures when treating real patients. Data show that medical residents and nursing students who participate in simulation-based training as part of their curriculum have: high levels of satisfaction; greater confidence in their skills/abilities; and improved knowledge, attitudes, and clinical skills.[2,3]

While simulation can help inexperienced healthcare providers enhance their skills, simulation can also be incorporated into continuing education efforts for more experienced healthcare professionals. For example, simulation can be used as part of ongoing training for those who change departments or units, as refresher training on procedures and situations that occur infrequently, and to assess proficiency during recertification. Simulation can similarly be added to ensure readiness when new equipment and technology is introduced, as well as to practice new processes and protocols.

Although studies of simulation have demonstrated its efficacy for knowledge and skill development, fewer studies have examined the extent to which the knowledge and skills gained through simulation translate into improved patient outcomes.

17.7.2 Methods

The question of interest for this review is, "Does simulation training on individual skills in clinical practice improve patient outcomes?"

To answer this question, two databases (i.e., CINAHL® and MEDLINE®) were searched to identify studies of simulation published between 2008 and 2018. Search terms included "simulation training," "patient simulation," "computer simulation," "virtual reality," "serious games," and "serious gaming," as well as other similar terms. Terms such as "patient harm," "patient safety," and "medical errors" were also included. No attempt was made to focus on any particular provider type. The initial search yielded 1,750 results. After duplicates were removed, 1,119 were screened for inclusion and 27 full-text articles

were retrieved. Of those, 11 were selected for inclusion in this review: 7 are single studies, 3 are systematic reviews, and 1 is a meta-analysis. Articles were excluded if the article was out of scope (including not quantitative), the study design was insufficiently described, the study did not evaluate patient outcomes, the study was conducted with junior medical or nursing students, the study focused on improving teamwork (which is included in the Teamwork and Team Training section), or the study was conducted outside of the United States.

General methods for this report are described in the Methods section of the full report.

For this patient safety practice, a PRISMA flow diagram and evidence table, along with literature-search strategy and search-term details, are included in the report appendixes A through C.

17.7.3 Review of Evidence

All studies took place in hospital settings, the majority of which were teaching hospitals or tertiary teaching hospitals. Across studies, simulation-based training generally included some level of didactic instruction, practice via the simulation technology, and feedback. Studies varied in the type of simulation used, including high-fidelity computer-based simulations and full-body mannequins. All studies examined whether simulation-based training translated to improved treatment and outcomes of real patients. Evidence related to clinical/patient outcomes and clinical/patient care processes are presented in the sections that follow.

17.7.3.1 Clinical/Patient Outcomes

Three review articles and one meta-analysis were identified that reported patient outcomes related to simulation-based training efforts delivered to medical residents or fellows. Seven individual studies were identified, five of which provided simulation training to medical residents as part of simulation-based medical education (SBME) and two of which incorporated simulation as part of the continuing education of nurses. While the number of studies may be relatively low, results generally support the efficacy of simulation-based training as a patient safety practice.

In their systematic review, Griswold-Theodorson et al. (2015) limited their focus specifically to studies that provided evidence of the effects of SBME on patient care practices, patient outcomes, and value outcomes (e.g., costs). The majority of the 14 studies identified compared traditional training with simulation-based training and provided support for simulation training on various levels. Specifically, a portion of the studies demonstrated a reduction in complication rates (e.g., central line-associated blood stream infection or CLABSI rates, pneumothorax rates, intraoperative and postoperative complications). Cost savings were estimated in four of the studies reviewed, with significant savings associated with reductions in central-line infections, overnight hospital days, or additional hospital days.[4]

A systematic review of simulation-based training studies conducted by Schmidt et al. (2013) reported results related to diagnostic procedures, surgical procedures, and central venous catheterization. The studies of diagnostic procedures produced mixed results on patient discomfort, and one study reported decreased complication rates related to thoracentesis. For surgical procedures, fewer errors for laparoscopic cholecystectomy were reported after simulation training. Finally, three studies demonstrated decreased rates of catheter-related bloodstream infections related to central venous catheterization, and mixed results for complication rates and patient safety events.[5]

In their qualitative review, McGaghie et al. (2011) discussed two simulation research programs conducted in the United States that examined the impact of SBME on patient outcomes. One study reported an 85-percent reduction in catheter-related bloodstream infections after medical residents who had received SBME began working in the intensive care unit. The rate of catheter-related bloodstream infections was both significantly lower than it had been in the baseline period (post-SBME intervention=0.50 infections per 1,000 catheter-days vs. pre-SBME intervention=3.20 infections per 1,000 catheter-days, p=0.001) and also significantly lower when compared with another intensive care unit in the same hospital (0.50 infections per 1,000 catheter-days vs. 5.03 infections per 1,000 catheter-days, p=0.001). Another study, conducted in ophthalmology, reported that the sentinel complication rate for patients receiving cataract surgery significantly decreased from 7.17 percent to 3.77 percent (p=0.008) when performed by medical residents in the simulation-based curriculum.[6]

Five individual studies measured clinical or patient outcomes related to their simulation-based education efforts. Madenci et al. (2014) conducted a meta-analysis to evaluate the efficacy of simulation training on central venous catheter (CVC) insertion and/or catheter manipulation. Five randomized control trials and prospective two-group cohort studies were identified in which simulation training was used for invasive vascular procedures on real patients. While the group that received simulation training had a lower proportion of adverse events (3.8%), this difference was not statistically significant from the traditionally trained group (4.9%, p=0.15).[7]

Mosier et al. (2015) studied the impact of a simulation-based curriculum on improving airway management for fellows in pulmonary/critical care medicine. The fellows received high-fidelity simulation training twice a month over the course of 11 months. The scenarios progressively increased in difficulty and required participants to consider many factors related to endotracheal intubation, including anatomical and physiological characteristics that would make intubation difficult. Seven complications related to intubation were measured, including hypotension, desaturation, esophageal intubation, aspiration, airway trauma, peri-intubation arrest, and surgical airway. The only significant improvement was found for desaturation, which significantly decreased in the post-simulation period (from 25.9% to 16.8%, p=0.002). The study noted that a limited number of complications occurred in the pre- and post-simulation periods, making it difficult to find meaningful improvements.[8]

A study of advanced cardiac life support events conducted by Wayne et al. (2008) compared the events led by second-year simulation-trained medical residents with events led by third-year medical residents who had been traditionally trained. The authors reported no differences in patient survival of the advanced cardiac life support event between the simulation-trained and traditionally trained residents (simulation group=45%, traditional group=46.4%).[9]

Another study, conducted in orthopedics, evaluated the effectiveness of simulation for improving patient outcomes and reducing costs. Bae et al. (2017) introduced a simulation-based curriculum in pediatric orthopedics to improve the reduction of a distal radial fracture, to properly apply and mold a short-arm cast, and to remove the cast with a cast oscillating saw. The performance of medical residents who received simulation training was compared with that of traditionally trained residents. Results indicated that 8 out of 188 cases in the pre-simulation period resulted in a cast saw burn (4.3% of patients were injured), whereas 3 out of the 439 cases included in the post-simulation period resulted in cast saw injuries (0.7% of patients were injured). These data demonstrated a significant reduction in patient harm (p=0.002). Further, the authors estimated that costs associated with cast saw burns in the

pre-simulation period were approximately $32,320, which were substantially reduced to approximately $5,188 in the post-simulation period.[10]

Harting et al. (2008) examined whether the use of computer-based simulation translated into better pain management for cancer patients. Medical residents participated in the simulation intervention during the first week of their oncology rotation. Each resident received a half-hour lecture that outlined pain care principles, completed two to three simulated cases in which immediate feedback was given on actions taken, and participated in 1 day of followup rounds with actual patients. Results indicated that pain control within the first 48 hours of care significantly improved in the post-simulation period ($p<0.01$). Specifically, while patients' reported pain had increased over the first 48 hours of care in the pre-simulation period, reported pain levels decreased over the first 48 hours of care for patients treated after the simulation intervention was introduced. Nine out of the 20 patients (45%) in the pre-simulation group had described their pain as "worsening" or "unchanged" during their admission, whereas only 4 of the 20 patients (20%) in the post-simulation group described their pain this way.[11]

Barsuk et al. (2009) examined the use of simulation to improve CVC procedural skills. Seventy-six internal medicine and emergency medicine residents received the simulation intervention 1 to 2 months prior to their medical intensive care unit rotation. The simulation intervention included 1 hour of videotaped lecture followed by 3 hours of ultrasound training, deliberate practice, and feedback. Twenty-seven medical residents who had received traditional training served as a historical control group. Although several processes improved for those who received simulation training, no differences were found between the simulation and control groups when examining rates of pneumothorax (an important complication) due to the small sample size.[12]

Two studies provided simulation training to nurses as part of continuing education. Research conducted by Gerolemou et al. (2014) provided simulation training to critical care nurses on sterilization techniques during central venous catheterization. To establish a baseline, each nurse was asked to complete the steps in sterile technique preparation during CVC up until needle insertion on a full-body mannequin in a simulation laboratory. Observations were made of each nurse's performance and each participant was debriefed. During the 30–45 minute debrief, each nurse watched a video of his/her performance, received feedback on individual steps, and engaged in repetitive practice. Effectiveness was evaluated by examining infection rates prior to and following the simulation intervention. Infection rates decreased significantly in the post-simulation period (pre-simulation=2.61 infections per 1,000 catheter-days, or 6 catheter infections in 2,297 catheter-days; post-simulation=0.4 per 1,000 catheter-days, or 1 catheter infection in 2,514 catheter-days; $p<0.02$).[13]

In addition, Hebbar et al. (2018) used simulation in an effort to reduce medication administration errors made by nurses at three children's hospitals. A total of 1,434 nurses completed the 2-hour simulation training, which included two to three scenarios, after which each was debriefed. The authors reported that the rate of medication administration events significantly decreased following the simulation intervention (pre-simulation=average of 2.5 events per month, post-simulation=average of 1.4 per month, $p=0.029$). Further decreases were noted during the 7-month post-simulation period, indicating sustained improvement (pre-simulation=average of 2.5 events per month, 7-month follow-up=average of 0.86 per month, $p=0.014$). The reduction in medication administration events also decreased the length of stay by an average of 2 days at an annual cost savings of approximately $165,000 to $225,000 (based on an annual decrease of 15 medication administration errors).[14]

17.7.3.2 Clinical/Patient Care Process Measures

The three review articles and one meta-analysis identified in the current effort also reported data supporting the effectiveness of simulation-based training on clinical/patient care processes. Further, six out of the seven individual studies also provided data related to processes and provided findings consistent with the review articles.

Studies included in Griswold-Theodorson et al.'s systematic review demonstrated that simulation improved procedural skills (e.g., cardiac auscultation, hemodialysis catheter insertion) and success rates of procedures (e.g., colonoscopy, laparoscopic surgery). For example, the length of successfully performed procedures on actual patients was reduced as a result of simulation interventions for colonoscopies, laparoscopic surgery, and hernia repairs.[4]

Schmidt et al.'s (2013) systematic review reported that simulation-based training was associated with mixed results on procedure times for diagnostic procedures. Overall performance of surgical procedures (e.g., cholecystectomies, cataract surgery, prostate resection) improved following simulation-based training. Studies of central venous catheterization reported that simulation-based training resulted in fewer needle passes. Results of this review provided moderate support for simulation-based training in the development of technical skills.[5]

In their qualitative review, McGaghie et al. (2011) discussed two simulation research programs conducted in the United States that examined the impact of SBME on patient care practices and/or patient outcomes. Several studies used simulation to improve CVC insertion skills, reporting that medical residents who received SBME reported significantly fewer needle passes, catheter adjustments, and arterial punctures than traditionally trained medical residents.[6] The meta-analysis of simulation training on CVC insertion and/or catheter manipulation reported positive results on the clinical processes examined (Madenci et al., 2014).[7] In comparing groups that received simulation training with those that receive traditional training, the simulation-trained group had a significantly higher proportion of successful CVC insertions (89.8% vs. 81.2%; relative risk, 1.09; 95% confidence interval [CI], 1.03–1.16; $p<0.01$) and required significantly fewer attempts (weighted mean difference, -1.42; 95% CI, -2.34 to -0.49; $p<0.01$).[7]

Six individual studies in our review also provided evidence on improved clinical/patient care processes, four of which provided simulation as part of SBME and two as part of continuing education. In their study of a simulation-based curriculum to improve airway management, Mosier et al. (2015) calculated the success rate of first-attempt intubations, which significantly improved following the introduction of the simulation curriculum. Specifically, successful first attempts increased from 73.5 percent in the pre-simulation period to 81.6 percent in the post-simulation period ($p=0.006$).[8]

As part of their study to improve pain management for cancer patients, Harting et al. (2008) also reported that medical residents who received the computer-based simulation training administered long-acting oral medications earlier in care (90% of cases) than did residents in the pre-simulation period (35% of cases, $p<0.001$). This was encouraging, as interviews that had been conducted prior to the simulation revealed that residents often failed to administer long-acting pain medication, because they feared that it would induce respiratory suppression.[11]

Barsuk et al. (2009), who introduced simulation to improve CVC procedural skills, reported improvements on several quality indicators for the medical residents who received the simulation

training. Specifically, residents who received the simulation training reported significantly fewer needle passes (total, p<0.005; internal jugular, p <.0.005); arterial punctures (total, p<0.005; internal jugular, p<.0.005); and CVC adjustments (total, p=0.002; internal jugular, p=0.001); and higher successful CVC insertion rates (total, p=0.005; internal jugular, p=0.018) than residents in the control group. They noted no differences between the simulation and control groups when assessing the quality of subclavian CVCs.[12]

Wayne et al. (2008) reported that medical residents who received simulation training demonstrated significantly higher compliance with the American Heart Association standards as compared with traditionally trained residents when dealing with real advanced cardiac life support events (simulation group=68%, traditional group=44%, p<0.001).[9]

In sum, the six individual studies that incorporated simulation-based training for medical residents and fellows provide evidence that simulation improves technical skills and clinical processes.

The two studies of simulation training delivered to nurses that reported a positive impact on patient outcomes also reported improvements in processes. First, Gerolemou et al. (2014) reported nurses' performance of sterilization procedures significantly improved following the simulation intervention. The median score was 7 out of 24 for sterilization techniques in the pre-simulation period and increased to 23 out of 24 in the post-simulation period, indicating that nurses had more knowledge of and adhered more closely to the sterilization protocol (p<0.01).[13]

In addition, the study conducted by Hebbar et al. (2018) that reduced medication adverse events also collected a process measure. They reported that compliance with recommended medication administration practices significantly increased following the simulation intervention (from 51% at month 1 to 84% at month 18, p<0.001). Together, the two studies of continuing education for nurses demonstrate the efficacy of simulation for enhancing knowledge of protocols as well as improving compliance with established practices.[14]

17.7.4 Conclusion and Comment

17.7.4.1 Implementation

The majority of studies in the current review were conducted in a hospital setting. Simulation-based training (most often delivered in a simulation laboratory) was introduced as a strategy for improving patient outcomes related to a variety of procedures, including CVC insertion, tracheal intubations, advanced cardiac life support, cancer-related pain management, orthopedic fractures, and cataract surgery. Although many of the studies had relatively small sample sizes, improvements in patient outcomes and clinical processes were reported. Taken together, the evidence suggests that simulation-based training is an effective strategy that allows less experienced healthcare professionals such as medical residents to develop the skills needed to provide safer patient care. Only two studies utilized simulation as part of continuing education, with both demonstrating the efficacy of simulation for improving patient outcomes, as well as improving clinical/patient care processes. Although the costs associated with setting up a simulation laboratory can be substantial, [5,15] one individual study in the review found that their simulation program was associated with considerable savings.[10]

17.7.5 Gaps and Future Directions

Medical research has demonstrated the utility of simulation-based training for individual skill development, but a limited number of studies have examined whether this strategy impacts patient outcomes. The studies presented in the current review illustrate the potential of simulation-based training to improve patient safety outcomes. Moving toward a more simulation-based training curriculum for medical residents and nursing students, or providing simulation training as part of continuing education efforts is not without its challenges. As highlighted by Rodriguez-Paz et al. (2009), additional personnel and equipment, as well as assessment and evaluation methods, may be required. Studies are needed that weigh the costs of simulation against the costs associated with medical errors, complication rates, re-admissions, and lawsuits in order to identify the real return on investment.[15] Additionally, more studies are necessary to provide a more comprehensive evaluation of the long-term impact of simulation-based training on outcomes of interest.

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Discussion

This report covers 47 patient safety practices (PSPs) chosen for the high-impact harms they address and interest in the status of their use. The harms include diagnostic errors, failure to rescue, sepsis, infections due to multi-drug resistant organisms, adverse drug events, and nursing-sensitive conditions. While going through the process of selecting PSPs to address specific harm areas, it became evident that several commonly recommended practices should also be reviewed. These cross-cutting practices are improving safety culture, teamwork and team training, clinical decision support, person and family engagement, cultural and linguistic competency, staff education and training, and data monitoring, audit, and feedback. All of the harm-specific PSPs and cross-cutting PSPs included in this report underwent focused systematic reviews to establish the current evidence base for their use.

Since the publication of the second Making Health Care Safer report in 2013, the volume of research on patient safety topics has continued to expand. PSPs that could previously be presented only at a high level, such as those related to diagnostic errors or opioid-related safety, now have enough literature for in-depth examination. For more established PSPs, such as the use of rapid response teams or screening for delirium, there is now a greater understanding of contextual factors associated with successful implementation. In addition, the follow-up time after initial implementation has increased, providing more evidence about the long-term impact and maintenance of PSPs.

The most significant harms patients face continue to be found in higher acuity settings, such as the emergency department and intensive care unit, and the research is biased toward those settings. Research on the use of sepsis screening tools, for example, predominantly takes place in the acute care setting. As the importance of early identification has gained traction, sepsis screening tools are now being investigated for use in pre-hospital and long-term care settings, although with widely varied results. Other harms, such as adverse drug events and diagnostic errors, occur in a variety of settings, and studies of PSPs for those harms follow suit. For example, reducing adverse drug events in the elderly using medication deprescribing practices or medication screening, as well as associated research, can be found in ambulatory settings, long-term care facilities, and acute care settings. Similarly, PSPs geared toward reducing diagnostic errors, such as the use of clinical decision support in the diagnostic process, peer review of radiology and pathology studies, or result notification systems, have been studied in both the ambulatory and acute care settings.

One aspect of care or “setting” that poses a unique threat to patients is the transition between one setting and another; from the hospital to the outpatient setting, in particular. As we move out from the silos required for setting-specific research, research needs to address transitions of care. For this report, we were able to focus on two PSPs that address harms associated with transitions of care: care transition models as a PSP to reduce readmissions and medication management across transitions to reduce adverse drug events.

Regardless of setting, several themes emerged from the report:

- More than one PSP can be used to reduce a given harm. The PSPs presented in the report are those that the project Technical Expert Panel and Advisory Group felt were ready for a fresh review of the literature or PSPs that were relatively new and needed to have an evidence base established. The PSPs represented in the report are wide ranging but not intended to be an all-inclusive list.

- Selecting a particular PSP for implementation in a specific healthcare facility or system should be based on the predominant root cause(s) of the harm at that facility or system. In one facility, the root cause of an increase in sepsis mortality may be a lack of recognition of patients with sepsis arriving to the emergency department. In another facility, it may be due to lack of monitoring of patients who are experiencing deterioration on a medical-surgical unit.
- When using a specific PSP, consideration must be given to potential new harms that can be introduced. For example, PSPs and strategies to reduce venous thromboembolism must take into account the potential to unintentionally increase anticoagulation-related events.
- PSPs are not implemented in isolation and are often part of a broader safety strategy. The strategy often relies on a strong safety culture, teamwork, communication, and involvement of the patient and family. These cross-cutting practices are the foundation for success.
- The context in which a PSP is implemented determines success. Understanding the impact of context through rigorous, large-scale research studies is hard. It is difficult, and sometimes may be impossible, to design a study that takes into consideration all potential contextual factors, such as staffing, other PSPs in place, safety culture, and leadership engagement, and to control for those factors across enough sites to make the findings generalizable.

Limitations

There are several limitations to conducting such a broad review of the literature as found in this report.

As our understanding of patient safety expands, there is an increasing amount of published research, with most showing positive effects of the intervention under question (i.e., publication bias). By conducting in-depth reviews for each PSP included in this report, we have made a concerted effort to find all published literature on a given PSP. With the exception of newer practices that are still being refined (e.g., use of clinical decision support in the diagnostic process), most of the published studies describe either improvement or, at worst, no effect on a given outcome. With the paucity of recent randomized controlled trials (RCTs) in the literature and the reliance on pre-post studies and observational studies, it is difficult to assess the impact of the biases introduced by study design on the findings.

The low number of RCTs in the patient safety literature is also a limitation in conducting focused systematic reviews such as those found in this report. Many of the PSPs under examination have been implemented in some form. Staff are aware of the implementation of the PSPs, so being blinded to the intervention is usually not possible. Since PSPs are typically implemented across an entire facility rather than a single unit, finding a control group for comparison can be difficult. There is the potential for using multiple facilities, but, as previously discussed, the context in which a PSP is implemented can be very different, making the comparison a challenge.

Lastly, some of the PSPs addressed were introduced as part of multicomponent interventions (e.g., strategies to reduce *C. difficile* infections). When a specific PSP is part of a multicomponent intervention, it is difficult to ascertain which of the components is the driver for success. In some cases, such as when a set of PSPs is implemented as a "bundle," there is not even an attempt to identify which component is a driver. This often has not been considered a problem if the bundle produces reductions in adverse events.

Conclusions

This report presents reviews of 47 different PSPs covering a wide variety of harms across multiple settings. The amount of research in patient safety has exponentially grown since the last report was published, with the studies being of variable quality. PSPs that are more well-established are now being investigated in light of emerging harms, such as infection-prevention-related PSPs to address multidrug-resistant organisms. Similarly, emerging PSPs are being investigated for use to address well-established harms, such as the use of clinical decision support to reduce diagnostic errors.

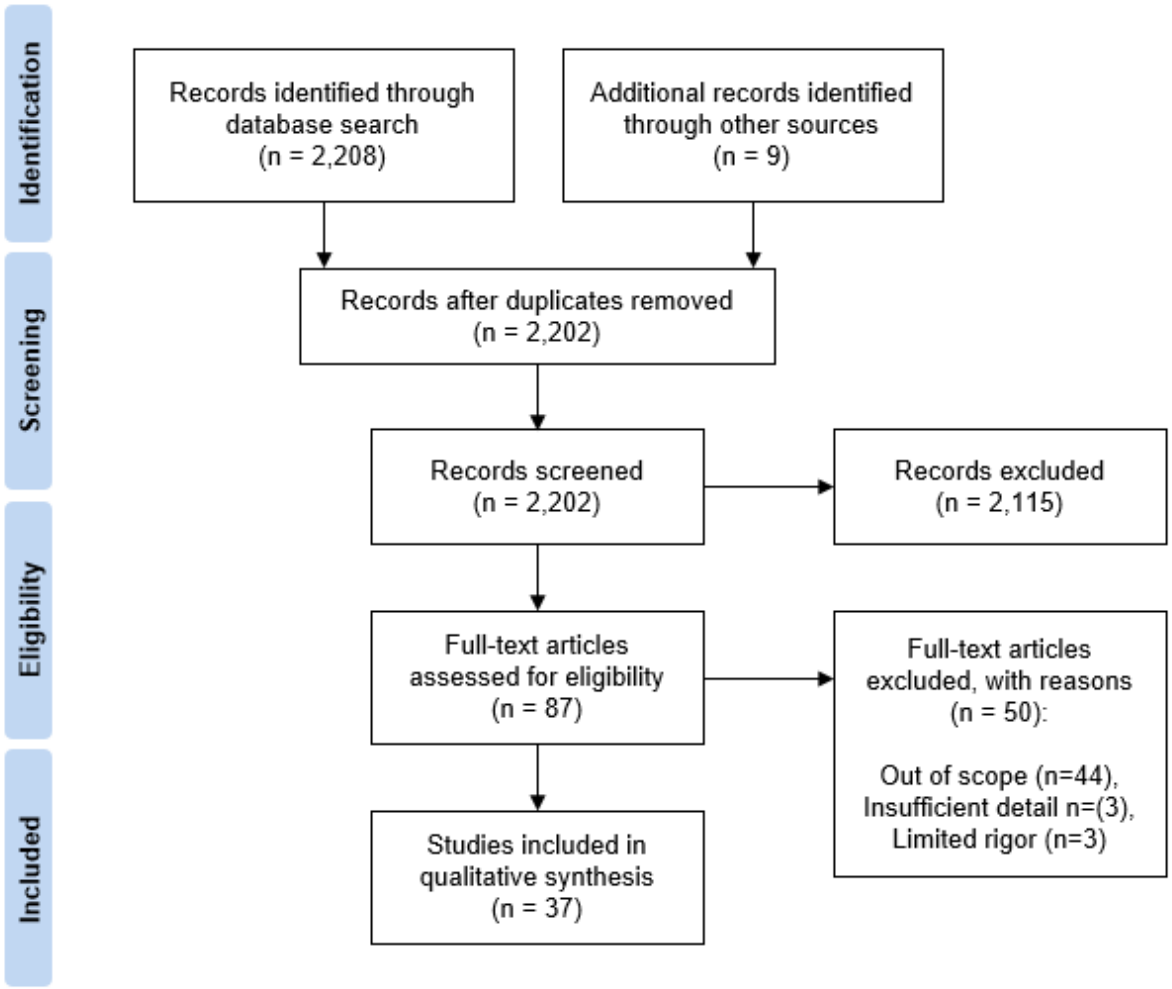
It is clear that many factors impact the success of any PSP on reducing harm. Patient safety culture, teamwork and communication, person and family engagement, providing culturally competent care, reinforcing good practice with education and training, and learning from data are all necessary to ensure success.

Future Research Needs

It is clear from the reviews of these PSPs that the importance of context for implementation cannot be overstated. Context plays a large role in the successful uptake and use of a PSP. Setting, safety culture, staffing and other organizational factors contribute to harm reduction as much as a PSP itself. More implementation research needs to be conducted across all of the PSPs to understand and work within real-world constraints, rather than conducting studies that may be rigorous but are stripped of that context. In an increasing number of cases, we now know what to do. Now the challenge is how to implement effective PSPs into a specific facility or setting and have them succeed.

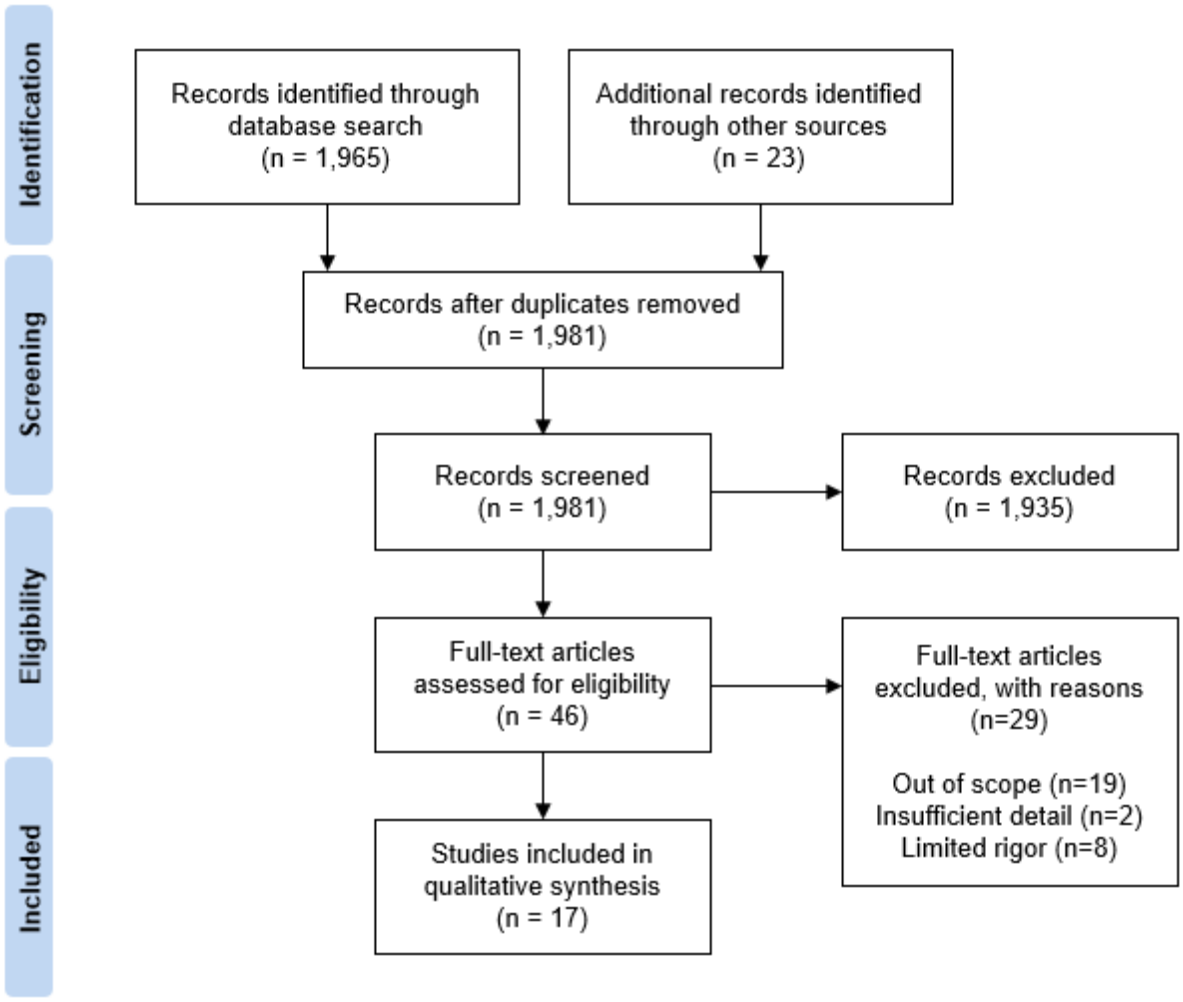
Appendix A. PRISMA Flow Diagrams

Figure A.1: Diagnostic Errors, Clinical Decision Support—Study Selection for Review



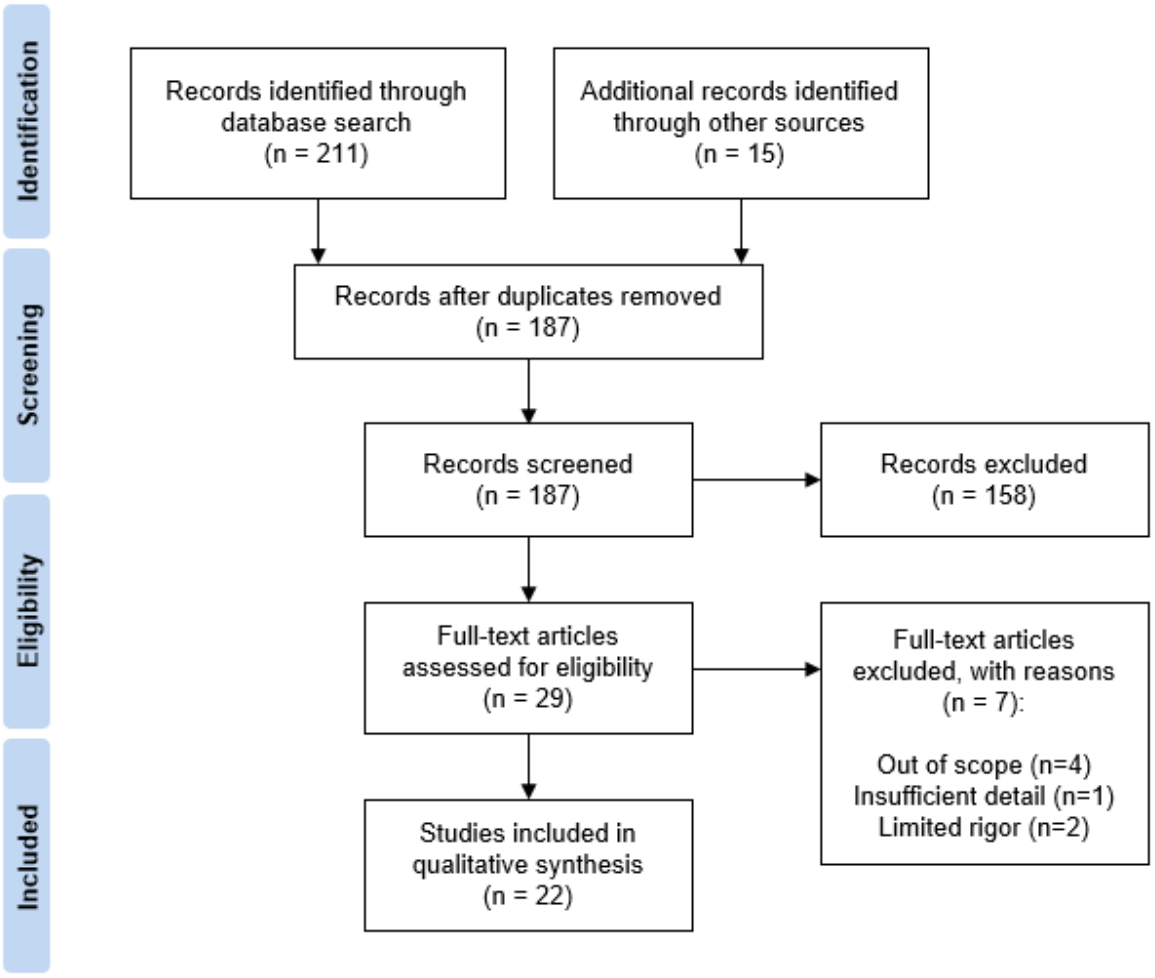
PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.2: Diagnostic Errors, Result Notification Systems—Study Selection for Review



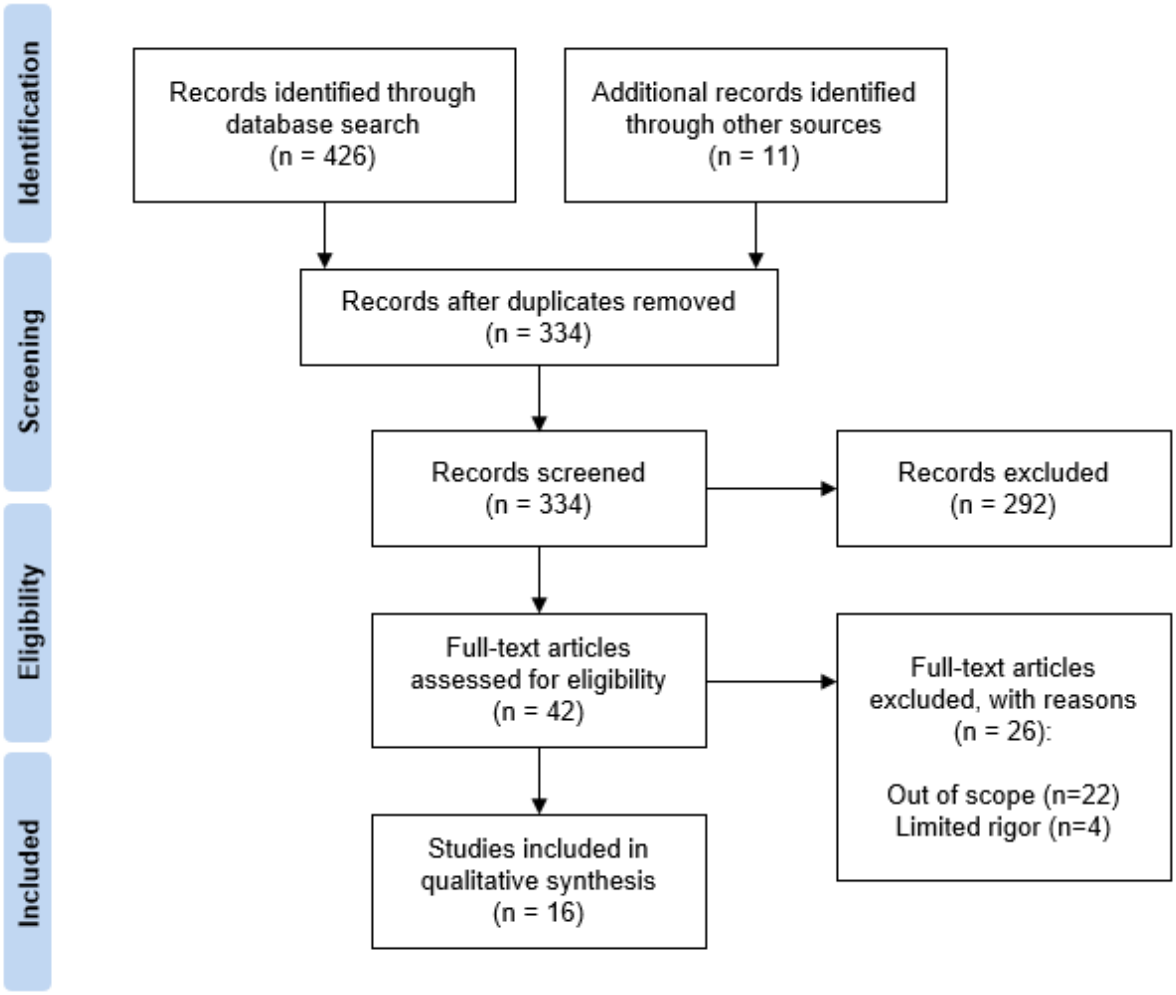
PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.3: Diagnostic Errors, Education and Training—Study Selection for Review



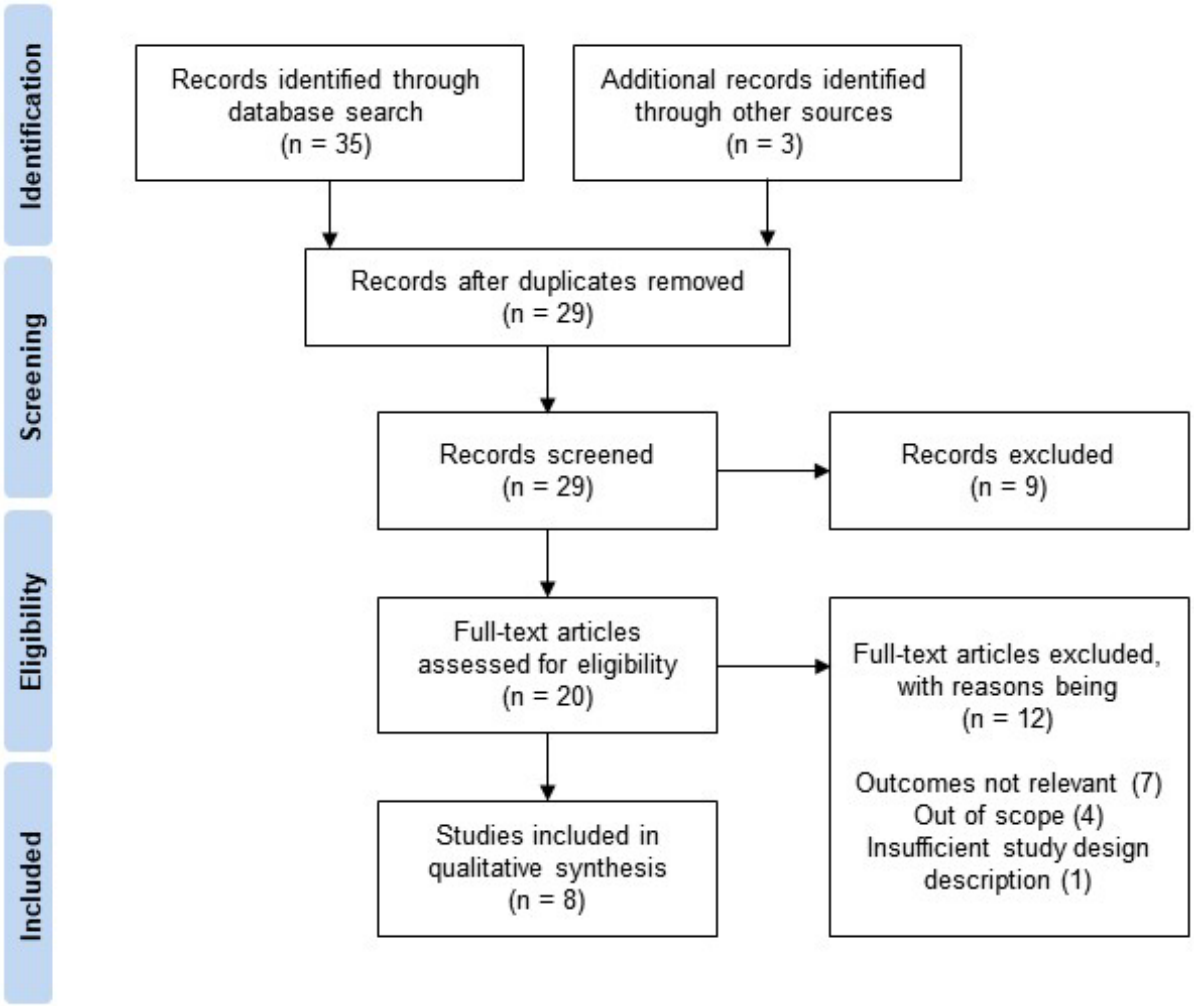
PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.4: Diagnostic Errors, Peer Review—Study Selection for Review



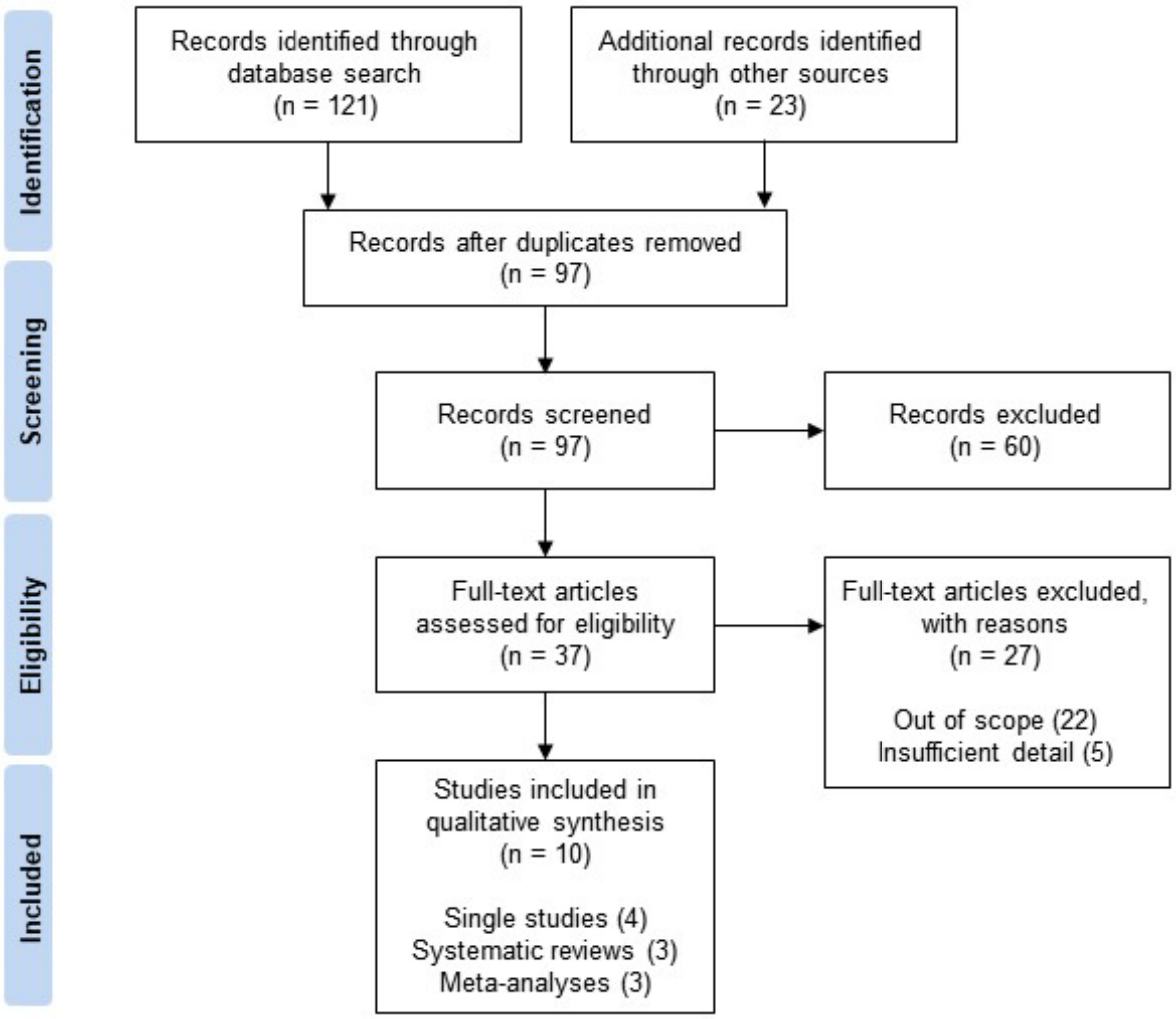
PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.5: Failure To Rescue, Patient Monitoring Systems—Study Selection for Review



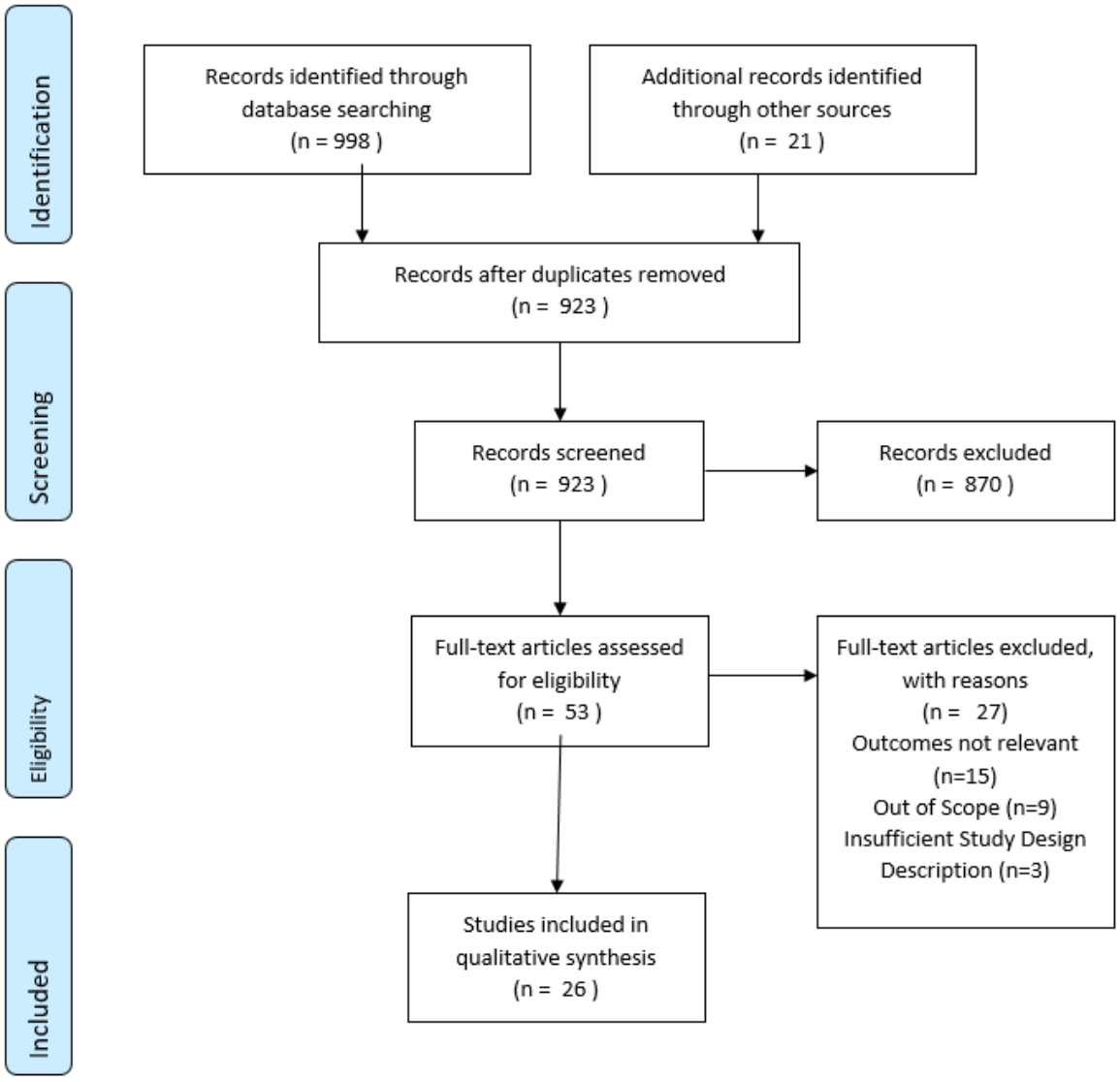
PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.6: Failure To Rescue, Rapid Response Teams—Study Selection for Review



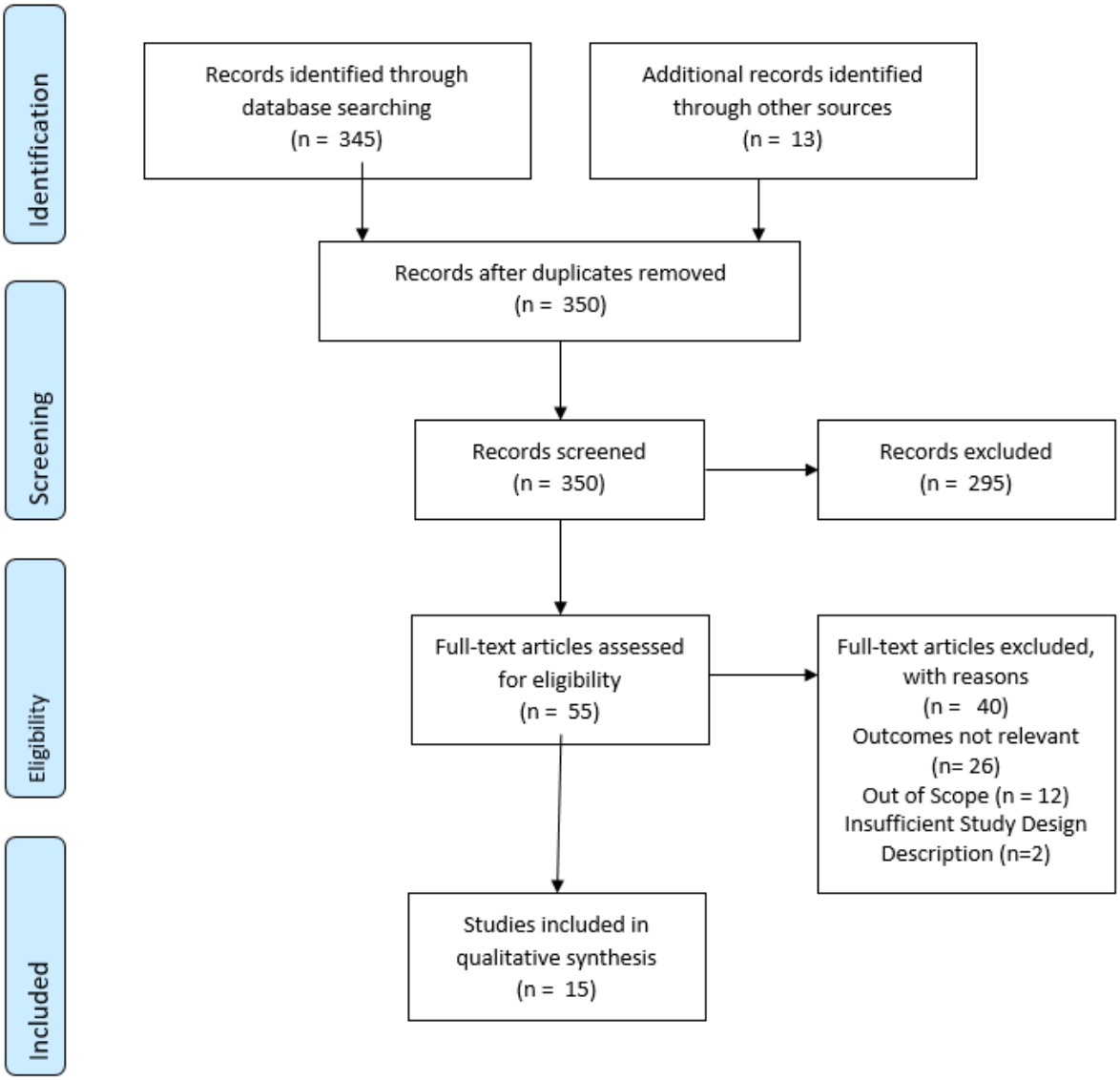
PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.7: Sepsis Recognition, Sepsis Screening Tools—Study Selection for Review



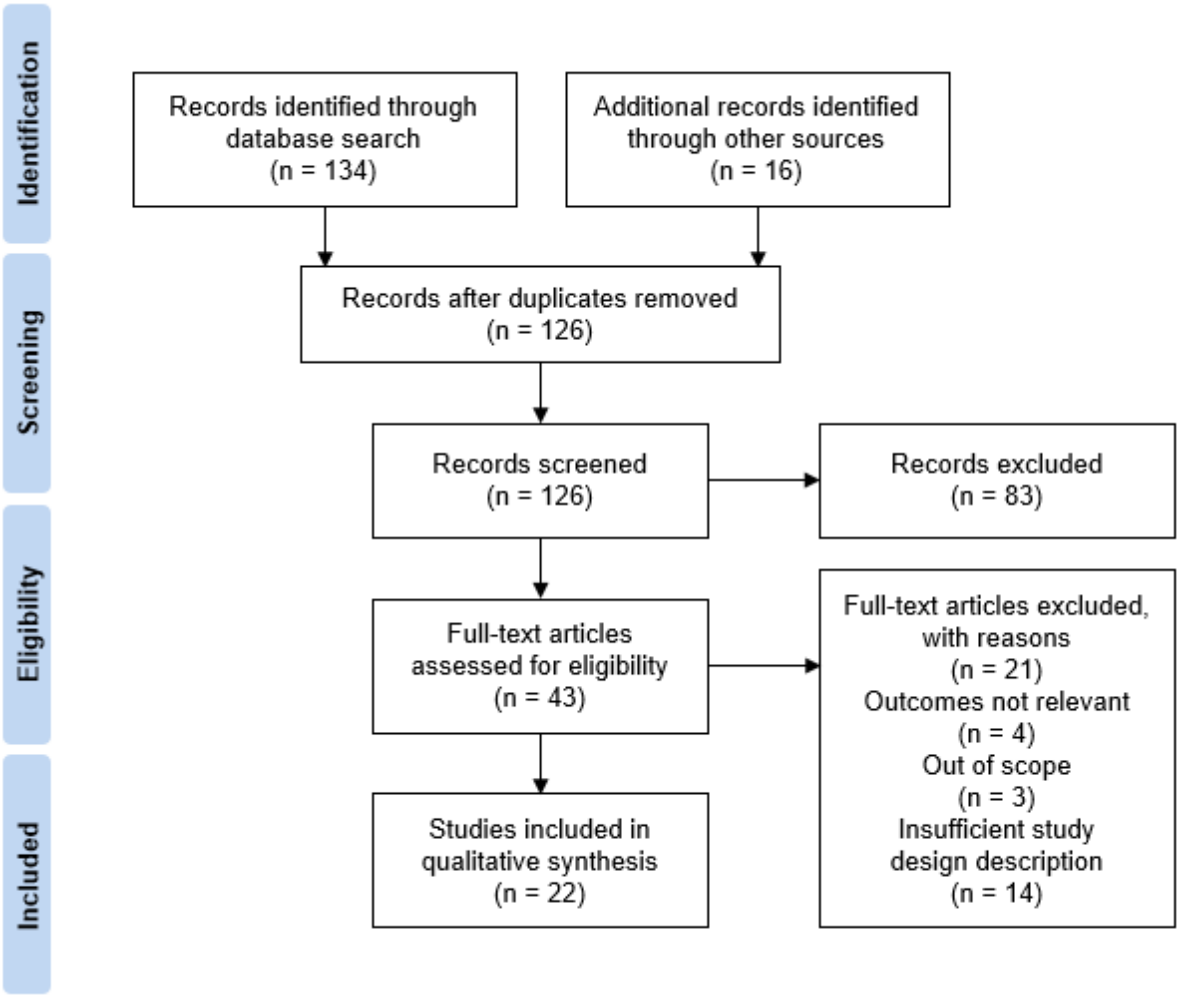
PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al.. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.8: Sepsis Recognition, Sepsis Patient Monitoring Systems—Study Selection for Review



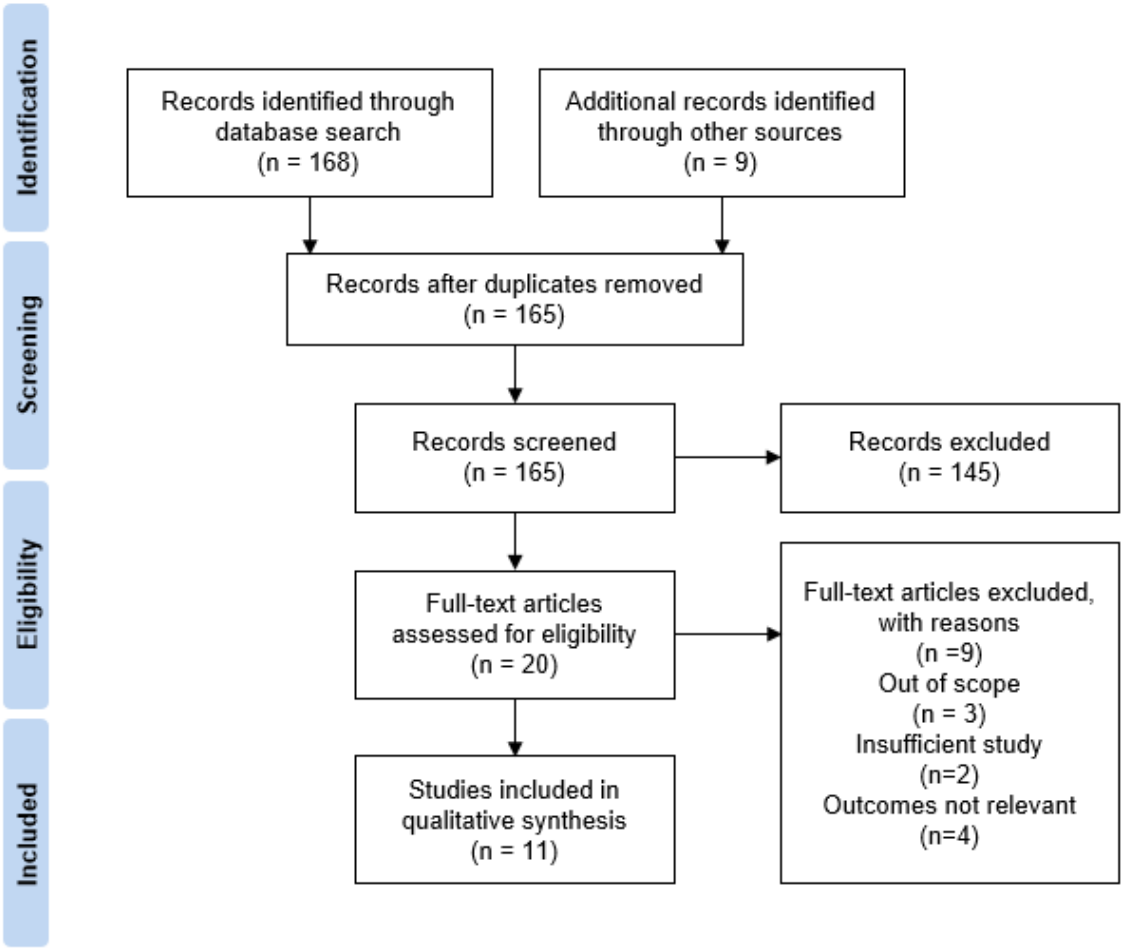
PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al.. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.9: Antimicrobial Stewardship Programs for *Clostridioides difficile*–Study Selection for Review



PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.10: Hand Hygiene for Clostridioides d*ifficile*–Study Selection for Review



PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.11: Environmental Cleaning and Decontamination for *Clostridioides difficile*–Study Selection for Review

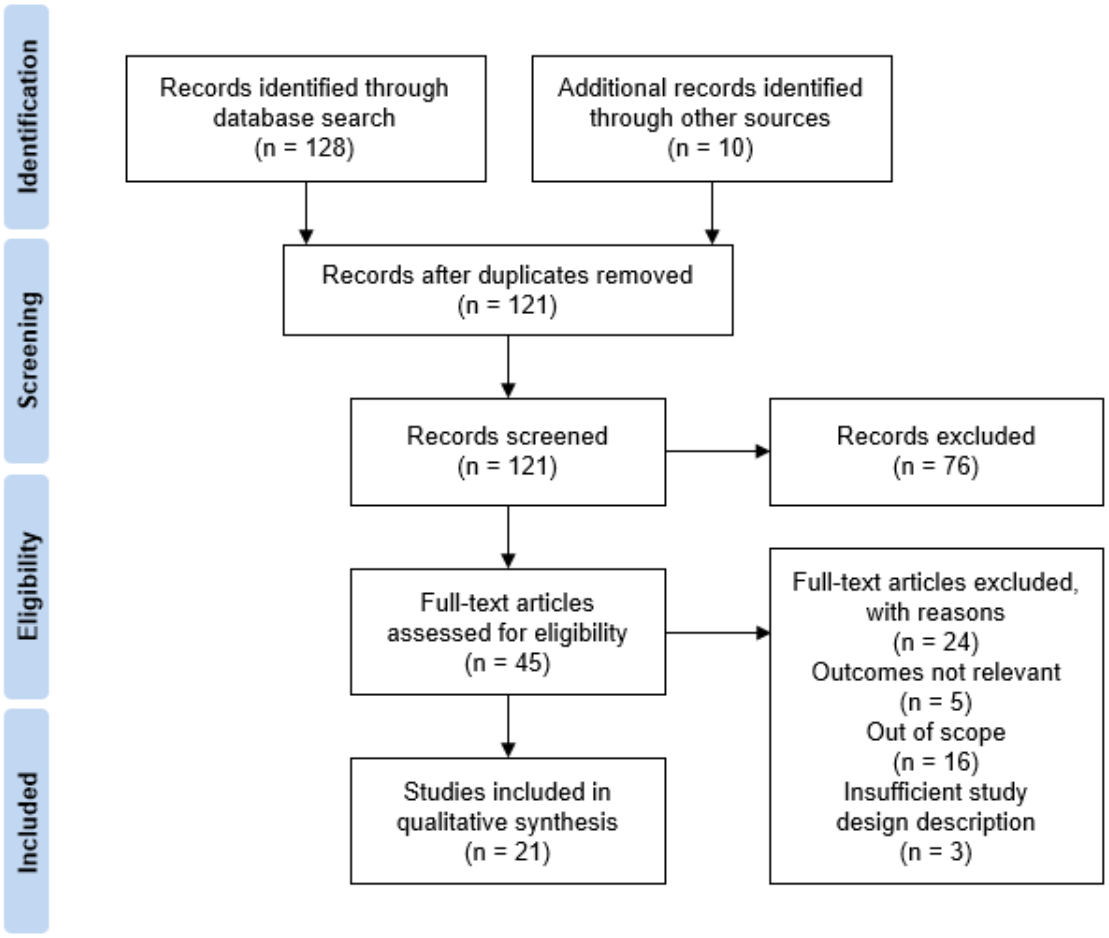


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Figure A.12: Surveillance for Clostridioides *difficile*–Study Selection for Review

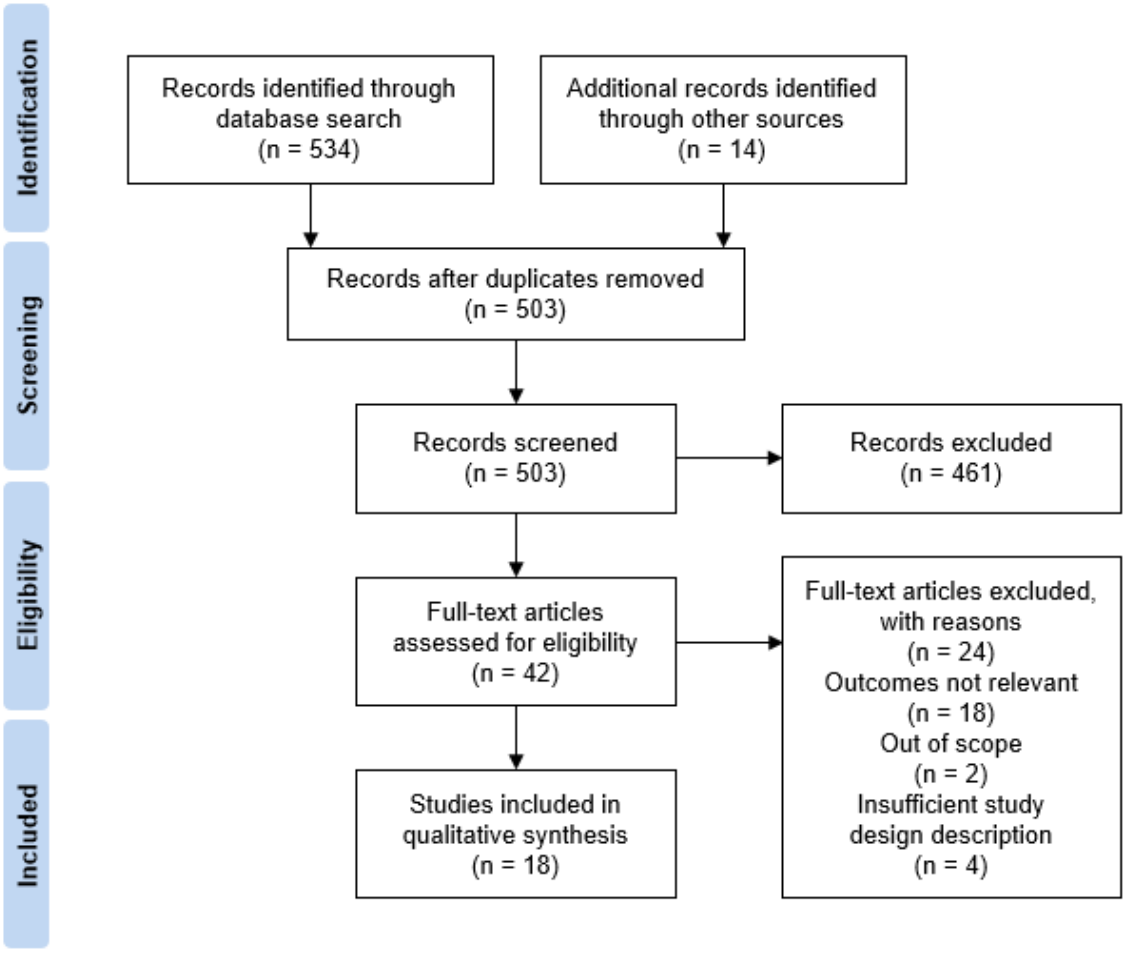

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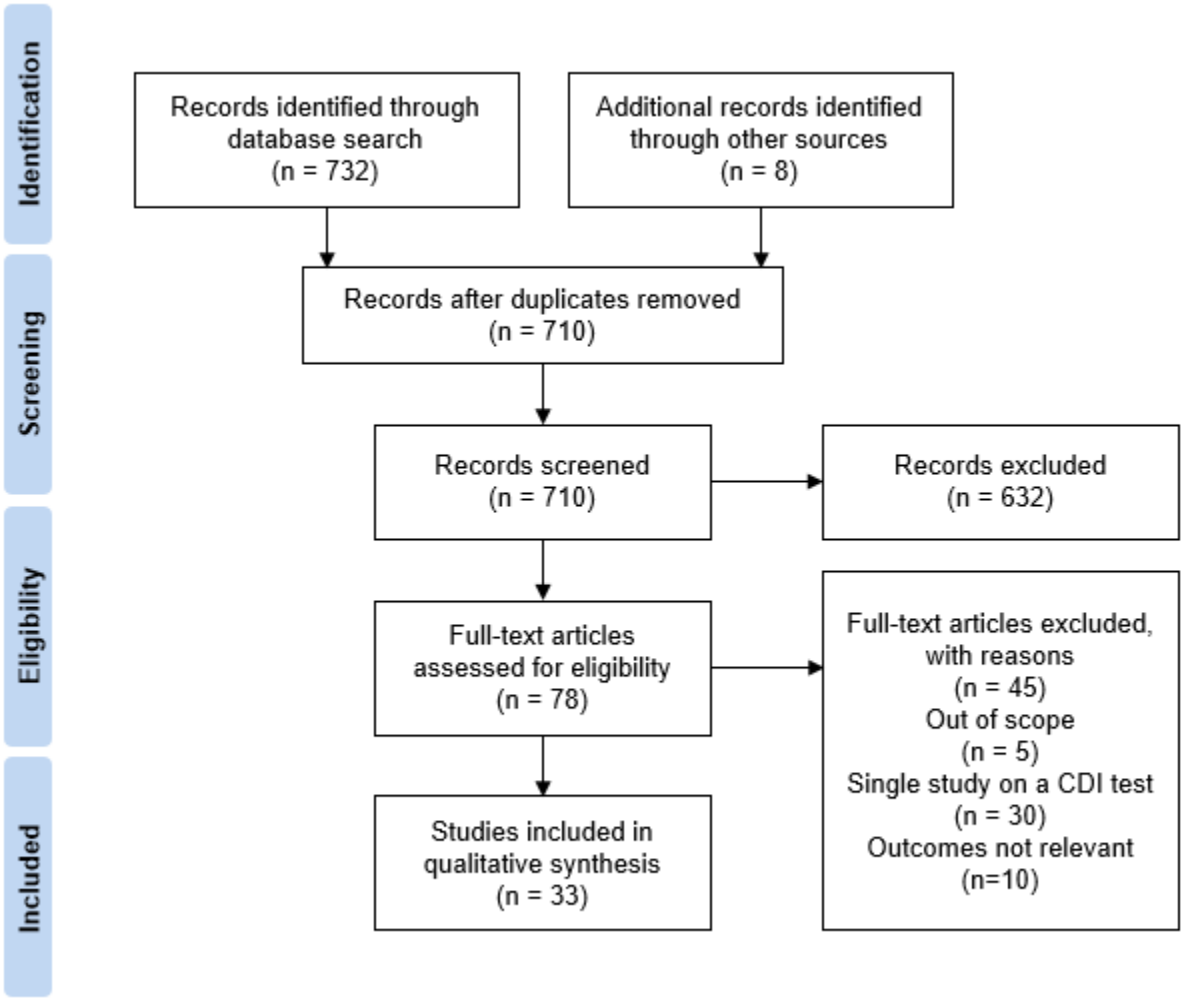
Figure A.13: Testing for *Clostridioides difficile*–Study Selection for Review



PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.14: Multicomponent Prevention Interventions for Clostridioides *difficile*–Study Selection for Review

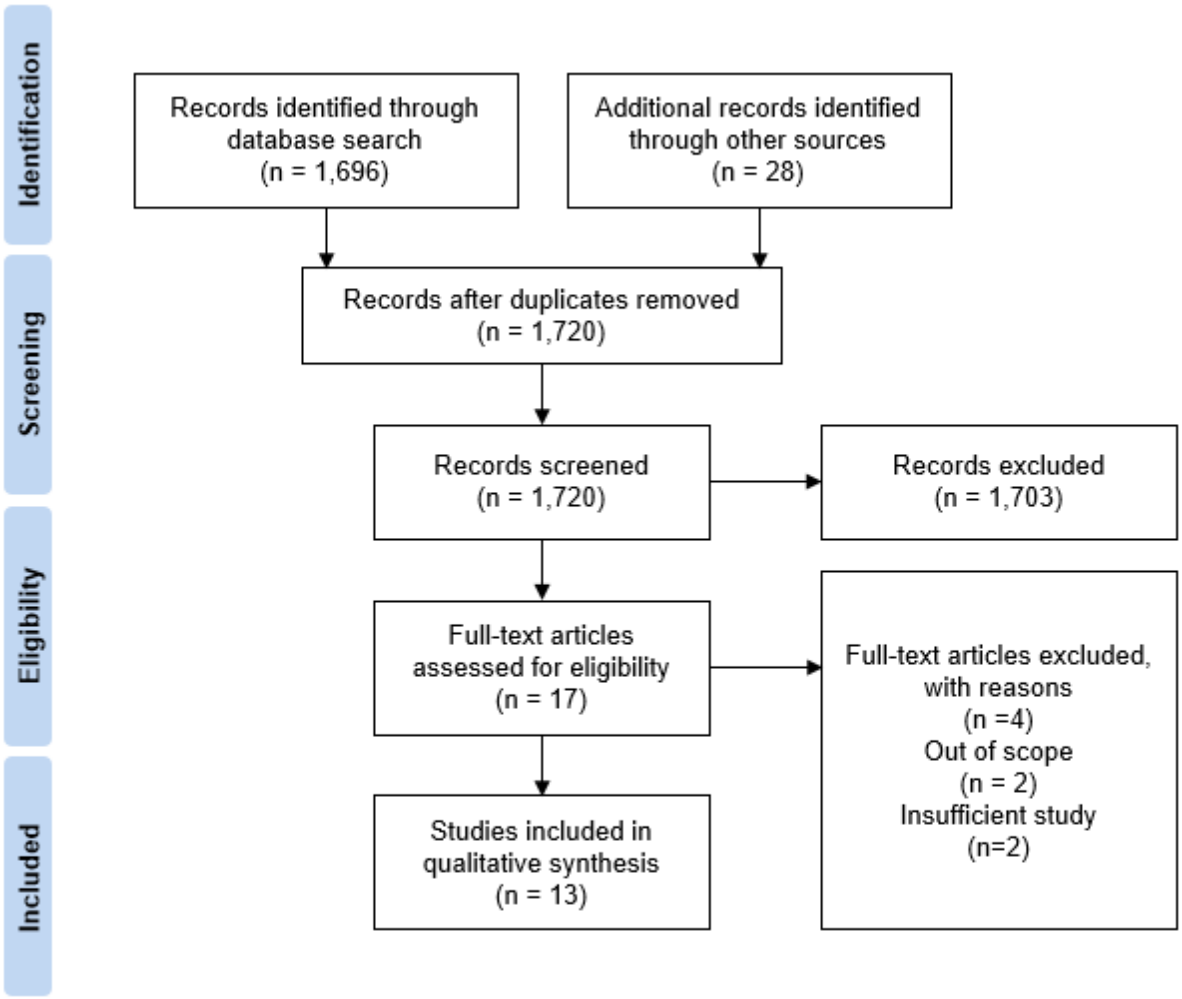


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Figure A.15: MDRO, Chlorhexidine Bathing—Study Selection for Review

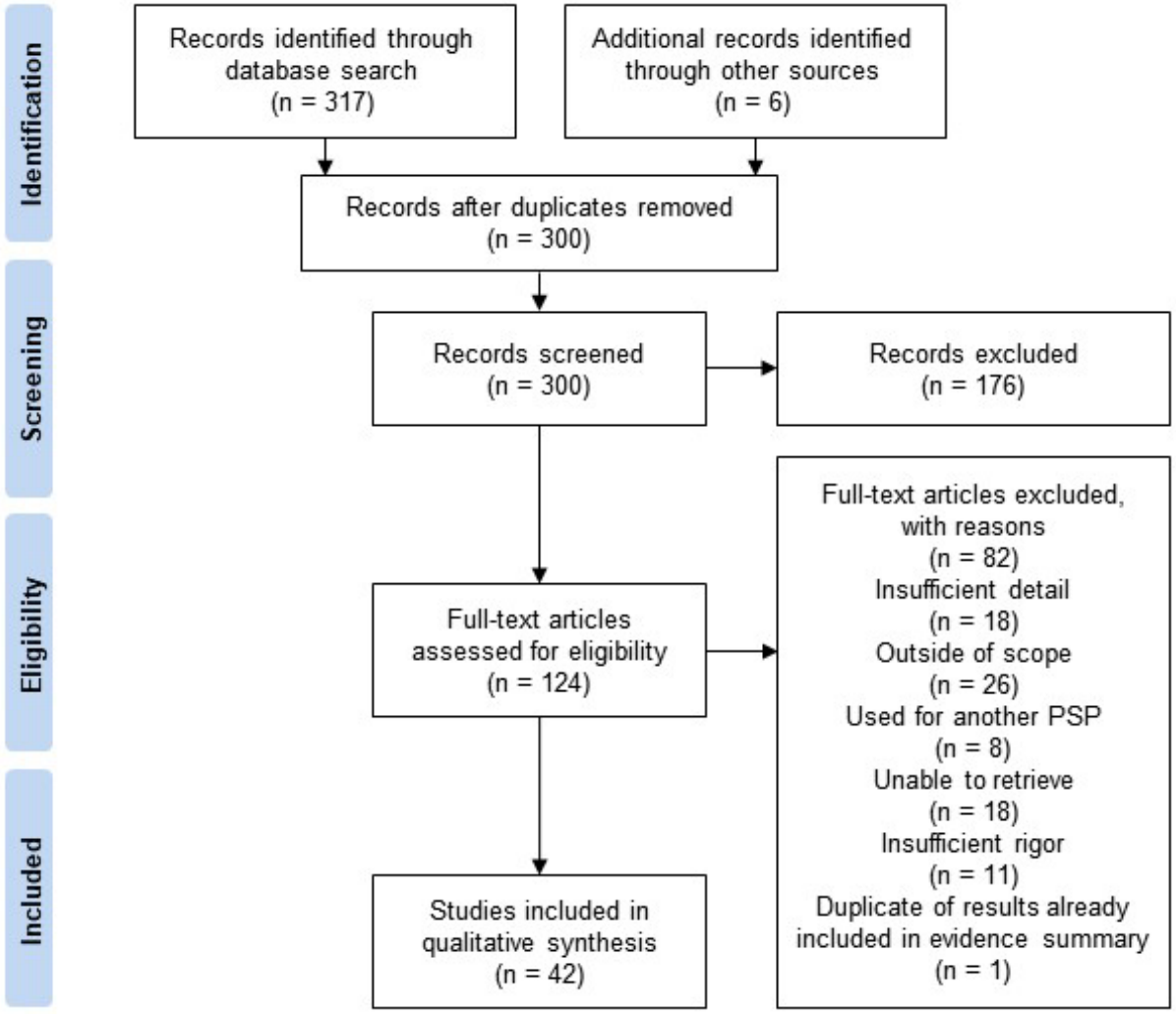

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Figure A.16: MDRO, Hand Hygiene—Study Selection for Review

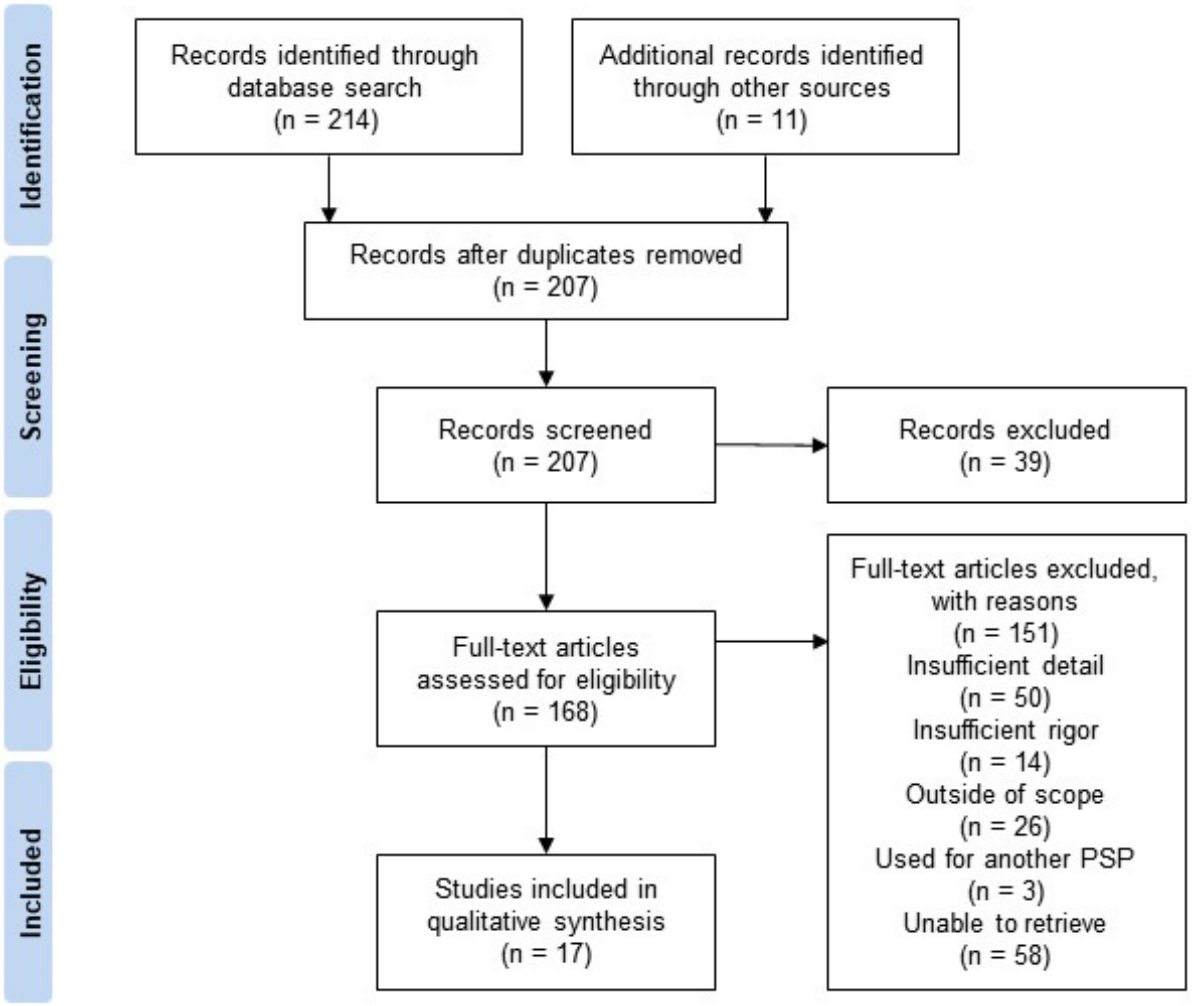

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Figure A.17: MDRO, Surveillance—Study Selection for Review

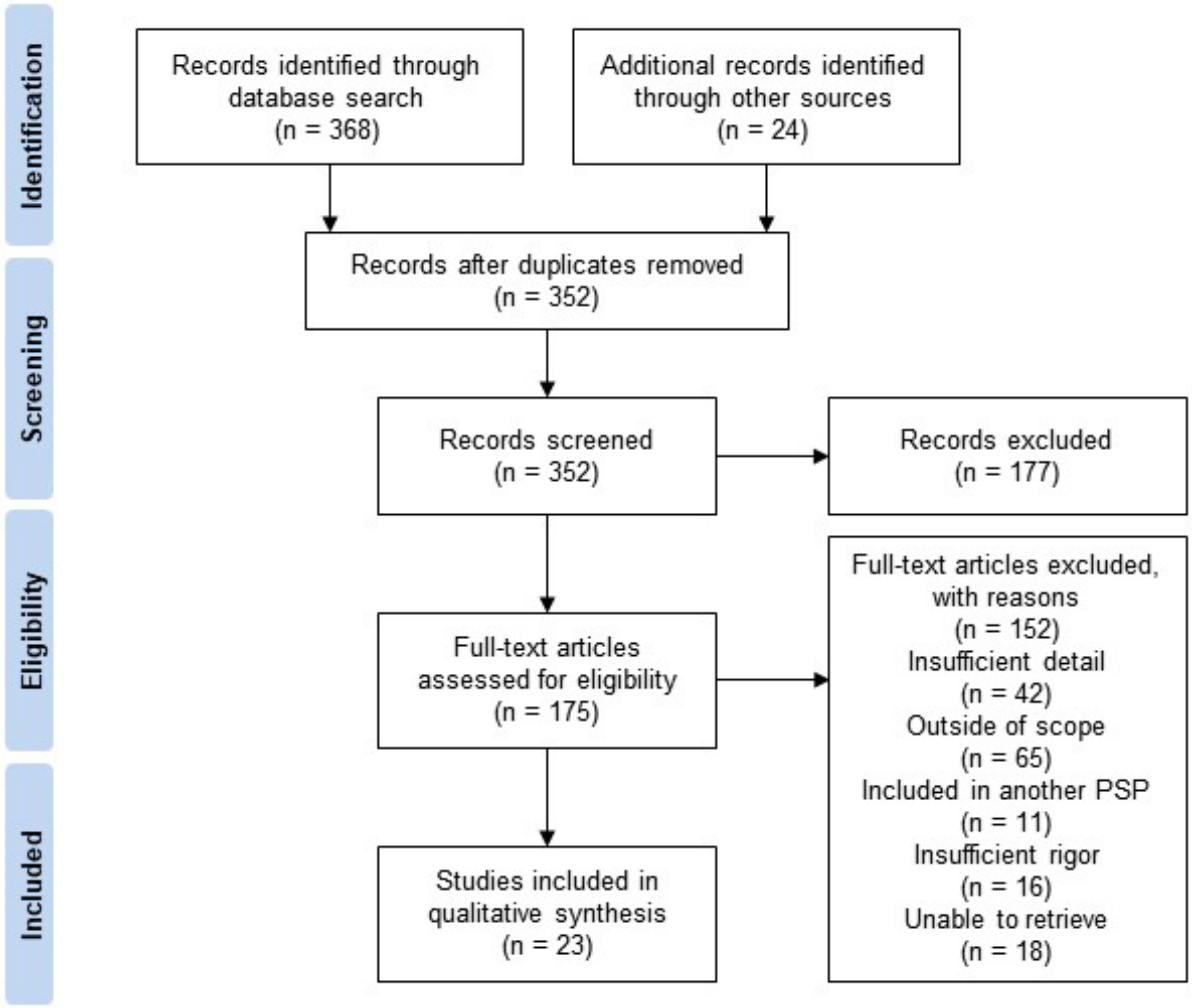

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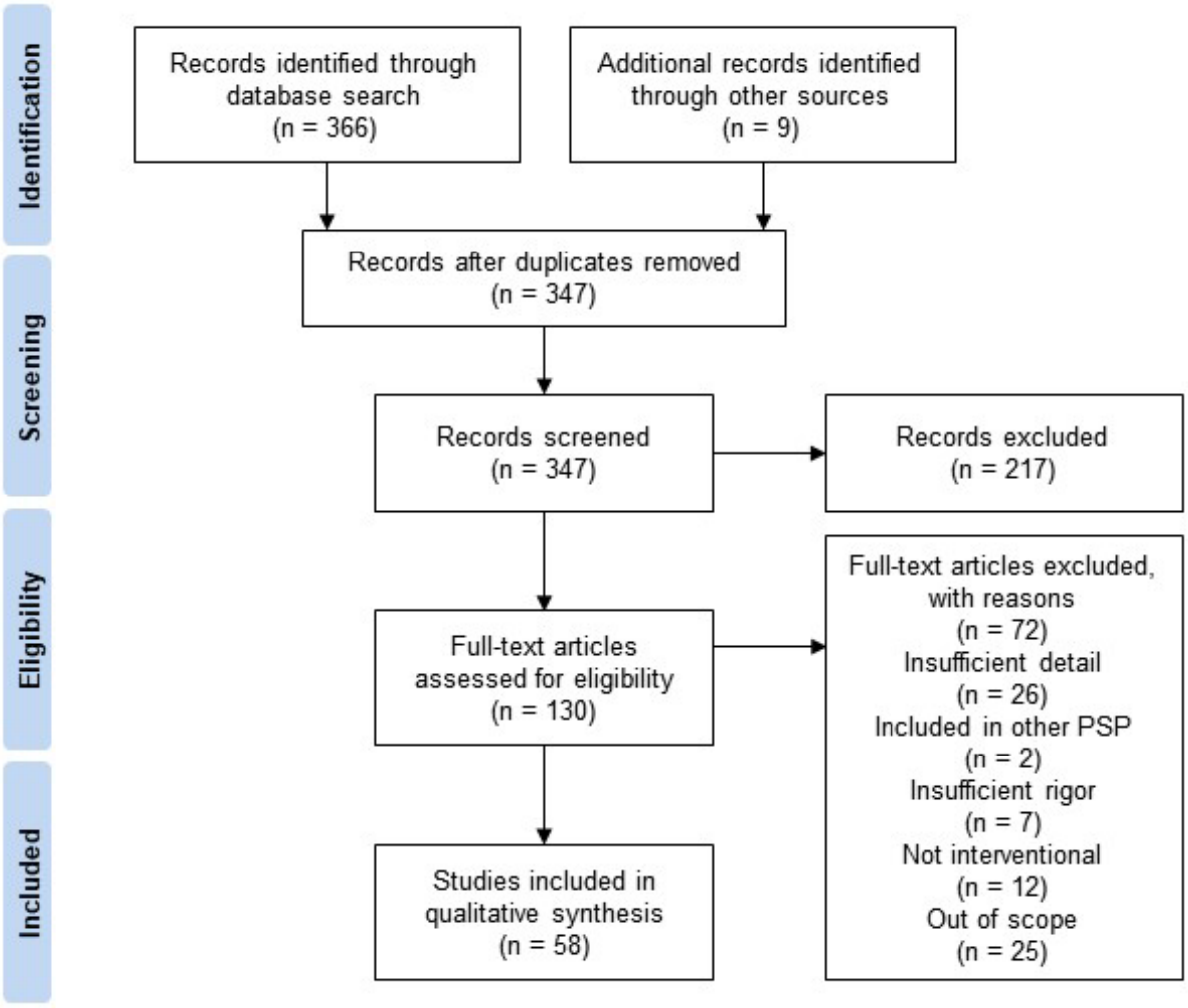
Figure A.18: MDRO, Environmental Cleaning and Disinfection—Study Selection for Review



PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al.. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.19: MDRO, Minimizing Catheter Use—Study Selection for Review

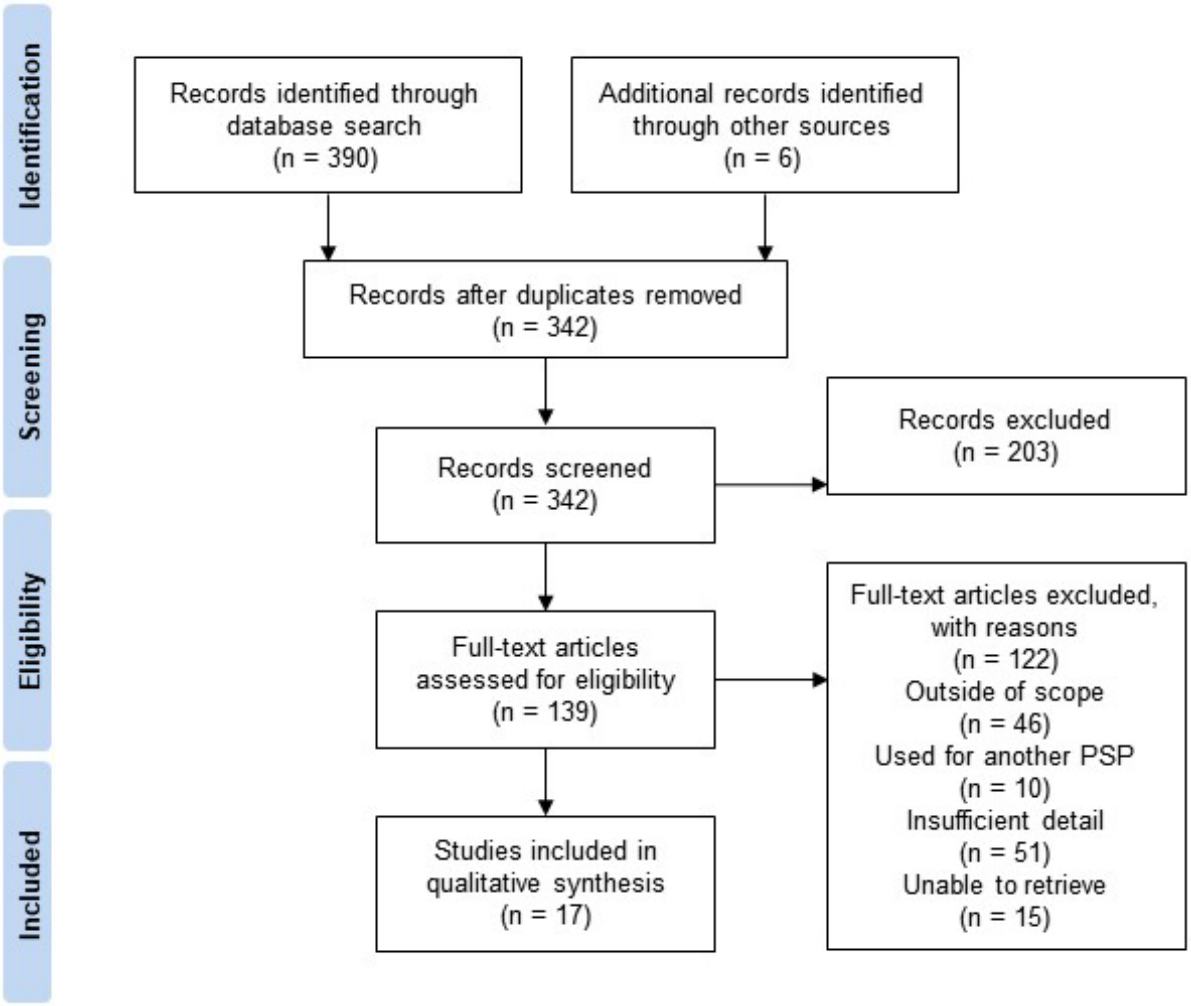


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Figure A.20: MDRO, Communication of Status—Study Selection for Review

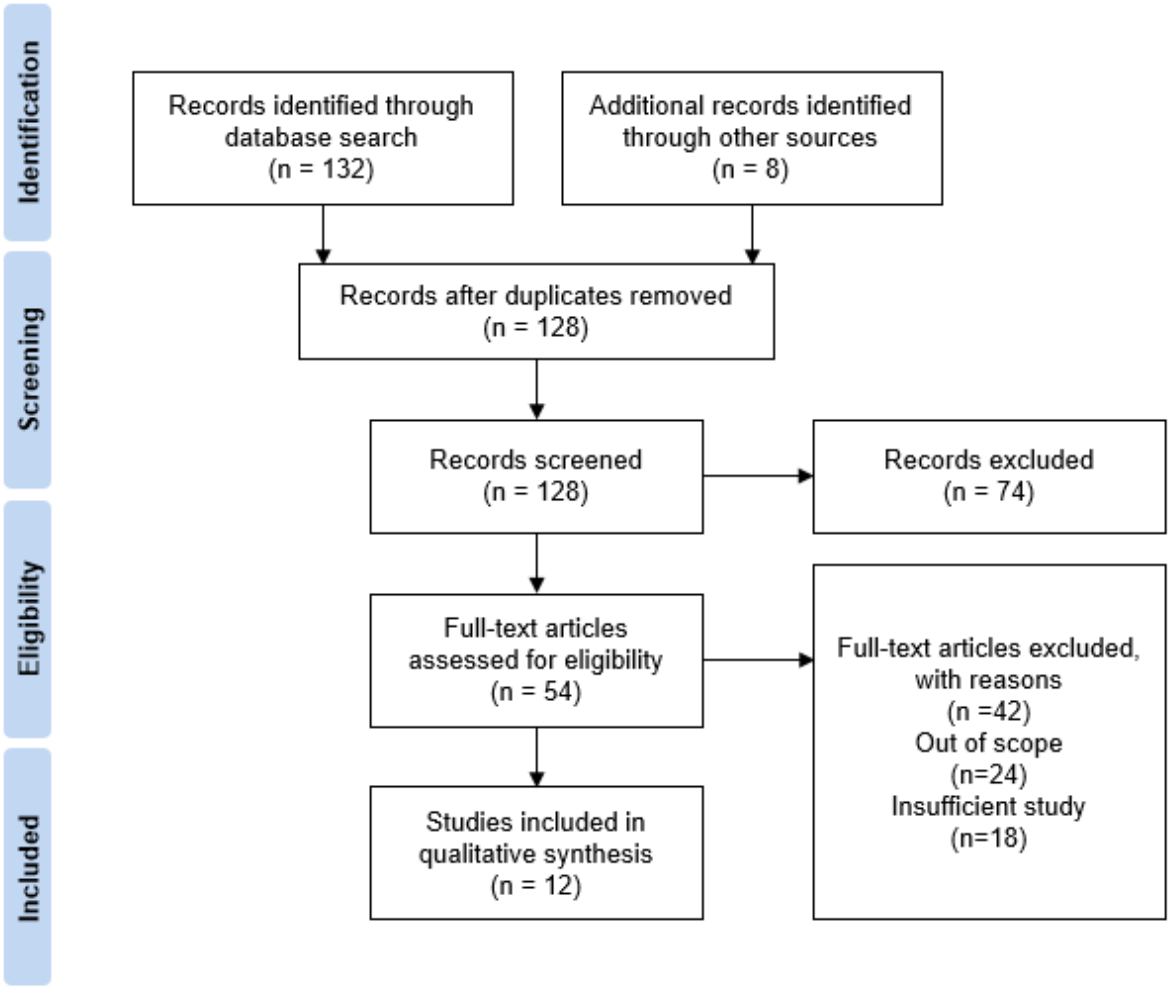

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Figure A.21: Carbapenem-Resistant *Enterobacteriaceae* Transmission-Based Precautions—Study Selection for Review

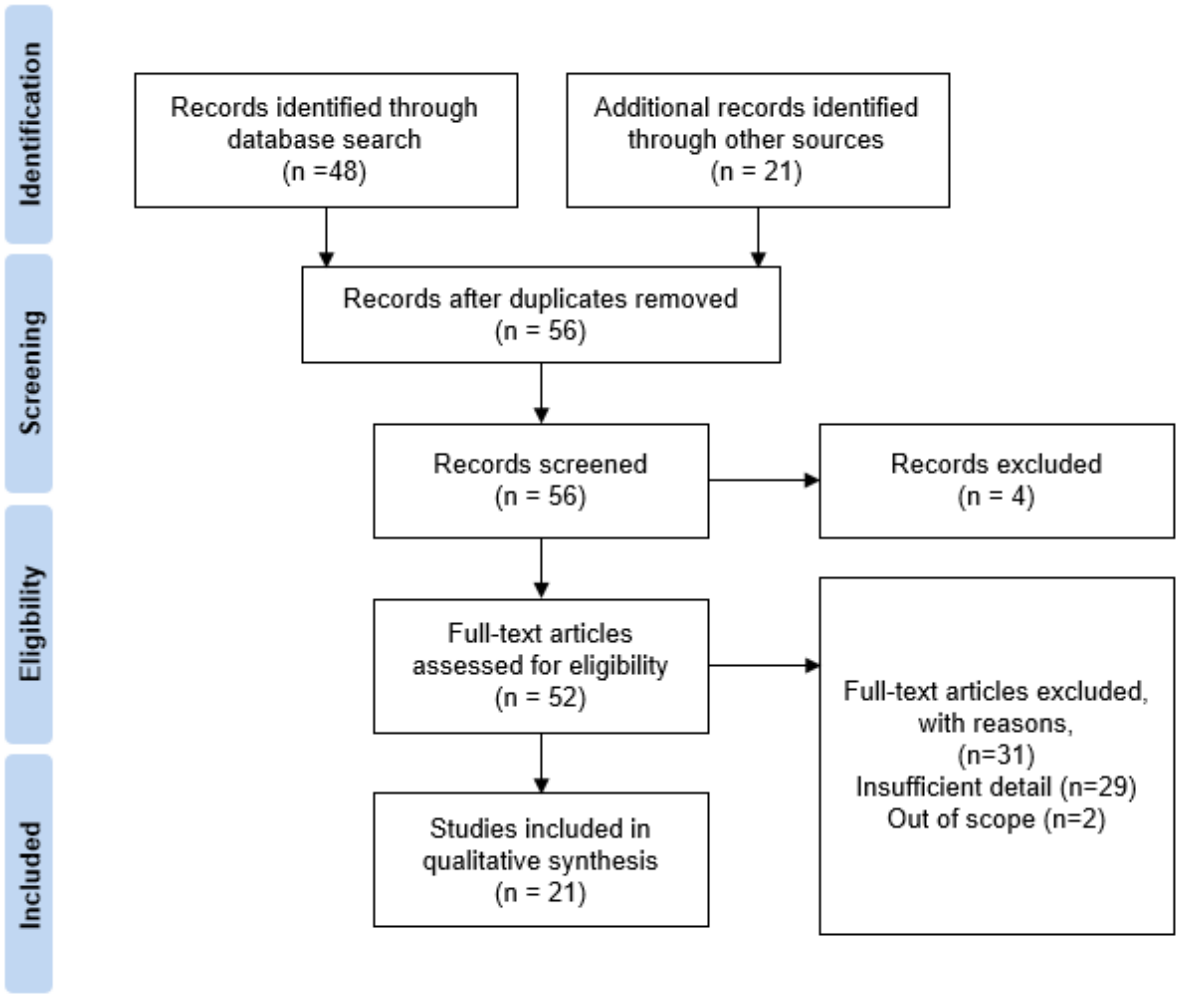

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Figure A.22: Anticoagulants, Management Service, Ambulatory Setting—Study Selection for Review

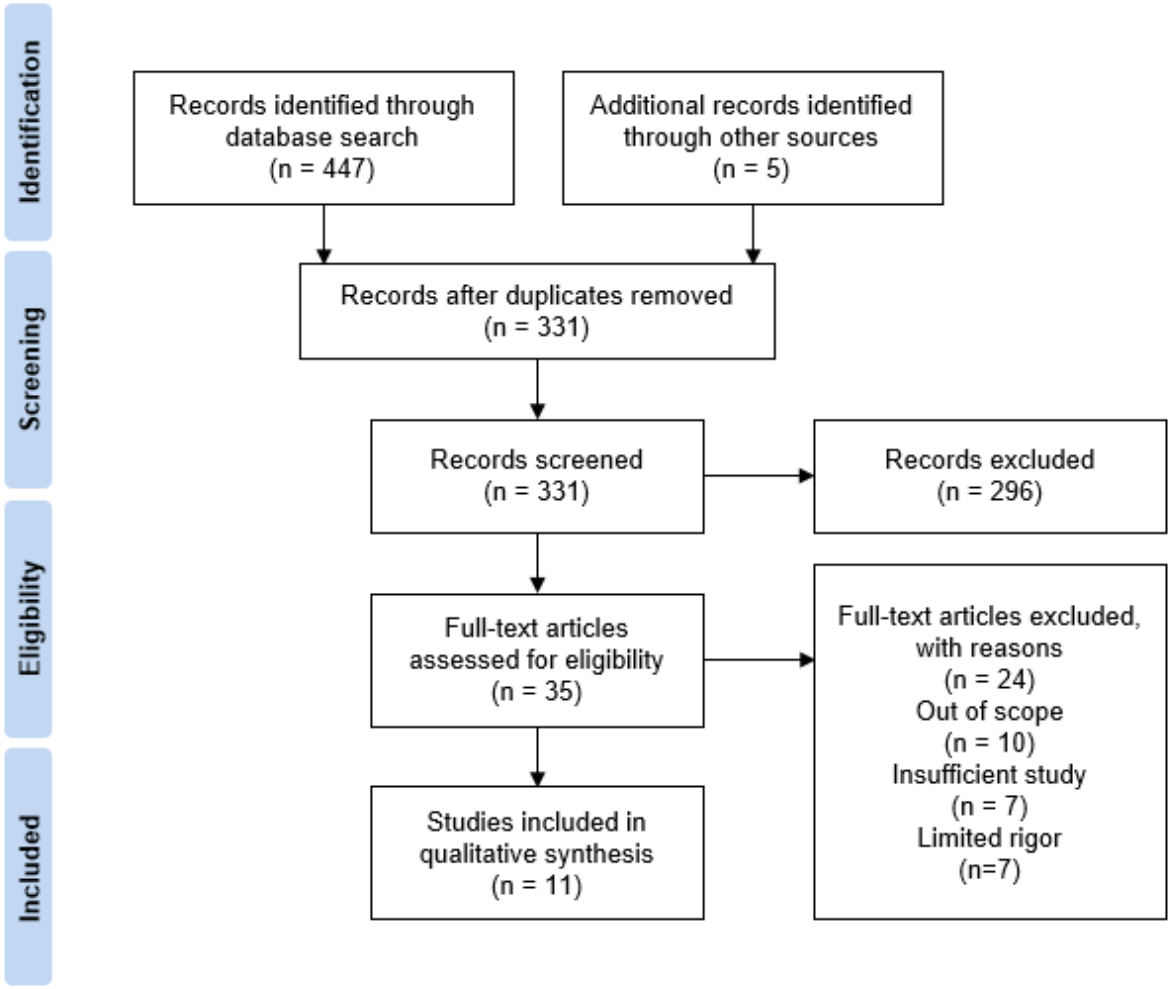

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Figure A.23: Anticoagulants, Protocols for Newer Oral Anticoagulants—Study Selection for Review

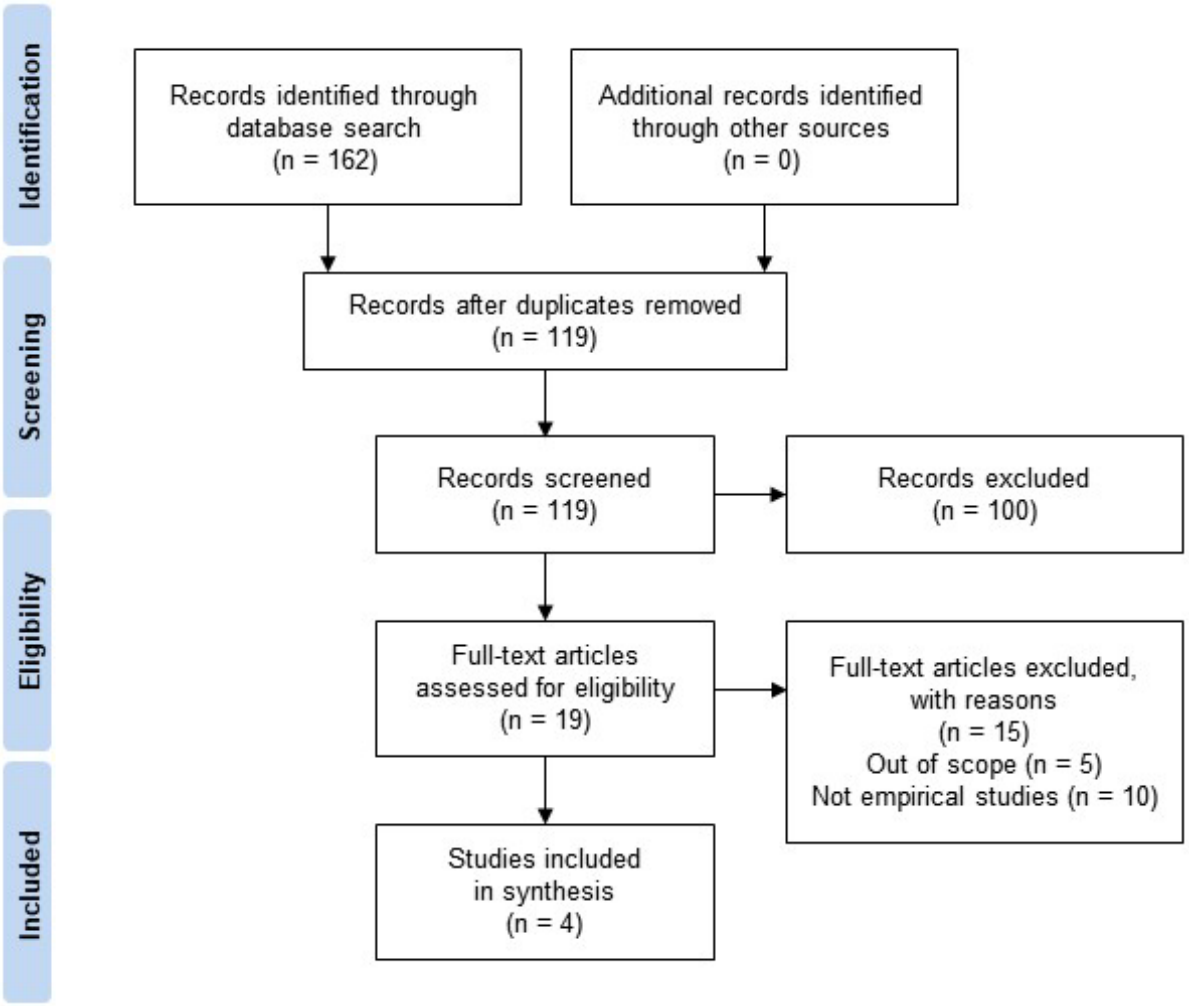

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Figure A.24: Anticoagulants, Transitions Between Hospital or Emergency Department and Home—Study Selection for Review

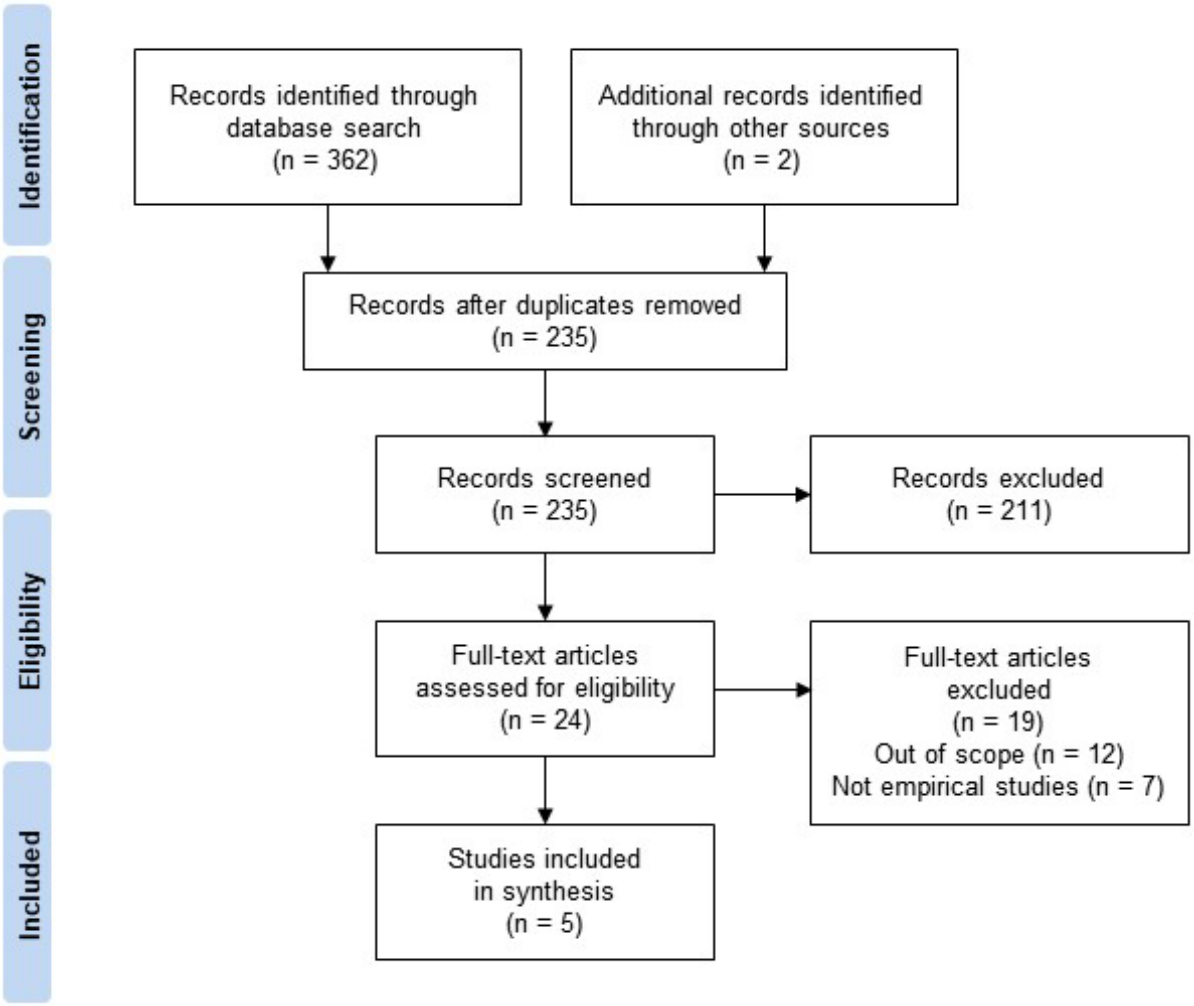

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Figure A.25: Harms Due to Diabetic Agents, Insulin Protocol—Study Selection for Review

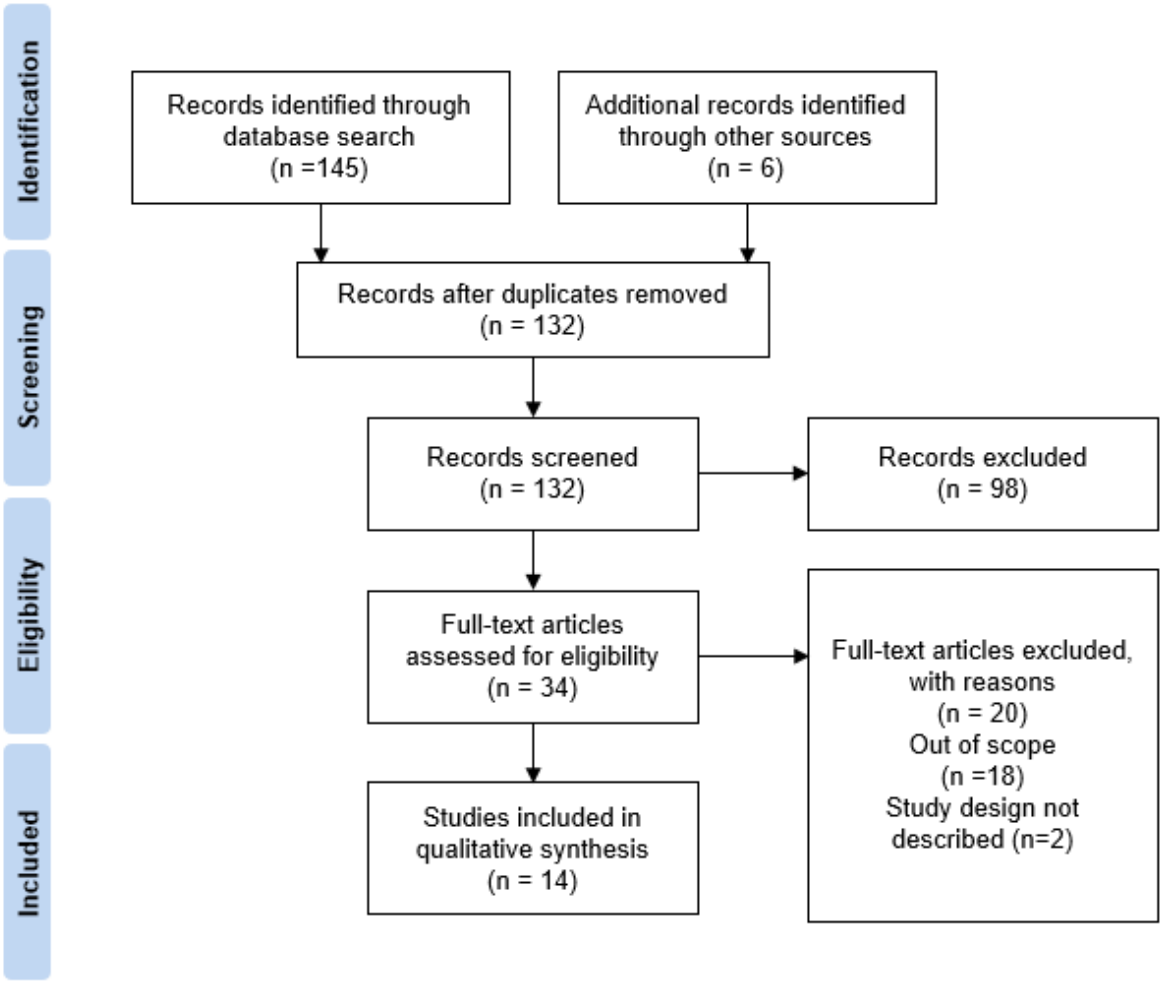

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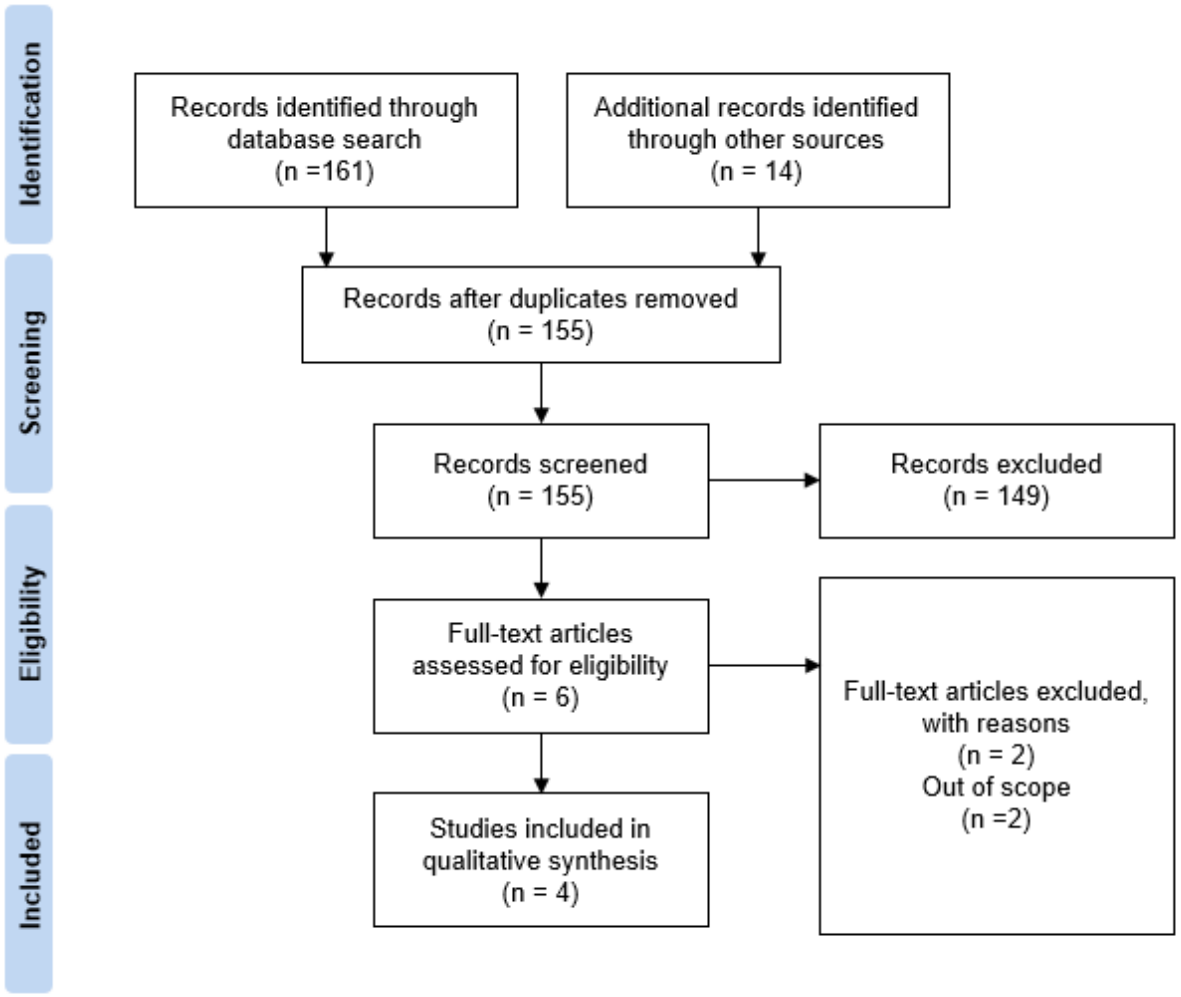
Figure A.26: Harms Due to Diabetic Agents, Teach-Back—Study Selection for Review



PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.27: Reducing Adverse Drug Events in Older Adults, Deprescribing To Reduce Polypharmacy—Study Selection for Review

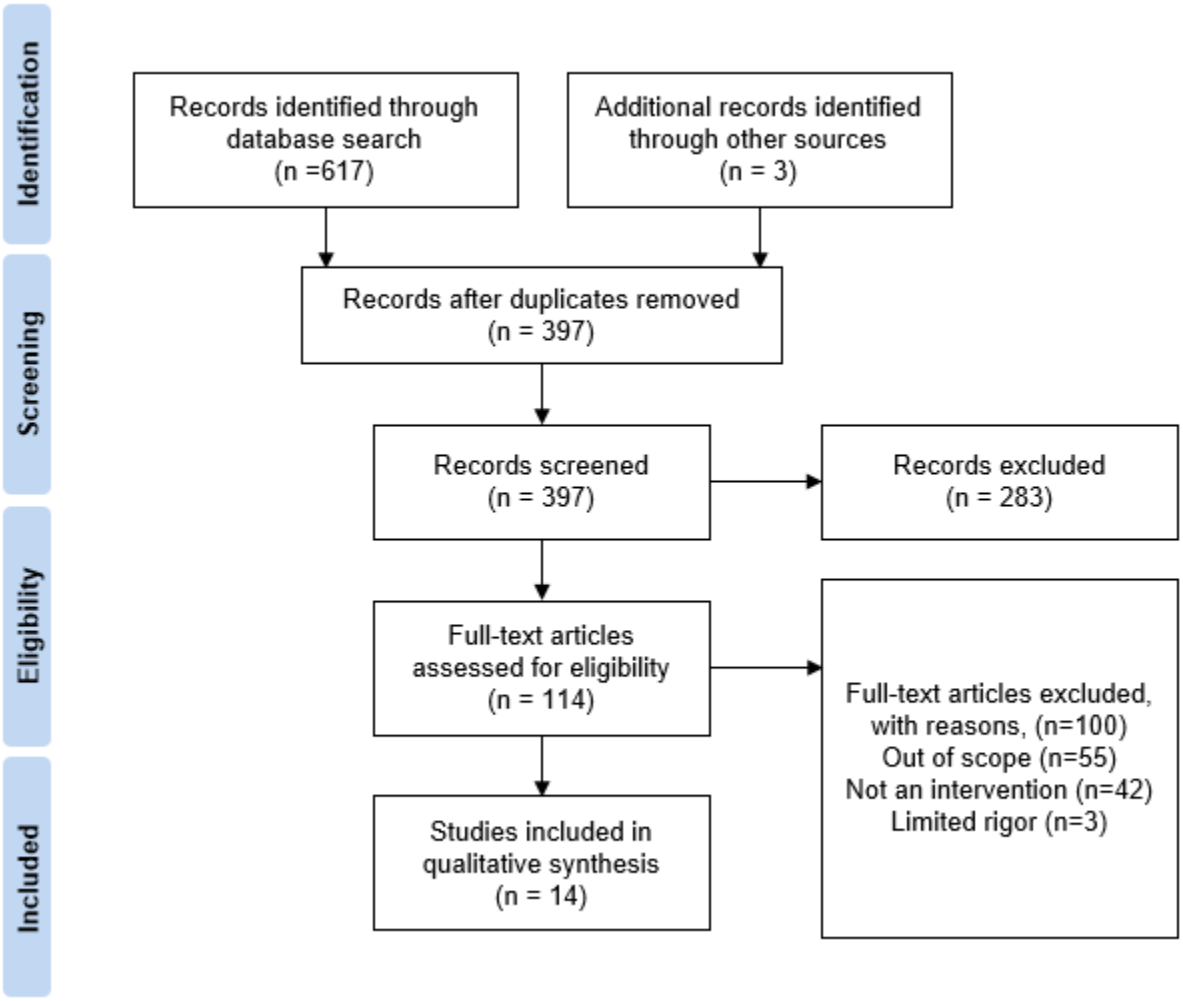


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Figure A.28: Reducing Adverse Drug Events in Older Adults, Using the STOPP (Screening Tool of Older Person's inappropriate Prescriptions) Criteria—Study Selection for Review

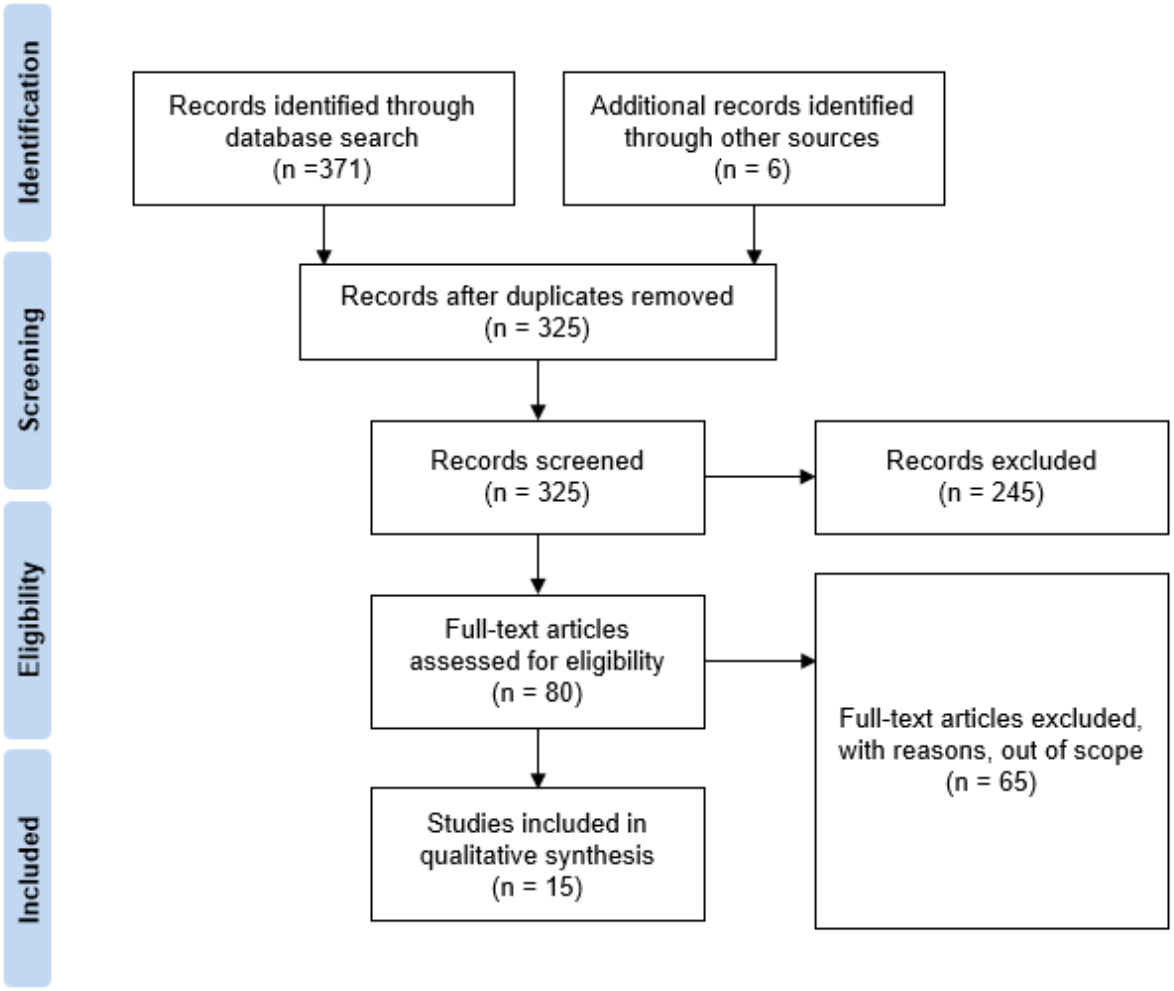

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Figure A.29: Opioids, Opioid Stewardship—Study Selection for Review

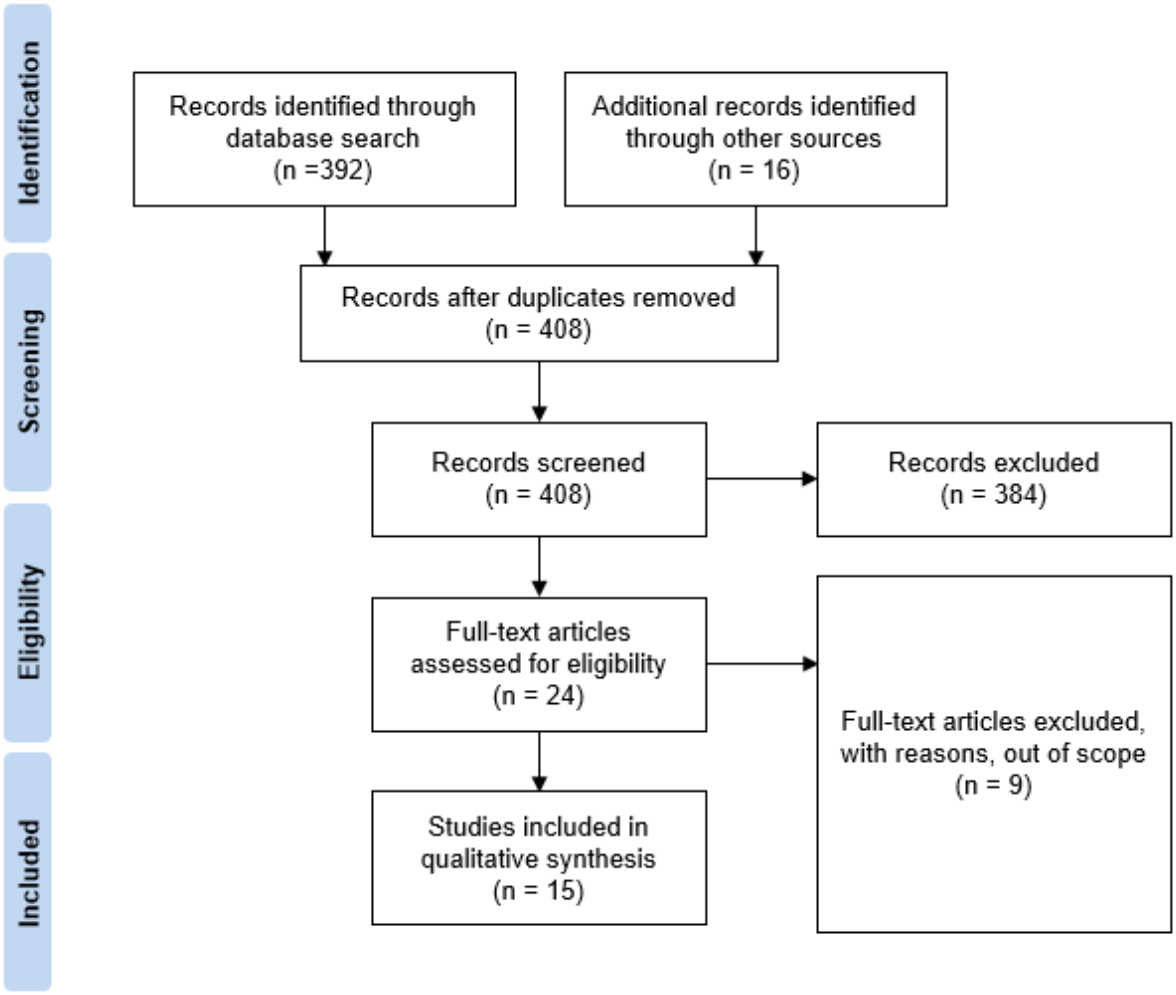

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Figure A.30: Opioids, Medication-Assisted Treatment—Study Selection for Review

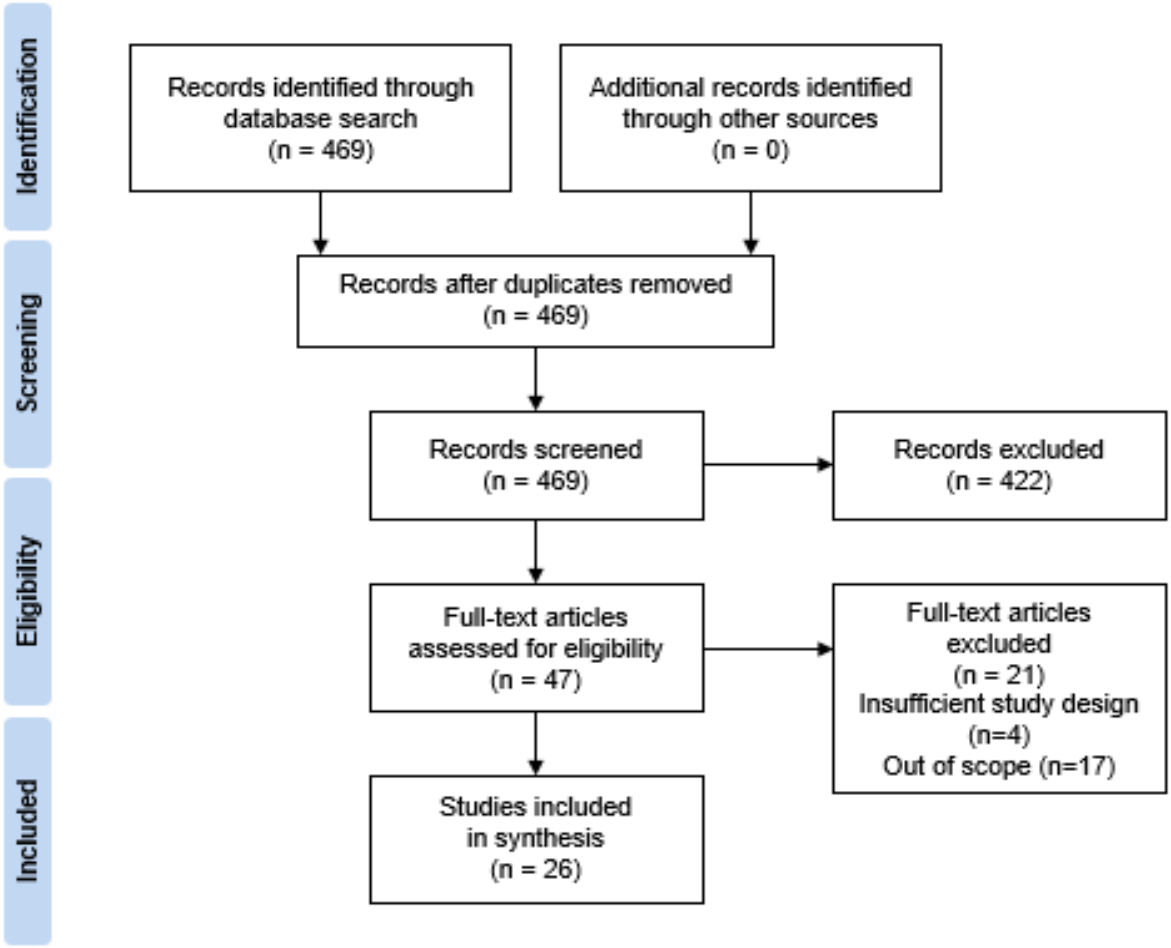

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Figure A.31: Patient Identification Errors in the Operating Room—Study Selection for Review

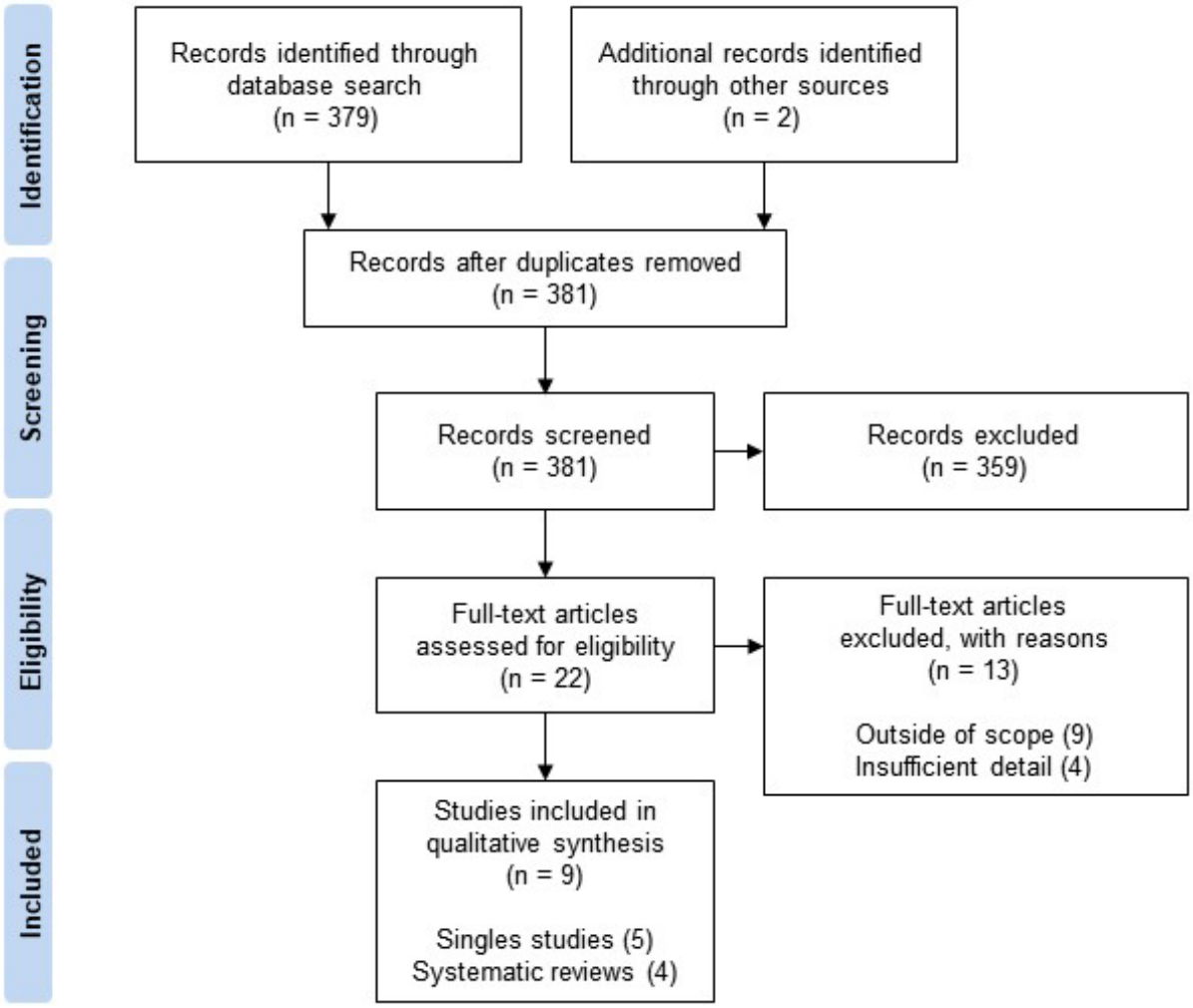

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Figure A.32: Infusion Pumps, Structured Process Change and Workflow Redesign—Study Selection for Review

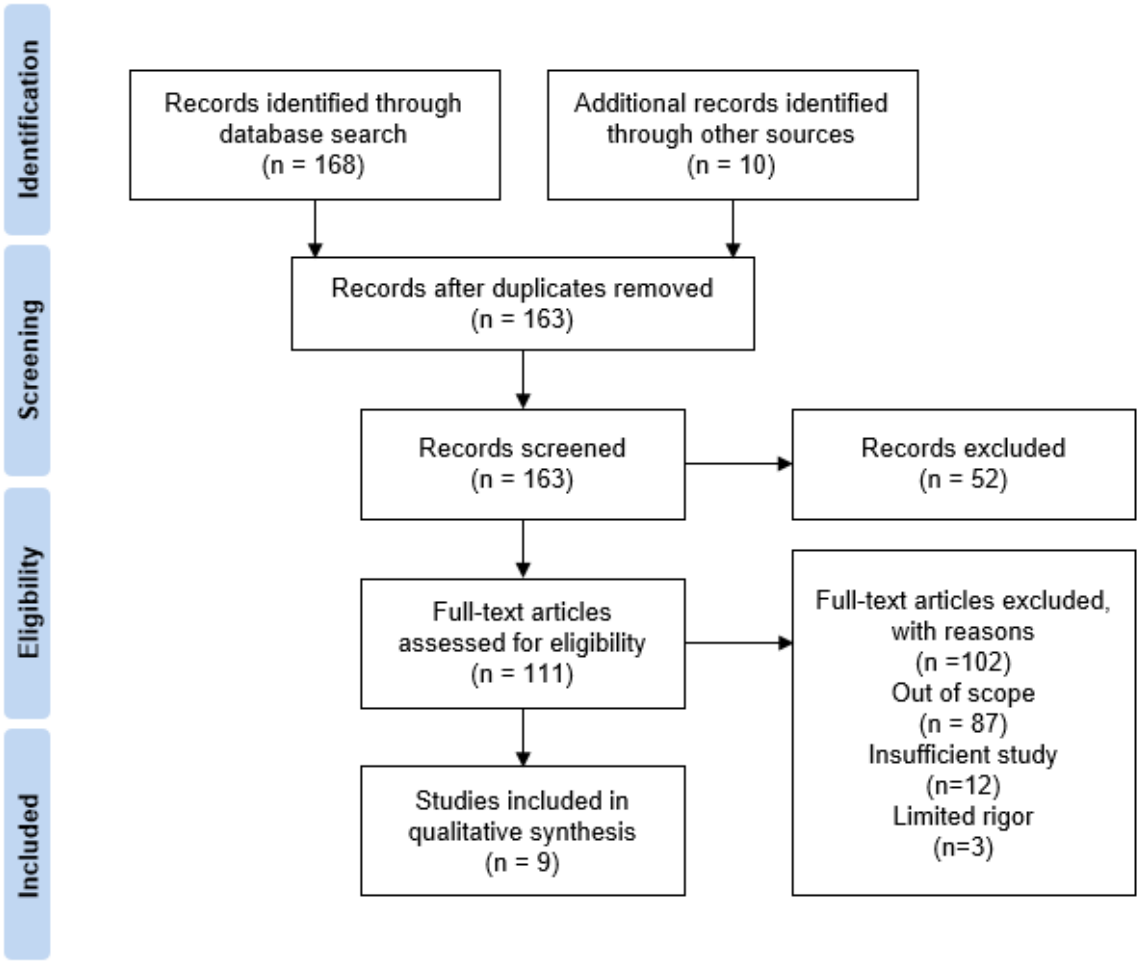

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Figure A.33: Infusion Pumps, Staff Education and Training—Study Selection for Review

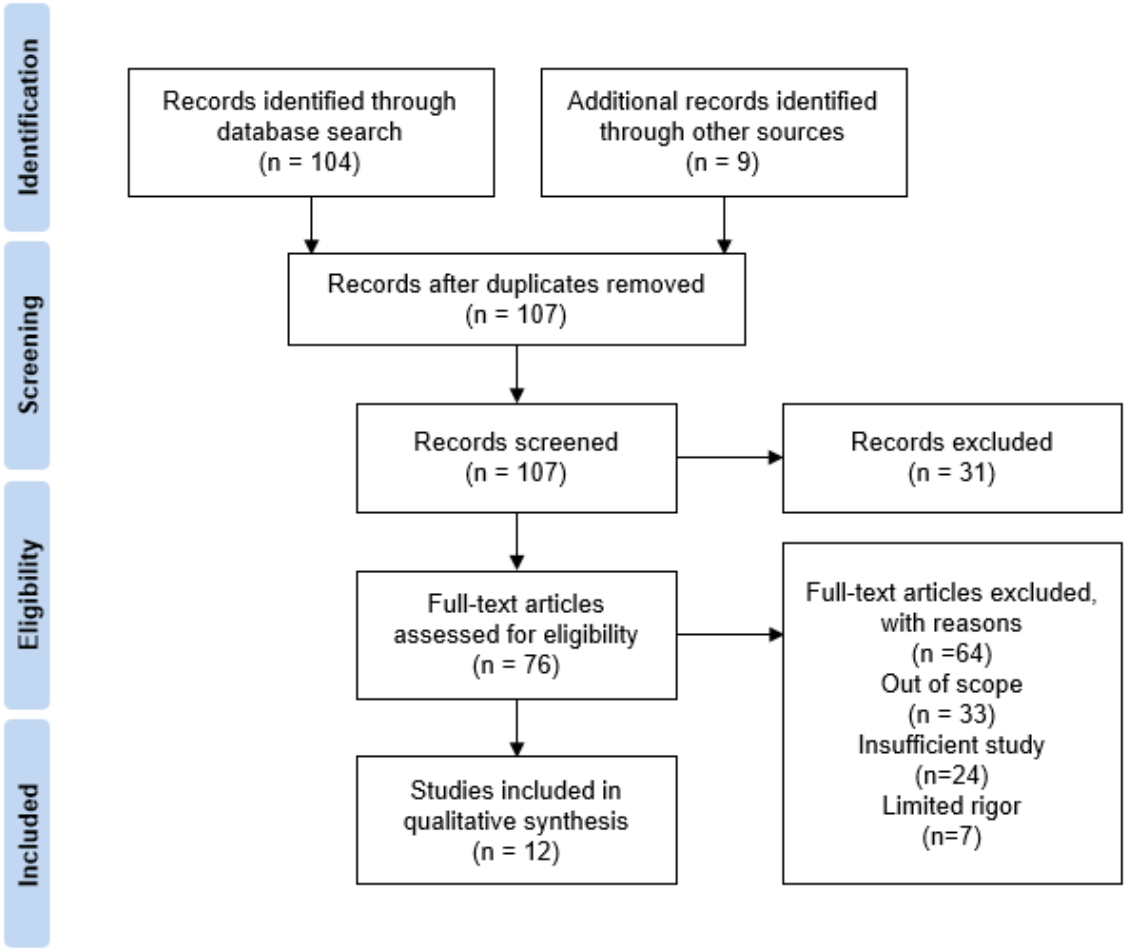

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Figure A.34: Alarm Fatigue, Safety Culture—Study Selection for Review

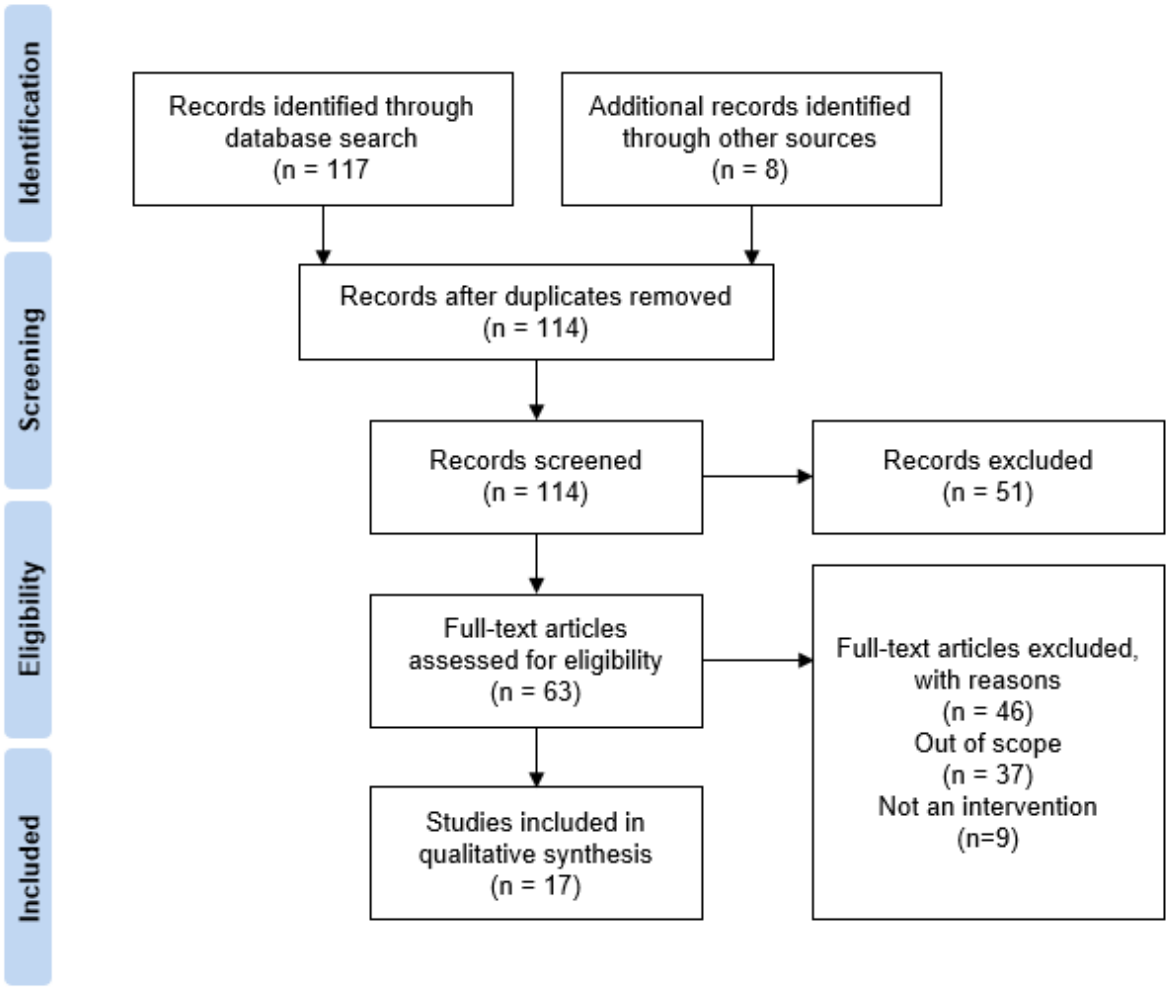

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Figure A.35: Alarm Fatigue, Risk Assessment—Study Selection for Review

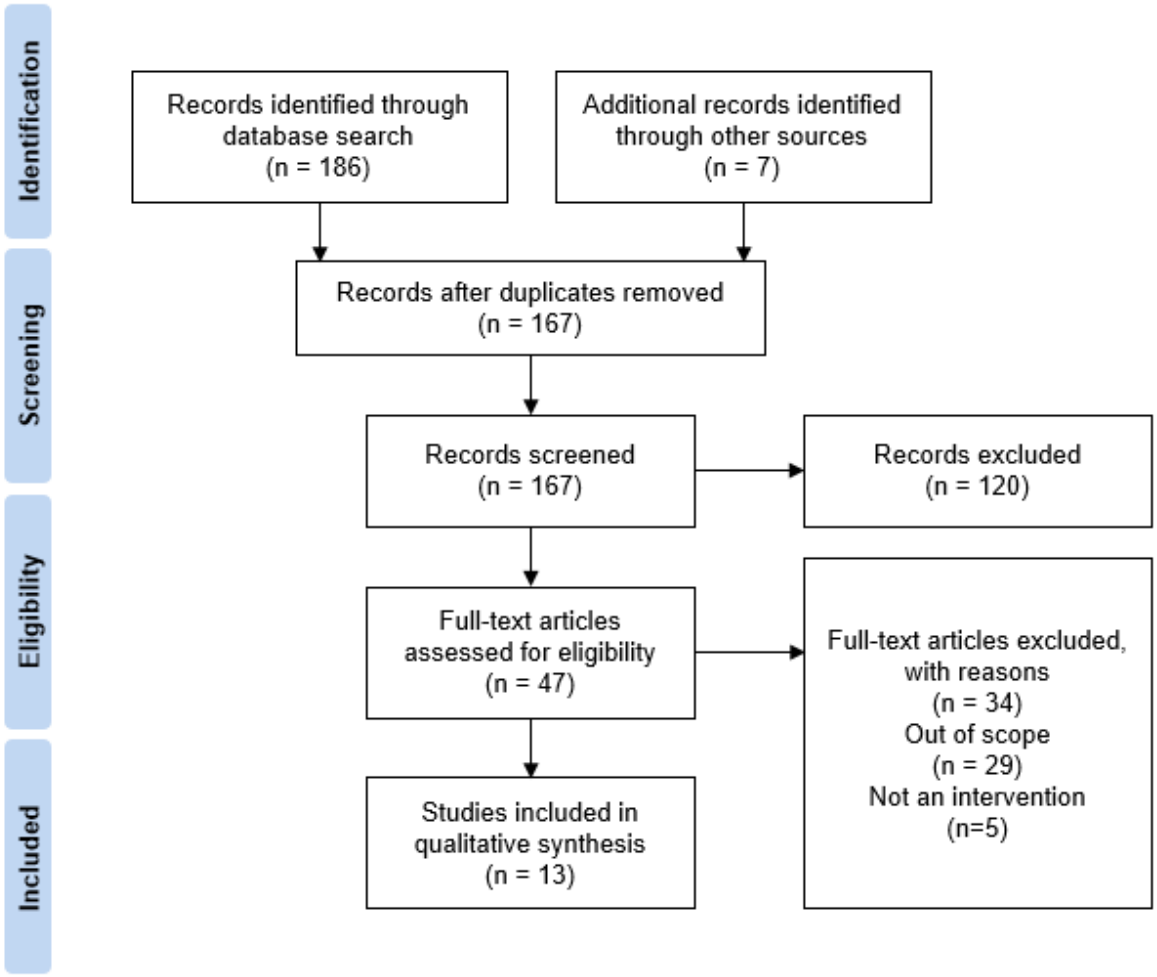

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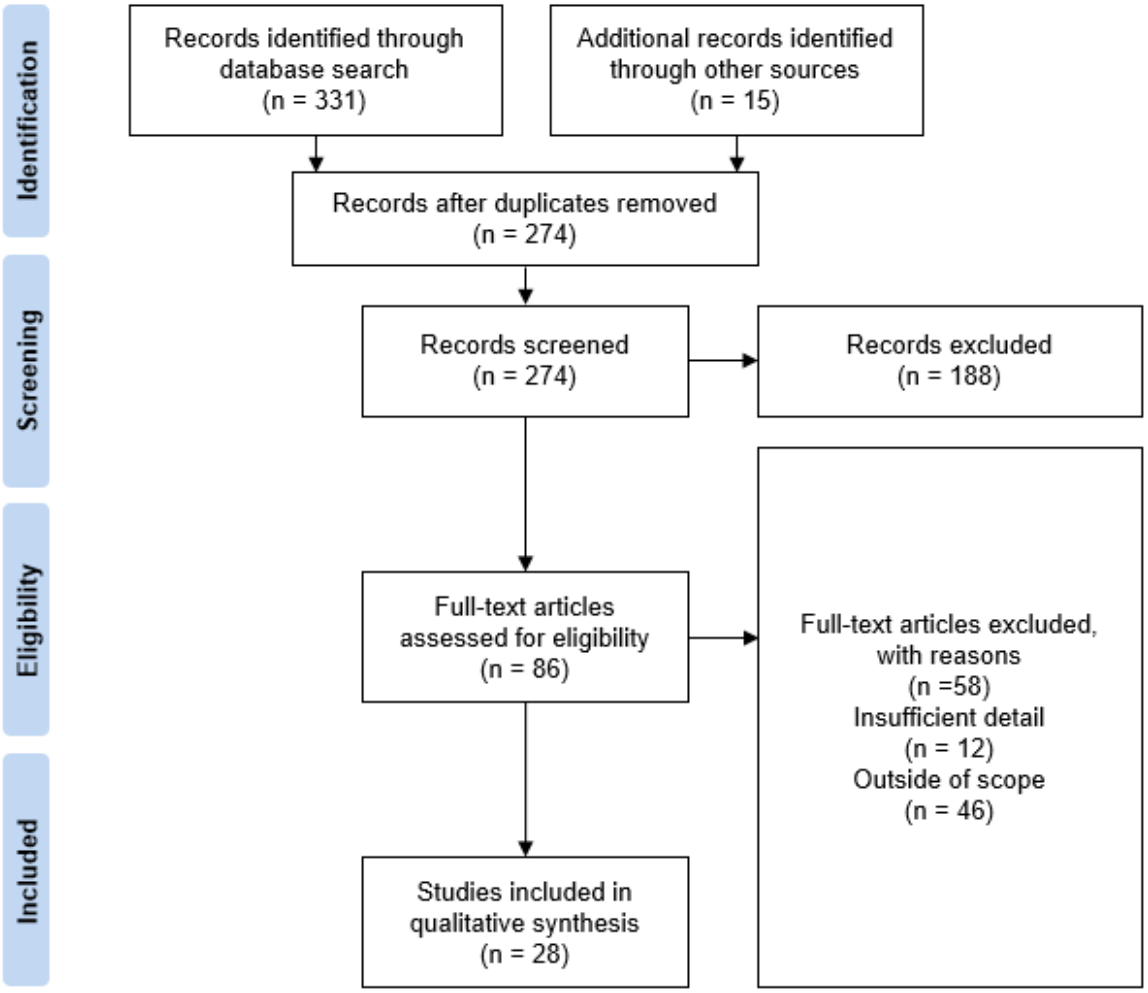
Figure A.36: Delirium, Screening and Assessment—Study Selection for Review



Criteria as described by Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Figure A.37: Delirium, Staff Education and Training—Study Selection for Review

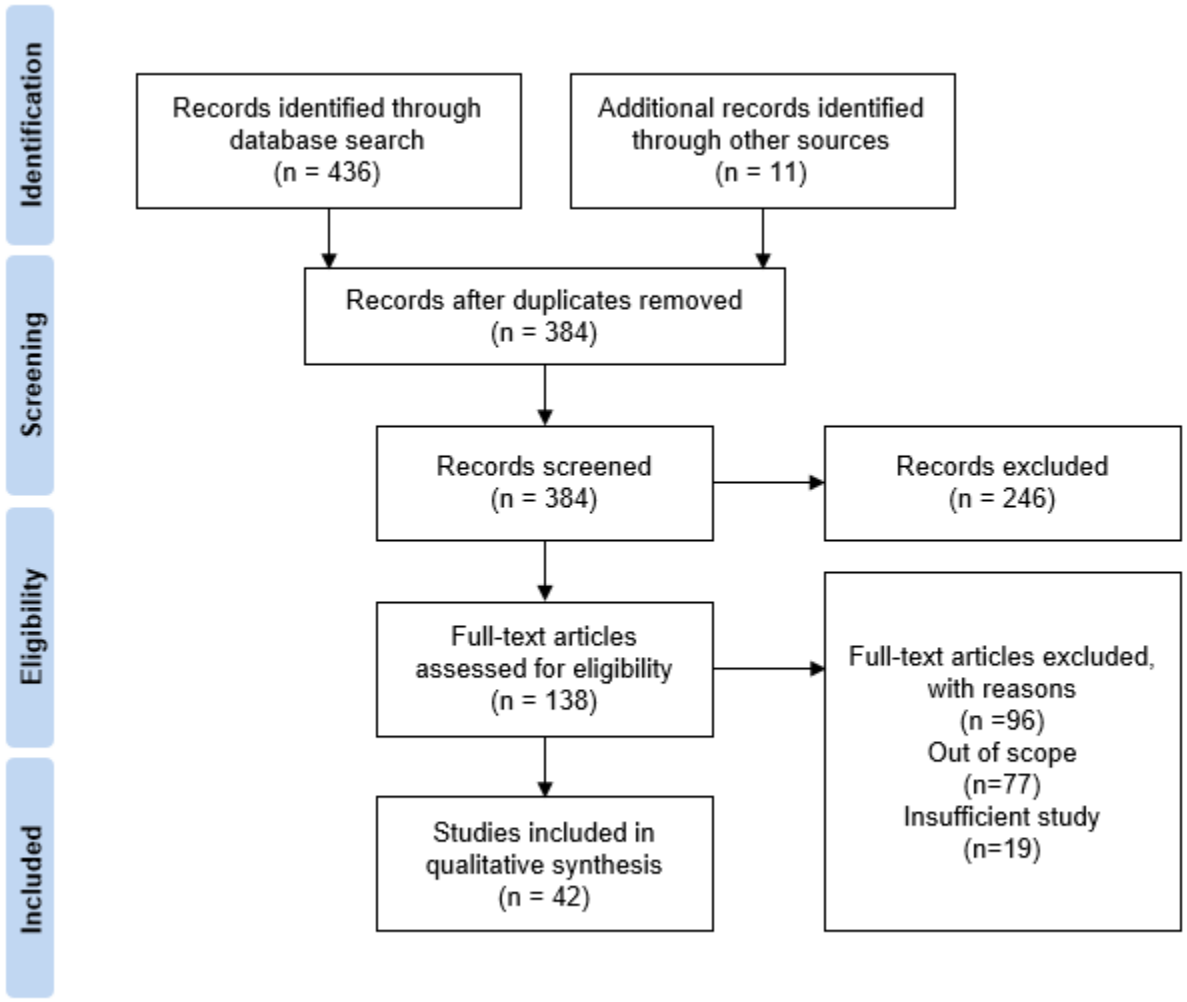


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Figure A.38: Delirium, Nonpharmacological Interventions To Prevent Intensive Care Unit Delirium—Study Selection for Review

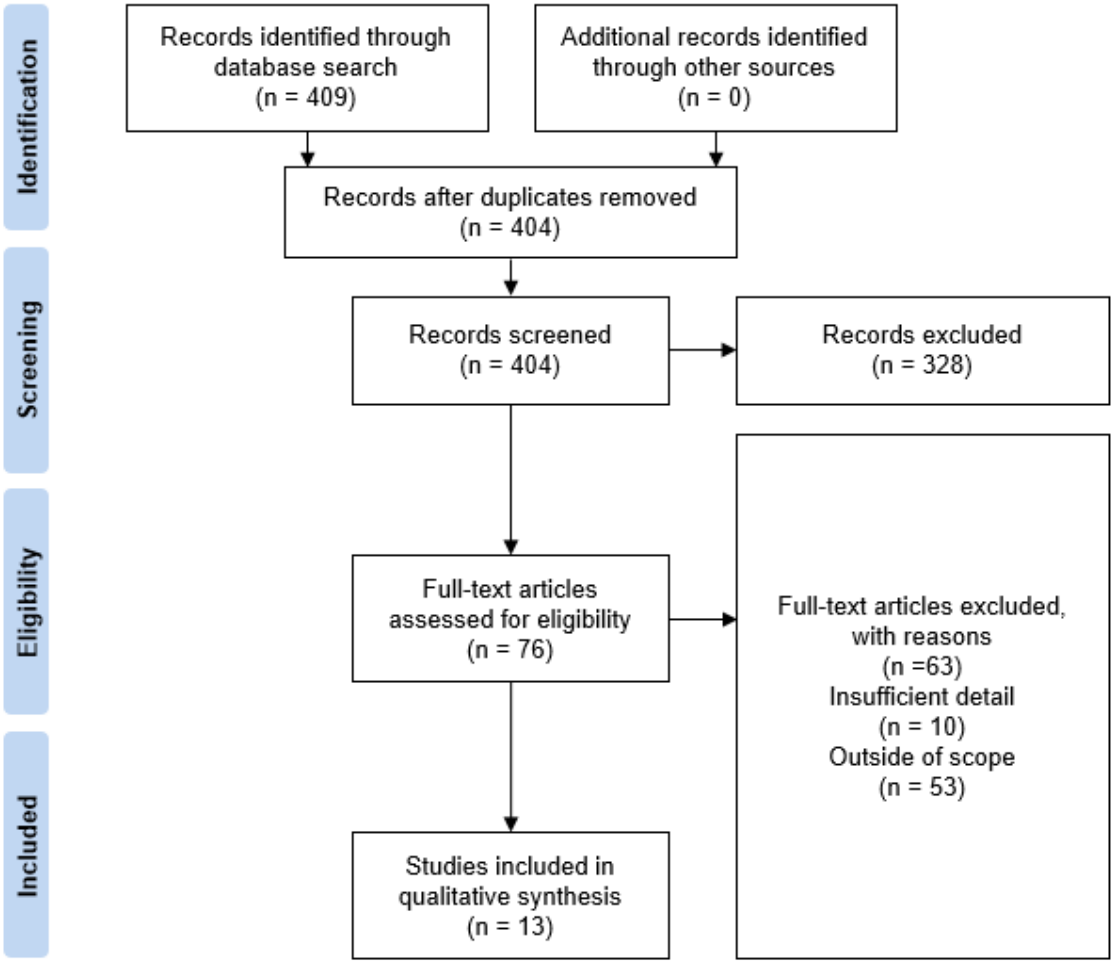

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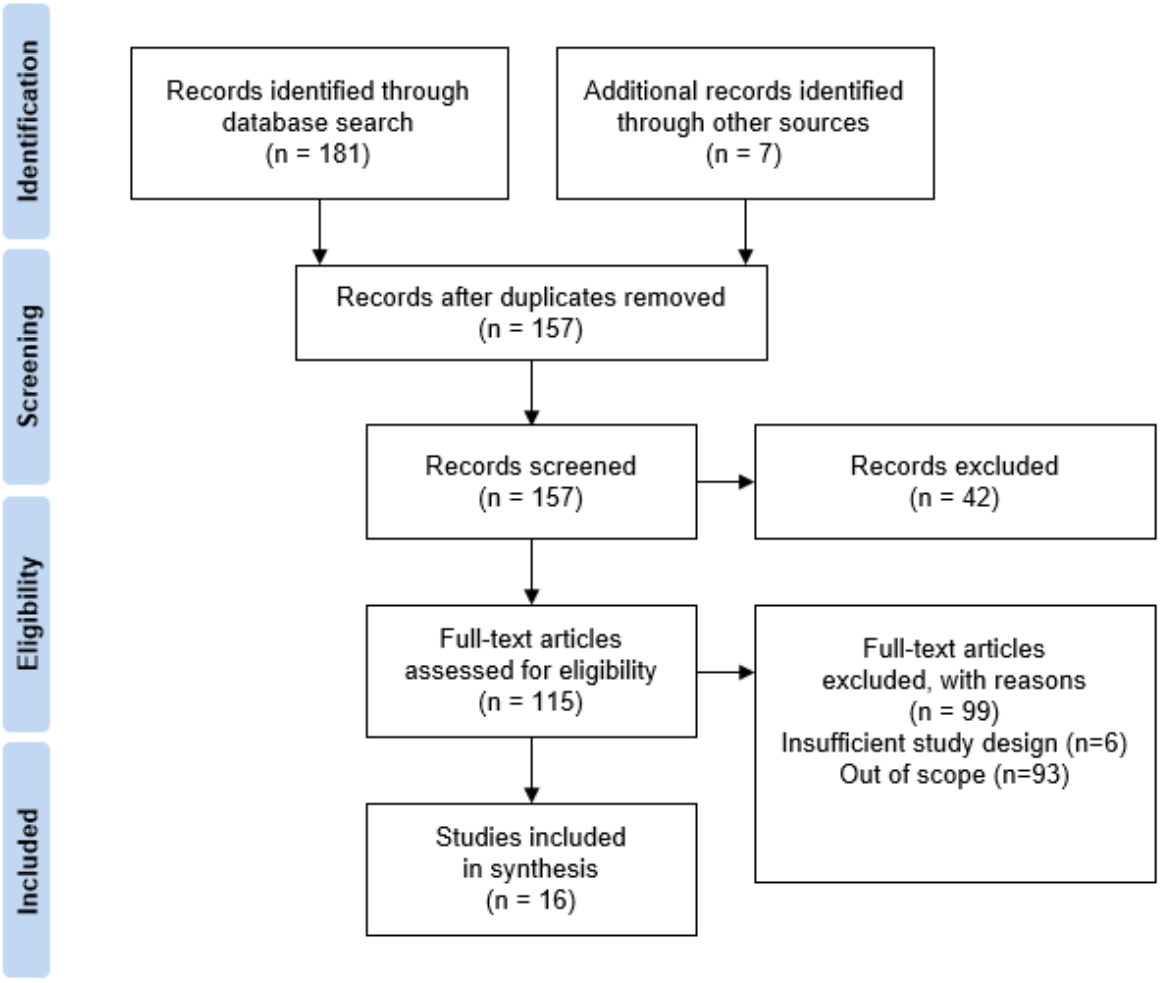
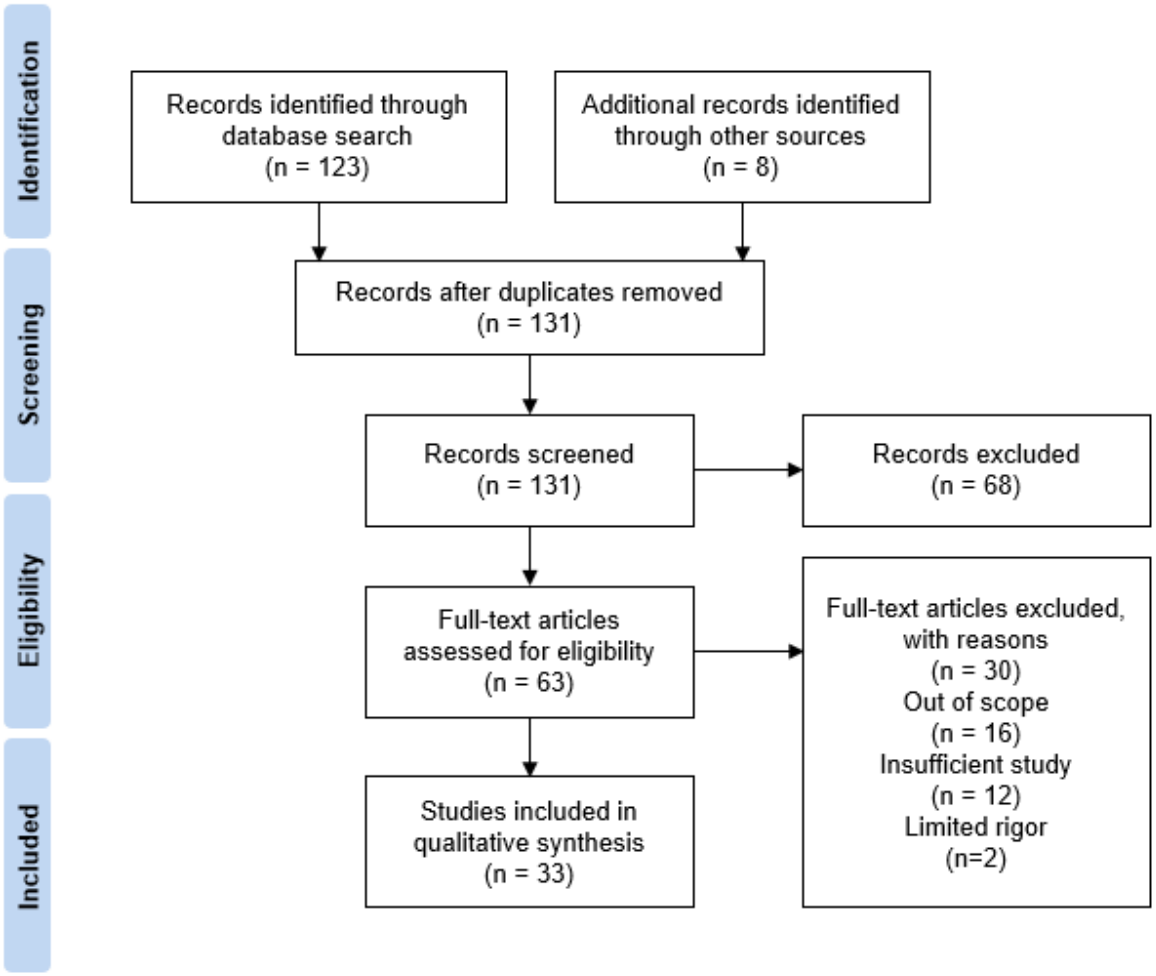
Figure A.39: Care Transitions, Use of Multi-Element Models To Improve Care Transitions—Study Selection for Review



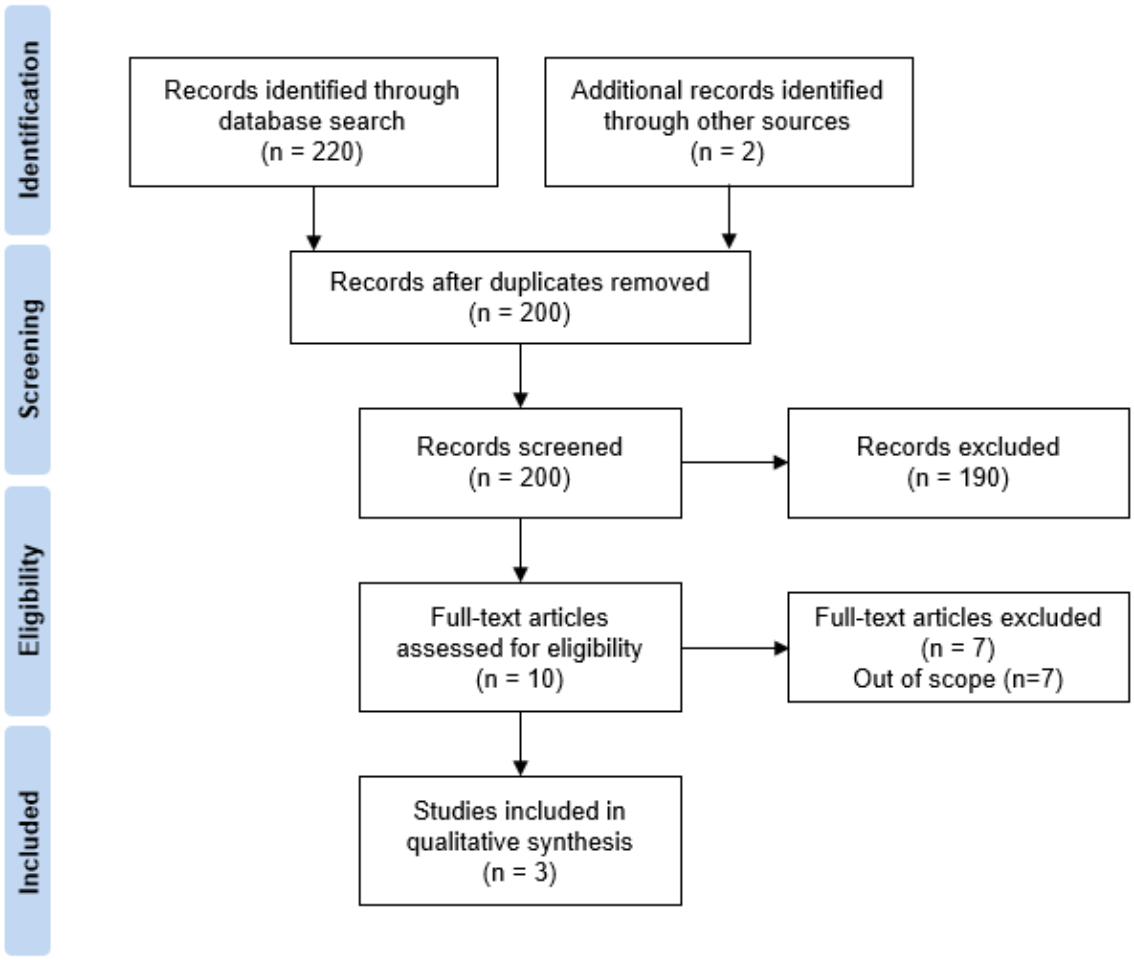
PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.40: Venous Thromboembolism Prophylaxis: Study Selection for Review



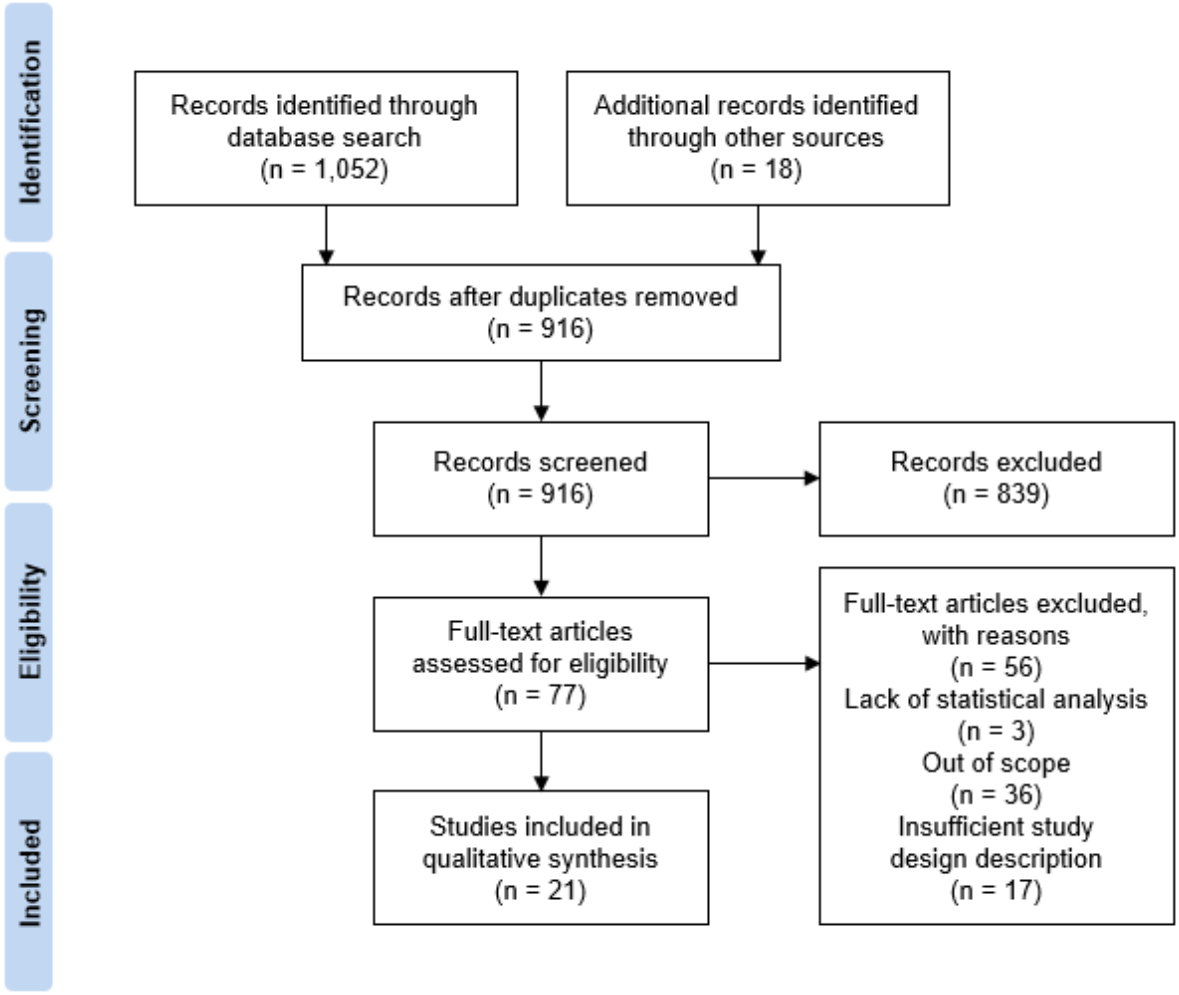
PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.41: Cross-Cutting Patient Safety Topics/Practices, Patient and Family Engagement—Study Selection for Review



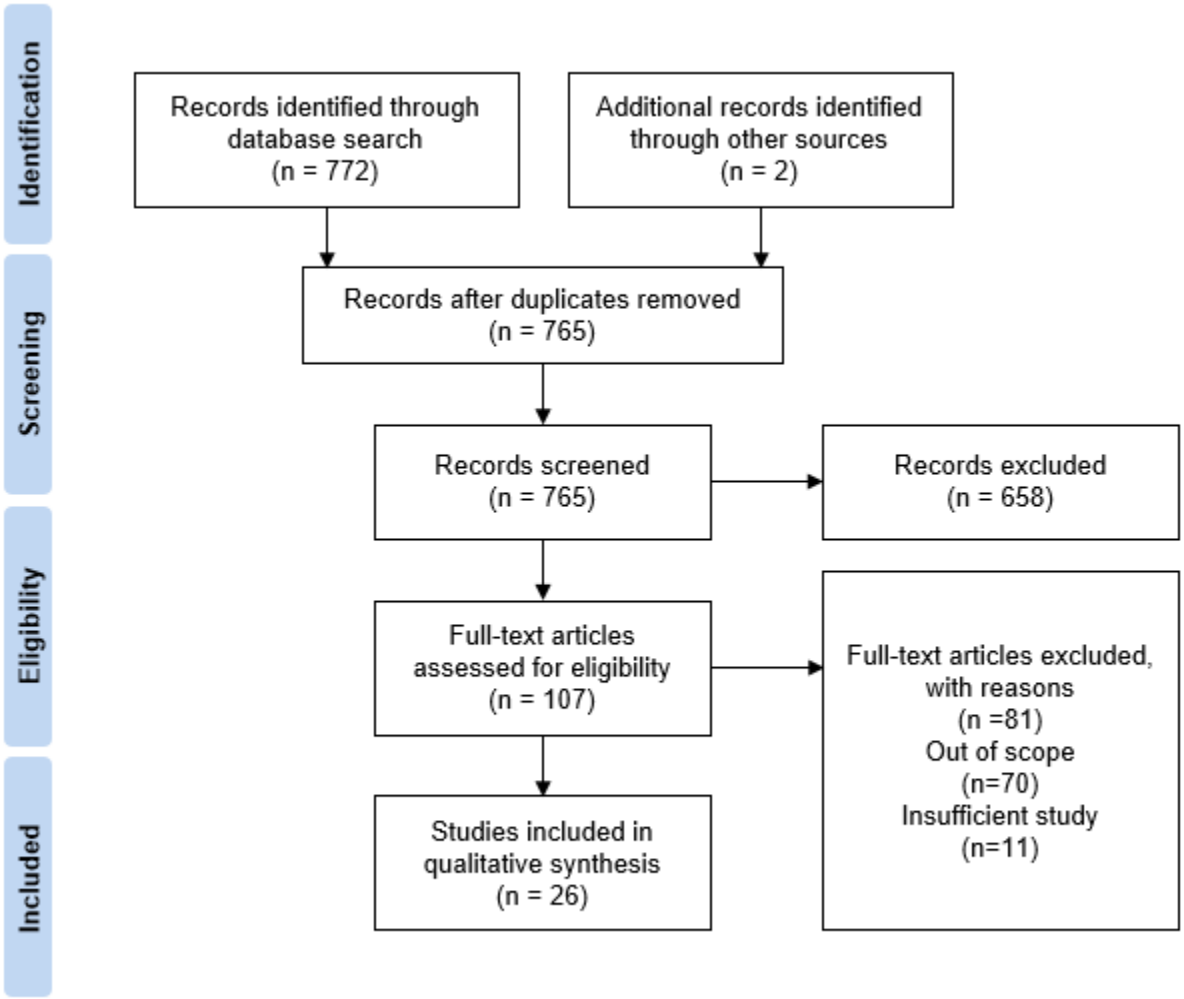
PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.42: Cross-Cutting Patient Safety Topics/Practices, Safety Culture—Study Selection for Review



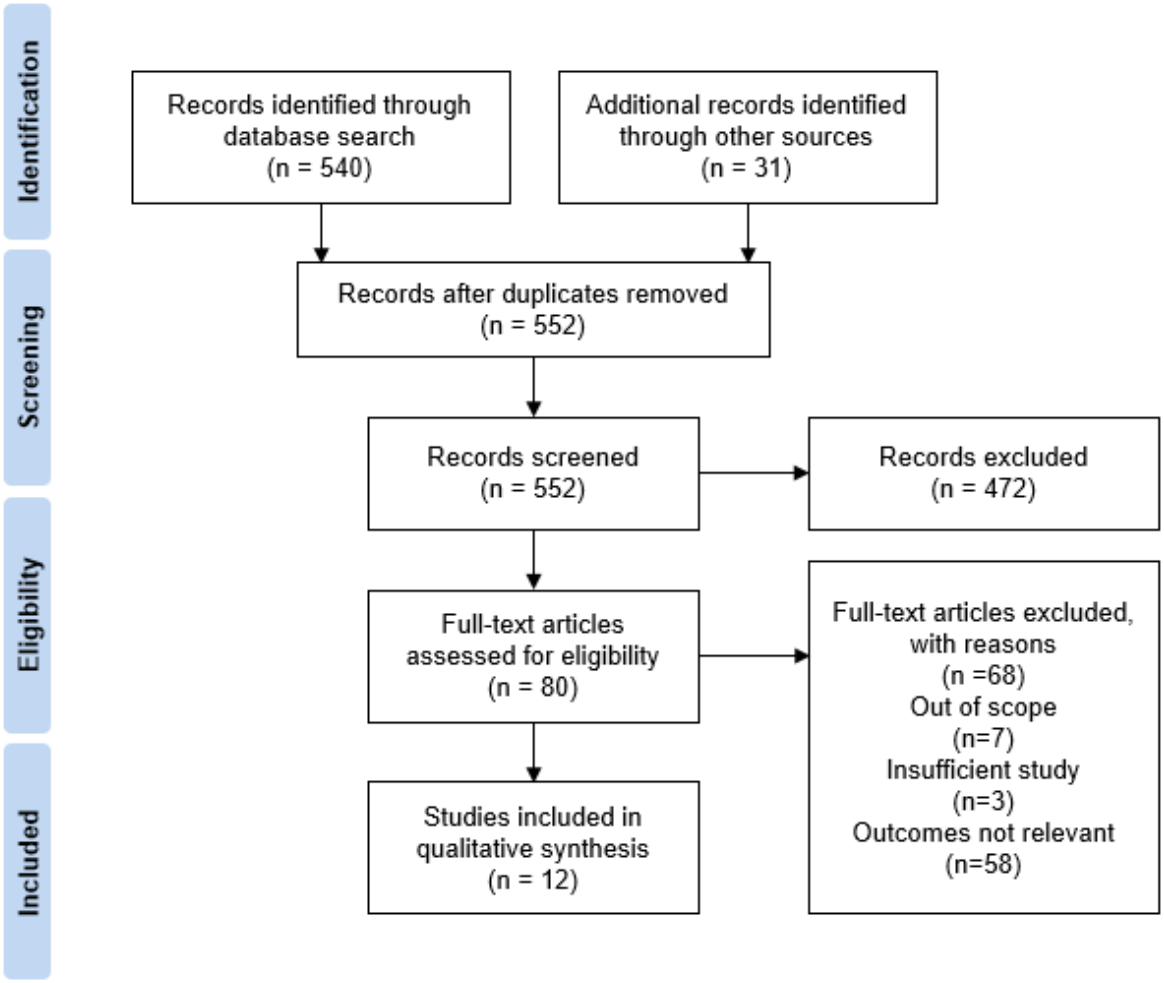
PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.43: Cross-Cutting Patient Safety Topics/Practices, Clinical Decision Support—Study Selection for Review



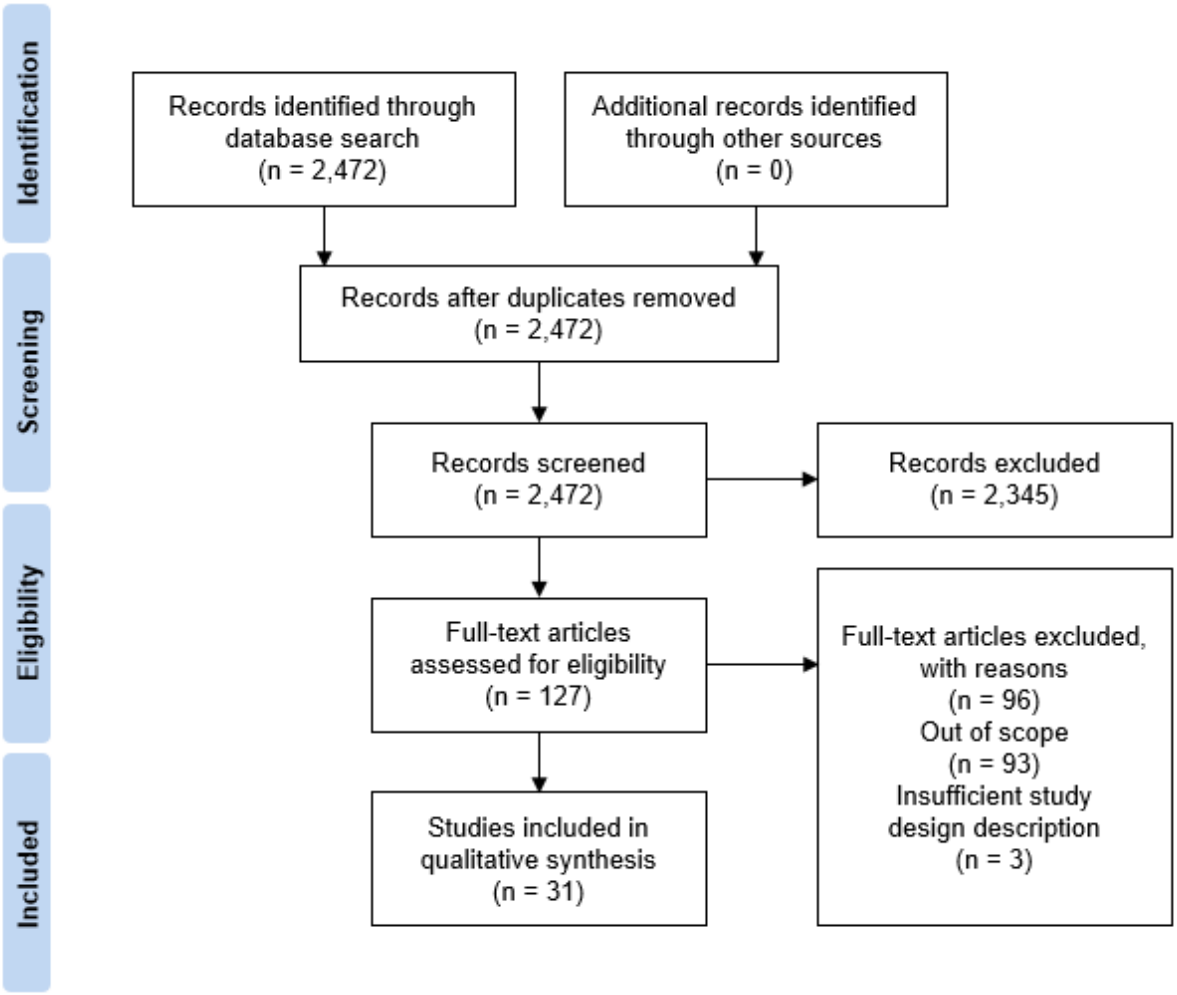
PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.44: Cross-Cutting Patient Safety Topics/Practices, Cultural Competency—Study Selection for Review



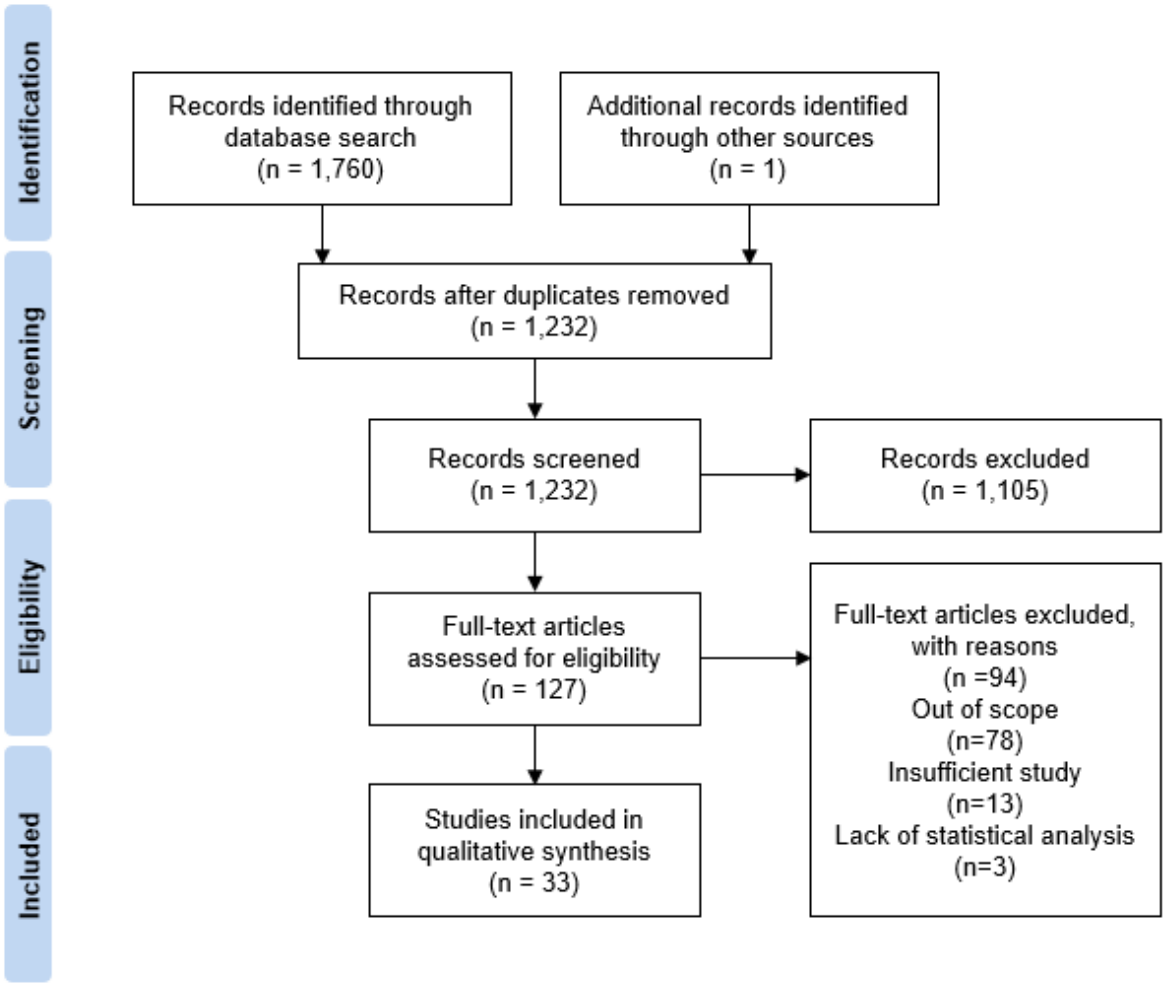
PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Figure A.45: Cross-Cutting Patient Safety Topics/Practices, Monitoring, Audit, and Feedback—Study Selection for Review



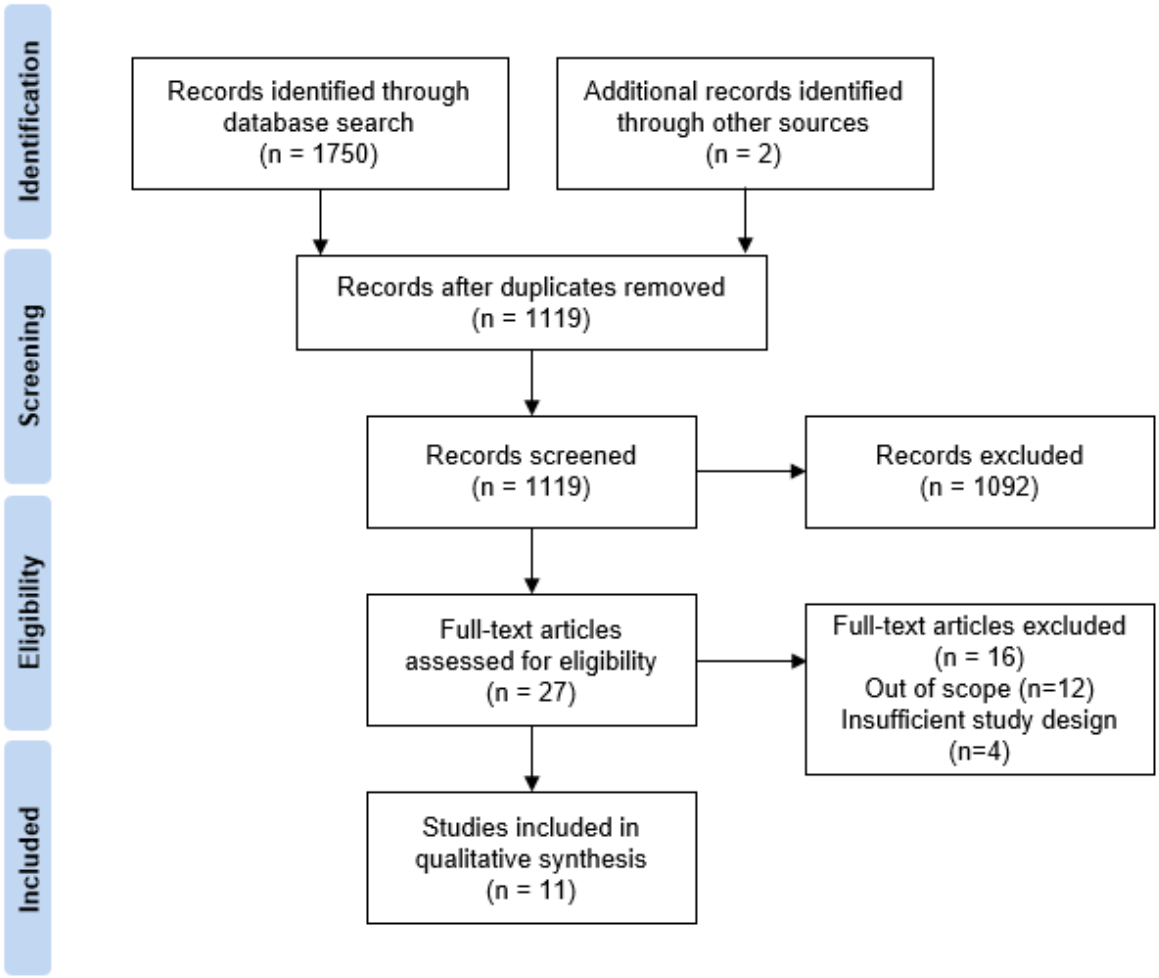
PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.46: Cross-Cutting Patient Safety Topics/Practices, Teamwork and Team Training—Study Selection for Review



PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Figure A.47: Cross-Cutting Patient Safety Topics/Practices, Education and Training Through Simulation—Study Selection for Review



PRISMA criteria described in Moher D, Liberati A, Tetzlaff J, et al. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009 Jul 21;6(7): e1000097. doi:10.1371/journal.pmed1000097.

Appendix B. Evidence Tables

Table B.1: Diagnostic Errors, Clinical Decision Support—Single Studies

Note: Full references are available in the Section 1.1 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Arthi et al., 2008[22]	A neuro-fuzzy system, using both artificial neural network (ANN) and fuzzy logic models, designed for the identification or diagnosis of autism	Evaluation of model performance; 194 samples.	Not specified	In this neuro-fuzzy model, the network was shown to learn quickly, and has an output error rate of 0.01, which remained constant after 400 epochs. The overall performance of this model is 85–90%, aiding in the diagnosis of autism.	Not provided	Low	None
Bien et al., 2018[27]	Automated deep learning model for detecting general abnormalities and specific diagnoses on knee magnetic resonance imaging (MRI) scans	Evaluation of model performance; internal validation using 1,370 knee MRIs performed between January 1, 2001, and December 21, 2002 (Stanford Univ. Medical Center). External validation using public dataset of 917 knee MRI exams (Clinical Hospital Center, Rijeka, Croatia).	Stanford University Medical Center, United States; Clinical Hospital Centre, Rijeka, Croatia	The model achieved area under the receiver operating characteristic curve (AUC) values of 0.937 (95% confidence interval [CI], 0.895 to 0.980) in detecting general abnormalities, 0.965 (95% CI, 0.938 to 0.993) for ACL tears, and 0.847 (95% CI, 0.780 to 0.914) for meniscal tears. Authors found no significant differences between the performance of the model and that of unassisted general radiologists in detecting abnormalities. Providing model predictions significantly increased clinical experts' specificity in identifying ACL tears ($p<0.001$; q-value 0.006).	Not provided	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Bond et al., 2012[5]	Differential diagnosis (DDX) generator	Analysis of performance of four DDX programs (Diagnosis Pro, DXPlain, Isabel, PEPID) using 20 test cases.	Not specified	The mean scores (95% CI) from performance testing on a five-point scale were Isabel 3.45 (2.53 to 4.37), DxPlain 3.45 (2.63 to 4.27), Diagnosis Pro 2.65 (1.75 to 3.55), and PEPID 1.70 (0.71 to 2.69).	Integration with electronic health record (EHR)—at the time of the publication, the DDX were limited by the data fields shared with the EHR. Better integration of the systems with the EHR would overcome this challenge.	Moderate	Included in Riches 2016, systematic review and meta-analysis
Cairns et al., 2017[32]	Electrocardiogram (ECG) interpretation support system (interactive progressive-based interpretation [IPI] system and differential diagnosis algorithm [DDA]) designed to augment the human interpretation process	Counterbalanced trial using convenience sampling; 35 participants completing 375 interpretations (215 control, 160 using support); training levels of subjects include medical students through cardiologists.	Classroom environment and remotely via website hyperlinks	IPI + DDA approach was shown to improve diagnostic accuracy by 8.7% (although this was not statistically significant). The percentage of correct interpretations for reading ECGs using the conventional approach was 42.61%. Interpretations using the IPI + DDA method were 51.35% (chi-squared p-value=0.1852).	Not provided	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Chamberlain et al., 2016[19]	Mobile smart phone application that consists of an electronic stethoscope, a peak flow meter application, and a patient questionnaire. Data from the app are combined with a machine-learning algorithm to identify patients with asthma and chronic obstructive pulmonary disease (COPD)	Evaluation of model performance; 119 healthy and sick participants used the app and also were examined by an experienced pulmonologist using a full pulmonary testing laboratory.	Not specified	Employing a two-stage logistic regression model, the algorithms were first able to identify patients with either asthma or COPD from the general population, yielding an AUC of 0.95. Then, the algorithm was able to distinguish between patients with asthma and patients with COPD, yielding an AUC of 0.97.	Not provided	Moderate	None
Chou et al., 2017[15]	Visually based, computerized diagnostic decision support system (VCDDSS, VisualDx)	Pre/post study design, no comparison group. Clinical diagnoses of 13 patients were made by 51 sixth-year medical students, 13 dermatology residents, and one consultant dermatologist.	Dermatology Teaching Clinic, China Medical University Hospital, Taiwan	There was an 18.75% increase in diagnostic accuracy after use of VCDDSS (accuracy rate before using VCDDSS 62.5%, after VCDDSS 81.25%; $p<0.01$).	Not provided	Moderate	None
David et al., 2011[9]	Visually based, computerized diagnostic decision support system (VCDDSS, VisualDx)	Descriptive analysis of model performance; 80 patients admitted with a diagnosis of cellulitis.	Harbor-UCLA Medical Center, United States	Twenty-eight out of 80 cases admitted for cellulitis had alternative diagnoses (i.e., were misdiagnoses). The admitting physician included the correct diagnosis in the DDX in 4/28 (14%) and the VCDDSS in 18/28 (64%) of the misdiagnosed cases ($p= 0.0003$).	Not provided	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Deleger et al., 2013[17]	Natural language processing (NLP) and machine-learning (ML) based automated method to risk stratify abdominal pain patients by analyzing the content of the EHR	Retrospective observational study; 2,100 pediatric emergency department patients with abdominal pain.	Pediatric emergency department (ED) in an urban, quaternary care children's hospital, United States	The system performance was comparable to that of physician experts, and achieved an average F- measure of 0.867 (recall or sensitivity, 0.869; precision or PPV, 0.863) for risk classification.	Not provided	Low-moderate	None
Elkin et al., 2010[39]	DXplain, a computer-based medical education, reference, and decision support system	Pre/post study design; residents doing month-long rotations on one of five general medicine services; 323 uses of the DXplain in the post-intervention period.	General medicine services at St. Mary's Hospital, a 1,200-bed hospital operated by the Mayo Clinic, Rochester, MN, United States	Five hundred sixty-four cases were identified as diagnostically challenging by the criteria during the intervention period, along with 1,173 cases during the control period. Total charges were $1,281 lower (p=.006), Medicare Part A charges $1,032 lower (p=.006), and cost of service $990 lower (p=.001) per admission in the intervention cases than in control cases.	Not provided	Low-moderate	Included in Riches, 2016, systematic review and meta-analysis
Farmer, 2014[25]	Diagnostic clinical decision support system (CDS) developed to assist primary care clinicians in diagnosing musculoskeletal shoulder complaints and to reduce diagnostic errors	Prospective observational audit; 93 patients attending the Shoulder Clinic between June and December 2012.	Orthopedic outpatient department at the Royal Hampshire County Hospital, part of the Hampshire Hospitals NHS Foundation Trust, United Kingdom	CDS showed significant high levels of sensitivity (91%), specificity (98%), positive likelihood ratio (53.12), and negative likelihood ratio (0.08), with a kappa value of 0.88 to a confidence level of 99% compared with expert diagnosis combined with arthroscopy findings or radiological imaging.	Not provided	Low-moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Gegundez-Fernandez et al., 2017[10]	A mobile app-based decisions support system for the differential diagnosis of uveitis	Retrospective case-series study; a series of 159 patients originally diagnosed by a uveitis specialist with specific uveitis (N=88) and idiopathic uveitis (N=71).	Two hospitals in Madrid, Spain	Diagnostic accuracy of the CDS was 96.6% (95% CI, 93.2 to 100).	The successful use of DDSS is fully dependent on proper assessment of symptoms and signs by the responsible clinician, because the computer will process only the data the human introduces.	Moderate	None
Graber et al., 2008[3]	Web-based CDS that accepts either key findings or whole-text entry and uses a novel search strategy to identify candidate diagnoses from the clinical findings	Descriptive analysis of model performance; tested 50 consecutive internal medicine adult medical case studies published in the New England Journal of Medicine.	Not specified	The clinical decision support system suggested the correct diagnosis in 48 of 50 cases (96%) with key findings entry, and in 37 of the 50 cases (74%) if the entire case history was pasted into the system.	Not provided	Moderate	Included in Riches. 2016 systematic review and meta-analysis
Gulshan et al., 2016[28]	Deep learning-trained algorithm for automated detection of referable diabetic retinopathy (RDR) and diabetic macular edema in retinal fundus photographs	Algorithm trained using a retrospective development data set of 128,175 retinal images, and validated using 2 separate datasets, both graded by at least 7 U.S. board-certified ophthalmologists.	Not specified	For RDR, the algorithm had an area under the receiver operating curve of 0.991 (95% CI, 0.988-0.993) for the first validation dataset and 0.990 (95% CI, 0.986-0.995) for the second validation dataset.	Not provided	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Hakacova et al., 2012[33]	Computer-based rhythm analysis software—Philips Medical (Software A) and Draeger Medical (Software B)	Descriptive analysis of model performance; 500 ECGs were analyzed manually by two senior experts and three non-expert clinicians, and automatically by two automated systems.	Emergency department, Lund University Hospital, Sweden	Accuracy of nonexpert reading was 85%, not significantly different when compared with the accuracies of the system readings of 80% for system A (p= 45) and 75% for system B (p=.11).	Not provided	Moderate	None
Herweh et al., 2016[29]	e-ASPECTS, a machine learning algorithm that is based on the Alberta Stroke Program Early CT score (ASPECTS), an established 10-point quantitative topographic computed tomography scan score to detect stroke on CT scans	Evaluation of model performance; images of 34 patients with stroke between January 2005 and December 2015; studies interpreted by three stroke experts and three neurology residents.	University Hospital, Heidelberg, Germany	e-ASPECTS showed a similar performance to that of stroke experts in the assessment of brain computed tomography (CT) scans of acute ischemic stroke patients with the Alberta Stroke Program Early CT score method.	Not provided	Moderate	None
Hughes et al., 2017[31]	Automated ECG computerized analysis	Prospective cohort study; 855 triage ECGs obtained between November 14, 2014, and March 3, 2015.	Adult ED, University of North Carolina, United States	A total of 222 (26%) ECGs were interpreted by the computer as normal. The negative predictive value for triage ECGs interpreted by the computer as “normal” was calculated to be 99% (95% confidence interval= 97 to 99).	Not provided	Low-moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Kharbanda et al., 2016[18]	Electronic CDS tool that includes three components: a standardized abdominal pain order set, a web-based risk stratification tool, and a "time of ordering alert"	Quasi-experimental study; 2,803 children age 3 to 18 years who presented with possible appendicitis to the pediatric emergency department (ED) between January 2011 and December 2013.	Two urban, tertiary care pediatric EDs, United States	Use of the CDS tool led to a 54% relative decrease in CT use, with an increase in ultrasound use. No differences in rates of missed appendicitis, ED revisits within 30 days, appendiceal perforation, or ED length of stay between time periods	Not provided	Low	None
Koopman et al., 2015[37]	Machine-learning algorithm-based system designed to match final radiology reports to final ED diagnosis to identify potentially missed diagnoses of fractures.	Evaluation of model performance; 2,378 free-text radiology reports of limb structures.	EDs of three large Australian public hospitals (adults, children, and mixed adults/children)	The PPV (precision) for all data sets=.92; sensitivity (recall)=.92, F-measure=0.92.	The reconciliation process is affected by the way ICD-10 codes are assigned, with many flagged cases being situations in which the abnormality was known but was not conveyed in the assigned ICD-10 code.	Low-moderate	None
Kostopoulou et al., 2017[14]	Prototype CDS integrated in an EHR system and designed to support a clinician's initial assessment by generating a list of possible diagnoses as the reason for encounter (RfE) is entered into the system	Within-subject study design using 12 manufactured scenarios with standardized patients, four for each of the available RfE.	Kings College, London, United Kingdom	Improvement in diagnosis using the CDS was statistically significant (odds ratio [OR] 1.41; 95% CI, 1.13 to 1.77; p=0.003), as were the improvements in diagnostic certainty and management.	Not provided	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Lee et al., 2013[23]	Preclustering-based ensemble learning (PEL) technique to assist in the diagnosis of acute appendicitis	Evaluation of model performance; 574 appendectomy cases, of which 110 were negative for appendicitis.	Tertiary hospital in southern Taiwan	The PEL technique had the best overall performance of classification systems and scoring systems, with an area under the curve measure of 0.619. PEL is more sensitive to identifying positive acute appendicitis than the commonly used Alvarado scoring system, and exhibits higher specificity in identifying negative acute appendicitis.	Not provided	Low	None
Li et al., 2018[30]	Endoscopic images-based nasopharyngeal malignancy detection model (eNPM-DM)	Evaluation of model performance; 27,536 biopsy-proven images from 7,951 individuals obtained from January 1, 2008, to December 31, 2016, split into the training, validation, and test sets; 1,430 images obtained from January 1, 2017, to March 31, 2017, used as a prospective test set.	Sun Yat-sen University Cancer Center; Guangzhou, China	The eNPM-DM attained an overall accuracy of 88.7% (95% CI, 87.8 to 89.5) in detecting malignancies in the test set. In the prospective comparison phase, eNPM-DM outperformed the experts: the overall accuracy was 88.0% (95% CI, 86.1 to 89.6%) versus 80.5% (95% CI, 77.0 to 84.0).	Not provided	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Lin et al., 2009[24]	Intelligent diagnosis model using classification and regression tree (CART) and case-based reasoning (CBR) techniques to increase the accuracy of liver disease diagnosis	Evaluation of model performance; 510 outpatients (300 with liver disease; 210 without) from 2005 to 2006.	Medical Center, Taiwan	Comparing the receiver operating characteristic (ROC) curves of these two models, CART demonstrated a greater sensitivity (0.931) for any given specificity than CBR (0.857). These results suggest the use of CART over CBR for the classification of liver disease. Tested by accuracy, sensitivity, and specificity, CART reports a greater classification capability than does CBR.	Not provided	Low-moderate	None
Martinez-Franco et al., 2018[13]	DXplain, a computer-based medical education, reference, and decision support system	Randomized controlled trial; 87 first-year family medicine residents (44 control, 43 intervention), solving 30 clinical diagnosis cases.	National Autonomous University of Mexico (UNAM) Postgraduate Studies Division in Mexico City, Mexico	There was a significant difference between the percent-correct scores for the control group (74.1±9.4) and the DXplain intervention group (82.4±8.5, p<0.001).	Not provided	Low-moderate	None
Mawri et al., 2016[34]	Computer-interpreted ECG (cECG)	Retrospective cohort study; 340 consecutive patients from September 2003 to December 2009 with STEMI who underwent emergent cardiac catheterization and percutaneous coronary intervention.	Henry Ford Hospital. Detroit, MI, United States	cECG failed to identify 30% of patients with STEMI. Protocol using the immediate review of ECGs by an emergency physician rather than depending on the cECG interpretation led to faster activation of the catheterization laboratory {19 minutes [interquartile range (IQR): 10–37] versus 16 minutes [IQR: 8–29]; p<0.029} and in median door-to-balloon times {113 minutes [IQR: 86–143] versus 85 minutes [IQR: 62–106]; p<0.001} in patients with STEMI.	If there are issues with the recording (e.g., incorrect lead placement, movement artifacts), the accuracy of the cECG interpretation will be affected.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Murphy et al., 2015[38]	Electronic triggers to identify patients at risk of diagnostic delays based on the following criteria: presence of a clinical clue or red flag; exclusion of records where further evaluation is not warranted (e.g., terminal illness); and presence of delay in diagnostic evaluation	Cluster randomized controlled trial; 72 full-time primary care providers (36 in control group, 36 in intervention group) seeing an estimated 118,400 patients in internal or family medicine ambulatory clinics from April 20, 2011, to July 19, 2012.	Urban Veterans Affairs facility (site A) and a private health system (site B), United States	Of 10,673 patients with abnormal findings, the trigger flagged 1,256 patients (11.8%) as high risk for delayed diagnostic evaluation. Times to diagnostic evaluation were significantly lower in intervention patients compared with control patients flagged by the colorectal trigger (median, 104 vs. 200 days, n= 557; p<.001) and prostate trigger (40% received evaluation at 144 vs. 192 days, n=157; p<.001) but not the lung trigger (median, 65 vs. 93 days, n=19; p=.59). More intervention patients than control patients received diagnostic evaluation by final review (73.4% vs. 52.2%, relative risk, 1.41; 95% CI, 1.25 to 1.58).	Not provided	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Niemi et al., 2009[16]	CDS, the Core Measure Manager (CCM), to identify core measure patients (HF and pneumonia) in real time and to provide alerts to the appropriate clinician with sufficient time to allow for intervention when performance measures were not being met	Descriptive analysis of system performance. Pneumonia study: patients 18 years and older with an ED visit, hospital admission, or both between October 1, 2006, and October 31, 2006 (986 admissions, 37 with pneumonia); heart failure (HF) study: patients 18 years and older admitted between February 11, 2007, and March 12, 2007 (1,037 admissions, 94 with HF).	Sutter Medical Center, Sacramento, CA, United States	The sensitivity for identification of pneumonia using the CDS in the ED was 89% and the specificity was 86%. The sensitivity for pneumonia admissions was 92% and the specificity was 90%. The sensitivity for HF identification was 94% and the specificity was 90%.	Not provided	Moderate	None
Segal et al., 2014[11]	CDS, SimulConsult, which generates different diagnoses based on input patient clinical findings	Evaluation of CDS using pre/post design; 16 pediatric neurologists (11 in the final year of pediatric neurology residency or subsequent year [‘‘junior’]) and 5 in practice for >10 years [‘‘senior’’]) tested 40 written case vignettes of patients with neurogenetic diagnoses.	Not specified	Diagnostic errors after using the decision support (‘‘aided’’) fell from 36% to 15% overall. There was an increase in the relevance of listed differential diagnoses after using the software ($p < .0001$).	A key factor that improved performance was taking enough time (>2 minutes) to enter clinical findings into the software accurately.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Segal et al., 2016[12]	CDS, SimulConsult, which generates different diagnoses based on input patient clinical findings	Evaluation of CDS using pre/post design. Twenty-six testers (7 general pediatrics, 9 emergency medicine, 10 pediatric rheumatology), eight case vignettes of real patients with confirmed diagnoses (six had pediatric rheumatologic diagnoses; two had other conditions with some rheumatologic findings).	Not specified	Significant reduction in diagnostic errors following introduction of the CDS, from 28% errors to 15% using decision support ($p< 0.0001$). Improvement was greatest for emergency medicine physicians ($p= 0.013$) and clinicians in practice for less than 10 years ($p= 0.012$).	Testers spent an average of 20 minutes per case, of which half was spent using the decision support.	Moderate	None
Song et al., 2016[26]	CDS, based on an online algorithm, that incorporates contextual information and makes diagnostic recommendations to physicians, aiming to minimize the false positive rate of breast cancer diagnosis, given a predefined false negative rate	Evaluation of the CDS algorithm using a de-identified dataset of 4,640 individuals who underwent screening and diagnostic mammograms at a large academic medical center.	Large academic medical center	Proposed approach outperforms the current clinical practice by 36% in terms of false positive rate given a 2% false negative rate.	Not provided	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Vandenberghe et al., 2017[35]	Computer-aided diagnosis using a convolutional neural network model (ConvNets) that automatically scores HER2, a biomarker that defines patient eligibility for anti-HER2 targeted therapies in breast cancer	Evaluation of model performance using a cohort of 71 breast tumor resection samples.	Not specified	In a cohort of 71 breast tumor resection samples, automated scoring showed a concordance of 83% with a pathologist. The 12 discordant cases were then independently reviewed, leading to a modification of diagnosis from initial pathologist assessment for 8 cases.	Not provided	Low-moderate	None
Wolf et al., 2013[20]	Four smartphone applications that allow the use of existing images of skin lesions to make assessments on the likelihood of malignancy risk	Case-control diagnostic accuracy study; a total of 188 lesions evaluated using the four applications (60 melanomas: 44 invasive and 16 in situ; 128 benign lesions).	Not specified	Sensitivity of the four tested applications ranged from 6.8% to 98.1%. Specificity ranged from 30.4% to 93.7%. Positive predictive value ranged from 33.3% to 42.1%, and negative predictive value ranged from 65.4% to 97.0%. The highest sensitivity for melanoma diagnosis was observed for an application that sends the image directly to a board-certified dermatologist for analysis, and the lowest sensitivity was observed for applications that use automated algorithms to analyze images.	Not provided	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Xiong et al., 2018[36]	Convolutional neural networks model to detect acid-fast stained tuberculosis bacillus	Evaluation of model performance using 246 samples of both positive and negative cases (45 in training set, 201 cas.es in testing set) collected from January 2016 to June 2017	Department of Pathology, Peking University First Hospital	The model achieved a high (97.94%) sensitivity and moderate (83.65%) specificity.	Not provided	Low	None

Table B.2: Diagnostic Errors, Clinical Decision Support—Systematic Reviews and Meta-Analyses

Note: Full references are available in the Section 1.1 reference list.

Author, Year	Description of Patient Safety Practice	Settings and Population	Summary of Findings	Comments
el-Kareh et al., 2013[1]	Diagnostic decision support systems and diagnosis-related health information technology (HIT)	Systematic review of HIT to reduce diagnostic error. The search strategy did not include limitations for settings or populations.	The use of HIT in diagnosis is still in its early stages. Many aspects of the diagnostic process have been targeted, but few tools and systems have been shown to improve diagnosis in actual clinical settings.	Included in Riches, 2016, systematic review and meta-analysis
Graber et al., 2012[7]	Interventions to prevent, reduce, or mitigate diagnostic errors, including CDS to support and improve cognition	Systematic review of cognitive interventions to reduce diagnostic error. The search strategy did not include limitations for settings or populations.	ISABEL has good sensitivity in both pediatric and adult settings, with sensitivity in the adult setting approaching 100%. Research on the use of Google searches yields the correct diagnosis in only 58% of difficult cases.	None
Nurek et al., 2015[40]	Computerized diagnostic decision support systems (CDDSS)	Meta-review of existing systematic reviews of CDS systems in primary care to improve diagnosis. Subjects (primary end-users of CDS) include individual clinicians; no specific criteria for setting.	Identified the following requirements for successful integration of a CDS: a more standardized computable approach to knowledge representation is needed, one that can be readily updated as new knowledge is gained, and a deep integration with the EHR is needed in order to trigger at appropriate points in cognitive workflow.	None
Riches et al., 2016[8]	Differential diagnosis (DDX) generators	Systematic review and meta-analysis investigate the efficacy and utility of DDX generators. Subjects include the individual user of the tool and the clinical case being entered into the tool; no specific criteria for setting.	The pooled accurate diagnosis retrieval rate of DDX tools was high, with high heterogeneity (pooled rate=0.70, 95% CI, 0.63 to 0.77; I2=97%, p<0.0001). DDX generators did not demonstrate improved diagnostic retrieval compared with clinicians, but small improvements were seen in the before and after studies, in which clinicians had the opportunity to revisit their diagnoses following DDX generator consultation.	None

Author, Year	Description of Patient Safety Practice	Settings and Population	Summary of Findings	Comments
Wagholikar et al., 2012[21]	Computer-assisted diagnosis models	Systematic review of modeling techniques to provide diagnostic support. The search strategy did not include limitations for settings or populations. (Search was focused on models.)	General trends in research of medical decision support: • Improvement in the accuracy of MDS application may be possible by modeling of vague and temporal data, research on inference algorithms, integration of patient information from diverse sources, and improvement in gene profiling algorithms. • Research would be facilitated by public release of de-identified medical datasets and development of open-source data-mining tool kits. • Comparative evaluations of different modeling techniques are required to understand characteristics of the techniques and to guide developers in the choice of technique for a particular medical decision problem. • Evaluations of MDS applications in the clinical setting are necessary to foster physicians' use of these decision aids.	None

Table B.3: Diagnostic Errors, Result Notification Systems—Single Studies

Note: Full references are available in the Section 1.2 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Chen et al., 2011[21]	Automated phone alert using short message service (SMS)	Pre/post design; total of 223 patients with acid-fast bacilli-positive tuberculosis (96 baseline, 127 post-intervention).	1,600-bed academic medical center, Taiwan	The laboratory delay (p<.001), response delay (p=.045), and interval from admission to transfer to the isolation room (P<.001) were all significantly reduced during the intervention phase. The proportion of patients transferred to isolation within 1 day increased significantly.	Not provided	Need adequate staffing levels to support the RNS and operational changes.	Low	None
Dalal et al., 2014[12]	Automated email system	Cluster-randomized controlled trial; 441 adult general medicine and cardiology patients who had one or more tests pending at discharge (TPAD) and their 117 attending physicians (241 patients/59 attending physicians in intervention arm, 200 patients/58 attending physicians in control arm).	Academic medical center: 720-bed tertiary-care hospital and academic medical center and primary care outpatient setting, United States	There was a statistically significant increase in the rate of awareness of TPAD results by attending physicians for patients assigned to the intervention compared with usual care (76% vs. 38%, adjusted/clustered odds ratio [OR] 6.30, 95% confidence interval [CI], 3.02 to 13.16, p<0.001).	Not provided	Need for connectivity between hospitals and primary care physicians (PCPs) outside of network. Integrate RNS into workflow.	High	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Dalal et al., 2018[13]	Automated email system	Cluster-randomized controlled trial. Attendings and PCPs caring for adult patients discharged from general medicine and cardiology services with at least one actionable TPAD between June 2011 and May 2012; 3,378 TPADs representing 1,522 patient discharges sampled.	Academic medical center: 720-bed tertiary-care hospital and primary care outpatient setting, United States	The proportion of actionable TPADs with documented action was 60.7% vs. 56.3% (p=0.82) in the intervention vs. usual care groups; similar for documented acknowledgment. Pathology tests were the type most commonly associated with documented followup.	Not provided	Need connectivity between hospitals and PCPs outside of network.	Moderate	None
Eisenberg et al., 2010[19]	Manual, web-based electronic messaging system	Post-intervention; 908,475 imaging exams performed, with 10,510 level 3 alerts (abnormal conditions that could result in considerable morbidity if they are not appropriately treated, but which are not immediately life-threatening) submitted to messaging system. Five hundred randomly selected alerts reviewed.	Single large academic medical center with several off-campus outpatient facilities, United States	All results were communicated to the referring providers, with 411 of 500 (82.2% +- 3.3) communications accomplished within the 48-hour policy goal. Note that day of week affected outcome, with more alerts submitted Monday-Thursday before 3 p.m. communicated within 48 hours (93.7% +/- 2.4) than those alerts generated on Thursday afternoon through Sunday (73.0% +/- 9.2).	Not provided	Need adequate staffing to support the RNS. Establish policies and procedures around RNS use.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
El-Kareh et al., 2012[27]	Automated email system	Cluster-randomized controlled trial; 157 results for 121 total inpatient and outpatient physicians (73 in intervention group, 48 in control group) caring for hospitalized adult patients with positive and untreated/ undertreated culture results returned after discharge.	Academic hospital (777 beds) and primary care outpatient settings; United States	Twenty-seven out of 97 (28%) results in the intervention group and 8 out of 60 (13%) in the control group (aOR 3.2, 95% CI, 1.3 to 8.4; p=0.01) had documented followup in the outpatient chart within 3 days of post-discharge result.	Not provided	Integrate RNS into workflow.	Low	None
Etchells et al., 2010[10]	Automated paging system	Randomized controlled trial; 165 critical lab values with documented response time (81 intervention; 84 control) on 108 patients admitted to the four general medicine clinical teaching units.	General medicine clinical teaching units at an urban academic hospital, Canada	There was a 23-minute reduction in median response time (interval between acceptance of the critical value into the LIS and the documented writing of order or documented time of treatment), but this was not statistically significant. Median response time was 16 min (IQR 2-141) for the automated paging group and 39.5 min (IQR 7-104.5) for the usual care group (p= 0.33).	Some critical results, such as those from repeated troponin tests, were viewed as nuisances. The physician-on-call had to carry numerous additional pagers and could not always discern which pager was alerting.	Automated physician scheduling integrated with RNS. Establish policies and procedures around RNS use.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Etchells et al., 2011[11]	Automated alerts via mobile phone or pager and link to CDS for alert	Randomized controlled trial (controlled stepped-wedge design); general internal medicine teaching units; 498 critical laboratory conditions on 271 patients.	General internal medicine clinical teaching units at two academic hospitals, Canada	Overall, 50% of potential clinical actions were carried out, and there were adverse clinical events within 48 hours for 36% of the laboratory conditions. The median (IQR) proportion of potential clinical actions that were actually completed was 50% (33%–75%) with alerting system on, and 50% (33–100%) with alerting system off (p=0.94, Wilcoxon rank sum test). When the alerting system was on (n=164 alerts) there were 67 adverse events within 48 hours of the alerts (42%). When the alerting system was off (n=334 alerts), there were 112 adverse events within 48 hours (33%; difference: 9% higher number of adverse events with alerting system on, p=0.06).	Not provided	Automated physician scheduling integrated with RNS. Establish policies and procedures around RNS use.	Low	None
Lacson et al., 2014[15]	Manual-triggered alert via pager or email	Pre/post design; 47,034 reports randomly sampled and manually reviewed (9,430 1 year prior to intervention; 37,604 4 years post-intervention).	Academic medical center (753 beds), United States	Adherence to the institutional policy for timely closed-loop communication of critical imaging results increased from 91.3% before the intervention to 95.0% after the intervention (p<0.0001). There was a ninefold increase in the critical results communicated via the system (chi-square trend test, p<0.0001).	Not provided	Establish policies and procedures around RNS use.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Lacson et al., 2016[16]	Manual-triggered alert via pager or email	Trend analysis; 10 semi-annual time periods from 42 randomly selected radiology reports from each of 10 semi-annual time periods between 2009 and 2014; total of 840 reports, 420 with documented communication and 420 without documented communication.	Single adult quaternary referral academic medical center, United States	After the implementation of the critical imaging test result policy and the ANCR, critical results lacking documented communication decreased nearly fourfold between 2009 and 2014 (0.19 to 0.05, p<0.0001).	There was concern over alert fatigue, a potential unintended consequence of implementing alerting systems, but authors did not find an increase in non-clinically significant results communicated through the system.	Establish policies and procedures around RNS use. Integrate RNS into workflow.	Low	None
Lin et al., 2014[23]	Automated phone text-message alert	Pre/post design. Patients with warfarin therapy managed by the hospital's outpatient clinics; 3,497 patients (30,981 tests) were included in the manual alert study period and 3,781 patients (32,297 tests) were included in the PHS alert group.	Outpatient department of a 2,500-bed tertiary teaching hospital, Taiwan	Incidence of major thromboembolic events was 1.6% pre-intervention and 1.6% post-intervention (p=0.709), and the rate of hemorrhagic events was 3.1% and 4.2% in the manual alert and PHS alert study periods (p=0.198).	Not provided	In hospital, need RNS technology to be available to all stakeholders.	Low	Study examines patient outcomes

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
O'Connor et al., 2016[17]	Manually triggered alert via pager or email/alert in electronic medical record (EMR)	Pre/post design; 171 PCPs at 13 affiliated outpatient practices; 5,931 outpatient nonurgent, clinically significant radiology alerts (1,503 pre-intervention; 4,428 post-intervention).	Tertiary academic medical center (793 beds) and affiliated outpatient practices, United States	There was 100% acknowledgement of non-urgent clinically significant ANCR-generated alerts, with the EHR used to acknowledge 15.5% of them. Ninety percent of alerts pre-intervention and 84% post-intervention were actionable (p=.29). PCPs acted on 94% (85 of 90; 95% CI, 88 to 98) of actionable alerts pre-intervention and 94% (79 of 84; 95% CI, 87 to 97) post intervention (p>.99).	Not provided	Integrate the RNS into workflow. Establish policies and procedures around RNS use.	Low	None
O'Connor et al., 2018[24]	Manually triggered alert via pager or email	Pre/post design; 5,595 pathology reports with malignancies (2,793 pre-intervention; 2,802 post-intervention).	Community hospital (150 beds) affiliated with an academic medical center, United States	Acknowledgment of the CSTR within 15 days, the institutional policy, was documented for 98 of 107 (91.6%) pre-intervention reports and 89 of 103 (86.4%) post-intervention reports (p=0.2294). Median time to acknowledgment was 7 days (interquartile range [IQR], 3, 11) pre-intervention and 6 days (IQR, 2, 10) post-intervention (p=0.5083). Post-intervention, median time to acknowledgment was 2 days (IQR, 1, 6) for reports with ANCR alerts versus 6 days (IQR, 2.75, 9) for reports without alerts (p=0.0351).	Not provided	Provide review and feedback about use of RNS. Establish policies and procedures for RNS use.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Park et al., 2008[20]	Automated phone alert using SMS and callback	Pre/post design; 217 critical hyperkalemia alerts (121 pre-intervention; 96 post-intervention).	Tertiary care academic medical center (2,200 beds), South Korea	Across all wards (intensive care units [ICUs] and general wards), the median and interquartile ranges of the clinical response times were significantly reduced, going from 213.0 min and 476.0 min to 74.5 min and 241 min, respectively (p<.001). The mean and median clinical response times in general wards were significantly decreased by 54.3% and 74.7%, respectively, in comparison to the pre-intervention response times (p<.001). The mean and median clinical response times in ICUs decreased by 11.8% and 51.8%, respectively, in comparison to those in 2001, but the change was not significant (p=.190).	Not provided	Need to account for technology limitations such as inconsistent phone reception within the hospitals.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Singh et al., 2009[18]	Automated EMR alert notification system	Post-intervention; 123,638 radiology studies generating 1,196 alerts, of which 979 (81.9%) were tracked as acknowledged and 217 (18.1%) were unacknowledged.	Single multi-specialty ambulatory clinic and five satellite clinics affiliated with U.S. Department of Veterans Affairs (VA), United States	Nine hundred seventy-nine (81.9%) alerts were tracked as acknowledged and 217 (18.1%) were unacknowledged. For 131 (11%) of alerts, there was no evidence of documented followup. There were 92 (7.7%) results without timely followup at 4 weeks after result transmission. Lack of acknowledgement was associated with physician assistants as ordering providers compared with attending physicians (OR: 0.46; 95% CI, 0.22 to 0.98), trainees as ordering providers (OR: 5.58; 95% CI, 2.86 to 10.89), and when dual as opposed to single communication was used (OR: 2.02; 95% CI, 1.22 to 3.36). There was no significant difference in rates of lack of timely followup between the acknowledged and unacknowledged alerts (7.3% vs. 9.7%; p=0.2).	Dual communication, intended to be a “safeguard” to protect against loss of followup, was unexpectedly associated with lack of timely followup.	Establish policies and procedures for RNS use.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Singh et al., 2010[5]	Automated EMR alert notification system	Observational/cross-sectional; 78,158 laboratory tests (HbA1c, Hep B Ab, PSA, TSH) performed, with 1,163 results transmitted as mandatory high-priority alerts (1.49% of results screened).	Single multispecialty ambulatory clinic and five satellite clinics affiliated with VA, United States	Of the alerts, 6.8% lacked timely followup at 30 days. Lack of acknowledgement was associated with allied health care providers as ordering providers (OR, 4.32; 95% CI, 1.21 to 15.52) and trainees as ordering providers (OR, 8.39, 95% CI, 2.97 to 23.68), compared with attending physicians. Specialty services were found less likely to acknowledge alerts compared with primary care providers (p<.0001). There was no significant difference in rates of lack of timely followup between acknowledged and unacknowledged laboratory alerts (6.4% vs. 10.1%; p=.13) and no significant differences in ordering provider types (p=.67), but there was a significant difference across specialties (p<.0001).	Not provided	Not provided	Low	None

Table B.4: Diagnostic Errors, Result Notification Systems—Systematic Reviews and Meta-Analyses

Note: Full references are available in the Section 1.2 reference list.

Author, Year	Description of Patient Safety Practice	Settings and Population	Summary of Findings	Implementation Themes/Findings
Liebow et al., 2012[8]	Automated notification systems; call centers	Nine articles met criteria for inclusion, as follows. Population: All patients in healthcare settings with lab results that include a critical value. Intervention: Automated notification systems and call centers for communicating critical values. Comparison: Manual critical values notification systems. Outcome: Timeliness and accuracy of reporting or receipt of critical values information, or timeliness of treatment based on critical values information.	Automatic notification systems (4 studies): only one study of "good quality"; average improvement from implementing automated notification systems is d=0.42 (95% confidence interval [CI], 0.2 to 0.62). Overall strength of evidence is suggestive. Call centers (5 studies): the average odds ratio for call centers is odds ratio [OR]=22.1 (95% CI, 17.1 to 28.6). Call centers are effective in improving the timeliness and accuracy of critical value reporting in an inpatient care setting, and are recommended as an "evidence-based best practice."	Automated notification systems may disrupt usual lines of communication and provide too much/too frequent information. Risk of losing back-up contact information; risk for HIPAA violations. Call centers may require additional communications with lab staff when caregivers require additional information that call centers may not have; staffing needs are significant.
Slovis et al., 2017[9]	Automated notification systems (asynchronous)	Thirty-four articles pertaining to asynchronous automated electronic notifications of laboratory results published through 2016.	Several asynchronous automated electronic notification systems for laboratory results have been successfully implemented with improvements in workflow and time to acknowledgement of results.	Though some critical alerts are necessary, not all critical results warrant notification, because not all critically abnormal laboratory values require emergent intervention. However, some studies have demonstrated that noncritical urgent and elective notifications can also improve clinical care.

Table B.5: Diagnostic Errors, Education and Training—Single Studies

Note: Full references are located in the Section 1.3 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
Coderre et al., 2010[20]	Use of querying an initial hypothesis to generate cognitive reflection in medical students	Pre/post study design with comparison groups; 67 first-year medical students	University of Calgary, Canada	Questioning an initial diagnosis through processing of additional data does not affect a correct initial diagnosis, but it does allow correction of an inaccurate initial diagnosis.	Not provided	Moderate
Dyre et al., 2017[38]	Error management training (2 components: active exploration during skill practice and the provision of error management instructions)	Randomized trial; medical students with no prior ultrasound experience; 32 students received error management training (EMT) and 28 received error avoidance training (EAT)	Department of Obstetrics, Rigshospitalet, Denmark	Providing error management instructions, rather than error-avoidance instructions, during simulation-based training improved the transfer of learning to the clinical setting. Mean test scores in the transfer test corresponded to a large effect size in favor of EMT (Cohen's d=1.11, 95% confidence interval [CI], 0.5 to 1.7).	Not provided	Low
Goodman and Kelleher, 2017[32]	Focused session of interpretation training at a local art gallery where art experts taught the trainees how to thoroughly analyze a painting	Pre/post study design, no comparison group; 15 first-year radiology residents	Not provided	Focused teaching on perception improved first-year residents' ability to localize imaging abnormalities. For the pretest, residents scored an average of 2.3 out of a maximum possible score of 15 (standard deviation (SD) of 1.4, range of 0–4). After training, average post-test score increased to 6.3 (SD of 1.8, range of 3–9) ($p < .0001$).	Not provided	Moderate
Mamede et al., 2010[17]	Structured reflection as taught through the use of five steps aimed at inducing reflective reasoning	Pre/post study design, with comparison group; 18 first-year and 18 second-year internal medicine residents	Erasmus Medical Centre, Rotterdam, Netherlands	When establishing diagnoses using nonanalytic reasoning, availability bias may occur in response to recent experience with similar cases. This bias may be counteracted by using reflective reasoning. Reflection improved all participants' diagnoses compared with nonanalytical reasoning.	Reflective practice may take its full effect only with more difficult clinical scenarios.	Low to moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
Mamede et al., 2012[18]	Compared structured reflection with providing a single diagnosis or generating differential diagnoses while practicing clinical cases	Three-phase experimental study; 46 fourth-year medical students	Erasmus Medical Centre, Rotterdam, Netherlands	Using structured reflection to diagnose cases increases the learning of clinical knowledge more effectively than using immediate diagnosis or differential diagnosis generation.	Not provided	Low to moderate
Mamede et al., 2014[19]	Compared structured reflection with providing a single diagnosis or generating differential diagnoses while practicing clinical cases	Two-phase experimental study; 110 fourth-year medical students	Erasmus Medical Centre, Rotterdam, Netherlands	Use of structured reflection was more effective in supporting learning than providing a single diagnosis or differential diagnoses.	Not provided	Low to moderate
McFadden and Crim, 2016[41]	Online simulation-based training activity to improve diagnosis; training supplemented with interactive practice opportunities and feedback delivered by an artificial intelligence–driven simulation/tutor	Pre/post design with comparison group using convenience sampling; 68 practicing primary care practitioners (27 in control group, 41 in treatment group)	Continuing medical education (CME) conference (control group), standalone online CME (intervention group)	There was no difference between control and intervention groups in pre-training diagnostic accuracy. The control group's post-training performance did not statistically significantly improve (p=.13); the intervention group's post-training diagnostic performance significantly improved, by 22% (p<.02).	Not provided	Low
Mohan et al., 2018[26]	Virtual simulation using two "serious" video games to train on the use of a heuristic, judgment by representativeness	A randomized controlled trial, using 257 board-eligible or board-certified emergency medicine physicians who worked primarily at non-trauma or level III/IV trauma centers	American College of Emergency Physicians Scientific Assembly	Both game interventions reduced under-triage events on the simulation compared with the control condition, whereas the text-based intervention did not.	Not provided	Low
Nendaz et al., 2011[21]	Weekly in-person case-based clinical reasoning seminars incorporating diagnostic reflection	Randomized controlled study; 29 medical students (14 in the control group and 15 in the intervention group, providing 28 and 30 encounters, respectively)	University of Geneva Faculty of Medicine, Switzerland	The case-based clinical reasoning seminars did not significantly affect the students' overall diagnostic or decisional competencies, but did aid in increasing the relevance of their differential diagnoses as written in the post-encounter notes.	Reflective practice may take its full effect only with more-difficult clinical scenarios.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
Pusic et al., 2012[35]	Radiographic training sets, which varied in their proportions of abnormal cases (30%, 50%, 70%)	Prospective, double-blind, randomized, three-arm education trial; 100 residents completed the study	Six academic training programs for emergency medicine and pediatric residents, United States	The two groups did not differ in accuracy on the post-test (p=0.20). The group with a low proportion of abnormal cases had the highest false negative rate, and missed fractures one-third more often than the groups that trained on higher proportions of abnormal cases. Manipulating the ratio of abnormal to normal cases the students are exposed to can alter their sensitivity and specificity.	Online educational intervention	Low
Reilly et al., 2013[22]	Three-part, 1-year curriculum in cognitive bias and diagnostic error	Pre/post study design with comparison group; 38 PGY-2 internal medicine residents	Perelman School of Medicine at the University of Pennsylvania, United States	Performance on the 13-item multiple-choice knowledge test improved post-curriculum when compared with both pre-curriculum performance (9.26 vs. 8.26, p=0.002) and the PGY-3 comparator group (9.26 vs. 7.69, p<0.001). Residents who participated in this curriculum improved their recognition and knowledge of common cognitive biases and heuristics.	Not provided	Moderate
Schwartz et al., 2010[39]	Four weekly case-based 1-hour in-person didactic sessions to help the students develop knowledge and skills in contextualizing patient care	Quasi-randomized controlled trial; 124 fourth-year medical students in internal medicine sub-internships	University of Illinois at Chicago and Jesse Brown Veterans Administration Medical Center, United States	Students who participated in the contextualization workshops were significantly more likely to probe for contextual issues in the standardized patient encounters than students who did not, and significantly more likely to develop appropriate treatment plans for standardized patients with contextual issues.	Not provided	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
Sherbino et al., 2011[14]	A 90-minute, standardized, interactive, case-based teaching seminar on cognitive forcing strategies (CFS)	Cross-over study design; consecutive enrollment of 56 senior medical students during their emergency medicine rotation	McMaster University	Preliminary findings suggest that application of CFS and retention are poor. Even immediately after instruction, in a test situation that is deliberately linked to the educational intervention, fewer than half the students in the study used CFS to correctly "de-bias" themselves. Two weeks post-CFS training, there was no evidence of de-biasing.	Not provided	Moderate
Sherbino et al., 2014[15]	A 90-minute, standardized, interactive, case-based teaching seminar on CFS	Prospective, controlled trial; 198 senior medical students in EM rotation (145 in intervention, 46 in control group)	McMaster University	The educational interventions employed to teach CFS failed to show any reduction in diagnostic error by novices.	Not provided	Low to moderate
Smith et al., 2009[40]	Four-month online didactic continuing education program to improve ability of rural radiographers to interpret plain musculoskeletal radiographic examinations	Pre/post design, no comparison group; 16 rural radiographers	Northern Sector of the Hunter New England Area Health Service, UK	Short-term intensive training can improve diagnostic accuracy of rural radiographers. There was a statistically significant improvement at the "general opinion" and "observation" levels for the more complex cases (paired t-test, $p<0.05$), while there was no change in image interpretation accuracy for less complex cases.	Online educational intervention	Moderate
Smith and Slack, 2015[16]	Workshop on debiasing (taught to recognize and respond to cognitive biases), including training reflective exercises	Pre/post study, no comparison group; 19 family medicine residents	Family Medicine Residency Program at David Grant Medical Center, Travis Air Force Base, California, United States	After the workshop, residents' formulation of an acceptable plan to mitigate the effect of cognitive bias increased from 84% (36 of 43) to 100% (33 of 33, $p=0.02$). There was no effect on preceptor concurrence with the residents' diagnoses, the residents' ability to recognize their risk of cognitive bias, or the preceptors' perception of an unrecognized cognitive bias in the residents' presentation.	Not provided	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
Soh et al., 2013[34]	One-hour online e-learning tutorial to improve visual perception skills	Randomized controlled trial, 14 first-year medical radiation sciences students (technologists)	Medical radiation science program, Australia	The experiment group demonstrated a 45% increase in the mean number of fixations per case (p=.047), with a 30% increase in sensitivity (p=.022), following the tutorial. The experiment group also demonstrated improved lesion detection overall and a 49% decrease in mean time to first fixation on the lesion (p=.016).	Online educational intervention	Moderate
van der Gijp et al., 2017[33]	Training on two visual search strategies, "scanning" and "drilling," used in radiology to improve visual perception	Randomized cross-over design; 19 first- and second-year radiology residents	Academic medical center's radiology residency program, United States	Perceptual performance following drilling search instructions outperformed performance following scanning search instruction in terms of true positives.	Not provided	Moderate
Wolpaw et al., 2009[9]	Training on the use of SNAPPS technique—Summarize history and findings, Narrow the differential; Analyze the differential; Probe preceptor about uncertainties; Plan management; Select case-related issues for self-study—for case presentations to facilitate learning	Post-test-only, comparison groups, randomized trial; 108 third-year medical students	Case Western Reserve University School of Medicine, United States	SNAPPS group showed more diagnostic reasoning than a feedback comparison and a control group.	Not provided	Moderate (qualitative analysis)

Table B.6: Diagnostic Errors, Education and Training—Systematic Reviews and Meta-Analyses

Note: Full references are available in the Section 1.3 reference list.

Author, Year	Description of Patient Safety Practice	Settings and Population	Summary of Findings
Cook et al., 2010[7]	Virtual patients	Studies published in any language that investigated use of a virtual patient to teach health professions learners. Virtual patient is "a specific type of computer program that simulates real-life clinical scenarios; learners emulate the roles of healthcare providers to obtain a history, conduct a physical exam, and make diagnostic and therapeutic decisions." No beginning date cutoff, and the last date of search was February 16, 2009.	Systematic review and meta-analyses. Included 4 qualitative studies, 18 no-intervention controlled studies, 21 noncomputer instruction comparative studies, and 11 computer-assisted instruction comparative studies. Use of virtual patients was associated with large positive effects compared with no intervention.
Graber et al., 2012[8]	Various interventions, including educational interventions	Articles and books that contained results from an intervention trial or suggested an intervention to reduce cognitive-related diagnostic error.	Review included 141 sources (42 empirical studies; 100 contained suggestions for interventions; and 1 had both). The review focused on three areas to reduce diagnostic errors: increase knowledge and experience, improve clinical reasoning, and get help.
McDonald and Matesic, 2013[36]	Patient safety strategies targeting diagnostic errors, including educational interventions	Studies that evaluated any intervention to decrease diagnostic errors (incorrect diagnoses or missed diagnoses) in any clinical setting and with any study design and patient outcomes.	Eleven studies used educational interventions aimed at various populations. Strategies targeted at clinicians produced improvements, but the studies were nonrandomized. Two randomized trials that targeted consumers in the diagnostic process found improvements.

Table B.7: Diagnostic Errors, Peer Review—Single Studies

Note: Full references are available in the Section 1.4 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Agrawal et al., 2017[18]	Simultaneous double-reporting of emergency teleradiology examinations with discrepancies adjudicated by the radiologists before finalization of the report	Descriptive analysis of retrospective data; 3,779 double-read radiological procedures over 4 months	International teleradiology practice and two non-teaching mid-sized to large community hospitals, United States	Of the 145/3,779 procedures (3.8%; 95% confidence interval [CI], 3.2 to 4.4) for which the double-reporting identified undetected or incompletely evaluated findings that led to report modifications, 69 were clinically significant. MRI spine studies contributed significantly more than other study types to these errors.	Not provided	To promote efficiency, limit double reviews to certain study types that have the greatest risk of diagnostic errors.	Moderate	In Geijer, 2018
Harvey et al., 2016[10]	Regularly scheduled consensus-oriented group reviews (3 or more radiologists) of randomly selected recently interpreted computerized tomography (CT), magnetic resonance imaging (MRI), and ultrasound cases (within 3–7 days)	Descriptive analysis of retrospective data. A total of 11,222 studies reported by 83 radiologists were peer-reviewed using COGR at 2,027 conferences during the 2-year study period	Radiology department at a 950-bed tertiary care academic center, United States	The average radiologist participated in 112 peer review conferences and had 3.3% of their available CT, MRI, and ultrasound studies peer reviewed. The discordance rate was 2.7% (95% CI, 2.4 to 3.0), with significant differences found on the basis of division and modality.	Not provided	Necessary to have stakeholder buy-in. Implementation associated with increased staffing needs, workload, and associated costs. Concern over maintenance of confidentiality may affect implementation.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Itri et al., 2018[11]	Peer review of randomly selected (20 cases/month adjudicated by third party) and nonrandomly selected (diagnostic errors found during routine clinical practice) radiologist interpretations and peer learning conferences (PLCs)	Descriptive analysis of retrospective data; 1,880 total abdominal imaging cases (190 identified via nonrandom peer review process; 1,690 identified via random peer review process) read by 10 radiologists	Abdominal imaging section of a radiology department in an academic tertiary care medical center, United States	Random peer review process: 1,690 cases reviewed, 2.6% with incidental errors. None considered to be significant or major discrepancies. Nonrandom process: 190 cases identified, 94 categorized as significant, 36 categorized as major discrepancies. CTs and MRIs accounted for 164 of the cases.	Not provided	Not provided	Moderate	None
Kamat et al., 2011[15]	Laboratory information system-driven pre-signout quality assurance tool to randomly select an adjustable percentage of pathology cases for peer review and adjudication by the pathologists prior to release of the final report	Descriptive analysis of retrospective data; 1,339 (7.45%) out of a total 17,967 non-gynecologic cytopathology cases over an 18-month period	Pathology department at a university medical center, United States	In 2.6% of cases there were discrepancies, including 34 minor and 1 major.	Not provided	Implementation associated with increased staffing needs, workload, and associated costs.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Lauritzen, 2016[19]	Prospective radiologist-requested double-reading of CT abdomen examinations	Retrospective cross-sectional study; 1,071 consecutive double-reported abdominal CT examinations of surgical patients	Multicenter study; five public hospitals, Norway	Of 1,071 reports, 146 contained clinically important changes (14%, 95% CI, 11.6 to 15.8), with changes to 108 reports (10%, 95% CI, 8.3 to 12.0) considered intermediate, 35 major (3%, 95% CI, 2.3 to 4.5), and 3 critical (0.3%, 95% CI, 0.06 to 0.8).	Not provided	Concern over maintenance of confidentiality may affect implementation.	Low to moderate	In Geijer, 2018
Lauritzen et al., 2016[20]	Prospective radiologist-requested double-reading of CT chest examinations	Retrospective cross-sectional study; 1,023 consecutive double-reported chest CT examinations	Multicenter study; five public hospitals, Norway	Report changes were classified as clinically important in 91 (9%) of 1,023 reports. Of these, 3 were critical (demanding immediate action), 15 were major (implying a change in treatment), and 73 were intermediate (affecting subsequent investigations).	Not provided	Not provided	Low to moderate	In Geijer, 2018

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Layfield and Frazier, 2017[14]	Random peer review (10% of all surgical pathology cases); nonrandom peer review (solicited review correlation of internal and external diagnoses; unsolicited correlation of internal and external diagnoses in cases sent for review at a second institution treating the patient; and review of all dermatopathology cases)	Descriptive analysis of retrospective data; all cases undergoing review by any of the four review protocols over a 1-year period were included	Department of Pathology and Anatomical Sciences at a university medical center, United States	The 10% random review detected 17 errors in 2,147 cases (0.8%); solicited case consultations detected 5 errors in 70 cases (7.1%); unsolicited reviews by outside institutions detected 3 errors in 190 cases (1.6%); and focused reviews of dermatopathology cases identified 5 errors in 59 cases (8.5%).	Not provided	Implementation associated with increased staffing needs, workload, and associated costs.	Moderate	None
Lian et al., 2011[22]	Retrospective review by two subspecialists of initially double-read CT angiography studies (head and neck); initial studies read by a staff neuroradiologist alone, by staff and diagnostic radiology resident, and by staff and neuroradiology fellow	Descriptive analysis of retrospective data; 503 sequential neck and intracranial CTA studies performed over a 6-month period	Unspecified	Reviewed 503 studies; 144 were originally reported by a staff neuroradiologist alone, 209 by staff and a diagnostic radiology resident, and 150 by staff and a neuroradiology fellow. Twenty-six significant discrepancies were discovered in 20/503 studies (4.0%).	Not provided	Not provided	Moderate	In Geijer, 2018

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Lindgren et al., 2014[25]	Retrospective interpretations of radiology studies (CT, MRI, and ultrasound abdominal studies) initially performed at an outside institution	Descriptive analysis of retrospective data; 398 abdominal imaging reinterpretations performed on 380 patients between 1/1/2010 and 7/15/2010	Single hospital, United States	Three hundred ninety-eight report comparisons were reviewed on 380 patients. The initial report had 5.0% (20/398) high clinical impact interpretive discrepancies and 7.5% (30/398) medium clinical impact discrepancies. The subspecialized secondary report had no high clinical impact discrepancies and 8/398 (2.0%) medium clinical impact discrepancies.	Not provided	Not provided	Moderate	In Geijer, 2018
Murphy et al., 2010[21]	Prospective, blinded double-reporting of minimal-preparation CT colon (MPCTC) with discrepancies resolved by followup colonoscopies	Prospective cohort of 186 consecutive patients undergoing MPCTC for lower gastrointestinal symptoms	Single hospital; UK	Of the 186 imaging reports, 111 had at least one discrepancy (60%). Sixty-seven clinically relevant extracolonic lesions were identified (25 identified in one report, 42 in both), and 24 clinically relevant colonic lesions (7 in one report, 17 in both). Of the 17 colonic lesions reported by both radiologists, 5 were false positives as determined by normal colonoscopies. Of, the 7 reported by one radiologist, 1 was a biopsy-proved cancer.	Increased false-positives. Double-reporting found one extra-colonic cancer, but at the expense of five unnecessary endoscopic procedures.	Implementation associated with increased staffing needs, workload, and associated costs.	Low	In Geijer, 2018

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Natarajan et al., 2017[23]	Retrospective reinterpretations by radiologists of plain radiographs initially read by pediatric orthopedists	Retrospective cohort; 1,570 consecutive pediatric orthopedic clinic patients with 2,509 radiographic studies during a 4-month period	Pediatric orthopedic clinic in an academic children's hospital, United States	Of 2,264 radiographic studies reviewed by a radiologist, new, clinically important information was added in 23 (1.0%) of studies. In 38 (1.7%) of the studies, the radiologist review missed the diagnosis or clinically important information that could affect treatment.	Not provided	Implementation associated with increased staffing needs, workload, and associated costs.	Low to moderate	In Geijer, 2018
Onwubiko and Mooney, 2016[24]	Retrospective reinterpretations of pediatric trauma CT scans initially performed at outside institution	Descriptive analysis of retrospective data; 168 patients transferred with CT abdomen and pelvis scans performed at outside institutions	Level 1 pediatric trauma center, United States	Ninety-eight CT abdomen/pelvis scans were reinterpreted, with 12 new, clinically significant injuries detected. Three patients had solid organ injuries upgraded and four were downgraded to no injury.	Not provided	Implementation associated with increased staffing needs, workload, and associated costs.	Low to moderate	In Geijer, 2018
Raab et al., 2008[12]	Random peer review (5% of cases) and focused secondary review (known diagnostically challenging case types) of surgical pathology cases	Nonconcurrent cohort study; 7,444 cases from random review process and 380 cases reviewed using focused review process	Single site within a large multihospital system, United States	The numbers of errors detected by the targeted 5% random and focused review processes were 195 (2.6% of reviewed cases) and 50 (13.2%), respectively (p<.001). The numbers of major errors for the targeted 5% random and focused review processes were 27 (0.36%) and 12 (3.2%), respectively (p<.001).	Not provided	To promote efficiency, limit double reviews to certain study types that have the greatest risk of diagnostic errors.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Swanson et al., 2012[13]	Peer review of randomly selected radiology studies (4 cases/shift) and voluntary, nonrandom case review with feedback	Descriptive analysis; peer review reports on 5,278 radiologic studies (4,892 mandatory random review; 386 voluntary review) conducted over 4-year period	Large urban multidisciplinary children's hospital, United States	The discrepancy rate was 3.6% between original interpretation and random peer review and 12% for the nonrandom review.	Not provided	Not provided	Moderate	None

Table B.8: Diagnostic Errors, Peer Review—Systematic Reviews and Meta-Analyses

Note: Full references are available in the Section 1.4 reference list.

Author, Year	Description of Patient Safety Practice	Settings and Population	Summary of Findings	Implementation Themes/Findings
Geijer and Geijer, 2018[16]	Double-reading of radiology studies	Included studies calculating the rate of misses and overcalls with the aim of establishing the added value of double reading by human observers.	Forty-six studies met inclusion criteria. The discrepancy rates varied from 0.4 to 22% in various studies. Double-reading by sub-specialists found high discrepancy rates. Double-reading generally increased sensitivity at the cost of decreased specificity.	To promote efficiency, limit double reviews to certain study types that have the greatest risk of diagnostic errors. Implementation associated with increased staffing needs, workload, and associated costs.
Pow et al., 2016[17]	Double-reading of radiology studies	Studies reporting on the effect of double-reporting on measures of diagnostic efficacy in all imaging modalities, both screening and diagnostic, including sensitivity, specificity, recall rate, and cancer detection rate were included.	Forty-one studies met inclusion criteria. The use of double- reading was found to increase sensitivity and reduce specificity, making it most useful for screening studies where high sensitivity is desired. The authors recommended the use of double-reading in trauma and found that the level of expertise of the reviewers influences the error rate, with those using a subspecialist for the second review having higher rates than for two radiologists with similar training.	To promote efficiency, limit double reviews to certain study types that have the greatest risk of diagnostic errors.

Table B.9: Failure To Rescue, Patient Monitoring Systems—Single Studies

Note: Full references are available in the Section 2.1 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Bailey et al., 2013[12]	An algorithm designed to predict the need for intensive care unit (ICU) transfer using electronically available data, with alerts sent by text page to the nurse manager	Randomized controlled crossover study; 28,927 hospitalizations on general wards; 19,116 distinct patients	Eight adult medicine wards in a 1,250-bed academic medical center; United States	Among patients identified by the early warning system, there were no differences in the proportion of patients who were transferred to the ICU or who died in the intervention group compared with in the control group.	The lack of clinical impact may have been due to relying on the alerted nursing staff to make phone calls to physicians, and not linking a specific and effective patient-directed intervention to the patient	Low
Bellomo et al., 2012[10]	Electronic automated advisory vital signs monitor to assist in the acquisition of vital signs and calculation of early warning scores	Before-and-after controlled trial; all patients admitted to the study wards included in the study: 18,305 patients	349 beds in 12 general wards in 10 hospitals in the United States, Europe, and Australia	During the control period, there were 205 rapid response team (RRT) calls (21.3/1,000 admissions), compared with 209 in the intervention period (24.1/1,000 admissions; p=.21). There was no significant overall change for in-hospital mortality (1.8% vs. 2.0%; p=0.36). However, there was a significant reduction in length of hospital stay, which was dependent on a particularly strong effect in U.S. hospitals (4 days vs. 3 days, p=<0.0001).	Findings seem to suggest that monitoring rather than intervention improves survival, because the need for all interventions decreased in the after-RRT call period.	Low-moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Brown et al., 2014[5]	Continuous heart rate and respiration rate monitoring	Controlled clinical trial; general medical, trauma, and surgical patients; 2,314 patients in intervention arm, 5,329 in control arm	Two 33-bed medical/surgical units in a 316-bed community hospital	Comparing the average length of stay, there was a significant decrease (from 4.0 to 3.6 and 3.6 days, respectively; p<.05). Total intensive care unit days were significantly lower in the intervention unit post-implementation (63.5 vs. 120.1 and 85.36 days/1,000 patients, respectively; p=.04). The rate of transfer to the intensive care unit did not change when comparing the treatment unit after implementation to the treatment unit before and the control unit (p=.19). Rates of Code Blue events decreased following the intervention, from 6.3 to 0.9 and 2.1, respectively, per 1,000 patients (p=.02).	Not provided	Low-moderate
Fletcher et al., 2017[7]	Electronic medical record-based dashboard	Quasi-experimental repeated treatment study; 6,736 eligible general medical/surgical ward patients 18 years of age and over	Inpatient general medical-surgical wards at an urban level 1 trauma center and teaching hospital with 413 beds (including 89 critical care beds) and approximately 19,000 annual admissions	There was no change in overall RRT activations (incidence rate ratio [IRR]=1.14, p=0.07), but a significant increase in first RRT activations (IRR=1.20, p=0.04). There were no significant differences in unexpected ICU transfers (IRR=1.15, p=0.25), cardiopulmonary arrests on general wards (IRR=1.46, p=0.43), or deaths on general wards (IRR=0.96, p=0.89).	The RRT dashboard allows the RRT and primary team members to monitor patients and review patients at risk, rather than relying exclusively on bedside nurses to activate an RRT.	Low-moderate
Kollef et al., 2014[8]	Electronic health record-based vital sign monitoring with real-time alerts sent to the RRT	Randomized controlled trial; 571 patients	Eight medicine units in a 1,250-bed academic medical center	ICU transfer (17.8% vs. 18.2%) and hospital mortality (7.3% vs. 7.7%) were similar for the intervention and control groups. The number of patients requiring transfer to a nursing home or long-term acute care hospital was similar for patients in the intervention and control groups (26.9% vs. 26.3%). Hospital duration was statistically shorter for the intervention group.	Communication between the RRT and the primary care teams was greater in the intervention arm, as was the use of telemetry and oximetry.	Low

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
McGrath et al., 2019[9]	Wireless patient sensors and pulse oximetry-based surveillance system monitors with advanced display and information systems	Quasi-experimental pre-post study with comparison group; 971.40 patient days in study units compared with 420.35 patient days for the comparison units	71 general care beds in two units	The enhanced monitoring system received high staff satisfaction ratings and significantly improved key clinical elements related to early recognition of changes in patient state. This included reducing average vital signs data collection time by 28%, increasing patient monitoring time (rate ratio 1.22), and increasing availability and accuracy of patient information. Impact on clinical alarms was mixed, with no significant increase in clinical alarms per monitored hour.	The significant decrease in time required to obtain and document vital signs allows staff the potential to spend time on additional patient-focused tasks. Despite the alarm rate increases, overall rates are still below the threshold where alarm fatigue would be a concern.	Low-moderate
Taenzer et al., 2010[4]	Pulse oximetry surveillance with nursing notification of violation of alarm limits via wireless pager	Quasi-experimental pre/post study with comparison units and control of confounders; over 43,000 patient days total; over 13,000 patient discharges	36-bed orthopedic unit with an average of 200 patient days and 53 patient discharges per week in a 395-bed hospital	Rescue events decreased from 3.4 (confidence interval [CI]: 1.89–4.85) to 1.2 (CI: 0.53–1.88) per 1,000 patient discharges (p=0.01) and intensive care unit transfers from 5.6 (CI: 3.7–7.4) to 2.9 (CI: 1.4–4.3) per 1,000 patient days (p=0.02), whereas the comparison units had no change.	Low nurse to patient ratios demand a different balance of sensitivity and specificity when compared with the operating room. Continuous patient surveillance can succeed only if it is not a burden to the already limited personnel resources, and thus, thoughtful implementation of the technology is the key.	Low-moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Weller et al., 2018[6]	Continuous multi-parameter patient monitoring. A wireless, portable, wearable multi-parameter vital sign monitor with automated nursing notification of alarms via smartphones.	Pre/post study with a comparison unit; 736 patients	26-bed adult, neurological/ neurosurgical unit (non-ICU) in an academic medical center	The RRT call rate was significantly reduced ($p<0.05$), from 189 to 158 per 1,000 discharges. ICU transfers per 1,000 discharges were insignificantly reduced, from 53 compared with 40 in the previous 5-month period in the same unit. Similar measures of comparison units did not change over the same period. Although unplanned patient deaths (non-compassionate care deaths) in the study unit were reduced during the intervention period, this finding was not statistically significant. Lengths of stay were similar between pre-pilot and intra-pilot study periods.	Nurses expressed a sense of increased knowledge about the status of their patient information visible on the in-room monitor (along with remote notification), reinforcing the likelihood that any increased nursing attention is a direct result of the new system, not a by-product of the guided implementation of the new process.	Low-moderate

Table B.10: Failure To Rescue, Patient Monitoring Systems—Systematic Reviews and Meta-Analyses

Note: Full references are available in the Section 2.1 reference list.

Author, Year	Description of Patient Safety Practice	Setting(s); Population(s)	Summary of SR Findings	Implementation Themes/Findings
McNeill et al., 2013[14]	Early warning systems (EWSs), emergency response teams (ERTs)	Hospital, inpatient; 43 studies reviewed	Overall evidence is of poor quality. For EWS, aggregate weighted scoring systems appear to be more effective than single parameter systems. For ERT, introduction of a medical emergency team does appear to improve hospital survival and reduces cardiac arrest rates.	Not provided
McGauhey et al., 2017[15]	EWS and rapid response system	275 studies reviewed; acutely ill patients on general hospital wards	Evidence supporting EWS validity and reliability showed that physiological variables (heart rate, blood pressure, RR) accurately predicted outcomes that were associated with an increased risk of unplanned intensive care unit (ICU) admission/readmission and of mortality in adult and pediatric patients within 24–48 hours. However, refuting evidence highlights that EWS-validated tools have largely been modified to individual localities, with the result that the sensitivity and positive predictive values were too low to predict patient deterioration in hospitals. As a result, the utility, validity, and reliability of EWS tools have been questioned.	Evidence suggests that the EWS protocols improve communication of vital signs and empower nurses to vocalize their concerns by "packaging" information using clinical judgment and quantifiable evidence to call for help.
Cardona-Morrell et al., 2016[12]	Continuous or intermittent vital signs monitoring	22 studies assessing the effect of continuous (9) or intermittent monitoring (13) and reporting outcomes on 203,407 patients in hospital wards across 13 countries	Continuous and intermittent monitoring practices led to: early identification of patient deterioration, increased rapid response activations, and improvements in timeliness or completeness of vital signs documentation. Innovative intermittent monitoring approaches are associated with modest reduction in in-hospital mortality over intermittent vital signs monitoring in "usual care." However, there was no evidence of significant reduction in ICU transfers or other adverse events with either intermittent or continuous monitoring. This review of heterogeneous monitoring approaches found no conclusive confirmation of improvements in prevention of cardiac arrest, reduction in length of hospital stay, or prevention of other neurological or cardiovascular adverse events. The evidence found to date is insufficient to recommend continuous vital signs monitoring in general wards as routine practice.	Not provided

Table B.11: Failure To Rescue, Rapid Response Teams—Single Studies

Note: Full references are available in the Section 2.2 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Blotsky et al., 2016[8]	Ward-based rapid response system (RRS) involving bedside nursing staff (activation) and senior medical resident (response)	Prospective before/after study; patients on medical clinical teaching unit (CTU); 95 calls were placed for 82 patients	48-bed CTU in a university-affiliated acute care teaching hospital; Canada	Total number of intensive care unit (ICU) admissions from the CTU was reduced from 4.8/1,000 patient days (±2.2) before intervention to 3.3/1,000 patient days (±1.4) after intervention (incidence rate ratio [IRR], 0.82, 95% confidence interval [CI], 0.69 to 0.99). CTU code blue rates decreased from 2.2/1,000 patient days (±1.6) before intervention to 1.2/1,000 patient days (±1.3) after intervention (IRR, 0.51, 95% CI, 0.30 to 0.89). Mortality rates did not change.	No additional clinical staffing required, so no additional funding required to implement.	Moderate
Chen et al., 2016[5]	RRS "Between The Flags" Program	Interrupted time-series population-based study; all adult hospital patients >18 years old; 9,799,081 admissions	All 232 public hospitals in New South Wales, Australia	Pre-intervention—trend of decreasing mortality, cardiac arrest rates, cardiac arrest-related mortality, and failure to rescue (FTR) rates, with stable mortality rate among low mortality diagnostic related group (LMDRGs) patients. Post-intervention—trends continued for all outcomes, including a new 20% ($p<0.001$) mortality reduction among LMDRG patients.	Not provided	Low-moderate
Moriarty et al., 2014[10]	Multidisciplinary team including a critical care nurse, critical care fellow, and respiratory therapist	Longitudinal study using control charts and Bayesian change point (BCP) analysis; all inpatients discharged between 9/1/05 and 12/31/10.	Two acute care hospitals and an inpatient psychiatric treatment center of the Mayo Clinic; Rochester, MN	A decrease in FTR, as well as an increase in the unplanned ICU transfer rate, occurred in the second-year post-RRT implementation, coinciding with an increase in RRT calls per month. No significant decreases were observed pre- and post-implementation for cardiopulmonary resuscitation events or overall mortality.	Findings support prior hypotheses that effects from RRT implementation may not be immediately noticeable.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Pain et al., 2017[9]	RRS "Between The Flags" Program	Prospective longitudinal study	225 public hospitals across New South Wales, Australia	Since the introduction of RRS, the cardiac arrest rate has declined by 42% ($p<0.05$) and the rapid response call rate has increased by 135.9% ($p<0.05$) in New South Wales.	Providing clarity about who is responsible for what at all levels of the system is crucial to successful implementation and long-term sustainability of the RRS. During implementation, consider strategies for reinforcing discretion and judgment by clinicians when patients have early warning signs.	Low-moderate

Table B.12: Failure To Rescue, Rapid Response Teams—Systematic Reviews and Meta-Analyses

Note: Full references are available in the Section 2.2 reference list.

Author, Year	Description of Patient Safety Practice	Settings and Population	Summary of Findings	Implementation Themes/Findings	Comments
Chan et al., 2010[4]	Rapid response teams (RRT)	Acute care hospital, non-intensie care unit (ICU) setting, adults and pediatrics; 18 studies published between 1950 and 2008	For adults, implementation of an RRT was associated with a 33.8% reduction in rates of cardiopulmonary arrest outside the ICU (relative risk [RR], 0.66; 95% confidence interval [CI], 0.54 to 0.80), but was not associated with lower hospital mortality rates (RR, 0.96; 95% CI, 0.84 to 1.09). For children, implementation of an RRT was associated with a 37.7% reduction in rates of cardiopulmonary arrest outside the ICU (RR, 0.62; 95% CI, 0.46 to 0.84) and a 21.4% reduction in hospital mortality rates (RR, 0.79; 95% CI, 0.63 to 0.98).	Not provided	None
Daniele et al., 2011[11]	RRT	Acute care hospital, non-ICU setting, adults; 26 studies published between 1989 and 2010	A statistically significant reduction in mortality rate was reported along with an equivocal result on length of stay in the cluster randomized control trial. An odds ratio of 0.52 (95% CI, 0.3 to 0.85) was calculated after RRT implementation.	There was no correlation between team composition and patient outcomes. Teams that were mature, dedicated, made rounds, and required mandatory activation had statistically significant results.	None
Maharaj et al., 2015[2]	Rapid response systems (RRS)	Acute care hospital, non-ICU setting, adults and pediatrics; 29 studies published between 1990 and 2013	The implementation of RRS has been associated with an overall reduction in hospital mortality in both the adult (RR, 0.87; 95% CI, 0.81 to 0.95) and pediatric (RR, 0.82; 95% CI, 0.76 to 0.89) inpatient population. There was substantial heterogeneity across studies for both populations.	There was no dose to response relationship between the duration of the implementation phase, the presence of a physician on the team, or the number of activations per 1,000 and hospital mortality.	None
McNeill et al., 2013[7]	Early warning systems (EWS), emergency response teams (ERT)	Hospital, inpatient	Overall evidence is of poor quality. For EWS, aggregate weighted scoring systems appear to be more effective than single parameter systems. For ERT, introduction of a medical emergency team (MET) does appear to improve hospital survival and reduces cardiac arrest rates.	Not provided	Also included in Patient Monitoring Systems

Author, Year	Description of Patient Safety Practice	Settings and Population	Summary of Findings	Implementation Themes/Findings	Comments
Solomon et al., 2016[3]	RRS	Acute care hospital, non-ICU setting, adults; 30 studies published between 2000 and 2014	The pooled analysis demonstrated that implementation of RRT/METs was associated with a significant reduction in hospital mortality (RR, 0.88; 95% CI, 0.83 to 0.93). There was heterogeneity among the contributing studies (I^2 =86%).	Not provided	Builds off of the meta-analysis of Chan et al., 2010
Winters et al., 2013[6]	RRS	Acute care hospital, non-ICU setting, adults; 43 studies published between 2000 and 2012	Systematic review found moderate strength of evidence that RRSs improve outcomes from both a high-quality systematic review through November 2008 and the additional literature published through October 2012.	Implementation processes differed widely across studies, and local needs and resources tended to dominate the processes. Education and promotion of the new service was often a factor in preparing for implementation. For staff training and education, several studies introduced new staff, such as a nurse educator.	None

Table B.13: Sepsis Recognition, Sepsis Screening Tools—Single Studies

Note: Full references are available in the Section 3.1 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Bayer et al., 2015[20]	Early sepsis detection score (PRESEP)	A retrospective analysis of consecutive patients who were admitted by emergency medical services (EMS) to the emergency department (ED); 375 patients.	EMS admission into ED	The area under the receiver operating characteristic curve (AUC) of the PRESEP score was 0.93 and was larger than the AUC of the MEWS. The PRESEP score surpassed MEWS and BAS 90-60-90 for sensitivity (0.74 and 0.62, respectively), specificity (0.75 and 0.83), positive predictive value (PPV) (0.45 and 0.51), and negative predictive value (NPV) (0.91 and 0.89). The Robson screening tool had a higher sensitivity and NPV (0.95 and 0.97), but its specificity and PPV were lower (0.43 and 0.32).	The PRESEP tool is simple and fast to calculate in the prehospital setting because all parameters are readily available and routinely assessed. One prospective observational study of patients with severe sepsis showed a significantly shortened time to initiation of antibiotic treatment (70 minutes vs. 122 minutes) and early goal-directed therapy (69 minutes vs. 131 minutes) if sepsis was already diagnosed by the EMS provider.	Low (based on Smyth, 2016)
Berger et al., 2013[28]	Shock index (SI) for the early recognition of sepsis	Retrospective cohort analysis. Adult patients presenting to the ED with a suspected infection; 2,524 patients.	ED at an academic community trauma center with 95,000 annual visits	Subjects with an abnormal SI of 0.7 or greater (15.8%) were three times more likely to present with hyperlactatemia than those with a normal SI (4.9%). The NPV of an SI ≥ 0.7 was 95%, identical to the NPV of SIRS. SI ≥ 1.0 was the most specific predictor of both outcomes.	Not provided	Low/ moderate
Filbin et al., 2018[22]	ED sepsis screening at triage	Retrospective, outcome-blinded chart review of a 1-year cohort; 19,670 ED patients.	ED in a large, urban tertiary care hospital	The triage concern-for-infection (tCFI) criterion improved specificity without substantial reduction of sensitivity. At triage, sepsis screens (positive quick sequential organ failure [qSOFA] vital signs and tCFI, or positive Shock Precautions on Triage [SPoT] vital-signs and tCFI) were 28% and 56% sensitive, respectively, and specificities were 97% and 95%.	Taken altogether, the findings of this analysis affirm the feasibility of sepsis screening at triage. Most septic shock patients could be identified upon triage, or shortly thereafter, using only vital signs and the patient's risk factors and symptoms. Such patients can and should be prioritized for rapid evaluation and diagnostic testing to confirm infection and initiate treatment expeditiously.	Low/ moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Goerlich et al., 2014[8]	Screening tool for the early identification of sepsis	Prospective, observational study of all patients who were seen at triage. Of 500 patients screened, 42 screened positive.	Academic tertiary referral hospital	The screening tool yielded a sensitivity of 85.7%, a specificity of 78.4%, a PPV of 26.7%, and an NPV of 98.4%.	Future modifications of the tool should elucidate the possibility of a source of infection. Thus, a modification of the screening tool that incorporates simple screening questions (analogous to a mini "review of systems" for tuberculosis screening) may aid in determining a potential source of infection and help limit false positives and false negatives.	Low/ moderate
Guerra et al., 2013[14]	A screening tool using point-of-care venous lactate meters	Prospective pilot cohort study. Patients with severe sepsis transported by EMS	Three tertiary care hospitals collectively care for > 80,000 ED patients annually	Trained EMS providers transported 67 severe sepsis patients. They identified 32 of the 67 severe sepsis patients correctly (47.8%). Sepsis alert protocol patients were intubated less frequently than nonalert patients (8% vs. 35%; p=0.003). Antibiotic administration was more prompt in the Alert protocol sample than non-Alerts, but the result did not reach statistical significance. There was no significant difference between alert patients and nonalert patients receiving central lines.	Unlike hospital-based Early Goal-Directed Therapy, no complex procedures, such as central-line placement, are required of EMS to initiate sepsis treatment. All procedures initiated are used frequently by EMS providers to treat hypoperfusion and shock. These prehospital measures, nearly universally available in the United States, can easily be applied by most EMS agencies. An EMS provider's sepsis knowledge base did not correlate with years of training or experience as an EMS provider.	Moderate/ high
Gyang et al., 2015[10]	Three-tiered, paper-based, nurse-driven sepsis assessment tool administered every 8 hours	Retrospective testing of a prospectively implemented tool on consecutive patients admitted to the unit. Of 245 patients screened, 39 screened positive.	Twenty-six-bed medical/ surgical intermediate care unit at a 613-bed academic medical center	Screening tool sensitivity and specificity were 95% and 92%, respectively. NPV was 99% and PPV was 54%. Overall test accuracy was 92%. There was no statistically significant difference in tool performance between medical and surgical patients. The authors did not find a significant difference in the proportion of patients receiving a sepsis-related clinical action before a screening result (positive or negative), which suggests that a positive screening test may have led to increased clinical action.	The researchers relied heavily on the nursing staff to assess for the presence or absence of infection and believe that the educational component prior to initiating the screening protocol was vital. EMR-based screening tools that rely purely on physiologic data have been considered for the early detection and management of sepsis, although they lack the specificity gained through the incorporation of clinical judgment.	Low/ moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Hunter et al., 2016[7]	Prehospital sepsis screening protocol	Retrospective analysis of a prospectively implemented tool. All patients admitted to the ED with a "sepsis alert"; 330 patients.	Eight advanced life support EMS agencies	Sepsis alerts that followed the protocol had a sensitivity of 90% (95% confidence interval [CI], 81-95%), a specificity of 58% (95% CI, 52-65%), and an NPV of 93% (95% CI, 87-97%) for severe sepsis.	While early identification and resuscitative efforts may improve outcomes in severe sepsis, obtaining lactate levels in the field can be difficult and expensive. However, prior studies have shown that prehospital providers can accurately obtain ETCO2 levels simultaneously with traditional vital signs. This suggests that using ETCO2 as an objective marker for hypoperfusion may help discriminate between potentially septic and severely septic patients.	Low/ moderate
Hunter et al., 2018[13]	Comparison of ETCO2 with qSOFA	Retrospective cohort study among patients transported by EMS; 287 patients.	A single EMS system for several regional hospitals	Sensitivity and specificity for ETCO2 as a mortality predictor were higher than for qSOFA score—80% (95% CI, 59-92) vs. 68% (95% CI, 46-84) for sensitivity and 42% (95% CI, 36-48) vs. 40% (95% CI, 34-46) for specificity.	Not provided	Low/ moderate
Hunter et al., 2019[32]	Prehospital identification of sepsis	Retrospective cohort study among septic patients who were identified as "sepsis alerts" in the ED. Of the 272 total patients, 162 had pre-arrival notification (prehospital sepsis alerts) and 110 did not.	Eight Advanced Life Support EMS agencies	Patients with prehospital sepsis alerts had a higher admission rate (100% vs. 95%, p=0.006) and a lower intensive care unit (ICU) admission rate (33% vs. 52%, p=0.003). There was no difference in mortality (11% vs. 14%, p=0.565) between groups.	Prehospital sepsis alerts were associated with a higher overall hospital admission rate but a lower ICU admission rate, which may reflect successful early resuscitative efforts. Both groups had similar mortality and lactate levels, suggesting that a differing disease severity was not the cause for these findings. Mortality is a difficult primary outcome to interpret in early sepsis intervention considering that many septic patients are older, have multiple comorbidities, and may have advanced directives for end-of-life care.	Low/ moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Larosa et al., 2012[17]	Written screening tool and an early alert system (Code SMART)	Prospective observational study; 447 screened, 58 patients were enrolled: 34 Code SMART and 24 non-Code SMART. All adult patients.	An ICU in a tertiary care, urban teaching hospital of 673 beds	The Code SMART group achieved greater compliance with timely antibiotic administration ($p<0.001$), lactate draw ($p<0.001$), and steroid use ($p=0.02$). Raw survival ($p<0.05$) and survival adjusted for age, leucopenia, and severity of illness scores ($p=0.01$) were greater in the Code SMART group	Not provided	Moderate
MacQueen et al., 2015[11]	Vital sign-based screening protocol	Retrospective cohort analysis. All general surgery inpatients undergoing abdominopelvic surgery. Of 478 total patients screened, 59 had positive screening tests.	Single public Safety Net hospital	The screening protocol had sensitivity 100% and specificity 88% for severe sepsis.	Not provided	Moderate
McClelland et al., 2015[24]	Prehospital sepsis recognition, including the use of a sepsis screening tool	Retrospective cohort analysis. Adult (>16 years) patients with sepsis documented by the hospital; 49 patients.	Regional ambulance service	EMS correctly identified 18/42 patients with sepsis (43% sensitivity, 14% specificity). EMS correctly identified 8/27 patients with severe sepsis (30% sensitivity, 77% specificity).	Not provided	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Patocka et al., 2014[15]	Triage screening tool	Retrospective chart review; 185 patients with severe sepsis or septic shock in the pre-triage tool group and 170 patients in the post-triage tool group.	Urban tertiary teaching hospital; 637 beds	Mean time to antibiotics decreased by 21%. Compared with the pre-triage tool cohort, patients in the post-triage tool cohort were more likely to have a serum lactate measured in the ED (20% in the pre-triage cohort versus 89.9% in the post-triage tool cohort; p<.0001) and less frequently admitted to hospital (88% vs. 79%).	The number of patients receiving antibiotics within an hour of triage was not different. Rather, the gains in time were seen between 1 and 4 hours after arrival in the ED. This suggests that very sick patients were identified regardless of the triage tool, whereas those with more occult sepsis might preferentially benefit from this tool.	Low/ moderate
Polito et al., 2015[25]	EMS screening tool for severe sepsis (PRESS)	Retrospective cohort study. Sequential adult, nontrauma, nonarrest, at-risk, EMS-transported patients; 555 patients.	A single EMS system	The PRESS score demonstrates a sensitivity of 86% and a specificity of 47%.	One of the advantages of the PRESS score is that it comprises various types of routinely and practically collected EMS data.	Low (based on Smyth, 2016)
Rincon et al., 2011[16]	Tele-ICU sepsis screening	Prospective observational study. Every ICU patient admitted. Of 89,921 screened, 5,437 patients met criteria for sepsis.	One hundred sixty-one ICUs at 10 hospitals across a geographical range of 500 miles.	Statistically significant increases in compliance with SSC's bundled care recommendations were realized during this study period with four initial elements: antibiotic administration increased from 55% in 2006 to 74% in 2008 (p=0.001), serum lactate measurement increased from 50% to 66% (p=0.001), the initial fluid bolus of ≥20 mL/kg increased from 23% to 70% (p=0.001), and central line placement increased from 33% to 50% (p=0.001).	Tele-screening is a viable solution to mitigate disparities of care across a large health system.	Low/ moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Scott et al., 2014[29]	Recording of clinical recognition signs by clinicians on a form	Prospective cohort study, Patients <19 years with fever and tachycardia and undergoing phlebotomy; 239 patients.	ED of a free-standing children's hospital	The sensitivity of exam findings ranged from 8% to 54%; specificity from 84% to 98%.	Not provided	Low/ moderate
Seymour et al., 2017[3]	Score for out-of-hospital prediction of development of critical illness during hospitalization	Retrospective cohort analysis of patients transported by EMS; 144,913 patients.	EMS system that transports to 16 receiving facilities	Using a score threshold of 4 or higher, sensitivity was 0.22 (95% CI, 0.20-0.23), specificity was 0.98 (95% CI, 0.98-0.98), positive likelihood ratio was 9.8 (95% CI, 8.9-10.6), and negative likelihood ratio was 0.80 (95% CI, 0.79-0.82). A threshold of 1 or greater for critical illness improved sensitivity (0.98; 95% CI, 0.97-0.98) but reduced specificity (0.17; 95% CI, 0.17-0.17).	Not provided	Low (based on Smyth, 2016)
Shapiro et al., 2008[30]	Clinical decision rule for obtaining blood cultures	Prospective, observational cohort study. ED patients with suspected infection: 3,730 (96%) were enrolled, with 305 (8.2%) episodes of true bacteremia.	ED in a 490-bed urban academic tertiary care center	The rule is highly sensitive in identifying patients who will have a positive blood culture. The sensitivity was 98.0% (95% CI, 96–100%) in the derivation set and 97.0% (95% CI, 94–100%) in the validation set. The specificity was 29.0% (95% CI, 27–31%) and 28.8% (95% CI, 26.2–31.4%) for each respective set.	If used in this population, the rule could appropriately reduce the use of blood cultures by approximately 27%, resulting in approximately 1,053 fewer cultures per year. At an estimated cost of $15.91 and a charge of $118 per culture set, this represents a potential savings of $16,758 in costs and $124,286 in charges (institutional data).	Low/ moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Shetty et al., 2016[35]	Severe sepsis screening algorithm	Retrospective analysis, Patients presenting to the ED with suspected sepsis; 747 patients.	ED in a tertiary hospital	Sensitivity and specificity of algorithms to flag severe sepsis ranged from 20.2% to 82.3% and 57.8% to 94.8%, respectively.	Not provided	Low/ moderate
Shiuh et al., 2012[26]	EMS Sepsis Protocol with Point-of-Care Lactate	Prospective cohort of consecutive out-of-hospital patients treated under an EMS sepsis protocol; 219 patients.	EMS patients transported to a large urban/ suburban 2-hospital health system	There was a final hospital diagnosis of severe infection or sepsis for 76.7% of sepsis alert patients (n=66) and 74.2% of sepsis advisory patients (n=72). In these patients, median time from arrival to broad-spectrum antibiotics was 59 min (IQR 42–91) in sepsis alert patients and 81 min (IQR 49.5–127.3) in sepsis advisory patients. ICU admission occurred in 50% and 23% of sepsis alert and advisory, respectively.	Not provided	Moderate
Singer et al., 2014[9]	Sepsis screening tool with subsequent lactate measurement if criteria met.	Prospective, observational study, A convenience sample of adult ED patients with suspected infection; 258 patients.	A suburban academic ED with an annual census of 90,000	Sensitivity was 34%, specificity 82%, PPV 89% (95% CI, 80%–94%), and NPV 23%.	Not provided	Low/ moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Sloane et al., 2018[5]	Comparison of five sepsis screening tools	Retrospective chart audit of all residents who had been hospitalized and returned to participating nursing homes (NH) during the study period; 236 NH residents.	Thirty-one community NHs in North Carolina, The mean NH bed size was 11.	Documentation of 1 or more vital signs was absent in 26%–34% of cases. Among people with complete vital sign documentation during the 12 hours prior to hospitalization, the most sensitive screening tools were the 100-100-100 Criteria (79%) and an oral temperature >99.0F (51%); and the most specific tools were a temperature >100.2F (93%), the qSOFA (88%), the Systemic Inflammatory Response Syndrome criteria (86%), and a temperature >99.0F (85%). Many SOFA data points were missing from the record; despite this, 65% of cases met criteria for sepsis.	Over a quarter of NH residents lacked documentation of vital signs in the 72 hours prior to hospital transfer. Better surveillance of people who undergo changes in status is, therefore, an important element of improved detection of early sepsis. During the 12 hours prior to transfer, only 19% of the sepsis admissions and 16% of the nonsepsis admissions had a medical note or other indication of a provider examination. A possible solution is telemedicine if the resources were put in place to make on-call physicians able to have a robust virtual visit to patients with changes in medical status, and if reimbursement were provided at an appropriate level for such services.	Low/ moderate
Tedesco et al., 2017[18]	Sepsis Management Algorithm	Prospective pre-post observational study. Patients in the ED; 247 patients	A community hospital ED with 320 beds that had approximately 40,000 ED visits each year	Mortality from sepsis was significantly reduced ($\chi 2$ [1, n=5.889, p=0.015]) from 18.4% in 2015 compared with 13.2% for the same timeframe in 2016, which represented a 28% reduction in mortality.	Not provided	Moderate
Tirotta et al., 2017[31]	MEWS	Retrospective analysis of a multicentric prospective study. Consecutive septic patients with positive blood culture; 526 patients.	Thirty-one medical hospital wards in Italy	When dichotomized as low risk vs. high risk (MEWS <4 vs. >4), the MEWS had a sensitivity of 35% and a specificity of 83%.	Not provided	Low

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Wallgren et al., 2014[27]	Comparison of two prehospital sepsis screening tools with clinical judgment by EMS personnel	Retrospective cross-sectional study of adult patients transported by the EMS, with a hospital discharge International Classification of Diseases code consistent with sepsis; 353 patients.	EMS services in Sweden	For sepsis, Robson tool: sensitivity was 75% (p<0.001), BAS 90-30-90: sensitivity was 43% (p<0.001), EMS clinical judgement: 12% accuracy (95% CI not reported).	A possible contributing factor toward the low detection of sepsis by clinical judgment in the current study is the lack of guidelines on documentation of the primary impression in EMS records in Sweden.	Moderate/ high (from Smyth, 2016)
Wawrose et al., 2016[12]	Comparison of a sepsis screening tool, the Sepsis Screening Score (SSS), with a commercially available sepsis screening tool, the St. John's Sepsis Agent (SJSA)	Prospective observational study of each patient in the surgical intermediate care unit (SIMU). SSS was twice daily, SJSA was EHR monitoring. Of 348 patients included in the study, 47 (13.5%) developed sepsis.	SIMU at Memorial Hermann Hospital, a tertiary referral hospital in Houston, Texas	The SJSA was determined to have a sensitivity of 44.7%, a specificity of 84.7%, a PPV of 31.3%, and an NPV of 90.7%, while the SSS was determined to have a sensitivity of 74.5%, a specificity of 86.4%, a PPV of 46.1%, and an NPV of 95.6%. The differences in sensitivity ($p < 0.001$), PPV ($p < 0.001$), and NPV ($p = 0.011$) were found to be statistically significant.	Unlike the SJSA, the SSS is based on parameters that are easily measurable from the bedside, which allows for rapid sepsis diagnosis and subsequent treatment.	Low/ moderate

Table B.14: Sepsis Recognition, Sepsis Screening Tools—Systematic Reviews

Note: Full references are available in the Section 3.1 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings
Nannan Panday et al., 2017[33]	Early warning scores (EWS)	Emergency Department (ED) and acute medical unit (AMU)	Forty-two studies were included: 36 studies reported on mortality as an endpoint, 13 reported Intensive Care Unit (ICU) admission, and 9 reported the composite outcome of mortality and ICU admission. For mortality prediction, National Early Warning Score (NEWS) was the most accurate score in the general ED population and in those with respiratory distress; Mortality in Emergency Department Sepsis score (MEDS) had the best accuracy in patients with an infection or sepsis. ICU admission was best predicted with NEWS; however, in patients with an infection or sepsis, Modified Early Warning Score (MEWS) yielded better results for this outcome.	Uniformity in the EWS used across all departments of the healthcare chain might be beneficial for the improvement of patient care. The ideal prognostic score should be easy to calculate, preferably without the need of laboratory results, and should show good predictive value. Simple bedside systems such as RTS, CRB-65, or quick Sepsis Related Organ Failure Assessment (qSOFA) are appealing due to their simplicity and ease of use; however, it is difficult to combine both simplicity and accuracy, as this review shows that simple prognostic scores were outperformed by more elaborate scoring systems such as the NEWS and MEDS.
Roney et al., 2015[34]	Modified early warning scoring system tools utilization	Adult medical-surgical/ telemetry units	There were limited high-level data, and no clinical trials linking use of modified early warning scoring system tool to robust outcomes were found. The literature review found no MEWS assessment tool combining nursing assessment findings adjusted for SIRS vital sign criteria and laboratory values to aid in identification of both at-risk and septic patients. Literature review research findings suggest MEWS tools' scoring of physiologic findings, including vital signs, have a positive relationship with earlier detection of clinical deterioration.	Critical assessment of patients prior to deterioration requires critically thinking nurses, not mere gathering and recording of vital signs. The clinical picture may be quantified with a scoring tool to assist bedside nurses' clinical decision making, thus leading to improved outcomes and decreased incidence of failure to rescue.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings
Smyth et al., 2016[6]	Prehospital sepsis screening tools	Prehospital EMS	Recognition of sepsis by ambulance clinicians is poor. The use of screening tools based on the Surviving Sepsis Campaign (SSC) diagnostic criteria improves prehospital sepsis recognition. Screening tools derived from EMS data have been developed, but they have not yet been validated in clinical practice. There is a need to undertake validation studies to determine whether prehospital sepsis screening tools confer any clinical benefit. The studies identified provide low-quality or very low-quality evidence to suggest that accuracy of prehospital sepsis recognition by ambulance clinicians varies considerably.	In many areas, paramedic education programs have not focused sufficient attention on sepsis as a clinical syndrome, and paramedic knowledge of sepsis is often poor.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings
Alberto et al., 2017[1]	Sepsis screening tools	General hospitalized patients	Electronic tools can recognize abnormal variables and activate an alert in real time. However, accuracy of these tools was inconsistent across studies, with only one demonstrating high specificity and sensitivity. Paper-based, nurse-led screening tools appear to be more sensitive in the identification of septic patients but were only studied in small samples and particular populations. The process of care measures appear to be enhanced with the use of screening tools; however, demonstrating improved outcomes is more challenging. High levels of accuracy were reported in the studies and reproduced for the purpose of this review with the screening tools used in three studies. However, two studies had small sample sizes, with accuracy tests calculated on random numbers of negatively screened participants. The remaining study reported control data collected retrospectively outside of the study period. Lower sensitivity and PPVs were reproduced and reported in the larger studies, where arguably more robust designs were used. The more complex screening tools appear to be more effective in ruling out patients with sepsis, but they performed poorly in correctly identifying septic patients. Nurses were always the first responders to sepsis alerts, although sometimes the rapid response coordinator and the covering medical provider were also alerted at this time. Overall, the frequency and time to use of diagnostic measures (lactate orders, blood cultures) improved significantly, whereas results pertaining to treatment (fluids and vasopressors) were inconsistent across studies, with some but not all demonstrating improvement. One study reported significant decrease in mortality and risk of death. Other studies showed positive trends in hospital mortality, hospital and ICU LOS, and ICU transfer.	The technology and the staff available, such as the nurse to patient ratio and the supporting steering committees, played a pivotal role in developing a strategy for sepsis screening in these studies. Reviewed screening tools have different levels of sensitivity and specificity, which need to be considered prior to identifying an instrument for implementation; this applies not only to the variables incorporated in the instrument but also the medium that is used, specifically either electronic or paper-based. If technology is available, electronic tools may be preferred over paper-based tools. However, due to the resource-limited settings worldwide, implementation of paper-based, nurse-driven tools could make a difference in sepsis care. Frequency of screening practice and review periods of variables to screen may depend on patient characteristics, staffing, and available technology.

Table B.15: Sepsis Recognition, Sepsis Monitoring Systems—Single Studies

Note: Full references are located in the Section 3.2 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Austrian et al., 2018[10]	Electronic health record-based sepsis alert system	Interrupted time series retrospective cohort study. Patients 18+ years of age who were seen in the urgent care center or emergency department (ED); 2,144 total hospitalizations with a final diagnosis of severe sepsis or septic shock.	ED and urgent care units in an urban academic medical center; 726 beds	The alerts had no effect on any intermediate outcome measures, including intensive care unit (ICU) admissions and length of stay (LOS), nor on the process of care measures for sepsis, including time to first lactate measurement or antibiotics prior to blood cultures. There was a 16% decrease in LOS with introduction of the sepsis alert system. However, this decrease did not quite reach statistical significance when accounting for multiple testing (p=.007). The authors found no evidence for differences in mortality in the pre- and post-alert period after adjustment. The alerts had no effect on any intermediate outcome measures, including ICU admissions and LOS.	Not provided	Because of the poor positive predictive value (PPV) of the alert system, repeated firings likely contributed to the well-documented phenomenon of alert fatigue. The isolated alert system trigger may have been insufficient to effect robust changes in ED workflow and clinical outcomes. High PPV is critical for successful deployment of clinical decision support interventions.	Low/ moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Berger et al., 2010[25]	Computer alert that automatically recognizes systemic inflammatory response syndrome (SIRS) criteria and recommends lactate testing	Quasi-experimental pre-post interventional design. All visits by ED patients 19+ were screened for SIRS; 5,796 subjects met SIRS criteria and had suspected infection during the study period.	Urban ED, a tertiary care level 1 trauma center with an established emergency medicine residency program and an annual adult volume of 70,000	Increase in lactate collection in the ED (5.2% before vs. 12.7% after alert implemented, absolute increase of 7.5%, 95% confidence interval [CI], 6.0% to 9.0%). Increase in lactate collection among hospitalized patients (15.3% vs. 34.2%, absolute increase of 18.9%, 95% CI, 15.0% to 22.8%); decrease in the proportion of abnormal lactate values (21.9% vs. 14.8%, absolute decrease of 7.6%, 95% CI, -15.8% to -0.6%). No significant difference in mortality (5.7% vs. 5.2%, absolute decrease of 0.5%, 95% CI, -1.6% to 2.6%, p=.6).	Not provided	The absolute number of patients with elevated lactate levels was higher in the alert phase of the study. However, the proportion of patients tested who had high lactate levels was lower in the alert phase. This reflects the trade-off between the ability to uncover occult severe sepsis through use of an alert to increase lactate testing as a screening tool versus the expense of testing a greater number of lactate levels among ED patients with sepsis. The mortality benefit of early goal-directed therapy in the treatment of patients with severe sepsis may make it worthwhile to cast a wide net and screen patients liberally to identify those who qualify for enrollment in the study.	Moderate	In Makam et al., 2015

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Croft et al., 2014[29]	System to provide surveillance, diagnosis, and protocolized management of surgical intensive care unit (SICU) sepsis	Prospective pre-post analysis. A paper system was used to manage 77 consecutive sepsis encounters in 65 patients. Then a computerized system was used to manage 132 consecutive sepsis encounters in 119 patients.	SICUs at UFHealth	Recognition of early sepsis tended to occur more using the computerized system (paper, 23%; computer, 35%). Hospital mortality rate for surgical ICU sepsis (paper, 20%; computer, 14%) was less with the computerized system.	Not provided	Not provided	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Hooper et al., 2012[14]	Listening application with automated identification, with physician notification of the systemic inflammatory response syndrome	A prospective, randomized, controlled, single-center study; 442 consecutive patients.	Medical ICU of an academic, tertiary care medical center	The median time from detection of modified SIRS by the listening application (LA) to an assessment by a physician was 0.9 (interquartile range .18 to 3.47) hours. The median time to new antibiotics was similar between the intervention and usual care groups, whether comparing among all patients (6.0h vs. 6.1h, p=0.95), patients with sepsis (5.3h vs. 5.1h, p=0.90), patients on antibiotics at enrollment (5.2h vs. 7.0h, p=0.27), or patients not on antibiotics at enrollment (5.2h vs. 5.1h, p=0.85). The amount of fluid administered following detection of symptoms matching modified SIRS criteria was similar between groups whether comparing all patients or only patients hypotensive at enrollment. Other clinical outcomes, including ICU length of stay, hospital length of stay, and mortality, were not shown to be different between patients in the intervention and control groups.	Not provided	Both ICU nurses and physicians are experienced in the early recognition and management of septic patients. The high rate of antibiotic administration prior to enrollment in our study suggests that infection had already been suspected, with treatment initiated, in many patients. Thus, as was the case with an electronic monitoring study in the emergency department, the biggest shortcoming of the LA may have been the failure to identify patients with modified SIRS before the treating physician did.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Jung et al., 2018[16]	Bedside clinical surveillance visualization system with a visual sepsis screen score (SSS)	Prospective observational. All SICU patients; 232 total patients, 37 with positive score.	Thirty-four-bed SICU in a single large academic medical center	SICU LOS was significantly shorter in the post-SSS group (19.1 +- 3.3 d vs. 7.6 +- 2.5 d, p<0.01) as was the total hospital LOS (29.6 +- 4.3 d vs. 10.8 +- 3.1 d, p<0.01). There was no significant difference in mortality between the two patient cohorts.	Not provided	Sequential organ failure assessment (SOFA) and quick SOFA use subjective data that require manual input into the electronic medical record. This manual input can be a source of delay in alert notification and identification of sepsis. Thus, the authors decided to incorporate the SSS, which is calculated based on automatically populated objective data, into the surveillance system. Nevertheless, physical examination and patient evaluation remain of utmost importance, and the authors stress that this alert system is a screening tool, and does not replace bedside evaluation and sound clinical judgment.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Manaktala et al., 2017[12]	Real-time surveillance of electronic medical record (EMR) data and delivered alerts to nursing staff's mobile devices at the point of care	Single-center, quasi-experimental study, with pre- and post-test analysis; 778 patients.	Two hospital floors, containing two respiratory units and one general medicine unit, comprising a total 58 inpatient beds.	Authors observed a 43-53% decrease in sepsis mortality on hospital units where the sepsis initiative had been implemented. A 30.8% change was noted in the study screening units, with an observed readmission rate of 19.08% during the control period and 13.21% during the study period (p=0.057). Difference in LOS was not significant.	Not provided	The sepsis screening algorithms used in the study were based on standard IHI guidelines. However, these algorithms also contained additional specifications to adjust for comorbid medical conditions and medications. The authors believe that the complexity of the system's algorithms is responsible for its high sensitivity and high specificity, and is a key contributor to the impressive outcomes reported.	Low/ moderate	In Alberto et al., 2017

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
McCoy et al., 2017[15]	Machine learning-based sepsis prediction algorithm with alerts to physicians	Prospective pre-post quality improvement study. All patients over 18 in the included units; pre-implementation period consisting of 407 cases and two post-implementation periods consisting of 336 cases and 381 cases, as well as 204 cases in the post-implementation steady-state period.	One regional community hospital; 242 beds; ED, ICU, progressive care unit, and medical/ surgical patients	Relative to in the pre-implementation period, the post-implementation period sepsis-related in-hospital mortality rate decreased by 60.24%, the sepsis-related hospital length of stay decreased by 9.55%, and the sepsis-related 30-day readmission rate decreased by 50.14%. There were approximately $3.6 million of cost savings per year due to shorter stays. The average annual 2016 SEP-1 (sepsis CMS core measure) bundle compliance rate at the CAPE Regional Medical Center was 49%; however, this rate increased to 72.7% following the use of the MLA.	Not provided	Clinicians indicated that more patients required bedside assessment due to the use of the algorithm than the clinical staff could accommodate. The quality improvement team responded by adjusting the alert threshold to reduce the number of flagged patients, increasing specificity of the alert. Furthermore, per request from end users, the quality improvement team incorporated a 6-hour “snooze” feature to prevent reassessment by the algorithm of any given patient in a 6-hour period. Due to the distance between the ED and other hospital units, it was quicker to direct all ED alerts to a charge nurse or clinical coordinator rather than to a hospitalist. Accordingly, calls were streamed based on patient location.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
McRee et al., 2014[26]	EMR sepsis surveillance	Retrospective review of pre- and post-implementation; patients admitted to an adult medical telemetry unit; 171 total sample. Seventy-five records were pre-EMR sepsis surveillance implementation and 96 were post implementation of the alert.	An adult medical telemetry unit in one hospital	Implementing EMR sepsis surveillance significantly improved home discharge (49.0% vs. 25.3%, p<.05) and reduced hospital mortality (1.0% vs. 9.3%, p<.05). Although there was no difference in the length of hospital stay for the whole group, patients in the surveillance group who triggered an alert on the EMR surveillance had a decreased length of hospital stay compared with those without an alert (7.2 +- 4.2 vs. 11.6 +- 9.4 days, p<.05).	Not provided	Not provided	Moderate	In Makam et al., 2015
Moorman et al., 2011[13]	Use of heart rate characteristics (HRC) monitoring to detect sepsis in infants in the neonatal ICU	Two-group, parallel, individually randomized controlled clinical trial of 3.003 very-low-birthweight infants.	Nine NICUs in the United States	There was a statistically significant and clinically important 22% relative reduction in mortality in infants whose HRC index was displayed (8.1 vs. 10.2%; p=0.04).	The tradeoff for lower mortality was 10% more blood cultures obtained, and 5% more days on antibiotics in the group with HRC monitor display.	Not provided	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Narayanan et al., 2016[8]	Severe Sepsis Best Practice Alert (SS-BPA), automated, real-time, algorithm-based detection of severe sepsis or septic shock via the electronic medical record system	Single-center, before-and-after observational study. Adult patients in the ED; 214 patients.	Single academic medical center	Time to antibiotics was significantly reduced in the SS-BPA cohort (29 vs. 61.5 minutes, pb .001). In addition, a higher proportion of patients received antibiotics within 60 minutes (76.7 vs. 48.6%; pb .001). On multivariable analysis, in-hospital mortality was not significantly reduced in the intervention group (odds ratio, 0.64; 95% CI, 0.26 to 1.57). Multivariable analysis of LOS indicated a significant reduction among patients in the SS-BPA cohort.	Not provided	Not provided	Low/ moderate	None
Nelson et al., 2011[27]	An automated, real-time electronic medical record query and caregiver notification system	Before-and-after, prospective study with consecutive enrollment; 398 patients activated sepsis notification system.	Academic ED with 68,000 annual visits	Only blood culture testing was performed significantly faster in the presence of decision support (median time to culture before intervention 86 minutes, IQR 31, 296 minutes; median time to culture after intervention 81 minutes, IQR 37, 245 minutes; p.032 by Cox proportional hazards modeling). The predominant shortcoming of the strategy was failing to detect severely septic cases before caregivers. The other two endpoints improved, but not in a statistically significant way (blood lactate OR 1.7, 95% CI, 0.9 to 3.2; administering antibiotics OR 2.8, 95% CI, 0.9 to 8.6).	Not provided	That patients require time to fully manifest their illness in the ED is not surprising, although the magnitude of this interval—with 50% requiring more than 2½ hours to meet severe sepsis criteria—was unexpected. Given that routine clinical practice in the department detected the condition more quickly in about half of cases, future algorithms should focus on identifying the subtler cues that prompt experienced caregivers before much of the formal sepsis-defining data are available.	Moderate	In Makam et al., 2015

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Sawyer et al., 2011[28]	Real-time computerized sepsis alert	Prospective, observational, pilot study. Patients identified by the sepsis screen while admitted to a medicine ward were included in the study. A total of 300 consecutive patients were identified, comprising the nonintervention group (n=200) and the intervention group (n=100).	Six medicine wards in Barnes-Jewish Hospital, a 1,250-bed academic medical center	Within 12 hours of the sepsis alert, interventions by the treating physicians were assessed, including new or escalated antibiotics, intravenous fluid administration, oxygen therapy, vasopressors, and diagnostic tests. Within 12 hours of the sepsis alert, 70.8% of patients in the intervention group had received ≥1 intervention vs. 55.8% in the nonintervention group (p=.018). Antibiotic escalation, intravenous fluid administration, oxygen therapy, and diagnostic tests were all increased in the intervention group.	Not provided	Not provided	Low	In Alberto et al., 2017
Shimabukuro et al., 2017[9]	Machine learning-based severe sepsis prediction system with alerts	Randomized controlled clinical trial. Adult patients (18+) admitted to participating units were eligible for this factorial, open-label study; it had 75 patients in the control and 67 patients in the experimental group.	Two medical-surgical intensive care units; 32 total unit beds	No adverse events were reported during this trial. Patients in the experimental group received antibiotics an average of 2.76 hours earlier than patients in the control group and had blood cultures drawn an average of 2.79 hours earlier than patients in the control group. Average length of stay decreased from 13.0 days in the control group to 10.3 days in the experimental group (p=0.042). In-hospital mortality decreased by 12.4 percentage points when using the MLA (p=0.018), a relative reduction of 58.0%.	Not provided	With extra time for intervention in the experimental group, patients might not have ultimately progressed to septic shock; this may have produced different prevalences in the experimental (1.5%) and control (5.3%) groups.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Umscheid et al., 2015[17]	Early warning and response system for sepsis	A prospective pre/post study with multivariable adjustment–measured impact. Adult non-ICU patients admitted to acute inpatient units. All inpatients on non-critical care services; 595/15,567 triggered alert in pre period; 545/15,526 in the post period.	Noncritical care units in an urban academic healthcare system; 1,500 beds	In unadjusted and adjusted analyses, ordering of antibiotics, intravenous fluid boluses, lactate, and blood cultures within 3 hours of the trigger increased significantly, as did ordering of blood products, chest radiographs, and cardiac monitoring within 6 hours of the trigger. Hospital and ICU LOS were similar in the pre and post periods. There was no difference in the proportion of patients transferred to the ICU following the alert. All mortality measures were lower in the post period, but no differences reached statistical significance.	Not provided	Not provided	Low/ moderate	In Alberto et al., 2017

Table B.16: Sepsis Recognition, Sepsis Patient Monitoring Systems—Systematic Reviews

Note: Full references are available in the Section 3.2 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings
Alberto et al., 2017[1]	Sepsis screening tools (electronic and paper)	General hospitalized patients	Electronic tools can capture and recognize abnormal variables and activate an alert in real time. However, accuracy of these tools was inconsistent across studies, with only one demonstrating high specificity and sensitivity. Paper-based, nurse-led screening tools appear to be more sensitive in the identification of septic patients than electronic tools but were studied only in small samples and particular populations. The process of care measures appears to be enhanced with both types of screening tools; however, demonstrating improved outcomes is more challenging. High levels of accuracy were reported in the studies and reproduced for the purpose of this review, with the screening tools used in three studies. However, two studies had small sample sizes, with accuracy tests calculated on random numbers of negatively screened participants. The remaining study reported control data collected retrospectively outside of the study period. Lower sensitivity and positive predictive values were reproduced and reported in the larger studies, where arguably more robust designs were used. The more complex screening tools appear to be more effective in ruling out patients with sepsis, but they performed poorly in correctly identifying septic patients. Nurses were always the first responders to sepsis alerts, although sometimes the rapid response coordinator and the covering medical provider were also alerted at this time. Overall, the frequency and time to use of diagnostic measures (lactate orders, blood cultures) improved significantly with screening tool use, whereas results pertaining to treatment (fluids and vasopressors) were inconsistent across studies, with some but not all demonstrating improvement. One study reported a significant decrease in mortality and risk of death. Other studies showed positive trends in hospital mortality, hospital and intensive care unit (ICU) length of stay, and ICU transfer.	The technology and the staff available (e.g., nurse to patient ratio and the supporting steering committees) played a pivotal role in developing a strategy for sepsis screening in these studies. Reviewed screening tools have different levels of sensitivity and specificity that need to be considered prior to identifying an instrument for implementation; this applies not only to the variables incorporated in the instrument but also to the medium that is used, specifically either electronic or paper-based. If technology were available, electronic tools might be preferred over paper-based tools. However, due to the resource-limited settings worldwide, implementation of paper-based, nurse-driven tools could make a difference in sepsis care. Frequency of screening practice and review periods of variables to screen may depend on patient characteristics, staffing, and available technology.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings
Despins, 2017[6]	Automated detection of sepsis using electronic medical record data	Emergency department (ED) and hospitalized neonatal, pediatric, or adult patients. All the studies except one took place at academic medical centers.	Care team alerts did not consistently lead to earlier interventions. Earlier interventions did not consistently translate to improved patient outcomes. Performance measures were inconsistent. Three studies noted decreased time to sepsis-related interventions (Nelson et al., 2011; Sawyer et al., 2011; Umscheid et al., 2015). Conversely, Hooper et al. (2012) found no difference in time to initiation of sepsis-related therapies. One study noted improved patient outcomes. McRee et al. (2014) observed a shorter hospital length of stay, more patients discharged to home, and fewer deaths. However, other researchers reported no significant effect of sepsis alerts on patient outcomes (Sawyer et al., 2011; Umscheid et al., 2015). Sepsis alerts prompting increased initiation of interventions did not significantly impact patient outcomes, such as ICU transfer rates, ICU and hospital length of stay, and mortality rates.	While automated approaches enable earlier recognition and therapy initiation, the risk of alert fatigue increases if these approaches have low to moderate positive predictive values and thus high false discovery rates. Microbiology culture studies provide results 24–72 hours after obtaining the sample, making them impractical in screening for early sepsis. More research is needed to determine the optimal variables to include in a detection algorithm, and the optimal performance indexes that minimize the risk of recognition delay and alert fatigue. It is possible that research should also focus on developing reliable automated early detection of general clinical deterioration that triggers secondary detection queries, which would provide the care team with a list of possible syndromes, including sepsis. Those developing sepsis detection algorithms should consider not only sensitivity and prediction indexes to minimize alert fatigue but also the timing of data availability to select algorithm components that optimize early sepsis detection. Likewise, sepsis alert development needs to incorporate knowledge of the workflow and care delivery process for each point-of-care discipline (e.g., physician, nurse). Knowledge pertaining to current alert notification processes and clinicians' EMR interaction is important to identify both the best discipline to receive the sepsis alert and the best means of delivering it.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings
Makam et al., 2015[7]	Automated electronic sepsis alert systems	ED or hospital	Diagnostic accuracy varied greatly, with positive predictive value (PPV) ranging from 20.5 to 53.8%; negative predictive value (NPV) 76.5 to 99.7%; positive likelihood ratio (LR+) 1.2 to 145.8; and negative likelihood ratio (LR-) 0.06 to 0.86. The alert system (Nelson et al.) that was triggered by a combination of SIRS criteria and hypotension (PPV=53.8%; LR+ =145.8; NPV =99.7%; LR- =0.37) outperformed the alert system (Meurer et al.) that was triggered by SIRS criteria alone. There was modest evidence for improvement in process measures (i.e., antibiotic escalation), but only among patients in non-critical care settings (medical ward and ED vs. medical ICU). Neither of the two high-quality studies that included a contemporaneous control found evidence for improving inpatient mortality or hospital and ICU length of stay. Minimal data were reported on potential harms due to false-positive alerts. Berger et al. showed an overall increase in the number of lactate tests performed but a decrease in the proportion of abnormal lactate values (21.9% vs. 14.8%, absolute decrease of 7.6%, 95% confidence interval [CI], -15.8% to -0.6%), suggesting potential over-testing in patients at low risk for septic shock. Automated sepsis alerts derived from electronic health data may improve care processes but tend to have poor positive predictive value and do not improve mortality or length of stay.	The fact that sepsis alert systems improve intermediate process measures among ward and ED patients but not ICU patients likely reflects differences in both the patients and the clinical settings. First, patients in the ICU may already be prescribed broad-spectrum antibiotics, be aggressively fluid-resuscitated, and have had other diagnostic testing performed before the activation of a sepsis alert, so one would be less likely to see an improvement in the rates of process measures assessing initiation or escalation of therapy compared with among patients treated on the wards or in the ED. The apparent lack of benefit of these systems in the ICU may merely represent a “ceiling” effect. Second, nurses and physicians are already vigilantly monitoring patients in the ICU for signs of clinical deterioration, so additional alert systems may be redundant. Third, patients in the ICU are connected to standard bedside monitors that continuously monitor for the presence of abnormal vital signs. An additional sepsis alert system triggered by SIRS criteria alone may be superfluous to the existing infrastructure. Fourth, most patients in the ICU will trigger the sepsis alert system, so there likely is a high noise-to-signal ratio with resultant alert fatigue. Little data exist to suggest the optimal design of sepsis alerts, or the frequency with which they are appropriately acted upon or dismissed. In addition, the authors found little data to support whether effectiveness of alert systems differed based on whether clinical decision support was included with the alert itself (e.g., direct prompting with specific clinical management recommendations), or the configuration of the alert (e.g., interruptive alert or informational). Most of the studies reviewed employed alerts primarily targeting physicians; little evidence was found for systems that also alerted other providers (e.g., nurses or rapid response teams).

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings
Warttig et al., 2018[5]	Automated systems for the early detection of sepsis (randomized trials only)	Med/surg ICU; 1,199 participants in total	Three studies were included in this review .Overall there were no significant differences in time to start of antimicrobial therapy (such as antimicrobial and antifungal treatments, very-low-quality evidence); length of stay in the intensive care setting (very-low-quality evidence); or mortality at 14 days, 28 days, or discharge (very-low-quality evidence), when automated monitoring systems were compared with standard care. Very-low-quality evidence was available on failed detection of sepsis, and data reporting was too unclear to enable analysis of this in a meaningful way. Other outcomes that the authors wanted to assess were not reported in any of the studies, such as time to initiation of fluid resuscitation (the process of increasing the amount of fluids in the body), mortality at 30 days, and quality of life.	Not provided

Table B.17: Sepsis Recognition, Multicomponent Sepsis Interventions—Systematic Reviews

Note: Full references are located in the Section 3.3 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Beardsley et al., 2016[1]	(1) Nurse-conducted screening for sepsis using a standard assessment instrument; (2) pager alerts notifying rapid-response, pharmacy, and other personnel of cases of suspected sepsis; (3) activation of an electronic order set including guideline-based antibiotic therapy recommendations based on local pathogen patterns; and (4) a protocol allowing pharmacists to select an antibiotic regimen if providers are busy with other patient care duties.	Prospective pre–post study. Sample size unknown.	Tertiary academic medical center with 885 beds and over 180 adult intensive care unit (ICU) beds	After the Code Sepsis initiative was implemented, the mean time from rapid response nurse arrival on the unit to antibiotic administration decreased from 396 minutes to 51 minutes for patients in noncritical care units. The time from a positive sepsis screen to antibiotic administration also decreased in the ICUs as the Code Sepsis rollout was extended to the various critical care units. The institution's sepsis-related mortality index dropped from a mean value of 1.65 for the five quarters prior to Code Sepsis implementation to 0.8 for the period April 2013–March 2014.	The Code Sepsis program enhanced cooperation among prescribers, pharmacy staff, and nursing personnel. Pharmacy personnel worked with representatives of the medical and nursing staffs to analyze all aspects of the medication-use process relating to antibiotics for sepsis. Processes were then improved, and antibiotic turn-around time decreased to a point that exceeded the expectations of most program participants. An important aspect of the Code Sepsis initiative was the implementation of a protocol that allows pharmacists to choose sepsis antibiotics. Allowing pharmacists to take on this responsibility freed up physicians to focus on other critical aspects of the patient's care without delaying the administration of antimicrobial therapy. It appears that this type of protocol is unique, as the authors were unaware of the existence of similar protocols at other institutions.	Moderate/ high	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Gatewood et al., 2015[2]	The three-tiered intervention consisted of (1) a nurse-driven screening tool and management protocol to identify and initiate early treatment of patients with sepsis; (2) a computer-assisted screening algorithm that generated a "Sepsis Alert" pop-up screen in the electronic medical record for treating clinical healthcare providers; and (3) automated suggested sepsis-specific order sets for initial workup and resuscitation, antibiotic selection, and goal-directed therapy	A before and after retrospective cohort study. All patients admitted to the emergency department (ED); 624 patients.	ED in a 450-bed academic hospital managing more than 18 000 inpatient admissions each year. A quaternary care facility.	Overall bundle compliance increased by 154%, from 28% at baseline to 71% in the last quarter of the study (p<0.001). Institution of nurse triage screening tool, nurse-initiated sepsis order set, and provider order sets increased total Surviving Sepsis Campaign (SSC) bundle compliance to 50%. Introduction of the automated sepsis icon and EMR alerts resulted in further performance improvement to 70% compliance. Bundle antibiotic and intravenous fluid compliance all increased significantly after launch of the sepsis initiative: bundle and intravenous fluid compliance increased by 74% and 54%, respectively (p<0.001). The mortality rate for patients in the ED admitted with sepsis was 13.3% before implementation and fell to 11.1% after implementation (p=0.230); mortality in the last two quarters of the study was 9.3% (p=0.107).	Not provided	Low/ moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Judd et al., 2014[3]	An electronic sepsis screening tool administered once per shift and a fast antibiotics program.	A retrospective observational study of consecutive adults with sepsis. Baseline data were collected for 181 patients; the intervention group included 216 patients.	Tertiary medical center with 433 beds.	After implementing the First-Dose STAT policy, average time from antibiotic order entry to administration was reduced from 154 ± 134 minutes to 84 ± 55 minutes by the end of the phase 1 intervention period ($p<0.001$). Average time from order entry to administration decreased to 57 ± 37 minutes by week 15 ($p<0.001$). The percentage of patients who received a first-dose intravenous (IV) antibiotic within 60 minutes increased from 25.6% to 54.3%. Similarly, the percentage of patients who received a first-dose IV antibiotic within 90 minutes increased from 36.6% to 80% by the end of week 15. Nonsignificant decreases in overall length of stay (LOS) (7.43 ± 5.68 days vs. 6.77 ± 5.0 days; $p=0.138$) and in-hospital mortality (13.8% vs. 8.8%; $p=0.113$) were observed in patients with sepsis Diagnosis-related groups (DRGs). Early recognition and treatment contributed to significant reductions in ICU LOS (5.85 ± 4.38 days vs 4.21 ± 3.64 days; $p=0.003$) and total cost per case ($14,378 vs. $12,311; $p=0.033$).	The average time from order entry to medication delivery remained low throughout the 3-month intervention period despite a significant improvement in the overall time to administration. These data suggest that efforts to improve antibiotic administration times should focus on the time from delivery to nurse administration. During the phase 1 intervention period, scheduled completion of an electronic sepsis screening tool aided in converting the sepsis population to a lower severity of illness based on the change in sepsis-related DRG coding assignments.	Low/ moderate	Bundle with fast antibiotics program.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
MacRedmond et al., 2010[4]	Manual management algorithm including early goal-directed therapy, a computerized physician order entry set for suspected sepsis, introduction of invasive hemodynamic monitoring and antibiotics stocked in the ED, and an extensive education campaign involving ED nurses and physicians.	Prospective pre–post study. Patients in the ED who had sepsis; 74 patients total, 37 pre and 37 post.	ED in a tertiary care teaching hospital of 500 beds, a "closed" medical-surgical ICU of 15 beds staffed by dedicated intensivists, and an ED that serves >60 000 patients per year.	Significant improvements were observed in mean time to initiation of early goal-directed therapy (3.2 vs. 10.4 h, p=0.001) and to achievement of resuscitation goals (10.4 vs. 30.1 h, p=0.007). There was a trend toward more rapid administration of antibiotics (1.4 vs. 2.7 h, p=0.06). This was associated with a decrease in crude hospital mortality rate from 51.4% to 27.0% (absolute risk reduction=24%, 95% CI, 3% to 47%). Improvements were sustained in the followup audit at 16 months.	After the education sessions, the researchers found significant improvement in the early identification of patients who had potential sepsis; they believe that increased awareness of the time-critical nature of sepsis treatment among ED nurses and physicians was key to the successful implementation of the protocol. The researchers did not measure compliance with specific elements.	Moderate	None
Mittal et al., 2018[5]	Increased the number of nurses, provided space for triage, and created a triage tool for recognizing patients with severe sepsis, which took less than a minute to complete.	Prospective pre–post observational. Children age 2 months to 17 years of age with severe sepsis were eligible for enrollment; 41 pediatric patients.	ED in a tertiary care hospital.	The median interquartile range time to administration of antibiotics from the time of admission decreased significantly, from 50 minutes (18, 65) to 20 minutes (15, 20) (p=0.02). Duration of hospital stay was longer in phase 1 than in phase 2 (12 days vs. 6 days). However, the difference was not statistically significant (p=0.1).	The major hurdles causing delay in antibiotic administration in phase 1 of the study were overcrowding, high patient load, difficult IV access, and atypical presentation leading to delayed recognition of severe sepsis The shortage of nurses in phase 1 was a hurdle in early initiation of antibiotics in the ED.	Moderate	None

Table B.18: Clostridioides *difficile*, Antimicrobial Stewardship–Single Studies

Note: Full references are available in the Section 4.1 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Carbo et al., 2016[26]	Antimicrobial stewardship in which automated protocols were not used, and the infectious diseases pharmacist reviewed each patient's chart daily. Complex cases were reviewed with the infectious diseases physician.	A retrospective cohort study encompassing the study period January 1, 2005–October 31, 2014. Population: Male veterans admitted for treatment of complicated urinary tract infection; (n=118 and n=123 in the pre-ASP and ASP group, respectively).	A 150-bed Veterans Affairs Healthcare System facility in Buffalo, NY	The incidence of CDI did not differ between stewardship groups (p=0.81). However, duration of antibiotic therapy was significantly shorter in the antimicrobial stewardship program (ASP) group (10.32 days vs. 11.96 days; p<0.0001), as was length of hospitalization (5.76 days vs. 6.76 days; p=0.015). Accepted interventions (n=153) occurred as follows: intravenous [IV] to oral conversion (n=48), de-escalation (n=39), duration of antibiotics (n=38), antibiotic selection (n=9), dose adjustment (n=9), escalation (n=7), and drug interaction (n=3). Interventions that were not accepted (n=17) included duration of antibiotics (n=10), de-escalation (n=2), escalation (n=2), IV to oral conversion (n=2), and antibiotic selection (n=1).	Not provided	The ASP included brief monthly educational conferences on antimicrobial stewardship and local antimicrobial resistance, to underline the importance of microbial cultures and to promote appropriate use of antimicrobial agents. The stewardship team consisted of a board-certified pharmacist and infectious diseases physician support.	Moderate	Article was not specifically targeted to CDI.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Chung et al., 2014[15]	A resource-efficient method for identifying antibiotic targets for antimicrobial stewardship interventions. Study was a prelude to a more extensive Agency for Healthcare Research and Quality (AHRQ)-funded project (Evaluation & Research on Antimicrobial Stewardship's Effect on Clostriodiodes *difficile*).	Exploratory evaluation about using different matching criteria with select control groups to determine target antimicrobials. A total of 126 cases were matched to six groups of 252 controls, using different matching strategies.	A 700-bed urban academic tertiary care center	Cases were more likely than five control groups to have been exposed to piperacillin and tazobactam, fluoroquinolones, and third- and fourth- generation cephalosporins; however, the magnitudes of the association varied. Five groups of controls were matched to cases (2:1 ratio) using group-specific matching criteria, including admission date, age, type of admission, length of stay (LOS) to discharge, and/or LOS to CDI diagnosis. The final control group was selected from patients who received antibiotics during hospitalization. Data, including demographics and antibiotic use, were compared between case and control groups. Researchers performed a sixth case-control study using only CDI-negative patients who received antibiotics and were rigorously matched to specific criteria as controls. Although the relationship between piperacillin and tazobactam and CDI remained, third- and fourth-generation cephalosporins and fluoroquinolones were no longer significantly associated with CDI.	Not provided	Because of differences in antimicrobial prescribing practices and formularies between institutions, it is important to use local data to select targets. It is also important to use thorough but feasible matching strategies. Using matching criteria may make it possible to identify high-risk antibiotics associated with CDI.	Low to moderate	Study is about how to determine antibiotic targets for ASPs.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Cruz-Rodríguez et al., 2014[22]	Pharmacy restriction of clindamycin (in an orthopedics ward with high rates of CDI)	Pre-/post-interventional study that consisted of two periods: a 7-month baseline period (December 2011 through June 2012) and a 16-month intervention period (July 2012 through October 2013); 684 patients were included during the baseline and 1,720 during the intervention period.	An orthopedics ward with high rates of CDI in a university teaching hospital in Mexico. 48-bed area with a mean of 1,200 admissions per year.	A reduction of 88% in CDI (1.07 to 0.12 per 1,000 patient days, p=0.056) and 84% for all-cause diarrhea (2.40 to 0.38 per 1,000 patient days, p=0.021) was achieved. Clindamycin was reduced 92.61% without an increase in other antibiotics.	Not provided	The intervention period consisted of a pharmacy restriction of clindamycin for the entire orthopedics ward. Only patients with a previous infectious disease consult could receive clindamycin in their antibiotic scheme.	Low to moderate	Several other studies are noted in which clindamycin reduction resulted in significant CDI reduction.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Dancer et al., 2013[29]	Restrictive policy banning the routine use of third-generation cephalosporins, specifically ceftriaxone, and quinolones throughout the hospital, following an educational campaign	Daily antibiotic doses, hospital-acquired CDI, MRSA, and extended spectrum beta lactamase (ESBL) cases measured 9 months before until 16 months after policy introduction. Population: the hospital admits adult patients only, specializing in care of older adults, as well as in respiratory medicine, endocrinology, and cardiology.	A 450-bed district general hospital in a rural area just outside Glasgow, UK	Between the first and final 6 months of the study, average monthly consumption of ceftriaxone decreased by 95% (from 46.213 to 2.129 DDDs/1,000 pt-bds) and that for ciprofloxacin by 72.5% (109.804 to 30.205 DDDs/1,000 pt-bds). Over the same periods, hospital-acquisition rates for *C. difficile* decreased by 77% (2.398 to 0.549 cases/1,000 pt-bds), for MRSA by 25% (1.187 to 0.894 cases/1,000 pt-bds) and for ESBL-producing coliforms by 17% (1.480 to 1.224 cases/1,000 pt-bds). Time-lag modelling confirmed significant associations between ceftriaxone and *C. difficile* cases at 1 month (correlation 0.83; $p<0.005$). An audit performed 3 years after the policy showed sustained reduction in *C. difficile* rates (0.259 cases/1,000 pt-bds), with additional decreases for MRSA (0.409 cases/1,000 pt-bds) and ESBL-producing coliforms (0.809 cases/1,000 pt-bds).	Consumption of empirical amoxicillin and gentamicin escalated throughout the study and could have confounded the overall effect. It is possible that the restrictive policy has had some impact on extreme drug resistance in this hospital.	It was decided to initiate an educational program encouraging prescribers to reduce consumption of cephalosporins and quinolones on a voluntary basis. This education included providing a series of lectures to all medical staff starting in January 2008 and weekly teaching for small groups of junior doctors. Feedback on HAI rates was sent to clinicians and managers. Gaining support was difficult. By far, the best method of restricting use of a particular drug was physical removal from ward stores by the pharmacists.	Low to moderate Strength: researchers state there were no additional infection control interventions over the study period.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Jenkins et al., 2015[24]	An antimicrobial stewardship program (ASP) in a hospital with low baseline antibiotic use	A time-series analysis to evaluate the impact of the ASP over a 6.25-year period (July 1, 2008–September 30, 2014) while controlling for trends during a 3-year pre-intervention period (July 1, 2005 to June 30, 2008).	A 525-bed public safety net hospital in Denver, CO	During the pre-intervention period, total antibacterial and antipseudomonal use were declining (−9.2 and −5.5 days of therapy [DOT]/1,000 patient days [PD] per quarter, respectively). Both continued to decline after the intervention, although at lower rates (−3.7 and −2.2 DOT/1,000 PD, respectively), resulting in a slope change of 5.5 DOT/1,000 PD per quarter for total antibacterial use (p=0.10) and 3.3 DOT/100 PD per quarter for antipseudomonal use (p=0.01). During the stewardship period, significant reductions were seen in high-risk antibiotics (imipenem-cilastatin, β-lactam/β-lactamase inhibitor combinations, fluoroquinolones, and aminoglycosides). Antibiotic expenditures declined markedly during the stewardship period (−$295.42/1,000 PD per quarter, p=0.002), largely as a result of declining antipseudomonal expenditures.	Not provided	A formal ASP was implemented by an infectious diseases physician and an infectious diseases pharmacist, with support from hospital leadership, infectious diseases physicians, data management and information technology specialists, and an infection prevention program. Focus in three areas: (1) preauthorization requirement for select broad-spectrum, toxic, or costly antibiotics; (2) postprescription review with real-time feedback to prescribers; and (3) development and implementation of local guidelines for common infections.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Jump et al., 2012[14]	Infectious Disease Consultation Service (audit and feedback, education)	Pre-/post-systemic antimicrobial use and the rate of positive *C. difficile* tests at the LTCF were compared for 36 months before and 18 months after the initiation of the infectious diseases consultation service using segmented regression analysis of an interrupted time-series.	A 160-bed Veterans Affairs (VA) urban LTCF	In contrast to the pre-intervention period, total systemic antibiotic administration decreased by 30% (p<.001), with a significant reduction in both oral (32%, p<.001) and IV (25%, p=.008) administration. Greatest reductions in tetracylines, clindamycin, sulfamethoxazole/ trimethoprim, fluoroquinolones. Rates of change for positive *C. difficile* tests at the LTCF declined in the post- versus pre-intervention periods (p=.04). (While the rate of change in positive *C. difficile* tests did not change significantly over time for the two individual periods, the difference in the rates of change between the two periods was significantly different.)	Not provided	The facility instituted an onsite LTCF Infectious Disease Consultation Service as a multifaceted intervention to improve the use of antimicrobials at the LTCF. The consult team consisted of an infectious diseases physician and nurse practitioner. They examined residents at the LTCF once each week and were available for remote consultation the remainder of the week.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Libertin et al., 2017[10]	Prospective audit with healthcare provider feedback and targeting 12 antimicrobial agents. An educational grand rounds lecture series was provided before implementation of the ASP to all prescribers. To improve this selection, prescribers were given algorithms to aid the selection of empirical antibiotics for specific infectious disease syndromes based on local antibiograms.	Pre-/post intervention comparison of CDI rates, antimicrobial costs. Data on use of 12 targeted antimicrobial agents were used for comparison with the post-ASP initiation.	A rural community hospital (with low patient census) in GA	CDIs decreased from 3.35 cases per 1,000 occupied bed days (OBDs) in 2013 to 1.35 cases per 1,000 OBDs in 2015 ($p<0.001$). Total targeted antimicrobial costs decreased 50% from $16.93 per patient day in 2013 to $8.44 per patient day in 2015. Annualized savings were $280,000 in 1 year, based on drug savings only.	Not provided	Authors note that development of a collegial environment for a healthcare provider's growth in ASP knowledge was important in achieving acceptance of the program. The approach on how to implement an ASP depends on many factors, including need for an infectious diseases consultant, an infectious disease-trained pharmacist, a person with a doctor of pharmacy degree, or a combination of these; institution size; composition of the providers; and resources provided by the institutional leadership.	Moderate; no sample size given. No control group. Small rural hospital—results may not be generalizable.	No formulary restriction and pre-authorization were used for the targeted antimicrobial agents. The intervention did not include strategies to limit antibiotic therapy to the shortest effective duration.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Lowe et al., 2017[27]	Targeted antimicrobial stewardship (audit and feedback) for patients with a viral respiratory tract infection. Prospective audit and feedback was implemented based on two criteria: microbiology (no positive bacterial cultures) and chest imaging (absence of pneumonia or consolidation on radiology dictation).	A quasi-experimental before-and-after study. Intervention was conducted for 1 year starting December 1, 2015; 92 patients were included in the prospective cohort and 118 in the retrospective cohort.	Two Canadian health centers	Antimicrobial stewardship recommendations for hospitalized patients with viral respiratory tract infections were accepted for 77% of cases. This targeted approach translated into a 1.3-day (95% confidence interval, 0.3 to 2.3; p<0.01) decrease in mean days of antibiotics post-viral diagnosis compared with the previous year without systematic interventions. There was a 32% reduction in antibiotic days per patient.	Not provided	Facility initiated a collaboration between the virology laboratory and the ASP team to integrate reporting of respiratory virus PCR with an ASP audit and feedback intervention. Algorithm used a combination of microbiology, radiologic imaging, and clinical context after discussion with the ASP team to de-escalate antibiotics.	Moderate	CDI was not the prime focus of the study. A review of patient outcomes did not reveal statistically significant differences for length of stay, ICU admission within 14 days, mechanical ventilation within 14 days, antibiotics prescribed within 14 days, CDI diagnosed within 30 days, or readmission within 30 days.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Ostrowsky et al., 2014[28]	Controlled use of target antibiotics. Facilities identified target antibiotics using case-control studies. All hospitals selected at least one back-end audit and feedback strategy as one of their intervention strategies, with up to three other interventions implemented per hospital.	A multicenter before-and-after 20-month intervention comparative study in 10 medical centers (six intervention, four controls). The six intervention hospitals reported 108,268 distinct episodes of antibiotic use for 68 antibiotics; 3,491 CDI cases were reported.	Ten medical facilities in greater New York City region. The mean bed size for intervention hospitals was 573 (range, 396 to 871). All were nonprofit facilities and combined had more than 240,000 inpatient admissions annually.	Intervention facilities identified piperacillin/ tazobactam, fluoroquinolones, or cefepime (odds ratio, 2.0 to 9.8 in CDI case patients compared with those without CDI) as intervention targets. Intervention hospitals reduced the use of targeted antibiotics to varying degrees, depending on the measures used and the intervention. Total target antibiotic use significantly decreased ($p<0.05$) when measured by days of therapy and number of courses but not by defined daily dose. Number of courses with all forms of these antibiotics was reduced ($p<.005$). Intervention hospitals reported fewer hospital-onset CDI cases (2.8 rate point difference) compared with nonintervention hospitals; however, there were no statistically significant decreases in aggregate hospital-onset CDI either between intervention and nonintervention groups or within the intervention group over time.	Not provided	Each intervention hospital did its own case control study to identify target antimicrobials. For piperacillin/ tazobactam and cefepime, hospitals did audits and feedback. For quinolone, hospitals used restrictions or algorithms asking the prescriber to reevaluate the choice. The implementation of ASP interventions was typically more complex than expected. Each site developed ASP activities to meet its needs and respond to local resource constraints.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Patton et al., 2018[19]	Following national guidance on restriction of antimicrobials associated with a high risk of CDI [high-risk antimicrobials in October 2008, the hospital policy for empirical treatment of infection changed to remove cefuroxime for any indication, include ceftriaxone only for meningitis, limit fluoro-quinolones to a few specific indications, and reduce use of clarithromycin, clindamycin, and co-amoxiclav. Cefuroxime was also removed from the policy for antibiotic prophylaxis in general surgery.	The study period was October 2006 to September 2010. The study was an observational pre-/post evaluation of intervention effects in medical and surgical wards. It included all patients age 18 years and older admitted through the acute medical unit or one of six general surgical wards.	An 855-bed university hospital, UK; medicine and surgery wards	Six months post-intervention, there were relative reductions in high-risk antimicrobial use of 33% (95% CI, 11 to 56) in the medicine ward and 32% (95% CI, 19 to 46) in the surgery ward. At 12 months, there was an estimated reduction in CDI of 7.0 cases/1,000 admissions (relative change -24% [95% CI, 55 to 6]) in Medicine, but no change in Surgery (estimated 0.1 fewer cases/1,000 admissions [-2% {95% CI, 116 to 112}]). Mortality was reduced throughout the study period, unaffected by the intervention. Pre-intervention CDI rates and trends influenced the intervention effects.	Not provided	Evaluation of the effect of real-world stewardship interventions on outcomes other than prescribing remains methodologically challenging and worthy of further effort. Pre-intervention outcome data should be examined before resource-intense interventions and evaluations are undertaken, and all evaluations should include balancing measures. There are limitations in using mortality as a stewardship outcome, due to confounding, but it does have value as a balancing measure, and most studies do not report any clinical outcome data.	Low to moderate	This article also includes a systematic review to compare findings with those of other studies. Authors measured mortality owing to concerns raised by clinicians about the change in antimicrobial policy.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Rahme et al., 2016[31]	H-AST =hospital-based antimicrobial stewardship teams working with an LTCF. Campaign that included (1) creation of LTCF urinary guidelines; (2) an in-service for providers on appropriate treatment of urinary tract infection (UTI), skin and soft tissue infection (SSTI), and respiratory tract infection (RTI); (3) an educational event for family members, discussing the risks of overusing antimicrobial agents; and (4) a telephone hotline for the LTCF to contact the H-AST for questions.	Pre- and post-intervention measures of target antimicrobials (12-month mean DDD per 1,000 resident days [RD]) and CDI rates in the LTCF. No sample size given.	A 520-bed, long-term skilled nursing facility (working with an infection prevention team from a community teaching hospital)	Significant 38.7% decrease in ciprofloxacin use. A decrease in overall antibiotic use: 11.68%, from 82.33 to 72.71 DDD per 1,000 RD (p=0.06). A comparison of infection rates per 1,000 RD pre- and post-intervention showed a 5.51% decrease in UTI diagnosis/treatment, from 1.71 to 1.61 (p=0.28), and a 5.73% decrease in RTI from 1.35 to 1.27 (p=0.67). There was an 11.10% increase in the rate of SSTI during the post-intervention period, from 0.92 to 1.04 (p=0.27). The rate of CDI in the LTCF decreased by 19.47%, from 0.094 to 0.076 (p=0.58) in the post-intervention period.	Not provided	The LTCF medical director, nursing manager, and infection prevention nurse collaborated with the H-AST. The education campaign focused on creating treatment guidelines for UTI, SSTI, and RTI. A pocket card outlining the recommendations was developed for each disease state. LTCF providers and nursing staff commonly stated that a large obstacle to appropriate antimicrobial prescribing is family pressure. Providing family member education was a unique element to this stewardship initiative.	Low to moderate; the LTCF performed environmental changes during the pre-intervention period that could have affected the CDI rates during the post-intervention period. Single site; no sample size given.	Levofloxacin and moxifloxacin use did not show a statistically significant change, going from 6.16 to 6.72 and 0.34 to 0.32 DDD per 1,000 RD, respectively (p = 0.65 and 0.93). Total FQ consumption (Cipro-floxacin, levofloxacin, and moxifloxacin) also did not change significantly.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Shea et al., 2017[12]	Healthcare system antimicrobial stewardship-initiated respiratory fluoroquinolone restriction and education program on its use, appropriate-ness of quinolone-based therapy based on institutional guidelines, and CDI rates.	A multicenter, quasi-experimental study	Four of 12 adult hospitals within Seton Healthcare Family, a large, urban, not-for-profit healthcare system located throughout Central Texas. The four hospitals ranged from 124 to 534 licensed beds.	Compared with pre-intervention, the four hospitals experienced 48% and 88% average reductions in use (DOT/1,000 PD) after education and restriction, respectively. Using segmented regression analysis, both education (14.5 DOT/1,000 PD per month decrease; p=0.023) and restriction (24.5 DOT/1,000 PD per month decrease; p<0.0001) were associated with decreased use. A significant reduction in the annual acquisition cost of moxifloxacin, the formulary respiratory fluoroquinolone, was observed postrestriction compared with pre-intervention within the healthcare system ($123,882 vs. $12,273; p=0.002). CDI rates decreased significantly (p=0.044) from pre-intervention using education (3.43 cases/10,000 PD) and restriction (2.2 cases/10,000 PD).	Not provided	Prior to this study, an extensive literature review was performed to guide the initial development of institutional treatment guidelines, including community-acquired pneumonia and antibiotic therapy in chronic obstructive pulmonary disease exacerbations. These literature findings and expert opinion were used to develop educational material, respiratory fluoroquinolone restriction criteria, and institutional treatment guidelines.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Taggart et al., 2015[25]	Antimicrobial stewardship audit and feedback program. ICU patients were reviewed Monday to Friday by a physician and pharmacist with infectious diseases training. Recommenda-tions related to appropriate antimicrobial use were presented to ICU teams during a dedicated daily meeting. Initiative was part of an Ontario-wide quality improvement project to introduce audit and feedback programs into ICUs.	A controlled interrupted time series analysis was used to compare outcomes in the 12 months before and after the intervention in 2012–2014; 2,635 ICU patients (from two ICUs). Cardiovascular and coronary care ICUs served as control units.	Four adult ICUs at St. Michael's Hospital, a 465-bed academic teaching hospital in Toronto, Ontario, Canada.	Mean total monthly antimicrobial use in defined daily doses (DDD) per 1,000 patient days was reduced 28% in the trauma and neurosurgery (TN) ICU (1,433 vs. 1,037), but increased 14 % in the medical surgical (MS) ICU (1,705 vs. 1,936). There was a significant reduction in antibacterials by 29% (p=0.0001), antibiotics with activity against *Pseudomonas* species by 44% (p<0.0001), and fluoroquinolones by 80% (p<0.0001). The rate of *C. difficile* infection in the TNICU decreased from 0.66 cases per 1,000 patient days pre-intervention to 0.48 cases per 1,000 patient days post-intervention. However, the result was not statistically significant (p=0.69). There were no significant changes in the use of the specific agents or classes of antimicrobials in the MSICU. There was a non-significant decrease in the rate of *C. difficile* infection in the MSICU. Rates in the control ICUs were also reduced.	One of the intervention groups showed a decrease in use of anti-microbials, but the other (MSICU) showed an increase.	Little change in overall antibiotic prescribing, but reduction in high-risk antibiotics. Before intervention, antibiotic selection was performed by ICU teams. During the post-intervention period, an infectious diseases trained pharmacist and physician reviewed all patients admitted to the intervention ICUs daily (weekdays only). Patients who remained in the ICU were reassessed every weekday until ICU discharge. The ICU team maintained prescribing autonomy.	Low to moderate	CDI reductions were not statistically significant, and the rates in the control ICUs were also reduced. The mean total cost of anti-microbials in the TNICU decreased from $18.40 per patient day before the intervention to $14.53 per patient day after the intervention (p=0.017).

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Talpaert et al., 2011[5]	Revised antibiotic guidelines for empirical treatment of common infections and enhanced stewardship on reducing broad-spectrum antibiotic use	A retrospective, quasi-experimental study using interrupted time series (ITS) over 12 months before and after the intervention (2005–2007). Population: all adult inpatients. Number of ASP patients: 386.	Adult medical and surgical wards, in a ~500-bed acute general hospital in London.	The intervention was associated with a significant reduction in the use of fluoroquinolones by 105.33 defined daily doses (DDDs)/1,000 occupied bed-days (OBDs) per month (95% CI, 34.18 to 176.48, p<0.001) and cephalosporins by 45.93 DDDs/1,000 OBDs/month (95% CI 24.11 to 67.74, p<0.0001). These changes in levels correspond to a 58.5% and 45.8% drop in fluoroquinolone and cephalosporin use, respectively. There was no significant change in total antibiotic, clindamycin, amoxicillin, or co-amoxiclav use. There was a significant increase in use of "low-risk antibiotics." There was a significant decrease in CDI following the intervention (IRR 0.34 [0.20 to 0.58], p<0.0001). No differences in clinical outcomes were associated with the intervention.	Not provided	The intervention included audit and feedback, education, and revised guidelines saying to avoid broad-spectrum antibiotics, for example, fluoroquinolones, cephalosporins, clindamycin, amoxicillin, and co-amoxiclav. Instead, "low-risk" antibiotics were recommended. Formation of an antibiotic management team (AMT) comprising a consultant microbiologist and an antibiotic pharmacist. Any high-risk antibiotic prescribed by clinicians or supplied by the Pharmacy Department was brought to the attention of the AMT.	Low to moderate	CDI was endemic at the facility: between April 2005 and March 2006, 349 cases of CDI were recorded. The limited information available indicates the emergence of the 027 ribotype during 2007.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Tedeschi et al., 2017[11]	An ASP was implemented based on systematic bedside infectious disease consultation and structural interventions (i.e., revision of protocols for antibiotic prophylaxis and education focused on the appropriate-ness of antibiotic prescriptions).	Quasi-experimental study of the periods before (from January 2011 to June 2012) and after (from July 2012 to December 2014) ASP implement-tation.	A 150-bed rehabilitation hospital dedicated to patients with spinal cord injuries.	Antibiotic consumption decreased from 42 to 22 defined daily dose (DDD) per 100 patient days ($p<0.001$). The main reductions involved carbapenems (from 13 to 0.4 DDD per 100 patient days; $p=0.01$) and fluoroquinolones (from 11.8 to 0.99 DDD per 100 patient days; $p=0.006$), with no increases in mortality or length of stay. The incidence of CDI decreased from 3.6 to 1.2 cases per 10,000 patient days ($p=0.001$). Between 2011 and 2014, the prevalence of extensively drug-resistant (XDR) strains decreased from 55% to 12% in *P. aeruginosa* ($p<0.001$) and from 96% to 73% in *A. baumannii* ($p=.03$). The prevalence of ESBL-producing strains decreased from 42% to 17% in *E. coli* ($p=0.0007$) and from 62% to 15% in *P. mirabilis* ($p=0.0001$). A trend toward lower mortality and a significant shortening of length of stay were observed.	Not provided	An ASP based on infectious diseases consultation was effective without affecting patient outcomes. The ASP intervention had two steps: First, a systematic bedside infectious diseases consultation activity. A dedicated infectious diseases consultant was present onsite three times a week and was available for remote consultations. Second, regular 6-monthly revisions of the internal protocol for antibiotic prophylaxis were performed and educational activities were conducted.	Low to moderate	The population at this setting is highly exposed to anti-microbials. Patients cared for in these facilities are prone to Infections. Rehabil-itation physicians are worried about antibiotic resistance but may remain unaware of the local epidemiology and the most common mechanisms of antibiotic resistance.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Wenisch et al., 2014[13]	An information campaign on CDI, formal restriction of moxifloxacin, and direct feedback	Pre-/post study. The pre-intervention period (period 1) was January through May 2013, and the intervention period (period 2) was June through December 2013. The study recorded the defined daily doses (DDD) of moxifloxacin and the number of CDI patients/ month.	A 1,000-bed tertiary care community teaching hospital with 1,081 beds (Vienna, Austria)	Moxifloxacin use was reduced from a mean (+/- standard error of the mean [SEM]) of 1,038 +/- 109 DDD per month (period 1) to 42 +/- 10 DDD per month (period 2) (p=0.0045). In total, quinolone use decreased by about 37% in period 2 compared with period 1. Total antibiotic use was stable. The mean (+/-SEM) numbers of CDI cases in period 1 were 59 +/-3 per month and in period 2 were 32 +/-3 per month (46% reduction; p=0.0044).	Not provided	The development of evidence-based practice guidelines incorporating local microbiology and resistance patterns is strongly recommended in antimicrobial stewardship programs. The numbers of CDI cases and ribotype 027 isolates seemed to be related to moxifloxacin (a high-risk broad-spectrum antibiotic) use. The antibiotic stewardship team was appointed by the hospital management and consisted of a clinical pharmacist, a pathologist, and infection control professionals.	Low to moderate	While the CDI numbers were stable at 200 patients per year from 2009 to 2011 (0.56, 0.51, and 0.50 per 1,000 patient days, respectively), an increase to 313 patients was observed in 2012 (0.88/1,000 patient days).

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Yam et al., 2012[30]	A multi-disciplinary team was formed to implement a stewardship program targeting six antimicrobials with a high potential for misuse. A key part of the program was the participation of a remotely located infectious diseases physician specialist in weekly case review tele-conferences.	Pre-/post-program evaluation. Measurements taken at 13 months after implement-tation.	A 141-bed rural hospital	The rate of nosocomial CDI decreased from an average of 5.5 cases per 10,000 patient-days to an average of 1.6 cases per 10,000 patient-days. An evaluation of the first 13 months of the initiative (May 2010–June 2011) indicated that pharmacist-initiated antimicrobial stewardship interventions increased dramatically after program implementation, from a baseline average of 2.1 interventions per week to an average of 6.8 per week. An analysis of 2010 purchasing data demonstrated a decrease in annual antibiotic costs of about 28% from 2009 levels (and a further decrease of about 51% in the first two quarters of 2011).	Not provided	After a review of baseline data, a novel process was developed. The strategy was to follow recommended IDSA–SHEA guidelines while addressing major gaps in hospital resources. Included use of a remotely located physician specialist in infectious diseases, improvement of existing information technology, and education and training of pharmacists to provide daily antimicrobial reviews were the major strategies used to provide an ASP for use in a rural setting.	Moderate: inability to quantify and evaluate the progress of the program due to the lack of consistent pharmacist reporting methods	None

Table B.19: Clostridioides *difficile*, Antimicrobial Stewardship–Systematic Review

Note: Full references are available in the Section 4.1 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Populations	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Baur et al., 2017[17]	Antibiotic stewardship programs	Hospitals	Search for studies published from January 1, 1960, to May 31, 2016. Excluded LTCF. Included 32 studies. The main outcomes were incidence ratios (IRs) of target infections and colonization per 1,000 patient-days before and after implementation of antibiotic stewardship. Meta-analyses were done with random-effect models, and heterogeneity was calculated with the I^2 method. Antibiotic stewardship programs reduced the incidence of infections and colonization with multidrug-resistant Gram-negative bacteria (51% reduction; IR 0·49, 95% CI 0.35 to 0.68; p<0·0001), extended-spectrum β-lactamase-producing Gram-negative bacteria (48%; 0.52, 0.27 to 0.98; p=0.0428), and methicillin-resistant *Staphylococcus aureus* (37%; 0.63, 0.45 to 0.88; p=0.0065), as well as the incidence of CDIs (32%; 0.68, 0.53 to 0.88; p=0.0029). Most effective when implemented with other measures. Significant heterogeneity between studies was detected. Among the different types of antibiotic stewardship interventions, antibiotic cycling was found to be the most effective, followed by audits and feedback and antibiotic restriction. The interventions became more effective over time, ranging from 10% reduction of antibiotic resistance for 1980 to 2000 to 32% reduction for 2006 to 2013. Studies of guideline implementation and single antibiotic classes did not show any effect for these interventions on resistance rates, perhaps because of short followup. ASPs were more effective in the hematology-oncology settings.	When planning future studies of ASPs, it would be advisable to use controlled interventional study designs and data-reporting consistencies. Implementation facilitators: high compliance among physicians, the additional educational effect of feedback, a closer working relationship between physicians and the antibiotic stewardship team because of audits, audits in conjunction with antibiotic stewardship programs, educational effects, and the Hawthorne effect due to putting electronic monitoring systems in place. Auditing is effective in all settings.	None

Author, Year	Description of Patient Safety Practice	Setting/s, Populations	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Davey et al., 2017[18]	Antimicrobial stewardship	Hospital inpatient	Review of articles published up to January 2015 to estimate the effectiveness and safety of interventions to improve antibiotic prescribing to hospital inpatients and to investigate the effect of two intervention functions: restriction and enablement. There was very low-certainty evidence about the effect of the interventions on reducing *Clostridium difficile* infections (median, -48.6%; interquartile range, -80.7% to -19.2%; seven studies). The duration of antibiotic treatment decreased by 1.95 days (95% CI, 2.22 to 1.67; 14 randomized controlled trials [RCTs]; 3,318 participants; high-certainty evidence) from 11.0 days. Information from nonrandomized studies showed interventions to be associated with improvement in prescribing according to antibiotic policy in routine clinical practice, with 70% of interventions being hospitalwide compared with 31% for RCTs. The risk of death was similar between intervention and control groups (11% in both arms), indicating that antibiotic use can likely be reduced without adversely affecting mortality (RD 0%, 95% CI, 1 to 0; 28 RCTs; 15,827 participants; moderate-certainty evidence). Antibiotic stewardship interventions probably reduce length of stay by 1.12 days (95% CI, 0.7 to 1.54 days; 15 RCTs; 3,834 participants; moderate-certainty evidence).	Both enablement and restriction were independently associated with increased compliance with antibiotic policies, and enablement enhanced the effect of restrictive interventions (high-certainty evidence). Enabling interventions that included feedback were probably more effective than those that did not (moderate-certainty evidence). One RCT and six nonrandomized studies raised concerns that restrictive interventions may lead to delay in treatment and negative professional culture because of breakdown in communication and trust between infection specialists and clinical teams (low-certainty evidence).	None

Author, Year	Description of Patient Safety Practice	Setting/s, Populations	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Feazel et al., 2014[16]	Antibiotic stewardship programs (ASPs) to prevent CDI in hospitals (non-outbreak situations)	Hospitals (non-outbreak situations)	Objective was to perform a meta-analysis of published studies to assess the effect of ASPs on the risk of CDI in hospitalized adult patients; 16 studies met inclusion criteria. The average quality of the studies was low, as measured by the modified Downs and Black tool. Most studies suffered from poor internal validity, particularly with respect to bias. Heterogeneity in studies' settings. When the results of all studies were pooled in a random effects model, a significant protective effect (pooled risk ratio 0.48; 95% CI, 0.38 to 0.62) was observed between ASPs and *C. difficile* incidence. When pooled results were stratified by intervention type, a significant effect was found for restrictive ASPs (complete removal of drug or prior approval requirement). Furthermore, ASPs were particularly effective in geriatric settings. The duration of each ASP also affected the magnitude of the effect, with longer studies resulting in a greater protective effect than shorter studies. Majority of studies are from UK, limiting generalizability.	ASPs effectively decrease the incidence of CDI. Restrictive policies that modified physician prescription practices were more effective than persuasive policies. ASPs are most effective with geriatric populations. Studies were subject to many biases. Future studies should use designs with higher internal validity, either through a cluster-randomized design or by the addition of non-equivalent control groups. Thus, given the apparent benefit of ASPs in reducing CDI, further research and implementation of active ASPs are needed in North America, as well as multiple measurement.	Articles went back as far as 1997 and up to 2013.
Louh et al., 2017[20]	Review of several interventions to reduce CDI, including hand hygiene, chlorohexidine bathing, probiotics, environmental cleaning, bundles, and ASPs	Acute care hospitals	Systematic search for ASP interventions to reduce the rate of CDI in acute care hospitals. Review of articles published between January 1, 2009, and August 1, 2015. Review identified 13 studies that implemented ASPs. Common approaches were prospective audit and feedback when targeted antimicrobials were prescribed, or preauthorization requirements for antimicrobials. Both methods appeared to be effective in reducing CDI in acute care hospitals. One study saw a decrease in CDI rates from 8.2 of 10,000 to 3.1 of 10,000 patient-days with an audit and feedback system for six high-risk antimicrobials, although this result may be confounded by a change in environmental cleaning practice made immediately preceding this evaluation. Similarly, another study implemented stewardship educational lectures and restricted use of ceftriaxone and ciprofloxacin, resulting in CDI reduction from 24 of 10,000 to 5.5 of 10,000 patient-days. Hospitals with relatively low baseline rates of CDI did not see a substantial change after deployment of an ASP.	ASPs were generally effective in reducing CDI. Audit and feedback and restrictions were primary methods. Better results for institutions with higher CDI rates. Institutions with few resources should strive to improve environmental practices, with implementation of bleach-based cleaning. Institutions with more resources should consider bundled interventions that incorporate environmental cleaning, *restrictive* ASPs, and checklists.	Authors found that, in prevention studies performed in acute care hospitals, bleach-based environmental disinfection appeared to have the most effect in preventing CDI. Bundled interventions and antimicrobial stewardship showed promise for reducing CDI rates.

Author, Year	Description of Patient Safety Practice	Setting/s, Populations	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Pitiriga et al., 2017[21]	Antimicrobial stewardship targeting quinolone prescribing	Hospital and community sites	Article synthesizes the impact of antibiotic stewardship practices, including interventions on (1) quinolone resistance rates and (2) healthcare-associated infections (MRSA, ESBLs bacteria, and CDI). Most of the existing stewardship studies document possible improvements in susceptibility rates among both nosocomial and community Gram-negative isolates and decrease in CDI (three CDI-focused studies). However, there are possible pitfalls in the existing study designs; more clinical data are needed. Article includes recommendations for quinolone-targeted practices such as: restriction policies, audit and feedback, prior authorization, IV switch to oral program, educational programs, and local antibiotic guidelines, as well as monitoring of Gram-negative susceptibility patterns. Novel approaches for identifying bacterial resistance include: use of molecular diagnostics, mass spectrometry, microarrays, and whole-genome sequencing, as well as prompt investigation of the clonality of quinolone-resistant strains.	Recommendations for quinolone-targeted practices include: restriction policies and prospective audits with feedback. However, clinicians should be aware of the ‘‘squeezing the balloon’’ effect—i.e., the association of restriction policies with progressive resistance to unrestricted antimicrobials. Quinolone bundling on the basis of antimicrobial spectrum; syndrome-specific interventions; multifaceted approaches.	Background: studies have linked use of quinolones with increase in antibiotic resistance and infections involving MRSA and *C. difficile*. (This article is not specific to *C. difficile*.)

Table B.20: Clostridioides *difficile*, Hand Hygiene–Single Studies

Note: Full references are available in the Section 4.2 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Al-Tawfiq et al., 2018[30]	The Joint Commission Centre for Transforming Healthcare's web-based Targeted Solutions Tool (TST) for improving hand hygiene; hand hygiene compliance	Trained unknown and known observers monitored compliance, and rates of hospital-acquired infections were tracked and correlated against the changes in hand hygiene compliance. In total, the secret observers recorded 5,669 hand hygiene observations; 4-month baseline; 1 year intervention period.	A 30-bed oncology/hematology inpatient unit and a 350-bed community hospital located in eastern Saudi Arabia	The compliance rate increased from 75.4% at baseline (May to August 2014) to 88.6% during the intervention (13 months) and the control periods ($p<0.0001$; not statistically significant). Reductions in healthcare-associated infection rates were recorded for *Clostridium difficile* infections from 7.95 (95% CI 0.8937 to 28.72) to 1.84 (95% CI 0.0241 to 10.26) infections per 10,000 patient-days ($p=0.23$).		The top contributing factors for noncompliance were improper use of gloves, hands full of supplies or medications, and frequent entry or exit in isolation areas. Researchers concluded that the application of TST allowed healthcare organizations to improve hand hygiene compliance and to identify the factors contributing to noncompliance. An action plan was developed to decrease improper glove use through education and focusing particularly on the primary noncompliant groups.	Low/ moderate—potential for Hawthorne effect; part of an overall quality improvement project. Single site, small.	The researchers identified obstacles to hand hygiene such as inappropriate use of gloves, particularly within the house-keeping department.
Edmonds et al., 2013[8]	Washing with plain soap and water	Pre/post-experimental study. This two-phase study was conducted to determine whether surrogate organisms were predictive of *C. difficile* spore removal and to compare the efficacy of various hand	Controlled experiment	A peracetic acid and surfactant formulation was the most effective test preparation and achieved significantly greater reductions of *C. difficile* spores than did the tap water control, the 4% chlorhexidine gluconate (CHG) hand wash, 0.5% bleach, 8% hydrogen peroxide,		Findings demonstrated that existing hand hygiene interventions have limited efficacy against *C. difficile* spores. Therefore, HCWs should continue to follow the recommendations for hand washing with soap and water and emphasize contact		The peracetic acid and surfactant formulation likely achieved the highest log reduction through a combination of spore removal and

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
		washing preparations at removing *C. difficile*. Nine subjects completed evaluations for a nonantimicrobial body wash or tap water for removal of spores of *B. atrophaeus*, *C. sporogenes*, and *C. difficile*. In phase 2, three to nine subjects completed evaluations for 10 test products and a tap water control for removal of *C. difficile* spores using a modification of a standard hand wash test method.		0.3% triclosan hand wash, nonantimicrobial hand wash, and nonantimicrobial body wash ($p<.05$). An ink and stain remover (applied with and without a brush) was significantly more effective than the tap water control, nonantimicrobial body wash, and 4% CHG hand wash ($p<.05$). The sodium tetraborate decahydrate powder was also significantly more effective than tap water ($p<.05$). The remaining preparations were statistically equivalent and not more effective than tap water alone.		precautions (especially gloves) for care of patients with CDI. The lack of readily available *C. difficile* spore suspensions makes it difficult to evaluate the efficacy of hand wash products against *C. difficile*. Surrogate organisms should not be used to predict efficacy of hand hygiene agents against *C. difficile* spores. The only other products to achieve significantly higher $\log_{10}$ reductions than the tap water were sodium tetraborate decahydrate powder and the ink and stain remover. However, these products also contain harsh ingredients that are unacceptable for routine use in healthcare environments.		inactivation. However, the active concentration or contact time would negatively impact skin tolerability.
Isaacson et al., 2015[37]	Hand washing using friction, that is, sand and water	Experimental comparison between different hand washing methods. Fourteen HCW subjects completed six study arms in randomized order: (1) no hand	Controlled experiment	Hand washing with sand resulted in an additional 0.5 log reduction in spore recovery compared with the current standard of soap and water. Sand was the only intervention statistically		Although the sand used in this study was well tolerated by participants and resulted in no irritation after a single use, abrasives might not be suitable for routine hand washing. This	Moderate—small sample—potential variation in technique across participants. Spores left	Study was based on the idea that augmenting the friction of hand washing would result in a reduction in

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
		washing; (2) negative hand washing control: 30 seconds of rubbing with 5 mL of water and 30 seconds of tap water rinsing; (3) 30 seconds of rubbing with 5 mL of 0.3% triclosan soap and 30 seconds of rinsing; (4) 30 seconds of rubbing with a paste consisting of 15 mL of sand mixed with 15 mL of tap water and 30 seconds of rinsing; (5) 15 seconds of rubbing with 5 mL of a 50% baking soda and 50% vegetable oil mix, and 15 seconds of rubbing with 5 mL of liquid dish detergent, followed by 30 seconds of rinsing; and (6) 60 seconds of rinsing. Contamination was measured after each method.		superior to water, removing an additional 0.36 log of spores (p=.019). Compared with triclosan soap/water, sand removed 0.5 log more spores (p=.003), and oil/baking soda followed by dish detergent removed 0.37 log more spores (p<.001).		study did not find a significant difference in residual spore counts after washing with triclosan soap versus tap water, consistent with findings from previous studies. This finding may occur because triclosan soap is not sporicidal and confers no additional friction.	over from the prior intervention. Did not use a "wash out" period, although they found that they did not necessarily need that.	contamina-tion.
Kirkland et al., 2012[29]	Hand hygiene compliance using (1) leadership/ accountability; (2) measurement/ feedback; (3)	Three-year interrupted time series with multiple sequential interventions and 1-year post-intervention followup. Tracked	383-bed teaching hospital, rural New Hampshire	HH compliance increased significantly from 41% to 87% (p<0.01) during the initiative and improved further to 91% (p<0.01) the following year. Nurses achieved higher	Not provided	Monthly data show that the single biggest improvement in HH overall, and in physician HH specifically, occurred after a year of measurement and	Low/ moderate—cannot precisely measure each intervention; single site,	When this initiative began, the culture was one in which autonomy was valued and enthusiasm

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	hand sanitizer availability; (4) education/ training; and (5) marketing/ communication.	two primary outcomes monthly: (1) HH compliance rates and (2) healthcare-associated infection rates. Between 2006 and 2008, HH observations increased from 244 to 498 average monthly observations.		HH compliance (93%) than physicians (78%). There was a significant, sustained decline in the healthcare-associated infection rate, from 4.8 to 3.3 ($p<0.01$) per 1,000 patient-days. Refills for wall-mounted dispensers increased 37%. In the final year, overall HAIs declined; and the CDI rate stayed the same (0.9 to 0.6 per 1,000 patient-days, $p=0.1$). The rates of *S. aureus* infection (2.5 to 1.6 per 1,000 patient-days, $p<0.001$) and bloodstream infection (2.1 to 1.4 per 1,000 patient-days, $p=0.004$) fell significantly.		monthly feedback citing poor performance. Physicians reported that, for them, regularly seeing data linking HH performance to healthcare- associated infections was important. Intervention built on the work of Goldmann, which framed the need for both system and personal accountability for HH. Routine HH audits on all units, with monthly unit-specific data, were published on an intranet site available to all staff, as were strategies to optimize availability of hand sanitizer (Purell, 62% ethyl alcohol formulation).	small; potential participant bias. Strength: covert observation; use of tracer condition—in comparison with OR (where intervention would not have made an impact), HAI rates decreased overall.	for quality improvement activities varied; such efforts typically attracted small groups of committed nurses. Infection rate reduction lags behind HH improvement.
Knight et al., 2010[27]	Hospital-wide alcohol-based hand rub (AHBR) policy	A retrospective chart review analysis to compare incidence rates of CDAD before and after implementation of the ABHR policy. Population: inpatient status between January 1, 2001, and June 30, 2008. Full implementation of the ABHR policy was completed by May 1, 2003. A total	A 795-bed community teaching hospital	The incidence rate of CDAD was 3.98 per 10,000 patient- days after implementation of the ABHR policy, compared with 4.96 per 10,000 patient days before implementation ($p=.0036$). The crude mortality rate in patients diagnosed with CDAD was 10.7% after implementation, compared with 13.3% before implementation	The rate of sepsis in patients diagnosed with CDAD was 19.6% after implemen-tation, compared with 5.2% before implement-tation ($p<.0001$).	Before implementation, only a 2% chlorhexidine-based soap product was available in the hospital. At the time of implementation, all existing antimicrobial products were removed and replaced with the alcohol-based hand foam. The only soap product available was a lotion soap with no antimicrobial activity.	Low/ moderate; single site. Possible other IPC improve-ments during period. Strengths: relatively long study period; controlled for doses of antibiotics as	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
		of 766 patients with healthcare facility-onset, healthcare facility-associated CDAD were identified.		(p=.275). After implementation of the ABHR policy, compliance with hand hygiene, including both ABHR and soap and water, rose dramatically.		During a cluster, outbreak, or evidence of nosocomial transmission of *C. difficile*, the authors recommend switching to soap and water only for hand hygiene.	a potential confounder.	
Oughton et al., 2009[2]	Hand washing with soap and water (vs. alcohol-based hand rubs)	Randomized crossover comparison among 10 volunteers with hands experimentally contaminated by nontoxigenic *C. difficile* (no hand washing training was conducted). A crossover format was used so that all volunteers would be exposed to all interventions once for each contamination protocol during the observation period of June–July 2007. Minimum of 24 hours between interventions; 318 observations; included use of control group.	Controlled experiment	Under the whole-hand protocol, the greatest adjusted mean reductions were achieved by warm water with plain soap (2.14 log10 CFU/mL [95% credible interval (CrI), 1.74 to 2.54 log10 CFU/mL]); cold water with plain soap (1.88 log10 CFU/mL [95% CrI, 1.48 to 2.28 log10 CFU/mL]); and warm water with antibacterial soap (1.51 log10 CFU/mL [95% CrI, 1.12 to 1.91 log10 CFU/mL]), followed by antiseptic hand wipes (0.57 log10 CFU/mL [95% CrI, 0.17 to 0.96 log10 CFU/mL]). Alcohol-based hand rub (0.06 log10 CFU/mL [95% CrI, 0.34 to 0.45 log10 CFU/mL]) was equivalent to no intervention. Hypothenar (odds ratio, 10.98 [95% CrI, 1.96 to 37.65]) and the fingertips (odds ratio, 6.99 [95% CrI, 1.25 to	Not provided	Alcohol-based hand rub produced a significant reduction in contamination, although of a lesser magnitude than was seen with the other hand hygiene interventions. The reason that antibacterial soap seems slightly inferior to plain soap according to the whole-hand protocol but not according to the palmar surface protocol is uncertain. It may be due to a higher concentration of organic matter present in the whole-hand protocol, which interferes with the activity of chlorhexidine.	Low/ moderate—in vitro study, no gloving, small sample, single site.	Study included surface (i.e., palms) and whole-hand contami-nation. With 10 paired assessments for each product, a power of more than 99% to detect a 1.0 log10 difference was calculated. All of the hand washing interventions studied were performed for less time than recommended by the manufacturers of the products.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
				23.41]) were less likely to remain heavily contaminated after hand washing.				
Pokrywka et al., 2017[35]	Patient hand hygiene (PHH)	A biphasic, quasi-experimental study was performed to increase PHH through education for staff and to provide education, assistance, and opportunities to the patient for hand cleaning. PHH practice was assessed by patient surveys and analyzed by Chi squared test. Phase 1: four medical-surgical nursing units: pre/post-intervention patient surveys; Phase 2: whole hospital pre/post-intervention patient surveys.	A 495-bed university-affiliated medical center in a large healthcare system	Patient-reported HH opportunities and frequency improved for patients in Phase 1 and 2, although the improvement was greater for Phase 1. CD SIRs for the study period showed a decrease in the number of observed hospital-onset (HO) LabID events in the first two quarters (Qs) after the implementation of PHH in March 2015, and a corresponding decrease in the HO SIRs from 0.834 to 0.572 and 0.497, respectively. SIR p-values for Q2 and Q3 (0.0157 and 0.0103, respectively) were significantly lower than expected ($p \leq 0.05$). The Q4 SIR, however, showed an increase to 0.3844 over the two preceding quarters.	The average frequency of PHH the patients reported did not change (average 2.4 before the initiative vs. 2.6 times after).	PHH may be a potentially underused preventive measure for CDI. Hospitalized patients are often not provided the opportunity to clean their hands. Limited patient mobility and acuity along with a lack of education present obstacles. Surveys of patients at the institution showed a need for increased PHH opportunities. Staff provided encouragement for PHH. Laminated signs were posted in each patient room with reminders for staff to assist patients in washing their hands throughout the day. This practice was augmented with screensavers and signage in staff areas. The increase in CDI in Q4 may show need for continued support and education.	Low/ moderate: surveys collected data from patients and were therefore susceptible to social desirability bias. CDI rates—small sample/ single site. Increased staff HH could have impact. Strength: no IPC changes were made during Phase 2.	None
Schweon et al., 2013[31]	Multimodal hand hygiene program	Quasi-experimental pre/post. Data were collected for 22	A 174-bed skilled nursing facility, in	CDI rate decrease 0.08 to 0.04, p=.36 (insignificant). Infection	Not provided	Not provided	Low/ moderate—resident	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
		months (May 2009 through February 2011). In March 2010, a comprehensive hand hygiene program was implemented, including increased product availability, education for healthcare personnel (HCP) and residents, and an observation tool to monitor compliance.	Stroudsburg, PA	rates for LRTIs were reduced from 0.97 to 0.53 infections per 1,000 resident-days (p=.01) following the intervention, a statistically significant decline. Infection rates for SSTIs were reduced from 0.30 to 0.25 infections per 1,000 resident-days (p=.65). A 54% compliance rate was observed among HCP.			compliance not monitored; single site.	
Sickbert-Bennett et al., 2016[32]	Clean In, Clean Out, cleaning hands before/after working with patient, covert observation, audit and feedback	Quasi-experimental: compared hand hygiene compliance data from the last quarter of the covert observations by infection preventionists and designated nursing staff with compliance data from the first month of the new program. Study used a Chi squared to compare the average historical HAI rate from January 2013 until the implementation of the new program in October 2013 with the average HAI rate during the study	853-bed hospital, North Carolina	The researchers found that a 10% improvement in hand hygiene was associated with a 14% reduction in HA-CDI (p=0.070). They found a significant increase in the overall hand hygiene compliance rate (p<0.001) and a significantly decreased overall HAI rate (p=0.0066), supported by 197 fewer infections and an estimated 22 fewer deaths. These reductions resulted in an overall savings of approximately U.S. $5 million.	Not provided	Engaging all hospital staff in measuring hand hygiene compliance created a Hawthorne effect. A key feature of the intervention was that the focus for observation was simply on cleaning hands upon entering and leaving patient rooms.	Low—single site. Strength: no other formal IPC efforts were being implemented at the same time.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
		period of October 2013 to February 2015, after implementation of the new program. More than 4,000 unique observers made more than 140,000 observations.						
Stone et al., 2012[26]	National "Cleanyour-hands" campaign in England and Wales, which included installation of bedside alcohol hand rub, materials promoting hand hygiene and institutional engagement, and regular hand hygiene audit.	Prospective, ecological, interrupted time series study of 187 trusts from July 1, 2004, to June 30, 2008 (4 years). Assessed associations between procurement and infection rates by a mixed effect Poisson regression model (accounting for bed occupancy, length of stay, hospital type, and timing of other national interventions targeting these infections).	Regional: 187 acute hospital trusts in England and Wales	Combined procurement of soap and alcohol hand rub tripled from 21.8 to 59.8 mL per patient bed-day; procurement rose in association with each phase of the campaign. Rates fell for MRSA bacteremia (1.88 to 0.91 cases per 10,000 bed-days) and CDI (16.75 to 9.49 cases). MSSA bacteremia rates did not fall. Increased procurement of soap was independently associated with reduced CDI throughout the study. The adjusted incidence rate ratio for 1mL increase per patient bed-day was 0.993 (95% CI 0.990 to 0.996; p<0.0001). Publication of the Health Act 2006 and visits by DPH improvement teams reduced CDI for at least	Not provided	The campaign took place in the context of a high-profile political drive and other national interventions to reduce MRSA bacteremia and CDI. It received central sustained funding and coordination. The World Health Organization currently offers a very similar intervention as part of its Save Lives initiative. Although caution should be exercised when extrapolating from these results, the campaign could offer a model for other countries to adopt or adapt.	Low/ moderate—large scope, controlled for confounders (although these are not listed), except antibiotics—which potentially would be a big confounder.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
				two quarters after the visit.				
Tomas et al., 2016[15]	A sporicidal formulation of ethanol for glove decontami-nation (to use before glove removal) to prevent CDI	Experiment and quasi-experiment: (1) Blind comparison of intervention versus bleach, 70% ethanol, and no cleaning. Gloves were contaminated with spores and then cleaned (the three ways listed); then samples were taken. (2) Study was repeated on gloved hands of personnel after caring for CDI patients. Sample size not given for artificially contaminated gloves. For personnel caring for *C. difficile* patients: 159 patient care episodes (67 by nurses, 52 by physicians, and 40 by allied health providers) involving 24 CDI patients.	Experiment at the Cleveland Veterans Affairs Medical Center	The reduction achieved by the sporicidal ethanol solution was equivalent to the 1:100 dilution of bleach (1.87 vs 1.69 logs; p=.97). A further reduction occurred when the solution was applied as a wipe. No personnel noted that the sporicidal ethanol solution had an adverse odor or caused respiratory irritation or staining of clothing (compared with bleach, which caused discoloration).	Use of a specific formulation of ethanol only for glove disinfection after care of CDI patients may be impractical to implement and might add to the cost of care. Although the sporicidal ethanol solution was not associated with adverse effects, the formulation tested has an acidic pH.	In the study, bleach wipes were effective in reducing spore contamination on gloves, but discoloration of clothing due to inadvertent spills, and aversion to the odor of bleach, were common complaints by personnel. Findings suggest that the sporicidal ethanol solution could be useful for glove disinfection before removal when caring for CDI patients. Glove disinfection might be useful but it would not replace the need for hand washing after glove removal when caring for CDI patients.	High	Study measures **glove contami-nation**, not impact on CDI rates.
Tomas et al., 2015[12]	Education on glove and PPE removal and use of bleach wipes for glove decontami-nation	Quasi-experimental study. Pre/post; 28 healthcare workers. Comparison of *C. difficile* hand contamination before and after education	Cleveland VA Medical Center	After phase 1 (education and practice on PPE removal), acquisition of *C. difficile* on hands occurred in 2 of 27 (7%) episodes of care. After phase 2 (disinfection of gloves	Although there were no reported adverse effects attributed to the use of bleach	In this study, researchers found that despite PPE use, healthcare personnel frequently acquired *C. difficile* spores on their hands while caring for patients with CDI. In a	Low—small sample is reflected by p-values	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
		intervention and glove contamination intervention.		with bleach wipes), contamination was significantly reduced compared with the pre-intervention period (0% vs. 16%; p=.04).	wipes, several personnel complained about the strong odor of bleach. In addition, some participants expressed a concern that staining of clothing or respiratory irritation would be a problem if bleach wipes were used routinely.	quasi-experimental intervention, improving PPE technique with education led to a nonsignificant reduction in contamination. Adding glove disinfection significantly reduced contamination, with no acquisition of spores detected during 30 episodes of patient care. The researchers postulate that the findings suggest that simple interventions may be effective in decreasing the risk for hand contamination while providing care to patients with CDI. Results are consistent with previous studies demonstrating that simulations using fluorescent lotions can be useful in improving infection control techniques, including PPE removal.		

Table B.21: *Clostridioides difficile*, Hand Hygiene–Single Systematic Reviews

Note: Full references are available in the Section 4.2 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Louh et al., 2017[25]	Hand hygiene	Acute care hospitals	Systematic search for controlled trials of interventions to reduce the rate of CDI in acute care hospitals. Search for articles published between January 1, 2009, and August 1, 2015. Review of four studies that evaluated the effect of hand hygiene campaigns. These used multifaceted campaigns that included access to alcohol-based hand rub, education, auditing, and feedback on hand hygiene compliance, in addition to advertising the use of hand hygiene. Mixed results. A nationwide hand hygiene campaign in hospitals in England and Wales showed significant reduction in CDI rates, but studies that investigated single-hospital campaigns showed no change in CDI acquisition. Hand hygiene was included in some but not all bundled interventions—bundled interventions all reduced CDI rates. Although older studies (before 2009) have shown a significant reduction in nosocomial infections from observing good hand hygiene, further benefit from promoting hand hygiene is unlikely, as the margin for improvement diminishes.	If an institution has adequate hand hygiene processes, incremental efforts to improve hand hygiene may not be as beneficial as other interventions. Institutions with few resources should strive to improve environmental practices, with implementation of bleach-based cleaning. Institutions with more resources should consider bundled interventions that incorporate environmental cleaning, restrictive ASPs, and checklists.	Review covers multiple PSPs. Environmental cleaning (daily/terminal with bleach) is found as most effective PSP of the five PSPs reviewed.

Table B.22: Clostridioides *difficile*, Environmental Cleaning–Single Studies

Note: Full references are available in the Section 4.3 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Alfa et al., 2008[42]	Accelerated hydrogen peroxide (AHP) cleaner (0.5% AHP) for cleaning toilets in non-outbreak situations	A prospective clinical comparison during non-outbreak conditions. A total of 243 patients and 714 samples were analyzed.	450-bed acute care facility	The efficacy of spore killing is formulation specific and cannot be generalized. The Oxivir$_{TB}$® AHP formulation resulted in statistically significantly (p=0.0023) lower levels of toxigenic *C. difficile* spores in toilets of patients with *C. difficile*-associated disease (CDAD) compared with the stabilized hydrogen peroxide cleaner formulation that was routinely being used (28% vs. 45% culture positive).	Not provided	The AHP formulation evaluated that has some sporicidal activity was significantly better than the currently used hydrogen peroxide cleaner formulation. It is a one-step process that significantly lowered the *C. difficile* spore level in toilets during non-outbreak conditions. The researchers report the formulation is less toxic than 5,000 ppm bleach. Interestingly, the background level of toxigenic *C. difficile* spores was 10% in toilets of patients with diarrhea not due to CDAD.	Low to moderate	Funds for this study were provided by Manitoba Medical Services Foundation as well as an unrestricted research grant from Virox Technologies Inc. and JohnsonDiversey Inc. All AHP used for this study was provided by Virox Inc.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Anderson et al., 2017[32]	Enhanced terminal room disinfection: rooms from which a patient with infection or colonization with *C. difficile* was discharged were terminally disinfected with one of two strategies, bleach or ultraviolet (UV) light and bleach	Cluster-randomized, crossover trial. Every strategy was used at each hospital in four consecutive 7-month periods. 31,226 patients were exposed. Convenience sample of multiple types of hospitals.	Nine hospitals in southeastern United States	The incidence of CDI among exposed patients was not changed after adding UV to cleaning with bleach (n=38 vs. 36; 30.4 cases vs. 31.6 cases per 10,000 exposure days; rate ratio 1.0, 95% CI 0.57 to 1.75; p=0.997).	4 minutes longer cleaning time, 10–20 minutes longer admit times	Adding UV to bleach cleaning had no impact on CDI rates although the researchers thought that in actuality, based on prior research, UV disinfection helped prevent CDI. This study was the most robust of the studies reviewed for this section. reviewed.	Low to moderate	Study covered interventions and harms in addition to *C. difficile*: MRSA (methicillin-resistant *Staphylococcus aureus*), VRE (Vancomycin-resistant enterococci), and multidrug-resistant *Acinetobacter*. Adding UV light to standard cleaning reduced incidence of these organisms (but not for *C. difficile*).

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Aronhalt et al., 2013[41]	The intervention used bleach wipes for daily and terminal patient room cleaning; a 1:10 (~6,000 ppm) dilution of hypochlorite solution	Post-intervention survey. 94 patients and 6 staff.	Patient care units at a single hospital with a relatively high incidence of CDI	Patients (n=94) (91%) continued to be very satisfied with how well their rooms were cleaned everyday. Bleach wipes were well tolerated by patients (n=44) (100%) surveyed on the medical units and less tolerated by patients (n=50) (22%) on the hematology-oncology units.	Environmental services housekeeping staff reported less satisfaction and more respiratory irritation during the initial month of the project.	Potential concerns for patients and employees include the appearance of residue left on surfaces, odors, and respiratory tract irritation. Patient and employee satisfaction with these processes is critical for sustainability of process improvement initiatives because the change process influences both populations.	Low	Qualitative study, measured patient/staff satisfaction with cleaning with bleach. However, does get into implementation challenges.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Barbut et al., 2009[40]	Hydrogen peroxide dry-mist system versus 0.5% hypochlorite solution for disinfecting surfaces contaminated with *C. difficile*	Prospective, randomized, before-and-after trial. 748 surface samples were collected (360 from rooms treated with hydrogen peroxide and 388 from rooms treated with hypochlorite).	Two hospitals, France	After disinfection, 23 (12%) of 194 samples from hypochlorite-treated rooms and 4 (2%) of 180 samples from hydrogen peroxide-treated rooms showed environmental contamination, a decrease in contamination of 50% after hypochlorite decontamination and 91% after hydrogen peroxide decontamination (HPD) ($p<0.005$).	Not provided	In this experiment, the hydrogen peroxide dry-mist disinfection system was significantly more effective than 0.5% sodium hypochlorite solution at eradicating *C. difficile* spores. Researchers note a need to find less corrosive and user-dependent alternatives to hypochlorite-based products. Hydrogen peroxide dry-mist disinfection process rooms do not have to be sealed.	Low to moderate	During the in vitro experiments, time-dependent sporicidal activity was observed for hypochlorite.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Best et al., 2014[33]	Deep cleaning and HPD, following a high incidence of CDI	Pre/post. Extensive environmental sampling (342 sites on each occasion) for *C. difficile* using sponge wipes was performed before and after deep cleaning with detergent/ chlorine agent immediately following HPD, and at two later occasions, 19 days and 20 weeks following HPD. *C. difficile* isolates underwent polymerase chain reaction ribotyping and multi-locus variable repeat analysis.	A single stroke rehabilitation unit (SRU)	*C. difficile* was recovered from 10.8%, 6.1%, 0.9%, 0%, and 3.5% of sites at baseline, following deep cleaning, immediately after HPD, and 19 days and 20 weeks after HPD, respectively. CDI incidence (number of cases on SRU per 10 months [January to October 2011]) declined from 20 before to 7 after the intervention.	Closed ward for 10 days. The whole ward had to be moved to alternative accommodation, which is a major undertaking and depends on the availability of decant space, an increasingly rare resource in some hospitals.	Emerging evidence shows that a minority of CDI cases is linked to other cases when endemic as opposed to epidemic infection rates prevail. There may therefore be an optimum level of CDI at which HPD is most likely to be cost effective. Results may demonstrate that HPD may be a useful method for decontaminating a hospital ward with a high CDI incidence.	Low to moderate	Determining a role for HPD should include long-term cost-effectiveness evaluations.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Boyce et al., 2008[31]	One-time decontamination followed by terminal disinfection using hydrogen peroxide vapor (HPV) decontamination of rooms occupied by patients with *C. difficile*-associated disease (CDAD)	A prospective before-and-after intervention study. Intensive HPV decontamination of five high-incidence wards followed by hospitalwide decontamination of rooms vacated by patients with CDAD. The pre-intervention period was June 2004 through March 2005, and the intervention period was June 2005 through March 2006 (8 months).	Five high-incidence wards at a 500-bed university hospital	On five high-incidence wards, the incidence of nosocomial CDAD was significantly lower during the intervention period than during the pre-intervention period (1.28 vs 2.28 cases per 1,000 p=0.047). Eleven (25.6%) of 43 cultures of samples collected by sponge from surfaces before HPV decontamination yielded *C. difficile*, compared with 0 of 37 cultures of samples obtained after HPV decontamination (p<0.001).	Not provided	The time required for the entire process was 3 to 4 hours for a patient room and approximately 12 hours for an entire ward. The HPV decontamination process used in this study was reported to be safe for use in healthcare facilities, as long as the area to be decontaminated is appropriately sealed and hydrogen peroxide levels outside the area being decontaminated are closely monitored. During the intervention period, hospital staff did not report any adverse effects attributable to the HPV decontamination process, among patients or personnel.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Ghantoji et al., 2015[38]	Pulsed xenon UV (PX-UV) light versus bleach (after standard cleaning)	Before-and-after quasi-experimental. High-touch surfaces in rooms previously occupied by *C. difficile*-infected patients were sampled after discharge but before and after cleaning using either bleach or nonbleach cleaning followed by 15 minutes of PX-UV treatment. A total of 298 samples were collected using a moistened wipe specifically designed for the removal of spores.	A single major comprehensive cancer center in the United States. The environmental surfaces in 30 *C. difficile* infection isolation rooms were sampled immediately after patients with a CDI were discharged.	Prior to disinfection, the mean contamination level was 2.39 colony-forming units (cfu) for bleach rooms and 22.97 for UV rooms. After disinfection, the mean level of contamination for bleach was 0.71 cfu (p=0.1380), and 1.19 cfu (p=0.0017) for PX-UV disinfected rooms. The difference in final contamination levels between the two cleaning protocols was not significantly different.	Not provided	The current study shows that PX-UV disinfection was equivalent to bleach in decreasing environmental contamination with *C. difficile* spores. PX-UV technology can be easily incorporated into routine environmental decontamination and has a potentially faster turnaround time than either HPV or bleach. Approximately 45 minutes to clean a room with bleach and 15 minutes with PX-UV, resulting in staff savings.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Haas et al., 2014[25]	Ultraviolet environmental disinfection (UVD) following discharge cleaning of contact precautions rooms and other high-risk areas	A retrospective study of the implementation of UVD following discharge cleaning of contact precautions rooms and other high-risk areas. Incidence rates of hospital-acquired multidrug-resistant organisms (MDROs) plus CDI before and during the UVD use were evaluated using rate ratios and piecewise regression. The period before UVD was 30 months (January 2009 to June 2011), and the UVD period was 22 months (July 2011 to April 2013).	A single 643-bed tertiary care academic medical center	The average time per UVD was 51 minutes, and machines were in use 30% of available time. UVD was used 11,389 times; 3,833 (34%) of uses were for contact precautions discharges. UVD was completed for 76% of contact precautions discharges. There was a significant 20% decrease in hospital-acquired MDRO plus CD rates during the 22-month UVD period compared with the 30-month pre-UVD period (2.14 cases/1,000 patient-days vs. 2.67 cases per 1,000 patient days; rate ratio, 0.80; 95% CI, 0.73 to 0.88, p<0.001). CDI before UVD: number, 390, rate, 0.79; CDI after UVD: number, 228, rate, 0.65; rate ratio, 0.83 (0.70 to 0.97) p=0.02.	UVD added an average of 51 minutes per discharge. This time included approximately 31 minutes for arrival, including setup of machine and blackout curtains in areas that had open bays or glass windows and walls. UVD machines were in use for approximately 30% of the total time available.	Facility used bleach-based (sodium hypochlorite 0.55%) disinfectants daily and at discharge for all rooms occupied by adults. In preparation for UVD use. An assessment of the number and timing of contact precautions discharges found the mean rate of contact precautions discharges was 0.87 per hour during peak discharge times of 2 p.m. to 6 p.m. Labor cost and availability should be considered in the budget and implementation plan for UVD. The machines were in use only 30% of the total available time in large part because of labor constraints.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Hacek et al., 2010[26]	Replacing quaternary ammonium compound as a room cleaning agent with diluted bleach (approximate concentration of 5,000 ppm sodium hypochlorite) to disinfect rooms of patients with CDI upon discharge	To determine the effectiveness of this program, rates of nosocomial CDI for all three hospitals were determined using the MedMined Virtual Surveillance Interface for 10 months prior to and 2 years after the cleaning intervention. Statistical significance was determined using Poisson regression analysis.	Three hospitals in a San Diego health system with approximately 850 beds and 40,000 annual admissions	There was a 48% reduction in the prevalence density of *C. difficile* after the bleaching intervention (95% CI, 36% to 58%, p<0.0001).	Not provided	Daily room cleaning routine remained unchanged during the study. The surfaces cleaned in each room remained the same; however, washing the walls was added to the list. Periodic, unannounced cleaning observations also were carried out by the infection control preventionists to assess compliance.	Low	Initiative was response to increase in CDI at three facilities.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Hooker et al., 2015[37]	A washable cover for the mattress and bed deck. The cover is removed and laundered with hot water, chlorine, and detergent. The covers are manufactured using material similar to that found in high-end bed mattresses. They are constructed to allow vapor-moisture transmission.	Two long-term acute-care hospitals (LTACHs) began using a launderable mattress and bed deck cover on beds starting in May 2013. One facility had 74 beds and the other had 30 beds. Covers were changed after every patient. The covers were laundered using hot water, detergent, and chlorine. Rates for CDIs were compared using Poisson regression between the 16 months before use of the washable cover and the 14 months after the cover started being used.	Two LTACHs in Indiana with single-patient rooms	At Hospital A, the use of bedcovers reduced the rate of CDIs by 47.8% (95% CI, 47.1 to 48.6), controlling for the rate of hand washing compliance and length of stay in days. At Hospital B, the use of bedcovers reduced the rate of CDIs by 50% (95% CI, 47.5 to 52.7), controlling for the rate of hand washing compliance and length of stay in days.	Not provided	Article states that after training, all environmental services employees could install the covers in approximately 2 minutes. A new cover was placed after terminal cleaning and patient admission. Although no formal time and motion studies were done, the researchers state that use of the washable covers should improve room turnover times because bed surface is no longer grossly contaminated and time is not needed to remove blood and organic material from the mattress. Could help reduce other healthcare-acquired infections as well.	Low to Moderate Study did not control for anti-microbial use. Strength: Controlled for hand washing.	National Institutes of Health funded

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Kundrapu et al., 2012[44]	Daily disinfection of high-touch surfaces in CDI and MRSA isolation rooms. A peracetic acid-based disinfectant (surface sporicide and disinfectant, branded by STERIS) versus terminal cleaning with bleach.	Quasi-experimental, randomized nonblinded trial. Compared percentage of positive cultures on gloved hands that touched the high-touch surfaces between the standard and enhanced cleaning rooms.	A single site: Cleveland Veterans Affairs Medical Center, a 215-bed hospital with an affiliated long-term care facility	Intervention was associated with a significant reduction in the frequency of acquisition of both pathogens on investigators' hands after contact with the surfaces and in the mean number of colony-forming units acquired. Daily disinfection samples: 0/20 (0%) positive; standard cleaning: 3/28 (11%) samples positive.	Disinfection of high-touch surfaces required about 20 minutes per room.	A peracetic acid-based disinfectant was chosen because preliminary studies indicated that it was as effective as sodium hypochlorite solution but less corrosive and irritating. High-touch surfaces included bed rails, bedside table, call button, telephone, chair, and wall-mounted items.	Low to moderate. Study nonblinded—could impact results. Small sample size. Strength: Similar comparison groups.	Prior to interventions, less than 10% of high-touch surfaces in CDI or MRSA rooms were cleaned daily by housekeepers during the study period. STERIS provided some financial support to the study (in addition to Department of Veterans affairs and AHRQ)

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Levin et al., 2013[28]	Portable pulsed xenon ultraviolet (PPX-UV) light after terminal cleaning (with chlorine-based agents)	During January 2011, the use of two PPX-UV devices to disinfect patient rooms was added to routine hospital discharge cleaning in a community hospital.	Single site: a 140-bed acute care community hospital	In 2010, the hospital-associated (HA) CDI rate was 9.46 per 10,000 patient days; in 2011, the HA CDI rate was 4.45 per 10,000 patient days (53% reduction, $p<0.01$). Previously rates were stable at an average of 9.22 for the years 2008 to 2010 (compared with 2011, 52% reduction; $p=0.002$). The number of deaths and colectomies attributable to HA CDI also declined dramatically.	It should be noted that, of the 15 patients who were diagnosed with HA CDI in 2011, 11 (73%) were placed in rooms that had not been treated with the PPX-UV device prior to occupation. Overall, 56% of discharged rooms received the UV light treatment.	Study used a chlorine-based product (Clorox Clean-up and Clorox Germ Wipes (The Clorox Company, Oakland, CA) in *C. difficile* rooms. This process was followed by the use of PPX-UV, for three 7-minute exposures (once in the bathroom and then in two locations in the main patient room). The overall room turnover time was extended by approximately 15 minutes over a standard terminal cleaning because cleaning could continue in the main room during PPX-UV treatment of the bathroom.	Low	Prior to implementation of PPX-UV, environmental services workers were trained in the use of the device as well as the important role the workers play in preventing illness and death. Although adding PPX-UV to their routine did increase their workload, as a group they felt great pride in being a part of the infection prevention team.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Manian et al., 2013[29]	"Enhanced cleaning" of patient room consisting of use of bleach followed by HPV decontamination. Since not all room could be targeted the intervention included use of a priority scale based on the pathogen and room location. Rooms vacated by patients with CDAD but for which HPV decontamination was not possible the same day underwent four rounds of cleaning with bleach instead.	A retrospective quasi-experimental before-and-after study. The intervention period was January 2009–December 2009, 196,313 patient days. During the pre-intervention period (January 2007 to November 2008), rooms vacated by patients with CDAD or on contact precautions for other targeted pathogens underwent one or more rounds of cleaning with bleach. During the intervention period (January–December 2009), targeted newly evacuated rooms underwent "enhanced cleaning" consisting of use of bleach followed by HPV decontamination using a priority scale based on the pathogen and room location.	A 900-bed community hospital	Of 334 rooms vacated by patients with CDAD (May–December 2009), 180 (54%) underwent HPV decontamination. The nosocomial CDAD rate dropped significantly from 0.88 cases/1,000 patient-days to 0.55 cases/1,000 patient-days (rate ratio, 0.63; 95% CI, 0.50 to 0.79, p<0.0001), a 37% reduction in the CDAD rate following institution of the described intervention.	Not provided	Use of HPV decontamination was found to be safe with no instances of any leakage of HPV outside of sealed patient rooms. The priority scale was developed primarily to help expedite assignment of rooms to HPV.	Low to moderate	Study design did not allow for assessment of the relative contribution of HPV versus four rounds of cleaning.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Miller et al., 2015[35]	PX-UV disinfection system for patient rooms and common areas	Quasi experimental, before and after; two intervention periods. Period one: reinforcement of infection prevention control procedures; Period two: use of UVD.	A single LTACF (bed count not provided)	In period two, CDI rates decreased from period one from 19.3 per 1,000 patient-days to 8.3 per 1,000 patient-days, a 56.9% reduction, p=0.02. Based on these outcomes, it is predicted that the facility was able to prevent 29 HA CDIs and generate over 210 additional patient bed days within the 15-month intervention. Each case results in $13,500 in hospital care costs; therefore, the intervention could have potentially resulted in net savings of approximately $300,000.	Not provided	Prior to UVD, a multidisciplinary *C. difficile* prevention team was formed and there was re-education around hand hygiene for CDI, disposable equipment implemented as well as additional sinks and reminders about equipment decontamination, reinforcement of contact isolation, and a checklist for terminal cleaning. The usage goal across the LTACF included all patient rooms after discharge and communal living areas on a weekly basis, such as dining rooms, rehabilitation areas, and lounges.	Moderate: Unclear if reductions in period two were, at least in part, the carryover result of the practices implement-ed in period one.	After discharge, rooms and bathrooms were terminally cleaned with a sodium hypochlorite solution.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Mosci et al., 2017[39]	Automated disinfection system with hydrogen peroxide <0.8 solution and silver ions versus bleach	A randomized multicenter trial. When patients with *C. difficile* were discharged, their rooms were randomized to one of two decontamination arms. The surfaces were sampled using swabs, before and after disinfection. Swab samples were cultured for quantitative detection of microbial mesophilic contamination and qualitative detection of *C. difficile*. 448 samples taken.	Hospital wards that had been occupied previously by patients with CDI; 28 hospital rooms across several hospitals	Hydrogen peroxide versus bleach. The difference in the overall reduction of contaminated rooms due to hydrogen peroxide and silver ions and sodium hypochlorite was not statistically significant (p=0.497), but a significant reduction after disinfection was noted in both groups. However, the disinfection with hydrogen peroxide and silver ions is preferable due to less dependence on operators.	Not provided	The complexity of environmental surfaces in healthcare facilities has increased and cleaning is highly operator dependent. A new technology is the use of hydrogen peroxide atomized by specific equipment, with associated silver compounds; however, this can only be used in vacated rooms, and total time for disinfection is roughly the same. Hydrogen peroxide and silver ion disinfection greatly reduces the environmental impact.	Low to moderate	No clinical outcomes—swabs taken from the environment. The most contaminated sites were the light and nursing call devices and the horizontal surface of the bedside table.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Nagaraja et al., 2015[36]	Terminal cleaning with PX-UVD in addition to standard cleaning	Pre/post intervention. This study compares a pre-UVD period (May 1, 2010, to April 30, 2011) with the UVD period (July 1, 2011, to June 30, 2012) for total CDI rates, hospital-acquired CDI rates, length of stay, and room occupancy. Pre-UVD was 139,677 patient-days and intervention was 132,574 patient-days.	ICU with 180 beds (The intensive care unit is a referral center for highly immune-compromised patients).	Compared with pre-UVD, during UVD, hospital-acquired CDI was 22% less (p=0.06). There was a 70% decrease for the adult ICUs (p<0.001), where the percentage of room discharges with UVD was greater (p<0.001). No significant difference was found in days to hospital-acquired CDI in rooms with a prior CDI occupant.	Oncology and pediatric rooms CDI rates increased.	Due to environmental contamination with *C. difficile* and cleaning performance variability, disinfection procedures that do not depend solely on individual practice are being used. Logistical barrier: the UV light is not effective at killing bacteria at greater distances (over 1.22 m).	Moderate. In some cases, during the intervention period, UVD was not applied due to logistical and other issues. Single site. Confounder: change to new environ-mental services company.	UVD machines cannot be used in occupied rooms. Evaluation of UVD should include data for hospitalized community-acquired CDI cases because these cases may impact the HA-CDI rate.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Orenstein et al., 2011[27]	Daily and terminal cleaning with germicidal bleach wipes (0.55% bleach) on wards with a high incidence of HA CDI	Quasi-experimental, pre/post-intervention measures. From August 1, 2008, through August 1, 2009, all rooms were cleaned daily and at hospital discharge with a quaternary ammonium compound. Intervention: From August 2, 2009, through July 31, 2010, housekeepers replaced this product with Clorox brand germicidal bleach wipes with 0.55% active chlorine.	Two medical units at a 1,249-bed hospital in Rochester, Minnesota. These units were selected because they were contiguous and had high endemic CDI incidence.	The intervention reduced HA-CDI incidence by 85%, from 24.2 to 3.6 cases per 10,000 patient-days ($p<0.001$) and increased the median time between HA-CDI cases from 8 to 80 days. Twenty-seven cases of HA CDI were prevented in this study. The incremental cost of an HA CDI is estimated to be between $5,000 and $8,000. Thus, between $135,000 and $216,000 of excess costs may have been averted by these simple measures.	All rooms were cleaned daily with bleach, regardless of whether the occupant had CDI. The process added little extra time to the housekeepers' daily routine.	Even though terminal cleaning with bleach has shown to be effective, because a substantial reservoir of colonized patients or asymptomatic carriers may not be in isolation, the researchers believe that *daily* cleaning may be more effective than discharge-only cleaning.	Low to moderate. Weak-nesses: Single site, unblinded Strength: Control for confounders	During the study, 444 buckets of bleach wipes were used at an annualized cost of $12,684. The bleach was allowed to dry to achieve the recommended 10-minute contact time to inactivate *C. difficile* spores.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Vianna et al., 2016[34]	PX-UV system for disinfecting all discharges and transfers after standard cleaning and prior to occupation of the room by the next patient. For all non-ICU discharges and transfers, the PX-UV system was only used for *Clostridium difficile* rooms	The intervention period was compared with baseline using a two-sample Wilcoxon rank-sum test. Beginning in November 2012, a PX-UV disinfection system was implemented as an adjunct to traditional cleaning methods on discharge of select rooms. PX-UV disinfection was implemented in >200 patient rooms per month from November 2012 to August 2014 (>4,400 rooms total) and compared with January 2011 to October 2012.	A single community hospital with 126 medical-surgical beds. The facility also houses an 80-bed psychiatric care unit.	A significant 29% facilitywide decrease in all three MDROs (*C. difficile*, MRSA, and VRE) was determined (p=0.01), statistically driven by a 41% decrease in *C. difficile* infection (p=0.01). In the ICU alone, all three infection types similarly experienced significant reductions (p=0.01) together. However, changes in VRE incidence was only statistically significant alone (p=0.01). Nonetheless, *C. difficile*, MRSA, and VRE rates decreased by 45%, 56%, and 87%, respectively. On all other non-ICU floors combined, only a 40% change in *C. difficile* infections alone was significant (p=0.04).	Not provided	According to the study, the difference in infection rates for the ICU compared with the non-ICU areas demonstrated the increased risk of infection in the ICU and the leverage that ICU-based interventions can have on facilitywide rates. Recommended PX-UV in an area of higher acuity and patient flow. A novel aspect of this study is that it examines two different deployment strategies for UVD: using UVD for every terminal discharge on a unit and for *C. difficile* isolation rooms only.	Low to moderate. Single site. An anti-microbial stewardship program was initiated in January 2012 (11 months before the ultraviolet device was introduced); and other confounders could have also influenced results.	None

Table B.23: Clostridioides *difficile*, Environmental Cleaning–Systematic Reviews

Note: Full references are available in the Section 4.3 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of SR Findings	Implementation Themes/Findings	Notes
Khanefer et al., 2015[30]	Environmental cleaning/ disinfection	Hospitals	Studies published between 1982 and December 2013 were reviewed. Nine studies on environmental cleaning/disinfection; most were part of bundles. The frequency of room disinfection varied depending on the study, being performed daily or on discharge. A significant decrease in CDI rate was observed after replacement of quaternary ammonium compound with bleach in highly endemic wards. The effect was more significant when bleach was used daily (85% vs. 47%). Compliance with recommended procedures should be monitored routinely. Checklists to instruct housekeepers on the cleaning sequence should be promoted. Moreover, education, implementation of standardized processes, and direct interaction with or immediate feedback to domestic staff are all interventions that have been reported to improve the efficiency of disinfection of contaminated surfaces. No-touch methods have good outcomes but high cost and turnaround times.	Disinfection with 1:10 hypochlorite solution is practical and inexpensive. It is challenging to develop a sporicidal and practical disinfectant for a wide variety of surfaces that is sufficiently nontoxic for routine application. A comparison of clinical and cost-effectiveness of eight *C. difficile* environmental disinfection methods has shown that the cheaper tradition of disinfection with a chlorine-releasing agent is as effective as modern techniques.	None

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of SR Findings	Implementation Themes/Findings	Notes
Louh et al., 2017[24]	Environmental cleaning. Recommend: Daily to twice daily cleaning of high-touch surfaces and terminal cleaning of patient rooms using chlorine-based products	Acute care hospitals	Systematic search for controlled trials of interventions to reduce the rate of CDI in acute care hospitals. Searched for articles published between January 1, 2009, and August 1, 2015. The five studies on environmental disinfection used a variety of interventions: daily bleach disinfection with auditing, terminal room disinfection with hydrogen peroxide vapor, terminal room UV treatment, and complete surface terminal bleach disinfection. Daily and terminal disinfection of the patient room with bleach-containing products in conjunction with auditing led to significant reduction in CDI. Terminal cleaning with UV light in addition to bleach cleaning had uncertain efficacy. Study quality weak. In the review of the recent CDI prevention studies performed in acute care hospitals, bleach-based environmental disinfection and bundled interventions appeared to have the most effect in preventing CDI. Bundled interventions with environmental efforts appeared to be more effective than those without them.	Institutions with few resources should strive to improve environmental practices, with implementation of bleach-based cleaning. Institutions with more resources should consider bundled interventions that incorporate environmental cleaning, restrictive ASPs, and checklists.	Review covers multiple PSPs. Environmental cleaning findings are summarized in this table. Environmental cleaning (daily/terminal with bleach) is found as most effective PSP of the five PSPs reviewed.
McLeod-Glover and Sadowski, 2010[17]	Cleaning products for *C. difficile*	Hospitals and inpatient rehabilitation care	Review of articles pertinent to the efficacy of cleaning products against *C. difficile* or studies with outcomes related to rates of CDAD. Evidence was level II. Evidence to support decision making about the use of environmental cleaners is weak. Search yielded nine studies and one research letter describing research into the efficacy of cleaning products against *C. difficile* spores. Chlorine-releasing agents are more effective than detergents for killing spores produced by *C. difficile*. No level I evidence is available to determine if the use of chlorine-releasing agents has an effect on rates of CDAD. Of interest is the effect of subinhibitory levels of cleaning agents on the sporulation capacity of *C. difficile*. One study showed that exposure to low levels of cleaning agents resulted in higher sporulation capacity compared with no exposure to cleaning agents, suggesting that sporulation capacity might increase in response to environmental stresses such as cleaning.	Hydrogen peroxide and peracetic acid had mixed results. Detergent alone or 70% isopropyl alcohol showed no benefit. Although chlorine-releasing agents are more effective for killing spores than detergents are in the laboratory setting, efficacy related to reducing levels of spores in the environment or rates of CDAD in the hospital has not been consistently shown.	None

Table B.24: Clostridioides *difficile,* Surveillance–Single Studies

Note: Full references are available in the Section 4.4 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Albert et al., 2018[32]	Reporting cases of healthcare facility-onset CDI (HO CDI) using the National Healthcare Safety Network (NHSN) CDI laboratory-identified (LabID) event definition.	Assessment of accuracy of facility reporting of HO CDI to NHSN. Retrospective chart review was performed on 212 NHSN LabID HO-CDI cases. The electronic medical record for each case was reviewed for various clinical events that contributed to *C. difficile* testing. The presence of fever, abdominal pain, and diarrhea was recorded from each case along with the timing and duration of symptoms.	A large urban medical center	Not provided	Study found only 62% of reported HO-CDI cases met clinical surveillance criteria. Of the reported HO-CDI cases, review of charts found that 13.6% were CA-CDI, 2.8% were recurrent, 1.9% were asymptomatic colonization, 18.4% were symptomatic colonization, 38.7% were possible HO CDI, and 24.5% were probable HO CDI. Within 24 hours of testing, 34.1% had received a stool softener and/or laxative.	Laxative use and failure to identify community-onset infection may contribute to misclassification of HO CDI. Many reported HO-CDI cases involved patients with underlying medical conditions that may mimic symptoms of CDI, highlighting challenges in distinguishing colonization from active disease. Of the reported HO-CDI cases, 103 had documentation of inflammatory bowel disease, chemotherapy, tube feedings, or gastrointestinal bleeding.	Moderate—small sample; chart review is imperfect.	Study about errors in classification / reporting of CDI to NHSN. An intervention was not tested.
Benoit et al., 2011[29]	Electronic laboratory and admission-discharge-transfer data from BioSense, a national automated	Retrospective, multi-center cohort study; validation of surveillance system by comparison with other widely accepted	Thirty-four hospitals sending inpatient emergency department and/or outpatient	Electronic laboratory data sent to the BioSense surveillance system were successfully used to produce disease rates of CDI comparable to those	Not provided	Laboratory codes and text-parsing methods were used to extract *C. difficile*–positive toxin assay results from laboratory data sent to BioSense from January 1, 2007, through June	Low. Did not include CO CDI, because data were limited to certain health	BioSense is a national automated surveillance system operated by the Centers for Disease

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	surveillance system. A total of 4,585 patients from 34 hospitals in 12 States had *C. difficile*–positive assay results.	surveillance results.	data to BioSense.	of other studies, which shows the feasibility of using electronic laboratory data to track a disease of public health importance. More than half (53.0%) of the cases were CO CDI, and 30.8% of these occurred in patients who were recently hospitalized. The overall rate of HO CDI was 7.8 cases per 10,000 patient-days, with a range among facilities of 1.52 to 7.8 cases per 10,000 patient-days.		30, 2008; these were merged with administrative records to determine whether cases were community-associated or healthcare onset. Although hospitals incur initial costs in capturing electronic data, the data are useful for tracking many diseases other than CDI. Few hospitals had LOINC- or SNOMED-coded laboratory test and result data, which emphasizes the need for widespread adoption of standard vocabularies to facilitate public health use of electronic data.	systems. Variability across hospitals in CDI onset type. The electronic data that were analyzed were not validated by comparison with hospital records.	Control and Prevention (CDC) that receives, analyzes, and visualizes electronic health data for public health use.
Dubberke et al., 2012[28]	Automated surveillance algorithm using electronically available data based on recommended surveillance definitions (Surveillance Definitions from CDC 2007)	Validation of an automated CDI surveillance algorithm, comparing the algorithm with chart review. A second chart review was performed for discordant results and determined to be the gold standard (the correct categorization). The study population	Four CDC Prevention Epicenter hospitals	A total of 1,767 patients had a positive *C. difficile* toxin test. Of these, 440 were CDI cases that the automated and chart review surveillance classified differently. The discordant cases were re-reviewed. The overall sensitivities, specificities, and kappa values of the algorithm by CDI onset compared with the gold	The algorithm did not have good agreement with chart review for hospital-onset CDI for hospital B. Community-onset and other healthcare facility–associated CDI showed a wide range of sensitivities (16% to 96%) and kappa values (0.25 to 0.93).	Previous research indicates electronic surveillance is more accurate and reliable than manual surveillance. Automated surveillance also requires less time, as it eliminates the need to do chart review, potentially allowing infection preventionists to devote more time to infection prevention efforts. Each hospital had to individualize the	Low to moderate. Each hospital had different data available. For example, Hospitals A, B, and C did not have discrete data on where a patient was	Study found that electronic surveillance performed better than chart review in identifying the types of onset of CDI.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
		included all adult patients ≥ 18 years of age admitted to four U.S. hospitals from July 1, 2005 to June 30, 2006. 1,767 patients with stool positive for *C. difficile* toxins were identified.		standard: hospital onset: 92%, 99%, and 0.90; community onset, study facility–associated: 91%, 98%, and 0.84; community onset, other healthcare facility–associated: 57%, 99%, and 0.65; community onset, community associated: 96%, 94%, and 0.69; indeterminate cases: 80%, 98%, and 0.76; and recurrent cases: 94%, 99%, and 0.94.	Similar trends were seen for community-onset, community-associated, and indeterminate CDI.	algorithm to their facility. Electronic surveillance requires access to an electronic health record (EHR) system.	admitted from (e.g., admitted from home, long-term care facility), whereas hospital D did.	
Dubberke, 2010[35]	ICD-9 code-based hospital-onset *Clostridium difficile* infection surveillance	Validation of ICD-9 codes for CDI surveillance (by comparison with toxic assay results). HO-CDI cases were identified at five U.S. hospitals between July 2000 and June 2006 using two surveillance definitions: positive toxin assay results (gold standard) and secondary ICD-9 diagnosis codes for CDI.	Five U.S. academic medical centers—MO, MA, OH, UT, IL. All study hospitals participated in the CDC Epicenter Program.	Of 8,670 hospital-onset CDI cases, 38% were identified by both toxin assay and ICD-9 code, 16% by toxin assay alone, and 45% by ICD-9 code alone. Nearly half (47%) of CDI cases identified by ICD-9 code alone were community-onset cases by toxin assay. The hospital-onset CDI rate was significantly higher by ICD-9 codes compared with toxin assays overall (p <0.001), as well as	Although ICD-9 codes appear to be adequate for measuring the overall CDI burden, use of the *C. difficile* ICD-9 code without present-on-admission classification is not an acceptable surrogate for hospital-onset CDI surveillance.	While ICD-9 codes may be an adequate surrogate for tracking the overall CDI burden, they may be less useful for tracking HO-CDI incidence compared with toxin assay results. In the future, present-on-admission codes—which became mandatory for Medicare patients discharged on or after October 1, 2007 (i.e., after the study period)—may add precision to ICD-9 code-based CDI surveillance. These codes might provide a	Low	ICD-9 codes significantly overreported the incidence of hospital-onset CDI compared with toxin assay results, and the degree to which this happened varied by year and by hospital.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
		Chi-square tests were used to compare incidence rates, linear regression models were used to analyze trends, and the test of equality was used to compare slopes. A total of 930,692 hospital discharges during the 6-year study period.		individually at three of the five hospitals ($p < 0.001$ for all). The agreement between toxin assays and ICD-9 codes was moderate, with an overall kappa value of 0.509 and hospital-specific kappa values that ranged from 0.489 to 0.570. Overall, the annual increase in CDI incidence was significantly greater for rates determined by ICD-9 codes than by toxin assays ($p=0.006$).		mechanism to distinguish pre-existing conditions, and ultimately reduce misclassification of community-onset CDI cases. Discharge diagnosis codes reflect conditions diagnosed or treated during the entire admission, but do not give information regarding the location or date of CDI onset.		
Durkin et al., 2015[31]	National Healthcare Safety Network (NHSN) reporting of laboratory identified (LabID) *Clostridium difficile* infection (CDI) versus traditional surveillance methods. LabID: designed to use electronically captured laboratory data	Validation of LabID surveillance using a cohort study. A period of 6 months (January 1, 2013, to June 30, 2013) of prospectively collected data using both LabID and traditional surveillance definitions. A total of 1,252 incident LabID CDI events were identified during 708,551 patient-days. CDI events with	A cohort of 29 community hospitals in the south-eastern United States	A total of 1,252 incident LabID CDI events were identified during 708,551 patient-days; 286 (23%) mismatched CDI events were detected. The overall HO-CDI rate was 6.0 versus 4.4 per 10,000 patient-days for LabID and traditional surveillance, respectively ($p < 0.001$); of 29 hospitals, 25 (86%) detected a higher	Hospital rank in the cohort differed greatly between surveillance measures. A rank change of at least five places occurred in 9 of 28 hospitals (32%) between LabID and traditional CDI surveillance methods.	LabID surveillance resulted in a higher hospital-onset CDI incidence rate than did traditional surveillance. Hospital-specific rankings varied based on the HO-CDI surveillance measure used. A clear understanding of differences in CDI surveillance measures is important when interpreting national and local CDI data. Hospitals that adopt the LabID surveillance method should expect	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	and hospital admission dates to determine hospital-onset (HO) versus community-onset (CO) surveillance categories.	mismatched surveillance categories between LabID and traditional definitions were identified and characterized further. Hospital-onset CDI (HO-CDI) rates for the entire cohort of hospitals were calculated using each method, then hospital-specific HO-CDI rates and standardized infection ratios (SIRs) were calculated. Hospital rankings based on each CDI surveillance measure were compared.		CDI rate using LabID compared with the traditional method.		to observe higher HO-CDI incidence rates than with traditional surveillance. Mismatched cases between LabID and traditional surveillance that are due to delays in diagnostic testing may potentially penalize hospitals on publicly reported SIR measures.		
Faires et al., 2014[24]	Outbreak investigation using the temporal scan statistic in a hospital	Case study. For patients detected with CDI from March 2010 to February 2011, stool specimens were obtained. *Clostridium difficile* isolates were characterized by ribotyping and investigated for the presence of toxin genes by	A Canadian hospital	Overall, 86 CDI cases were identified. Eighteen specimens were analyzed and nine ribotypes were classified, with ribotype 027 (n=6) the most prevalent. The temporal scan statistic identified significant CDI clusters at the hospital (n=5), service (n=6), and	Not provided	Application of the temporal scan statistic identified several clusters, including potential outbreaks not detected by hospital personnel. The identification of time periods with decreased or increased CDI rates may have been a result of specific hospital events. Understanding the clustering of infectious diseases,	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
		PCR. CDI clusters were investigated using a retrospective temporal scan test statistic. Statistically significant clusters were compared with known CDI outbreaks within the hospital. A negative binomial regression model was used to identify associations between year, season, month, and rate of CDI cases.		ward (n=4) levels ($p \leq 0.05$). Three clusters were concordant with the one *C. difficile* outbreak identified by hospital personnel. Two clusters were identified as potential outbreaks.		spatially or temporally, can help identify risk factors, facilitate detailed investigations to determine the association between exposures and disease interventions, and detect outbreaks. A commonly used statistical technique to detect disease clusters, the scan statistic has been used to investigate a wide array of infectious diseases or pathogens.		
Gase et al., 2013[30]	NHSN surveillance versus clinical infection surveillance	30 facilities collected 6 months of data using a clinical infection surveillance definition, while also submitting the NHSN LabID event for CDI. The datasets were matched and compared to determine whether the assigned clinical case status matched the LabID case status. A subset of mismatches was	30 New York State acute care hospitals	A total of 3,301 CDI cases were reported. Analysis of the original data yielded a 67.3% (2,223/3,301) overall case status match. After review and validation, there was 81.3% (2,683/3,301) agreement. The most common reason for disagreement (54.9%) occurred because the symptom onset was less than 48 hours after admission but the positive	Not provided	Use of the NHSN LabID event minimizes the burden of surveillance and standardizes the process. With a greater than 80% match between the NHSN LabID event data and the clinical infection surveillance data, the New York State Department of Health decided to use the NHSN LabID event CDI data for public reporting purposes.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
		evaluated further, and reasons for the mismatches were quantified.		specimen was collected on hospital day 4 or later. The NHSN LabID hospital-onset rate was 29% higher than the corresponding clinical rate.				
Hardy et al., 2010[22]	Use of measure of period of increased incidence (PII) to identify clusters and trigger interventions	Case study. Observational 18-month study of 102 PIIs involving 439 patients. For January 2008 to September 2008, multiple interventions were implemented, with PCR ribotyping of isolates being carried out on those PIIs with more than 10 cases. From October 2008 to July 2009, isolates from all PIIs were ribotyped 9. A PII was classified as an outbreak of CDI if there were two or more cases of the same PCR ribotype within a 28-day period.	A large teaching hospital with a total of 1,800 beds at three different sites	During roughly 1.5 years of the intervention, the number of PIIs investigated per month decreased, from a peak of 14 per month in February 2008 to 1 in June 2009. In the first 9 months of the study, isolates were ribotyped on those PIIs with more than 10 cases; for the last 8 months of the study, isolates were ribotyped for all PIIs. In this case, an outbreak was defined as two or more cases of the same PCR ribotype within a 28-day period. In the final 8 months, ribotyping of the isolates confirmed nine (32%) of these PIIs to be outbreaks, with three being due to ribotype 027, two	Not provided	The current study aimed to preempt and prevent outbreaks of CDI from becoming established, as opposed to being reactive and trying to control CDI once an outbreak was evident. The early identification and notification of PIIs enabled actions to be prompt and targeted. The authors postulate that concentrating on selected PII wards reduced the potential environmental sources of CDI transmission to the rest of the hospital.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
				to ribotype 078, and all the others being distinct ribotypes.				
Jones et al., 2012[37]	ICD 10 data for CDI surveillance	Evaluation of ICD-10 codes for CDI surveillance. Retrospective data analysis; during 2000–2010, 317,040 hospitalizations. Laboratory results and/or the ICD-10 code for *C. difficile* infection were positive for 698 cases.	A 750-bed university-affiliated public hospital in Paris	Sensitivity of the ICD-10 code, with laboratory results as the standard, was 35.6% (95% CI, 31.9 to 39.5), and specificity was 99.9% (95% CI, 99.9 to 100.0). The positive and negative predictive values were 79.2% (95% CI, 73.9 to 83.7) and 99.9% (95% CI, 99.8 to 99.9).	The sensitivity of ICD-10 codes in this study is inferior to that of values previously reported in the United States (71%–78%) and in Singapore (49.6%).	Compared with use of laboratory results, use of ICD-10 codes to estimate incidence of *C. difficile* infection resulted in underestimates. The relationship between methods for yearly incidence during the 11-year period was strong. Low sensitivity could be due to poor coding.	Low	None
Lavan et al., 2012[23]	Monitoring CDI in an acute hospital with limited resources/ technology: prevalence or incidence studies?	Comparison of two CDI surveillance methods (incidence and prevalence). Prevalence of CDI, antibiotic use, and associated co-morbidity was assessed weekly on two wards over 6 weeks. In addition, CDI incidence surveillance was performed on all new CDI cases over a 13-week period. Cases	Two wards in an acute hospital, Ireland	*Clostridium difficile* infection prevalence was 3.5% (range 2.9% to 6.1%) on the medical ward and 1.1% (range 0 to 3.5%) on the surgical ward. In the context of the study, it took, on average, 25 minutes per ward per week to measure prevalence. The workload to calculate incidence amounted to an average of 2.15 hours per day in the current study and depended on the	Not provided	The studies were done without sophisticated technology—case counting and Excel spreadsheets were used. CDI prevalence surveillance gives a broad overview of CDI, and pointed to areas that required more-detailed surveillance and required little time. However, patient-based CDI incidence surveillance provided a more useful analysis of CDI risk factors, disease, and outcomes for planning preventive programs and focusing	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
		were assessed for CDI risk factors, disease severity, response to treatment, and outcome at 6 months. A prospective Microsoft Excel database was created. Fisher's test was used for comparisons between count data, and continuous variables were assessed with two-sample t-test or Mann–Whitney test for nonparametric data.		number of ongoing cases. In contrast to the prevalence study, the incidence study was able to provide data on risk factors, symptoms, treatment, and patient outcomes.		antibiotic stewardship efforts.		
Quan et al., 2015[12]	A system for MDROs and *C. difficile* tracking that automated the following three main surveillance and tracking activities: monitoring microbiology results and initiation of chart-based flags, ordering contact precautions on admission, and	Quasi-experimental before-and-after study. In 2012, the system automatically reviewed daily positive laboratory results for 110,212 patient-days and cross-checked these results with historical MDRO and *C. difficile* flags, to determine whether 2,375 positive results	A 410-bed tertiary care academic medical center	Automation saved 43 infection preventionist hours per 1,000 admissions (850 hours of infection preventionist time annually). It also saved previously unquantified hours spent reviewing MDRO history for every admission. Automatic retiring of certain MDRO flags ensured removal of contact precautions after a specified	Not provided	Automated tracking useful for determining when to start/ discontinue contact precautions/ put patients in single person rooms. When the EHR system detected a finalized positive laboratory test result, it automatically checked whether an organism-specific flag was already present and added the flag if needed. For *C. difficile* specifically, because precautions are based	Low to moderate	Automated ordering prevented missed precautions, which might be caused by errors, such as admitting providers not noticing a flag, or healthcare workers missing history of infection on

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	ensuring appropriate removal of precautions.	represented incident cases.		time. A point-prevalence assessment of eligibility for discontinuation found that all precautions were appropriate, with none of them eligible for removal.		on diarrheal symptoms, any readmission within 60 days of an initial flag resulted in an automated order for precautions. Discontinuation criteria were displayed for review when physicians attempted to discontinue a precaution order.		manual review.
Saeed et al., 2018[18]	*Clostridium difficile* multidisciplinary team root cause analysis (MDT-RCA) (vs. on-the-spot investigation) of a breached case	Investigation of the financial impact of MDT-RCAs to the Trust. Methodology: over 2 years, the MDT-RCA forum reviewed 84 hospital-onset CDI cases. HFT serves a population of approximately 600,000.	Three hospitals in UK totaling over 850 beds	In total, 543 staff attended the MDT-RCAs at a potential cost to the Trust of £23,795.74 to £51,670.10. Over 24 months, the Trust had appealed against financial penalties for 27 cases, and 14 appeals were successful. This suggests that £140,000 would have been avoided had 14 cases not breached hospital CDI case targets. (Hospital groups, i.e., trusts, are required to demonstrate year-on-year reductions in CDI cases. Breaches of *C. difficile* targets—in this case, 37 cases for the first year—	In the end, targets were breached by only two cases, meaning £20,000 in fines was avoided. Deducting this from the total costs of the MDT-RCA meant the Trust lost £3,795.74 to £31,670.	Over the 2 years reviewed, the MDT-RCA proved to be costly to the Trust, with "no additional learning or quality improvement measures identified." Key learning themes from the 84 cases: the delay in isolating symptomatic patients and the delay in sending stool samples to the laboratory. Concerns were also raised with lack of documentation, such as the clinical and nursing teams not completing the *C. difficile* care pathway and diarrhea and vomiting risk assessment. One possible benefit of the MDT-RCA meetings may have been heightening the awareness of CDI	Low to moderate	Touches on issues of financial penalties for "preventable" CDI cases. Article is about financial implications of RCA specific to the commission-ing groups in the UK.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
				incur financial penalties to the Trust to the value of £10,000 per case.) After the appeal, only two cases breached the threshold.		among staff that attended.		
Schlackow et al., 2012[41]	Biomarker-based surveillance: automated electronic systems providing early warning of the changing severity of infectious conditions. Iterative sequential regression (ISR)-based severity monitoring.	Assessed the generalizability of ISR-based severity monitoring. Study of 5,551 toxin-positive and 20,098 persistently toxin-negative patients tested for CDI between February 1998 and July 2009, in a group of hospitals. Investigated 28-day mortality and biomarkers of inflammation collected at diagnosis using ISR, a novel join point-based regression technique. Assessed the generalizability of ISR-based severity.	A group of UK hospitals	ISR-based severity monitoring allowed the detection of the severity change years earlier than mortality monitoring. Among *C. difficile* toxin-positive patients in the Oxford hospitals, mean neutrophil counts on diagnosis increased from 2003, peaked in 2006–2007, and then declined; 28-day mortality increased from early 2006, peaked in late 2006–2007, and then declined. Molecular typing confirmed these changes were likely due to the ingress of the globally distributed severe *C. difficile* strain, ST1. Strong associations found between isolation of the ST1 severe strain and	One concern is feasibility. The samples used to predict severity were routinely collected and came from inpatients. Although in many hospitals in high-income countries, such samples are taken in most admissions, this may not be the case in lower resourced settings.	General methods of detecting changing virulence that would permit early recognition and control, and optimal management of such threats, would be highly desirable. The studied method requires that there be at least one routinely collected biomarker associated with disease-related mortality for each target condition. Researchers envisage that initially a number of potential severity markers could be investigated for each infection—retrospectively, using historical data if available, or prospectively, based on routine electronic databases. Comparing historical data with mortality retrospectively, and/or investigating any ‘‘signals’’ prospectively,	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
				higher neutrophil counts at diagnosis in two unrelated large multi-center studies. Similar trends were		would identify which biomarkers were most useful for passive severity monitoring.		
Schmiedeskamp et al., 2009[36]	Use of ICD-9 codes and use data to identify nosocomial CDI (vs. ICD-9 code alone)	Validation sample cross-sectional study. Laboratory and medical records were queried to identify symptomatic CDI toxin–positive adult patients with nosocomial CDI and were compared with records of patients whose cases were predicted to be nosocomial by means of ICD-9-CM code and CDI therapy data. Administrative claims data from July 1, 2004, to June 30, 2005, were queried. Population/sample size: 23,920 adult patients discharged from the hospital.	An academic health center in Virginia	The sensitivity of the ICD-9-CM code alone for identifying nosocomial CDI was 96.8%. The specificity was 99.6%, the positive predictive value was 40.8%, and the negative predictive value was 100%. When CDI drug therapy was included with the ICD-9-CM code, the sensitivity ranged from 58.1% to 85.5%, specificity was virtually unchanged, and the range in positive predictive value was 37.9% to 80.0%.	Combining the ICD-9-CM code for CDI with drug therapy information increased the positive predictive value for nosocomial CDI, but decreased the sensitivity.	Beginning October 1, 2008, the Centers for Medicare & Medicaid Services required hospitals to indicate which diagnoses were present on admission. The method proposed in this investigation should be useful to help determine the post-admission day that nosocomial CDI became evident. A limitation in using ICD-9-CM codes to identify CDI is the inability to determine which cases are nosocomial, because ICD-9-CM codes are assigned to all patients with CDI at any time during hospitalization.	Low to moderate	The purpose of this study was to determine whether combining the ICD-9-CM code with medication treatment data for CDI in hospitalized patients could be used to distinguish between patients with nosocomial CDI and patients who were admitted with CDI.
Truong et al., 2017[33]	Real-time electronic tracking of diarrheal episodes and	A quasi-experimental study from June 22, 2015, to June 30, 2016, on	An academic hospital	Use of *C. difficile* testing decreased upon implementation from an average of 208.8	Not provided	Real-time electronic clinical data tracking is an effective tool for verification of *C. difficile* clinical testing	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	laxative therapy for verification of *Clostridium difficile* clinical testing criteria	consecutive inpatients with *C. difficile* test orders; 2,321 cancelled *C. difficile* test orders		tests to 143.0 tests per 10,000 patient-days (p<0.001). HO-CDI incidence rate decreased from an average of 13.0 cases to 9.7 cases per 10,000 patient-days (p=0.008).		criteria and safe reduction of inflated HO-CDI rates. Oral vancomycin days of therapy decreased from an average of 13.8 days to 9.4 days per 1,000 patient-days (p=0.009). Clinical complication rates were not significantly different in patients, with 375 canceled orders, compared with 869 episodes with diarrhea but negative *C. difficile* results.		
Wilcox, et al., 2012[39]	Enhanced surveillance in England using the *Clostridium difficile* Ribotyping Network	Case study/system evaluation. Criteria used to assess the service include investigation of increases in the frequency of CDI cases (or high baseline rates) and increased severity, recurrence, complications, or mortality associated with CDI. A standardized request form for clinical and epidemiological data is used and	Regional, UK	Overall in England, mortality decreased, as did CDI incidence. In the first 3 years (2007 to 2010), the CDRN service processed 12,603 fecal specimens for culture and ribotyping. The average proportion of patients in England with reported CDI from whom samples were sent for ribotyping over the whole analysis period (2007 to 2010) was 10.8%. The reasons cited by requestors for referral to CDRN	Not provided	Access to CDRN ribotyping is limited to several regional microbiology laboratories in England, which aim to provide timely access to *C. difficile* culture and ribotyping according to standardized criteria for submission of fecal samples. The target turnaround time for delivery of ribotyping results, is <2 weeks. There was a 61% reduction in reports of *C. difficile* in England (36,095, 25,604, and 21,698 in 2008 to 2009, 2009 to 2010, and 2010 to 2011, respectively). The reduction was	Low to moderate	Responding to a national public health need, the Health Protection Agency created the CDRN for England, as part of an enhanced surveillance program for *C. difficile* in 2007.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
		is available via a web-based electronic requesting (and reporting) portal.		did not change over this time: case clusters (46% to 55%); unexplained increase in CDI rate (12% to 13%); and increased severity of symptoms (10% to 13%).		coincident with the control of the epidemic *C. difficile* ribotype 027, which accounted for 55%, 36%, and 21% of samples submitted to CDRN in 2007 to 2008, 2008 to 2009, and 2009 to 2010, respectively.		

Table B.25: Clostridioides *difficile*, Surveillance–Systematic Reviews

Note: Full references are available in the Section 4.4 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Goto et al., 2014[20]	Administrative Code Data (ACD) for surveillance ACD include International Classifications of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes.	General healthcare	This systematic review summarizes evidence for the accuracy of ACD for the detection of selected HAIs and includes a meta-analysis for surgical site infections (SSIs) and CDIs, where acceptable numbers of primary studies were available. For these two conditions, ACD have moderate sensitivity and high specificity, but evidence for detection of other HAIs is limited. With current low prevalence of HAIs, the positive predictive value of ACD algorithms would be low. ACD may be inaccurate for detection of many HAIs and should be used cautiously for surveillance and reporting purposes. The systematic literature review included 19 studies. Of those included studies, seven (five in the U.S.) reported results for CDI. When these parameters were applied to currently reported incidence of CDI (8.75 per 1,000 discharges) in U.S. acute care hospitals, estimated positive predictive value (PPV) was 87.0% (95% CI, 66.2 to 100), and estimated negative predictive value (NPV) was 99.7% (95% CI, 99.6 to 99.9). This systematic review found that ACD detect CDI and SSI with moderate sensitivity and high specificity compared with traditional surveillance.	These findings suggest that ACD may be useful as part of algorithmic automated HAI surveillance but should not be the sole primary case finding method in hospital performance measurement or epidemiologic research. The moderate sensitivity for CDI and SSI means that ACD may miss important cases of HAI. In addition, the relatively low prevalence of HAIs will limit the positive predictive value of ACD, despite their moderate sensitivity and high specificity. Thus, as increasing attention is paid to HAI prevention, lower infection incidence in the future with the accompanying lower PPVs will further compromise the utility of ACD.	According to article, the major limitations of ACD are that they were developed for the entirely different purpose of billing, and their coding criteria may differ from public health surveillance definitions. Also, coding for billing generally focuses on physician documentation and provided care, rather than clinical information of the patient's status.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Krutova et al., 2018[21]	Key components of surveillance for CDI	Acute care hospitals in Europe	The review provides a summary of components of CDI surveillance and includes suggestions. According to the review, the key components for CDI surveillance are appropriate case definitions of CDI, standardized CDI diagnostics, agreement on CDI case origin definition, and presentation of CDI rates with well-defined numerators and denominators. Incorporation of microbiological data is required to provide information on prevailing PCR ribotypes and antimicrobial susceptibility to first-line CDI treatment drugs. Implications: incidence rates of CDI, obtained from a standardized CDI surveillance system, can be used as an important quality indicator. In the future, surveillance data will be linked to antimicrobial use and real time CDI surveillance data. Linkage of hospital administrative information systems to microbiological information systems will eventually permit automated reporting of CDI data, enabling rapid identification of outbreaks. Such centers could also provide molecular typing support for CDI outbreaks in healthcare facilities and early intervention.	Use recommended testing practices: when to test and which test (e.g., two-step algorithm); appropriate case origin (CA, HA, recurrent, or unknown); calculate incidence rate or incidence density rate; use PCR ribotyping for CDI surveillance. In the future, technology will help improve speed and accuracy of surveillance.	Article also includes surveillance protocol for Europe.

Table B.26: Clostridioides *difficile*, Testing–Single Studies

Note: Full references are available in the Section 4.5 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Aichinger et al., 2008[30]	Not repeating negative CDI tests within 7 days of initial result	Retrospective review of stool testing for *C. difficile* from June 2006 through December 2007. 5,788 patients tested by enzyme immunoassay (EIA) and 2,827 patients tested by polymerase chain reaction (PCR).	An unspecified healthcare facility	The group of EIA patients tested only twice consisted of 792 subjects (13.7% of patients tested with EIA). Twenty (2.5%) patients had a negative result on the first test with subsequent positive results on the following tests. Thirty-eight (4.8%) went from positive to negative. For PCR, 351 were tested twice; 2% (7) went negative to positive and 2.9% (10) went positive to negative.	Not provided	The researchers concluded that the diagnostic gains of repeat testing are equally low for PCR and EIA and that repeat testing for *C. difficile* should not be routine. Several authors have suggested that it may be useful to test more than one stool specimen for *C. difficile* toxin by use of an immunoassay. Nevertheless, there are limited data supporting this practice.	Not provided	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Archbald-Pannone et al., 2015[60]	Clinical factors to predict mortality following *C. difficile* infection (CDI)	A parsimonious predictive model was chosen using Akaike information criterion (AIC) and a best subsets model selection algorithm. Area under the receiver operating characteristic (ROC) curve was used to assess the model's comparative, with AIC as selection criterion for all subsets to measure fit and control for over-fitting. 362 inpatients diagnosed with CDI who did not have chronic diarrhea. Followed them for 30 days after CDI diagnosis or until death.	U.S. academic hospital/ University of Virginia clinical laboratory	The area under the ROC curve was 0.804. The bootstrap estimate of optimism was -0.034; suggesting that this model applied to a novel cohort is expected to have an area under the curve (AUC) of 0.770. With this model, 1 point corresponds to approximately an 11% increase in the odds of death within 30 days. The selected model included Charlson comorbidity index (CCI), white blood cell count (WBC), blood urea nitrogen (BUN), intensive care unit, and delirium. The logistic regression coefficients were converted to a point scale and calibrated so that each unit on the CCI contributed 2 points, ICU contributed 5, unit of WBC (natural log scale) contributed 3, unit of BUN contributed 5, and delirium contributed 11.	Not provided	Clinicians could use this tool to enhance the early recognition of high-risk patients with CDI, implement a more intensive treatment regimen, and aid in the decision for earlier surgical consultation. The predictive model was directly calculated from the five retained variables: Charlson score, ICU at diagnosis, WBC, BUN, and delirium. Patients who were admitted from a long-term care facility, who were diagnosed in the ICU, and who developed delirium were at highest risk of dying within 30 days of CDI diagnosis.	Moderate	Background: According to article, current models to define severe CDI lack either sensitivity or specificity.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Bogaty et al., 2017[41]	Different CDI testing strategies (and their association with CDI incidence rates): EIA, glutamate dehydrogenase (GDH), GDH plus toxigenic cultures, nucleic acid amplification tests (NAATs)	Cross-sectional study of 95 hospitals by surveys conducted in 2010 and in 2013 to 2014. The association between testing strategies and institutional CDI incidence rates was analyzed via multivariate Poisson regressions.	95 hospitals in Quebec, Canada	Between 2010 and 2014, 35 institutions (37%) modified their algorithm. Institutions detecting toxigenic *C. difficile* instead of *C. difficile* toxin increased from 14 to 37 ($p<0.001$). Institutions detecting toxigenic *C. difficile* had higher CDI rates (7.9 vs 6.6 per 10,000 patient-days; $p=0.01$). Institutions using single-step NAATs, GDH plus toxigenic cultures, and GDH plus cytotoxicity assays had higher CDI rates than those using an EIA-based algorithm ($p<0.05$).	Not provided	Infection control professionals should be aware that local CDI incidence rates may be influenced by the local choice of diagnostic test. The research found that laboratory detection of CDI has changed since 2010 and there is an association between diagnostic algorithms and CDI incidence. The heterogeneity of available tests can pose a significant threat to the validity of surveillance systems regarding interinstitutional comparisons.	Low to moderate	Background: Many surveillance programs, including Quebec's, provide no recommendations regarding the choice of laboratory tests to use, and CDI incidence rates are not adjusted to take this variable into consideration.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Casari et al., 2018[42]	Use of NAAT plus clear sampling criteria (unformed stool)	Prospective, pre/post study. Analyses of sample numbers, numbers of positive results, and proportion of cases assessed as healthcare acquired over a 6-year period during which the testing method was changed from a toxin A/B immunoassay to a standalone commercial nucleic acid test after the first 2 years (2012)	A 750-bed tertiary care university hospital in Milan	Sample numbers and numbers of cases assessed as healthcare-acquired CDI fell after the introduction of the NAAT and sampling guidance, while infection rates in other hospitals in the same region remained relatively stable. A total of 8,680 samples were tested for CDI over the study period: 2,841, 2,746, 677, 768, 805, and 843 tests in 2010, 2011, 2012, 2013, 2014, and 2015, respectively. For the corresponding years, the total number of positive samples and those categorized as healthcare acquired was 106/105 for 2010, 108/104 for 2011, 92/79 for 2012, 95/75 for 2013, 93/76 for 2014, and 91/78 for 2015, respectively.	Not provided	This study showed that moving from a toxin EIA to a standalone NAAT resulted in fewer samples tested and lower positivity rates, largely due to a reduction in the number of healthcare-associated cases. According to the authors, the reasons for these findings are likely to be multifactorial. Lack of confidence in the sensitivity of the toxin tests meant that clinicians often repeated the test up to three or more times before declaring the patients free from *C. difficile* infection and releasing them from isolation, resulting in a poor use of isolation facilities.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Cooper et al., 2013[44]	An electronic screening tool to help identify patients at risk of CDI	Logistic regression was used to weigh six variables, and then a predictive model was devised to help identify which patients may be at risk for developing CDI. A retrospective review of 29,453 records of hospitalizations was conducted, including 274 cases of *C. difficile* toxin-positive patients, to retrieve data for the model.	A 255-bed, community hospital located in Virginia's Shenandoah Valley	The final model resulted in an area under the curve of 0.929, which suggests that the electronic screening tool will be an accurate predictor of predisposition to the disease. Model testing suggests a positive relationship between the total weight or score and the probability of developing the disease.	The impact of the tool to the prevalence and control of the disease itself may be difficult to ascertain in isolation from other infection control measures. Further studies are warranted on the economic benefits of the electronic screening tool and how it affects physician decision making.	This study suggests that an electronic screening tool for CDI can be devised locally and result in reasonably accurate screening of patients at risk of developing the disease. This model could be applied to the electronic medical record to automatically generate updated lists of patients who may need monitoring for prompt testing, isolation, or treatment. Being alerted that a patient is at high risk for CDI may help the clinician to consider prompt isolation and empiric treatment in cases when the laboratory test (especially EIA) is negative or is still pending.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Cruz-Betancourt et al., 2016[45]	A predictive preventive model for prevention of *Clostridium difficile* infection in patients in ICUs	A predictive screening tool was developed based on risk factors identified in the literature and validated by retrospective analysis of all HA-CDI cases occurring in critically ill patients during 2013. The tool was used to screen all patients admitted to an intensive care unit. Evidence-based interventions (bundle) were implemented for patients identified as being at high risk for HA CDI. Effectiveness of the model was measured by reduction of the HA-CDI rate during the intervention period compared with the pre-intervention period.	A vascular-thoracic ICU, a 20-bed unit providing care to patients following vascular surgery as well as to patients with chronic ventilator dependency	During the study period, 1,066 patients were screened using the predictive screening tool; 217 high-risk patients were identified as infected with *Clostridium difficile*. Sixty-two of these met exclusion criteria, resulting in a study population of 157 patients. During the pre-intervention phase, 10 cases of HA CDI occurred (overall incidence rate, 14.7). During the 12-month study period, two cases of HA CDI were identified (incidence rate, 3.12). The reduction was statistically significant.	Not provided	The combination of a predictive screening tool with preventive interventions in the vascular-thoracic ICU appeared effective in reducing HA-CDI rates. The two patients who developed CDI during the implementation period did not have the preventive bundle measures instituted due to procedural deviation. The major pharmacologic interventions related to adjustment or discontinuation of acid suppression therapy. Improved environment cleaning to reduce transmission in addition to improved hand hygiene rates also likely played a role in reducing HA-CDI rates, according to the authors.	Low to moderate	This study describes both the use of a predictive model and its integration into daily practice of interdisciplinary efforts at CDI reduction to demonstrate a method of clinical use of a predictive model.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Figh et al., 2017[63]	Two published clinical prediction tools (CPTs): the Velazquez-Gomez Severity Score Index (VGSSI) and ATLAS scores	A retrospective review of the charts of 271 hospitalized patients with CDI. VGSSI and ATLAS scores were assigned. Means and correlations of these scores with mortality were evaluated. Multivariate logistic regression analysis was performed on 32 known potential mortality predictor variables. The review included 271 patient charts.	A hospital	Mortality was overall strongly associated with VGSSI and ATLAS scores with poor correlation within the intermediate ranges. Mean scores for nonsurvivors indicated poor calibration.	Although both CPTs revealed the ability to discriminate patients at greater risk for mortality, precision and overall calibration were lacking.	An external validation of VGSSI and ATLAS scoring systems showed that these two CPTs are inaccurate in stratifying patients into the appropriate severity index score for severe CDI. In the application of the VGSSI and the ATLAS score, it is clear that there is an overall correlation of these models with mortality.	Low to moderate	These tools are used to predict the *severity* of CDI. There is a wide range of CDI severity. Approximately 25% will progress to pseudo-membranous colitis, and in this high-risk group, another 1–8% will become fulminant CDI.
Islam et al., 2013[32]	Cohorting patients—recognize risk of reinfection	Data describing patient demographics, comorbidity, CDI severity, and treatment were collected for 248 CDI patients between October 2008 and June 2011. The primary outcome was symptomatic recurrence within 30 days of diagnosis.	A single hospital ward	A total of 158 (55.6%) CDI patients was admitted to the cohort ward. On multivariate analysis, cohorting (3.94; 95% CI 1.23 to 12.65; p=0.021) and urinary infection (4.27; 1.62 to 11.24; p=0.003) were significant predictors of recurrence.	Not provided	Patients admitted to a *C. difficile* cohort ward may be at increased risk of recurrence because they are at increased risk of reinfection. Study suggests that hospitals using cohort wards to control *C. difficile* should manage patient flow through the cohort to minimize this risk.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Kassam et al., 2016[61]	CDI-related mortality prediction tool to prevent CDI mortality: *C. difficile* Associated Risk of Death Score (CARDS)	Retrospective analysis of United States 2011 Nationwide Inpatient Sample (NIS) database. All CDI-associated hospitalizations were identified using discharge codes (ICD-9-CM, 008.45). Predictive properties of model discrimination were assessed using the c-statistic and validated in an independent sample using the 2010 NIS database.	A large U.S. database, 374,747 cases with an associated diagnosis of CDI	The overall risk score in the cohort ranged from 0 to 18. Mortality increased significantly as CARDS increased. CDI-associated mortality was 1.2% with a CARDS of 0 compared with 100% with a CARDS of 18. The model performed similarly in the validation cohort. The severity scoring system had a comparable performance with a c-statistic of 0.77.	Not provided	The CARDS model displayed good discriminative ability, which was validated in an independent CDI cohort. Age has been identified as a risk factor of initial CDI development and CDI-associated mortality. ICU admission was also a strong independent predictor of CDI-associated mortality (odds ratio 5.23, 95% CI, 4.79 to 5.72). A number of chronic comorbidities are important predictors of CDI-associated mortality. Inflammatory bowel disease, malignancy, and liver disease were all independently identified to increase the odds of CDI-associated death in the model.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Koo et al., 2014[38]	Taking into account false positives for real-time PCR for *Clostridium difficile*-associated disease (CDAD) detection	CDAD rates were compared before and after real-time PCR implementation. After real-time PCR introduction, all hospitalized adult patients were screened for *C. difficile* by testing a fecal specimen by real-time PCR, toxin enzyme-linked immunosorbent assay, and toxigenic culture. The study included 199 enrolled hospital subjects.	A 600-bed university hospital in Houston, TX	CDAD hospital rates significantly increased after changing from cell culture cytotoxicity assay to a real-time PCR assay; 199 hospitalized subjects were enrolled, and 101 fecal specimens were collected. *C. difficile* was detected in 18 subjects (18%), including 5 subjects (28%) with either definite or probable CDAD and 13 patients (72%) with asymptomatic *C. difficile* colonization.	The difficulty in interpreting the clinical significance of *C. difficile* detected by NAATs is emphasized by recent studies describing the importance of confirmation of *C. difficile* toxin production. In spite of the high sensitivity of NAATs for *C. difficile* detection, PCR assays cannot distinguish asymptomatic colonization from symptomatic disease; i.e., there are false positives	Study reports that most healthcare-associated diarrhea is not attributable to CDAD, and the prevalence of asymptomatic *C. difficile* colonization exceeds CDAD rates in healthcare facilities. PCR detection of asymptomatic *C. difficile* colonization among patients with non-CDAD diarrhea may be contributing to rising CDAD rates and a significant number of CDAD false positives. PCR may be useful for CDAD screening, but further study is needed to guide interpretation of PCR detection of *C. difficile* and the value of confirmatory tests. A gold standard CDAD diagnostic assay is needed.	Moderate	Most subjects identified with *C. difficile* were asymptomatic, irrespective of the detection method, including 8 of 12 (67%) *C. difficile*-positive subjects by PCR. The only significant difference between subjects with CDAD and *C. difficile*-colonized patients was the mean number of stools passed in the previous 24 hours. Limitations of this study include enrollment of 51% of eligible patients and fecal specimen collection from only half of enrolled subjects.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Kuntz et al., 2014[48]	Tool to predict risk of CDI after an outpatient visit	Developed and validated a prognostic risk score to predict CDI risk for individual patients following an outpatient healthcare visit. A cohort of Kaiser Permanente Northwest (KPNW) patients with an index outpatient visit between 2005 and 2008, and identified CDI in the year following that visit. Researchers applied Cox regression and synthesized a priori predictors into a CDI risk score, which was validated among a Kaiser Permanente Colorado (KPCO) cohort. They calculated and plotted the observed 1-year CDI risk for each decile of predicted risk for both cohorts.	Cohort of 356,920 patients from a health system	Among 356,920 KPNW patients, 608 experienced CDI, giving a 1-year incidence of 2.2 CDIs per 1,000 patients. The Cox model differentiated between patients who do and do not develop CDI: there was a c-statistic of 0.83 for KPNW. The simpler points-based risk score, derived from the Cox model, was validated successfully among 296,550 KPCO patients, with no decline in the area under the receiver operating characteristic curve: 0.785 (KPNW) vs. 0.790 (KPCO).	Not provided	The predicted risk for CDI agreed closely with the observed risk. The CDI risk score used data collected during usual care to successfully identify patients who developed CDI, discriminating them from patients at the lowest risk for CDI. The prognostic CDI risk score provides a decision-making tool for clinicians in the outpatient setting. The patient characteristics that contributed >30 points to the risk score, indicating an approximate doubling of risk, were: age 55 years and older (38 to 100 points, depending on age category); hospitalization of 7 days (37 points); liver disease (47 points); inflammatory bowel disease (43 points); and cephalosporin use (38 points) or clindamycin use (58 points).	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Lanzas and Dubberke, 2014[20]	Screening patients at admission to detect asymptomatic *C. difficile* carriers and placing positive patients into contact precautions	An agent-based transmission model for *C. difficile* that incorporates screening and contact precautions for asymptomatic carriers in a hospital ward. Simulation of scenarios that vary according to screening test characteristics, colonization prevalence, and type of strain present at admission.	Electronic data were collected retrospectively from six medicine wards at Barnes-Jewish Hospital in St. Louis, Missouri	On average, testing for asymptomatic carriers reduced the number of new colonizations and hospital-onset (HO)-CDI cases by 40% to 50% and 10% to 25%, respectively, compared with the baseline scenario. Test sensitivity, turnaround time, colonization prevalence at admission, and strain type had significant effects on testing efficacy.	Not provided	Screening patients at admission to detect and isolate asymptomatic carriers could decrease the number of new colonizations and HO-CDI cases at the ward level. Simulations indicated that tests with a sensitivity greater than 90% and turnaround times less than 2.5 days could reduce the number of secondary new colonizations (and subsequent CDIs) caused by asymptomatic carriers. Additional research is needed to determine the costs, feasibility, and impact of screening on patient outcomes.	Low to moderate	Simulation: "The contribution of symptomatic cases to transmission and new infection is likely to be lower than previously thought, and the likelihood of transmission and infection appears to also be *strain specific.*"

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Longtin et al., 2016[19]	Detecting and isolating *C. difficile* asymptomatic carriers at hospital admission	Controlled quasi-experimental study between November 19, 2013, and March 7, 2015; 7,599 patients screened at admission.	A 354-bed Canadian acute care facility	During the intervention, 38 patients (3.0 per 10,000 patient-days) developed an HA CDI compared with 416 patients (6.9 per 10,000 patient-days) during the pre-intervention control period ($p<0.001$). The researchers estimated that the intervention had prevented 63 of the 101 (62.4%) expected cases. By contrast, no significant decrease in HA-CDI rates occurred in the control groups.	Not provided	The cost-benefit of this strategy is unknown, but preliminary estimates suggest that the intervention may be cost effective. The intervention cost U.S. $130,000 over 17 periods and prevented approximately 63 cases. Because each case costs U.S. $3,427 to $9,960, the savings in averted CDI (U.S. $216,000 to $627,000) are greater than the costs of the intervention.	Low	Context: “Present guidelines do not recommend screening and isolating asymptomatic carriers.”

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Maghdoori and Moghadas, 2017[21]	Screening at the time of hospital admission, and screening in-hospital patients with potential exposure to *C. difficile*, to detect colonized/ asymptomatic patients (in the context of imperfect patient isolation)	Stochastic modeling for the transmission dynamics of CDI in a hospital ward. Simulation of various scenarios for detection and isolation of colonized patients. Model incorporated several parameters representing the level of patient screening, effectiveness of isolation, treatment failure, and level of susceptibility to infection.	A hospital ward with 50 beds (simulation)	When the effectiveness of patient isolation was 100%, the daily incidence of *C. difficile* was reduced by over 79% (95% CI, 78% to 79.6%) as a result of 92.5% *rapid* screening *at the time of hospital admission*. For isolation with less than 100% effectiveness, the benefits of screening and detection of colonized patients were reduced as a result of within-ward transmission. Compared with the results for rapid testing, results that take 2 days (without patient isolation) significantly lowered the effect of admission screening on reducing the prevalence of CDI. When screening 90% of *in-hospital patients starting on day 100*, there was an increasing trend in the percentage reduction of *C. difficile* incidence over time, reaching levels over 76%.	Findings indicate that if infection control measures are implemented inefficiently, within-ward transmission can potentially offset the benefits of patient screening.	The analysis found that if rapid screening of patients at the time of hospital admission and screening of in-hospital patients are implemented individually, then the former would always outperform the latter in terms of reducing the prevalence and incidence of CDI irrespective of the reproduction number, time delay in the release of laboratory tests, or effectiveness of patient isolation. Model shows that impact of screening at admission or day 100 is dramatically reduced when test results take 2 days.	Moderate	Study is based on several simulations. Addresses the issue of asymptomatic carriers in CDI transmission and suggests screening for asymptomatic carriers may be effective under certain conditions.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Moehring, et al., 2013[40]	Change from nonmolecular to molecular testing techniques—impact on surveillance	Comparison of the relative change in incidence rate (IRR) of healthcare facility-associated (HCFA) CDI among hospitals in the Duke Infection Control Outreach Network before and after the date of switch from nonmolecular tests to polymerase chain reaction (PCR) using prospectively collected surveillance data from July 2009 to December 2011. Data from 10 hospitals that switched and 22 control hospitals were included. Individual hospital estimates were determined using Poisson regression. 1,805 cases of CDI over 4,038,447 patient days.	32 hospitals in the Duke Infection Control Outreach Network	For those hospitals that switched to PCR, mean incidence rate of HCFA CDI before the switch was 6.0 CDIs per 10,000 patient-days compared with 9.6 CDIs per 10,000 patient-days after the switch. After adjustment in the mixed-effects model, the overall IRR comparing CDI incidence after the switch to before the switch was 1.56 (95% CI, 1.28 to 1.90). Time-trend variables did not reach statistical significance. Hospitals that switched from nonmolecular to molecular tests experienced an approximate 56% increase in the rate of HCFA CDI after testing change.	Improved test sensitivity because of the change to molecular diagnostic testing can produce both positive and negative effects. A molecular test is more expensive to implement, may cause confusion among ordering providers, and may be overused because of its novelty. Also, the more sensitive test may be "too good" at identifying patients who are colonized but not truly infected with *C. difficile*.	Study shows that increase in CDI rates in the United States up to 2009 were due at least in part to "surveillance bias" (e.g., changing definitions and new testing methods). The purpose of this study was to adjust for time-dependent factor and isolate the impact of the change in testing method. All 10 hospitals that switched to PCR testing used the Cepheid Xpert *C. difficile* assay (Xpert CD assay; Cepheid). In the context of testing for potentially transmittable diseases within the hospital setting, the improved sensitivity of molecular tests allows infected and colonized patients to be rapidly and reliably identified.,.	Low to moderate	Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network surveillance definitions were used to identify incident cases of community-onset HCFA and HO HCFA CDI. The study period corresponds with introduction of the 2008 change in CDC surveillance definitions for CDI, which included source type interpretations. should be noted. In fact, two hospitals in the study saw a numerical decrease in their incidence rates after the switch.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Mostafa et al., 2018[29]	Factors for conversion from negative to positive PCR CDI test	A retrospective chart review of 20,866 laboratory test orders (2 years) for *C. difficile* PCR was conducted. The test result, clinico-pathologic patient features, and previous test results were recorded. Univariate and multivariate analysis were conducted to compare patients with initial and repeat negative results (n=248) with a group of patients with conversion from negative to positive results within 7 days.	Medical college and diagnostic laboratory	Among these charts, 1,637 (8.0%) were tests repeated within 7 days of previously valid test result. Based on only single repeat test orders, 970 (59.3%) followed an initial negative and 554 (33.8%) followed an initial positive test result. An additional 113 (6.9%) tests were repeated more than once within 7 days of the original test. Patients with a history of *C. difficile* confirmed by PCR within the 60 days prior to initial test were 19 times more likely to have a repeat positive result within 7 days of a negative result (95%, CI, 6.64 to 54.17, p<0.001). Conversely, patients with history of any antibiotic therapy within 14 days prior to initial test were 3.9 times more likely to have a repeat negative result (95% CI, 1.6 to 10.0, p=0.003).	Not provided	Identification of prior *C. difficile* infection as the only factor significantly correlated with conversion from negative to positive *C. difficile* test result within 7 days aids in selective test use and reduces the costs associated with unnecessary laboratory testing. The study demonstrates a potential for cost savings. Over a 2-year period, they found that 8% of tests were repeated within 7 days of a valid result, with an estimated cost of $61,537.50. Limiting repeat testing within 7 days to only those patients with a history of CDI within the previous 60 days would reduce this cost by ~90%.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Napierela et al., 2013[24]	PCR testing	Pre/post. The 20-month interval of *C. difficile* toxin A/B EIA testing that directly preceded commencement of *C. difficile* tcdB PCR was reviewed, as well as the first 20 months of PCR testing.	Three hospitals with 166, 538, and 260 beds	All three hospitals experienced significant reductions in healthcare-associated CDI upon introduction of molecular diagnostics ($p \leq 0.05$). Site-specific *C. difficile* testing volume decreased by 32.5–53.9% following implementation of tcdB PCR.	Not provided	These data suggest a strong influence of *C. difficile* toxin testing modality on healthcare-associated CDI. Conversion from *Clostridium difficile* toxin A/B EIA to tcdB PCR for diagnosis of CDI resulted in significant decreases in laboratory testing volume, reducing the workload. There were generally unchanged *C. difficile* toxin detection rates.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Planche et al., 2013[14]	Toxin (cytotoxin assay) testing as a CDI reference method	Prospective, observational multicenter study, cytotoxigenic culture and cytotoxin assays on 12,420 fecal samples in four U.K. laboratories. Also performed tests that represent the three main targets for CDI detection: bacterium (glutamate dehydrogenase), toxins, or toxin genes. Use of routine blood test results, length of hospital stay, and 30-day mortality to clinically validate the reference methods. Data were categorized by reference method result.	Four U.K. laboratories	A multivariate analysis accounting for potential confounders confirmed the mortality differences between groups 1 and 3 (odds ratio 1.61, 95% CI, 1.12 to 2.31). Multistage algorithms performed better than did standalone assays. In more than 6,000 patients with diarrhea, no increase in mortality occurred when a toxigenic *C. difficile* strain alone was present (cytotoxigenic culture positive, cell cytotoxin assay negative). By contrast, toxin (cell cytotoxin assay) positivity was associated with clinical outcome. Other clinical indicators were worse for cell cytotoxin assay-positive cases, but no difference was noted between cytotoxigenic culture-positive, cell cytotoxin assay-negative cases, and negative controls.	Not provided	Researchers found that toxin (cell cytotoxin assay) positivity was associated with clinical outcome and state that this reference method (of the three groups) best defines true cases of *C. difficile* infection. A positive cell cytotoxin assay indicates that the diarrhea was probably caused by CDI infection, whereas a positive cytotoxigenic culture indicates that a patient could be infectious even though the diarrhea might have resulted from another cause. A new diagnostic category of potential *C. difficile* excretor (cytotoxigenic culture positive but cytotoxin assay negative) could be used to characterize patients with diarrhea that is probably not due to *C. difficile* infection.	Low	Highly technical. Article looks at predictor of disease severity. Background: Cytotoxigenic culture detects toxigenic CDI and gives a positive result more frequently (because of colonization, which means that individuals can have the bacterium but no free toxin) than does the cytotoxin assay, which detects preformed toxin in feces.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Reigadas et al., 2015[27]	Systematic testing of diarrheal stool for CDI regardless of clinician request	Prospective study in which systematic testing for toxigenic *C. difficile* on all diarrheic stool samples was performed regardless of the clinician's request. A total of 3,673 unformed stool samples from patients age >2 years was processed for detection of toxigenic *C. difficile*.	A 1,550-bed hospital	Testing found 249 episodes of CDI. Of these, 45 episodes (18.1%) were excluded because they did not fulfill the criteria for diarrhea (3 unformed stools/24 h). Therefore, 204 CDI episodes met the inclusion criteria (CDI episodes in patients age >2 years); of these, 178 had raised clinical suspicion and 26 (12.7%) had no clinical request for toxigenic *C. difficile* testing. Community-acquired cases and young age were risk factors for clinical underdiagnosis.	Not provided	The introduction of a systematic search for toxigenic *C. difficile* in all diarrheic stools arriving at a microbiology laboratory reveals a significant proportion of unsuspected cases and provides a more complete picture of the situation of CDI in a nonselected population. The main risk factors for lack of clinical suspicion were community-associated CDI and young age. In this study, 31.4% of CDI patients had not previously received antibiotics.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Saab et al., 2015[33]	CDI screening of hospitalized patients with cirrhosis	A Markov model was used to compare costs and outcomes of two strategies for the screening of CDI. The first strategy consisted of screening all patients for CDI and treating if detected (screening). In the second strategy, only patients found to have symptomatic CDI were treated (no screening).	Hospital simulation	The results of the model showed that screening for CDI was consistently associated with improved healthcare outcomes and decreased healthcare use across all variables in the one- and two-way sensitivity analyses. Using baseline assumptions, the costs associated with the no-screening strategy were 3.54 times those of the screening strategy. Moreover, the mortality for symptomatic CDI was lower in the screening strategy than the no-screening strategy.	Not provided	Evidence demonstrated that cirrhotic patients may be particularly affected by CDI. The results of the study showed that screening and treating *C. difficile* in asymptomatic patients are not cost effective but cost saving.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Schroeder et al., 2014[43]	PCR or GDH plus on-demand PCR as most cost-effective diagnostic strategies	Decision analysis from the hospital perspective to compare multiple CDI testing algorithms for adult inpatients with suspected CDI, assuming patient management according to laboratory results; 10,000 symptomatic adults	Hospital simulation	A cost-benefit analysis (including estimated costs of missed cases) favored standalone on-demand PCR (vs. batch PCR) in most settings but favored on-demand PCR preceded by lateral-flow testing if a missed CDI case resulted in less than $5,000 of extended hospital stay costs and <2 transmissions, if lateral-flow GDH diagnostic sensitivity was >93% or if the symptomatic carrier proportion among the toxigenic culture-positive cases was >80%. These results can aid guideline developers and laboratory directors who are considering rapid testing algorithms for diagnosing CDI.	Not provided	This economic evaluation found that rapid testing is likely to be cost saving and more effective relative to the other technologies. Under most reasonable scenarios, standalone on-demand PCR as a one-step test is the strategy that minimizes false-negative results and costs to the healthcare system. However, where costs of a missed CDI diagnosis are minimal, where lateral-flow GDH/on-demand PCR or lateral-flow GDH-Tox/on-demand PCR can be performed with high diagnostic sensitivity, or where the symptomatic carrier proportion is high, testing with lateral-flow GDH or lateral-flow GDH-Tox before on-demand PCR is a justifiable option.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Silva et al., 2017[28]	PCR testing *plus* clinical assessment to diagnose CDI	A matched case-control study was conducted on inpatients in a tertiary care center. The first 50 patients with diarrhea and a positive PCR were identified as cases. Control patients were hospitalized patients receiving antibiotics, but with no diarrhea, housed in a room as close as possible to each case during the same admission time. A convenience sample of healthcare workers who cared for *C. difficile*-infected patients was also tested.	A tertiary care center. a 670-bed facility in the city of Sao Paulo, Brazil	There were two positive PCR results for *C. difficile* in controls (4.1%). None of the healthcare workers were positive for *C. difficile* by PCR. There was no difference between groups with respect to overall antibiotic use before the requested PCR for *C. difficile* (p=0.359). Most cases had a high proportion of gastrointestinal disorders (71.4%) compared with control (8.2%), p<0.001.	Not provided	The only non-antimicrobial predictor for CDI was gastrointestinal symptoms (p<0.001). Recommend assessing patients for diarrhea and interpreting laboratory results considering the clinical setting and the likelihood of other etiologies. The significance of a positive PCR result creates difficulties for clinical interpretation, due to the large number of positive tests from individuals without disease. According to the study, the use of molecular tests alone to diagnose CDI, without the toxin or host response tests, will likely lead to an excessive number of positively diagnosed cases, excessive treatment, and increased healthcare costs.	Low to moderate	Background: The diagnosis of CDI increases concern that asymptomatic carriers of toxigenic *C. difficile* may be diagnosed with CDI.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Stites et al., 2016[46]	A predictive model that identifies patients at high risk for CDI at the time of hospitalization. This approach to early identification was evaluated to determine if it could improve upon a pre-existing antimicrobial stewardship (AMS) program. The hospital's AMS program was administered as part of routine care, consistent with the guidelines of the Infectious Diseases Society of America.	Logistic regression and ROC curve analyses were used to develop an analytic model to predict risk for CDI at the time of hospitalization in a retrospective cohort of inpatients. The model was validated in a prospective cohort. Concurrence between the model's risk predictions and a pre-existing AMS program was assessed. This cohort study analyzed electronic medical record (EMR) data from 42,120 patient admissions retrospectively in 2014, and prospectively for 10,990 admissions between July and September 2015.	A large safety-net hospital in Philadelphia, PA (inner city)	The model identified 55% of patients who later tested positive as being at high risk for CDI at the time of admission. One in every 32 high-risk patients with potentially modifiable antimicrobial risk factors tested positive for CDI. Half (53%) tested positive before meeting the risk criteria for the hospital's AMS program (c-statistic 0.77, 95% CI, 0.69 to 0.84). The model was faster than the AMS program. One in four patients in the highest risk category at the time of admission later experienced one or more of the AMS program antimicrobial risk factors during hospitalization. Approximately half (53%) tested positive after being identified by the PIPAR model but before meeting the criteria for the AMS program. All results were similar in the prospective cohort.	Over half of the patients who tested positive (55%) were identified at the time of admission by the PIPAR model as "very high risk" (highest of six categories). Approximately 2 in every 100 of these patients tested positive for CDI while hospitalized. (Thus, almost half were not identified as the highest risk, although still more accurate and timely than the existing system.)	Identification of patients predisposed to CDI at the time of admission would allow the AMS program to target high-risk patients earlier than current standard practice, which relies on retrospective chart reviews, and to use multiple strategies. By using the risk data to identify patients proactively, the AMS program could implement a prospective control system to ensure that antimicrobial therapy is appropriate at the time of initiation, including choice of agent, dose, and duration.	Low	Testing criteria: The laboratory only tested samples from patients with more than three liquid stools within a 24-hour period.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Tabak et al, 2015[47]	An HO-CDI predictive model using electronic health records clinical data present at time of admission	Retrospective data analysis of 78,080 adults discharged from six acute care hospitals between January 1, 2007, and June 30, 2008; 323 HO-CDI cases (including 310 nonrecurrent and 13 recurrent CDIs) were identified. A logistic regression model to predict the risk of HO CDI and validation of the model using 1,000 bootstrap simulations.	Six U.S. acute care hospitals	About 21% patients within the higher risk strata accounted for 65% of all HO-CDI cases. The logistic regression model yielded 14 independent predictors, including hospital community-onset CDI pressure, patient age ≥65, previous healthcare exposures, CDI in previous admission, admission to the ICU, albumin ≤3 g/dL, creatinine >2.0 mg/dL, bands >32%, platelets ≤150 or >420 10^9/L, and WBC >11,000 mm3. The model had a c-statistic of 0.78 (95% CI, 0.76 to 0.81) with good calibration. For 79% of patients with risk score of 0–7, there were 19 HO CDIs per 10,000 admissions; for patients with risk score of 20+, there were 623 HO CDIs per 10, 000 admissions (p<0.0001)	Not provided	Using clinical parameters available at the time of admission, this HO-CDI model displayed good predictive ability. It may have utility as an early risk identification tool for HO-CDI preventive interventions and outcome comparisons. Application of the risk score needs to be tested prospectively, preferably in hospitals with advanced electronic health records. The number needed to treat with an intervention to prevent one case of HO CDI will be required to determine the overall cost-effectiveness of the tool.	Low	There are risk factors due to the care process (e.g., hospital antimicrobial exposure) but also those present on admission. The researcher asserted that on-admission risk stratification may help with prevention.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Van Beurden et al., 2017[62]	Three published prediction tools for patients at risk of a complicated course of CDI. The three models were from: Hensgens (2014), Na (2015), and Welfare (2011). A course of CDI was considered complicated if any of the following criteria were met within 30 days after the diagnosis of CDI: (1) death as a direct or indirect consequence of CDI, (2) admission to the ICU for treatment of CDI or its complications, (3) surgery (colectomy) for toxic megacolon, perforation or refractory colitis.	The validation cohort comprised 148 patients diagnosed with CDI between May 2013 and March 2014. During this period, 70 endemic cases of CDI occurred as well as 78 cases of CDI related to an outbreak of *C. difficile* ribotype 027. Model calibration and discrimination were assessed for the three prediction rules. To quantify how close predictions are to the actual outcome (calibration), the authors plotted the observed number of complicated cases against the predicted number of complicated CDI courses in the simplified risk categories provided by the original studies.	A 750-bed tertiary care center in Amsterdam	For those patients diagnosed with CDI due to nonoutbreak strains, the prediction model developed by Hensgens performed the best, with an AUC of 0.78. For entire cohort, AUC was 0.68. This prediction model can therefore be used in an endemic setting to identify patients at risk for CDI complications, aiding clinicians in deciding which patients to monitor closely for CDI-related complications. In conclusion, the study shows that a prediction rule can only be used in a cohort comparable with the derivation cohort.	The performance of all three prediction models was poor when applied to the total validation cohort with an estimated AUC of 0.68 for the Hensgens model, 0.54 for the Na model, and 0.61 for the Welfare model.	Early identification of patients at risk of a complicated course or death could help clinicians inform patients and might help doctors guide antibiotic treatment. All three prediction models performed poorly when validated using the total cohort, which included CDI cases from an outbreak as well as endemic cases. The prediction model of Hensgens performed relatively well for patients diagnosed with CDI due to nonoutbreak strains, and this model may be useful in endemic settings.	Low to moderate	Search of PubMed and Embase for studies on prediction tools for a severe or complicated course of CDI up to February 2016 (Appendix A). Selected studies that (1) predicted at least one relevant outcome (i.e., severity, complications, mortality) and (2) developed a prediction model or risk score.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Van der Wilden, 2014[49]	A risk scoring system (RSS) for patients at risk of developing fCDC (fulminant *C. difficile* colitis)	All patients (746) with *C. difficile* colitis admitted to Massachusetts General Hospital were prospectively enrolled in a specific database aiming to collect data on *C. difficile* infections. Various criteria/weighted risk factors were collected. Univariate analysis was performed to compare patients with and without fCDC.	Massachusetts General Hospital	The RSS successfully discriminates patients with *C. difficile* infection from those who have fCDC (AUC, 0.98). Calibration was low (Brier score of 0.019), indicating that the possibility of developing fCDC could be estimated accurately. A cutoff of 6 points was used to divide patients at high risk of developing fCDC, which classified 97.9% of patients correctly. In combination with a high specificity (88.4%) and excellent negative predictive value (99.8%), this scoring system proved it has the potential to be used at the bedside in order to safely rule out the possibility of fCDC.	The positive predictive value of 36.7% is low and should be considered against the background of its estimation in a low-prevalence setting (6.4% of total cohort was diagnosed with fCDC).	The researchers believe that the next step would be to externally validate the RSS to allow widespread implementation.	Moderate	The RSS included four variables: Age >70 years, WBC ≥20.000/µL or ≤2,000/µL, cardiorespiratory failure (defined as CDC-related vasopressor and/or mechanical ventilation requirement), and diffuse abdominal tenderness on physical exam.

Table B.27: Clostridioides *difficile*, Testing–Systematic Reviews

Note: Full references are available in the Section 4.5 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Bagdasarian et al., 2015[25]	Test only symptomatic patients. Multistep algorithms using polymerase chain reaction (PCR) for the toxin genes or single-step PCR on liquid stool samples have the best test performance characteristics.	Healthcare general; adults	Review of articles published between January 1978 and October 31, 2014. Recommendations include that CDI diagnosis requires presence of diarrhea (3 unformed stools in 24 hours) or radiographic evidence of ileus or toxic megacolon; and a positive stool test result for toxigenic *C. difficile* or its toxins, or colonoscopic or histopathologic evidence of pseudomembranous colitis. Diagnostic testing for CDI should be performed only in symptomatic patients. Laboratory testing cannot distinguish between asymptomatic colonization and symptomatic infection with *C. difficile*. The gold standard for detecting toxigenic *C. difficile* in stool is toxigenic culture; however, this method is time intensive and requires specialized equipment and personnel. Diagnostic approaches are complex due to the availability of multiple testing strategies. Multistep algorithms using PCR for the toxin genes or single-step PCR on liquid stool samples have the best test performance characteristics (for multistep, sensitivity was 0.68–1.00 and specificity was 0.92–1.00; for single step, sensitivity was 0.86–0.92 and specificity was 0.94–0.97). In one study, 56% of patients who responded to treatment asymptomatically shed *C. difficile* spores for as many as 6 weeks. Thus, a test of cure is not recommended.	Test only symptomatic patients. Laboratory testing cannot distinguish between colonization and infection. Diagnostic testing strategies for CDI vary. Multistep approaches using PCR for the toxin genes or single-step PCR on liquid stool samples have the highest sensitivity and specificity. Test of cure is not recommended after CDI treatment.	Article is also a review of treatment practices.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Butler et al., 2017[28]	Early diagnosis of CDI; diagnostic testing methods	Adult patients	Review of four databases from 2010 through April 2015 plus reference lists of included studies and recent systematic reviews. Included 37 studies on diagnostic tests. Research on diagnostic testing for and interventions to treat CDI expanded considerably in 4 years. High-strength evidence showed that nucleic amplification tests were sensitive and specific for CDI when using culture as the reference standard. Clinicians are not always well informed on the best diagnostic test to use, the operating characteristics of the tests used in their practice setting, or the relatively low likelihood of a false-negative result (e.g., evidence suggests retesting with the same test is common practice, yet not recommended).	NAATs are sensitive and specific; tests for toxin A/B are insensitive and specific; tests for GDH are sensitive but less specific; multistep steps are insensitive but specific.	Review provides pooled sensitivities, specificities, positive likelihood ratios and negative likelihood ratios, and 95% CIs for each class of tests. Also a review of prevention and treatment.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Crobach et al., 2016[4]	Diagnostic testing methods and criteria	Adult patients	Review/meta-analysis by the European Society of Microbiology and Infectious Diseases. Searched four databases for articles published between 2009 and June 2014. A total of 56 studies (15 from the previous meta-analysis and 41 published since 2009) were included in the meta-analysis. Toxin A/B EIAs tended to be the most specific assays, while GDH EIAs and NAATs were more sensitive tests. Although many toxin A/B EIAs belong to the least sensitive tests, the sensitivity of this category of assays is not as low as reported earlier. Different reference tests provide different results since each test has different targets. A rapid CDI diagnosis is associated with more prompt CDI treatment and fewer unnecessarily treated patients. However, two problems arise: First, the positive predictive values (PPVs) of even the most specific tests are inadequate at low disease prevalence. Second, as the targets identified by the index tests are (just like the targets of the reference test) different from each other, a positive index test does not necessarily indicate a real CDI case. Recommend a two-step algorithm—tests can be combined in such a way that the percentage of false-positive results can be decreased. After application of a first sensitive test (GDH EIA or NAAT), the toxin A/B EIA can then be performed as a second step on all samples that tested positive by NAAT or GDH EIA. Samples with a positive second test result can be classified as CDI likely to be present. However, samples with a first positive test result but a negative toxin A/B EIA need to be clinically evaluated.	According to the review, no single commercial test can be used as a standalone test for diagnosing CDI as a result of inadequate PPVs at low CDI prevalence. Therefore, the use of a two-step algorithm is recommended. Samples without free toxin detected by toxins A and B EIA but with positive GDH EIA, NAAT, or toxigenic culture (TC) results need clinical evaluation to discern CDI from asymptomatic carriage.	Review provides pooled sensitivities, specificities, PPV and negative predictive value, and 95% CIs for each class of tests.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Furuya-Kanamori et al., 2015[15]	Enhanced IPC for those at high risk for asymptomatic CDI; no active screening for asymptomatic *C. difficile* patients	Asymptomatic *C. difficile* colonized patients; healthcare settings	A narrative review was performed in PubMed for articles published from January 1980 to February 2015 using search terms "*Clostridium difficile*" and "colonization" or "colonisation" or "carriage." The review explores information about the definition, epidemiology, and biology of asymptomatic CDI colonization. The authors found there is no consistent definition for asymptomatic *C. difficile* colonization. Due to the findings, they agree with the guidelines not to perform active screening for asymptomatic *C. difficile* colonization for infection control purposes. Given the transmission potential of asymptomatic *C. difficile*-colonized patients, the increased prevalence among certain clinical groups, limited management options, and the limited utility of screening, instead, intensive infection control practices, normally reserved for diseased patients, should be targeted at individuals or clinical areas with higher risk of asymptomatic *C. difficile* colonization. Empirical research should be conducted into the impact of targeted, risk-based, intensive infection control programs before changes to the current SHEA guidelines for asymptomatic *C. difficile* colonized patients are considered.	Recommends: Intensive infection control practices (e.g., gloves and environmental cleaning), normally reserved for diseased patients, should be targeted at individuals or clinical areas with higher risk of asymptomatic *C. difficile* colonization. A standard definition for asymptomatic *C. difficile* colonization is needed. Suggest that patients with diarrheal symptoms with nontoxigenic strains of *C. difficile* should be considered colonized unless there is definitive evidence of disease. Estimates of asymptomatic colonization may be too low as stool culture is not practical in a clinical setting; however, this constitutes important future epidemiological study.	Review is mostly about the epidemiology, risk factors, transmission, toxin production, and duration of asymptomatic CDI. Article does address whether to test for asymptomatic colonization.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Marra and Ng, 2015[16]	Diagnostic testing for *C. difficile*: PCR or a two-step algorithm to improve sensitivity and specificity.	Not specified	A search for systematic reviews, clinical practice guidelines, and randomized control trials (RCTs) was conducted on articles going back to 1966. Article discusses findings for different testing methods, when to test, risk factors, epidemiology, and treatment of *C. difficile*. Each testing method has pros and cons in terms of time to conduct test, availability, and sensitivity and specificity. The stool culture test, also known as the cell culture cytotoxicity neutralization assay (CCCNA), has high sensitivity but is labor intensive and time consuming, taking 48–96 hours for results, and is not very specific. Using a procedure known as TC can overcome this problem by placing stool in a culture medium and then testing isolates with an immunoassay designed to detect toxin production. Compared with CCCNA, TC has a sensitivity of 67% to 79% but is too slow to be clinically useful (taking 4–7 days to obtain results). Enzyme immunoassays are fast and inexpensive but insensitive and not very specific. It is unclear where exactly PCR should be used; some laboratories are using it as a standalone test, while American College of Gastroenterology guidelines suggest it should be used as a confirmatory test. CDI testing algorithms suggest using GDH as the initial screening test, followed either by NAAT such as PCR or by EIA testing for GDH-positive specimens only. Only GDH-positive specimens undergo additional testing. The use of PCR has rapid turnaround to detect the gene for toxin production (tcdB gene) is promising as a standalone test for CDI but and has a rapid turnaround but costs 510 times more than EIA.	Diagnostic testing for CDI is in a state of flux. Review found that recent evidence and guidelines are suggesting a two- or three-step algorithmic approach to improve specificity and PPV. A few days may be necessary before confirmatory tests become available. Therefore, it is paramount that when CDI is suspected, appropriate antimicrobial therapy is initiated without delay and is reassessed once the laboratory testing is complete.	The objectives of this review are: to review the incidence of *C. difficile* infections around the world.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
O'Horo et al., 2012[34]	Two rapid molecular diagnostic techniques, PCR and loop-mediated isothermal amplification (LAMP)	Healthcare general	Systematic review and meta-analysis. Search yielded 25 PCR studies, including 11,801 samples that met inclusion criteria and 6 heterogeneous studies that evaluated LAMP. For PCR, with TC as a standard, pooled sensitivity was 0.92 (95% CI, 0.91 to 0.94); specificity, 0.94 (95% CI, 0.94 to 0.95); and diagnostic odds ratio, 378 (95% CI, 260 to 547). With cytotoxicity as a standard, pooled sensitivity was 0.87 (95% CI, 0.84 to 0.90); specificity, 0.97 (95% CI, 0.97 to 0.98); and diagnostic odds ratio, 370 (95% CI, 226 to 606). The six studies about LAMP used heterogeneous reference methods.	Review found that PCR is a highly accurate test for identifying CDI. Likelihood ratios, in particular when compared with a TC reference standard, indicate that the test is useful in determining post-test probability of CDI. Heterogeneity in LAMP studies did not allow meta-analysis; however, further research into this promising method is warranted.	None
Wei et al., 2015[37]	LAMP for the diagnosis of CDI	Healthcare general	Meta-analysis of studies on accuracy of LAMP for diagnosing CDI. Search of four databases up to February 2014. Nine studies met inclusion criteria for the present meta-analysis. The pooled sensitivities and specificities for diagnosing CDI were 0.93 (95% CI, 0.91 to 0.95) and 0.98 (95% CI, 0.98 to 0.99), respectively. The positive likelihood ratio was 47.72 (95% CI, 15.10 to 150.82), negative likelihood ratio was 0.07 (95% CI, 0.04 to 0.14), and diagnostic odds ratio was 745.19 (95% CI, 229.30 to 2421.72). The area under the ROC was 0.98. Meta-regression indicated that the total number of samples was a source of heterogeneity for LAMP in detection of CDI. The funnel plots suggested no publication bias. Compared with other non-culture-based methods, LAMP is a sensitive and specific method, although more expensive than traditional assay. LAMP can be performed in any laboratory without special requirements such as separate pre- and post-PCR rooms, which are necessary for real-time PCR or other PCR-based techniques, and LAMP cost-efficiency ($26) compared with the Xpert *C. difficile* assay ($46).	The LAMP test meets the minimum desirable characteristics of a diagnostic test of sensitivities and specificities, as well as other measures of accuracy in the diagnosis of CDI, and it is suitable as a rapid, effective, and reliable standalone diagnostic test, potentially decreasing morbidity and nosocomial spread of CDI.	None

Table B.28: Clostridioides difficile, Multicomponent Interventions–Single Studies

Note: Full references are available in the Section 4.6 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, moderate, Low)	Comments
Abbett et al., 2009[4]	The intervention included three components: an educational campaign, a prevention bundle, and a treatment bundle. The prevention checklist included: testing on suspected CDI, discontinuation of nonessential antimicrobials, contact precautions, hand hygiene reminders, dedicated stethoscope, flagging/ communication (sign on patients' doors, communication to team), isolation, terminal bleach cleaning for CDI rooms, and confirmation with supervisor that bleach cleaning was used. Guidelines were from Infectious Diseases Society of America and Society for Healthcare Epidemiology of America (IDSA/SHEA).	Observational before-and-after study of adult patients admitted to a tertiary care, university-affiliated hospital from January 2004 through December 2008. Followed patients for a total of 1,047,849 patient-days.	A 750-bed tertiary care, university-affiliated hospital, United States	Four years of data. Healthcare-associated CDI incidence rates fell from an average of 1.10 cases per 1,000 patient-days (95% confidence interval [CI], 1.00 to 1.21) before intervention to 0.66 cases per 1,000 patient days (95% CI, 0.60 to 0.72) after intervention. This statistically significant decrease amounts to a 40% reduction in incidence after the intervention. The decreasing rates of CDI noted after the implementation are even more striking because of the more complete ascertainment of cases of CDI that would be expected with an increased frequency of *C. difficile* toxin testing. No changes in chance of mortality.	Number of *C. difficile* toxin tests sent to the microbiology laboratory increased significantly from the pre-intervention period (rate, 28.0 tests per 1,000 patient-days [95% CI, 27.5 to 28.5]) to the post-intervention period (rate, 32.1 tests per 1,000 patient-days [95% CI,31.7–32.6]).	The intervention did not include antimicrobial stewardship, citing resource intensiveness of this PSP. Bundle delineated individual responsibilities for physicians, physician assistants, nurse practitioners, floor nurses, microbiology staff, infection control practitioners, and environmental services personnel. The bundle begins with "provider suspicion," which is defined as the ordering of a stool *C. difficile* toxin test. Intervention relied on increasing provider suspicion for CDI. Authors report that providers may be under pressure from payers who may no longer reimburse for cases of CDI and other healthcare-associated infections, and may be pushed to limit toxin testing and other documentation of CDI. Researchers suggest use of checklists to increase/measure compliance.	Low to moderate	Cost-effectiveness not measured

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, moderate, Low)	Comments
Barker et al., 2017[1]	Eight multiple-intervention bundles at reducing hospital-onset (HO) CDI and asymptomatic *C. difficile* colonization	An agent-based model of *C. difficile* transmission in a 200-bed adult hospital using studies from the literature, supplemented with primary data collection. The model includes an environmental component and four distinct agent types: patients, visitors, nurses, and physicians. Each model run simulates a 1-year period.	Simulated 200-bed adult hospital	Daily cleaning with sporicidal disinfectant and *C. difficile* screening at admission were the most effective single-intervention strategies, reducing HO CDI by 68.9% and 35.7%, respectively (both p <0.001). Combining these interventions into a two-intervention bundle reduced HO CDI by 82.3% and asymptomatic hospital-onset colonization by 90.6% (both, p <0.001). Adding patient hand hygiene to healthcare worker hand hygiene reduced HO CDI rates an additional 7.9%.	Visitor hand hygiene and contact precaution interventions did not reduce HO CDI compared with baseline. Excluding those strategies, healthcare worker contact precautions were the least effective intervention at reducing hospital-onset colonization and infection.	Article concludes that identifying and managing the vast hospital reservoir of asymptomatic *C. difficile* by screening and daily cleaning with sporicidal disinfectant are high-yield strategies. These findings provide data regarding which interventions to prioritize for optimal *C. difficile* control. The optimal bundle for CDI prevention is unknown, which hinders CDI prevention. Computer simulation modeling can allow examination of counterfactual scenarios that can identify the isolated effects of individual interventions to reduce CDI. Agent-based models can account for the indirect effects and underlying complexity of hospital infection control dynamics.	Moderate	Study also examined nine single interventions.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, moderate, Low)	Comments
Brakovich et al., 2013[5]	A tiered approach that included environmental cleaning and disinfection, diagnostics and surveillance, contact isolation, contact precautions, hand hygiene (soap and water) for CDI patients, and antibiotic stewardship. Approach was based on the IDSA/SHEA guidelines.	Pre/post-intervention measurements. Patients are admitted from surrounding hospitals, have an expected stay of at least 25 days, and are acutely ill. Most of the patient population is ventilator dependent, immune compromised, and treated with antimicrobials.	A 50-bed long-term acute-care hospital (LTACH) in the southeastern United States	Based on year-end results, the facility achieved a 27.61% decrease in the CDI rate. Over the course of 2 years, the CDI rate decreased 44.25%. The program was cost efficient barring the contract for the decontamination service. The hydrogen peroxide vapor (HPV) equipment and services contracted by the facility incurred the cost of $1,800 per month. This cost included decontamination of all rooms previously occupied by patients with CDI. The cost of microfiber mops and environmental services staff education was approximately $650.	Not provided	Researchers believed that training for environmental services was crucial. They also noted the development of a cleaning checklist and use of HPV for disinfection of rooms occupied by patients with CDI. Isolation signs for patient doors were redesigned to include guidelines for staff and families on appropriate isolation attire. Strict adherence to hand hygiene, which included washing with soap and water while applying friction, was strongly enforced and hand sanitizers were removed from patient rooms. Use of Interdisciplinary team. Researchers emphasized importance of surveillance, ongoing education, and reinforcement of intervention during daily meetings.	Low to moderate	Ventilated patients, patients requiring extended intravenous antibiotic therapy, and medically complex patients make up the population of an LTACH.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, moderate, Low)	Comments
Cheng et al., 2015[3]	Education, monitoring hand hygiene, antimicrobial stewardship, dedicated medical equipment, and items such as bedpans and commodes. Hand washing with soap and water was the preferred method of hand hygiene after caring for patients with CDI. The patient's room was cleaned at least twice daily with sodium hypochlorite 1,000 ppm. Cleaning staff were trained on high-touch surfaces. Terminal cleaning of the patient's room for 30 minutes and change of curtains.	Pre/post-observational study of 329 patients with healthcare-associated CDI	A university-affiliated acute hospital and three extended-care hospitals with a total of 3,200 beds, Hong Kong	The incidence rates of HA CDI per 10,000 admissions and 10,000 patient-days increased significantly by 15.3% and 17.0%, respectively, per quarter ($p<0.001$) from 2008 1Q to 2010 1Q by segmented Poisson regression. Coincident with the promotion of hand hygiene using alcohol-based hand rubs (ABHRs), the overall compliance of hand hygiene increased from 57.8% (2008) to 78.6% (2012), while the proportion of hand washing using soap and water gradually decreased from 19.0% (2008) to 13.3% (2012). The consumption of broad-spectrum antibiotics presented as divided daily dose per 1,000 acute bed-day occupancy was 140.9 and 152.3 per quarter before and after infection control interventions, respectively.	Not provided	More about the intervention: Cleaning staff were trained for 20 minutes with specific emphasis on the meticulous disinfection of high-touch areas, such as bedrail, bedside table, and locker. Education health talks were given to infection control-linked persons and ward staff four times a year. The compliance of hand hygiene of healthcare workers was monitored. Three or more CDI patients epidemiologically linked to the same ward were identified. An antibiotic stewardship program was maintained throughout the study period. The consumption of broad-spectrum antibiotics was monitored.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, moderate, Low)	Comments
Koll et al., 2014[9]	Collaborative intervention, interdisciplinary teams, environmental cleaning, data reports, checklists, contact precaution for all patients with diarrhea, personal protective equipment readily available and used, adherence to hand hygiene protocol, dedicated rectal thermometers, private room for CDI (confirmed or suspected), patient cohorting, if private room unavailable, as a last option, dedicated bathroom for CDI patients in a shared room with non-CDI patient	Quasi-experimental pre-post. Data were collected monthly from March 2008 to December 2009. Hospitals collected and reported total patient days and discharges, as well as 14 patient-level data elements for each CDI case. Data were received for 14,591 cases of CDI.	35 acute care hospitals in the New York metropolitan region. Mostly teaching hospitals.	Before data collection, 52% of hospitals measured and monitored prevention practices. The mean reported compliance with the prevention bundle was 95%; the mean compliance reported for the environmental cleaning protocol was 96%. There was a pronounced downward trend in the hospital-onset (HO)-CDI rate from ~13.5 per 10,000 patient-days to ~8.2 per 10,000-patient days (no exact figure given) based on the chart. A regression analysis demonstrated that the predicted HO reduction over time was significant over the course of the project ($p<0.001$). Hospitals reporting the highest CDI rates at the project's beginning generally demonstrated the greatest reductions.	Not provided	Study reports that implementing interventions to interrupt and prevent *C. difficile* transmission may be more successful regionally than at individual hospitals because existing evidence suggests community and regional factors, including transferring patients between healthcare facilities, contributes to the epidemiology of *C. difficile*. In the intervention, hospitals were asked to establish an internal interdisciplinary team to drive CDI reduction efforts that comprised, at a minimum, infection preventionists, physician and nurse champions, support staff from environmental and transport services, and quality improvement personnel. Hospitals received monthly data reports to monitor performance changes over time.	Low	Weakness: no control group, inconsistencies in implementation across hospitals. Strength: large sample.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, moderate, Low)	Comments
Power et al., 2010[6]	Enhanced cleaning, hand hygiene audits, education, antimicrobial stewardship	Interrupted time series in five collaborative wards (intervention group) and 35 non-collaborative wards (control group)	An 850-bed university teaching hospital, United Kingdom	At baseline, the non-collaborative wards had 1.15 (95% CI, 1.03 to 1.29) cases per 1,000 occupied bed days. In August 2007, cases decreased 56% from baseline (0.51, 95% CI, 0.44 to 0.60), which has been maintained since that time. In the collaborative wards, there were 2.60 (95% CI 2.11 to 3.17) cases per 1,000 occupied bed days at baseline. A shift occurred in April 2007, representing a reduction of 73% (0.69, 95% CI, 0.50 to 0.91) from baseline, which has been maintained.	Not provided	Study found that a collaborative learning model can enable teams to test and implement changes that can accelerate, amplify, and sustain control of *C. difficile*. Teams worked together over a 9-month period (mid-March to mid-December 2007). They attended learning sessions, which provided instruction in the theory and practice of improvement, participated in action periods in which they tested changes. During the 6 months that predated the collaborative, changes were made to infection control throughout the hospital. These included the introduction of a rapid response cleaning team, a deep clean program, and a focus on hand hygiene and uniform protocols.	Low	Context: 2006, Salford Royal had 350 cases of CDI in patients over 65, the fourth highest rate of infection in northwestern England. In spite of systemwide changes in infection control, infections rose, peaking at 115 cases during the first quarter of 2007.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, moderate, Low)	Comments
Price et al., 2010[8]	The initiative introduced had two main components: (1 the opening of an 11-bed cohort ward for patients with CDI and (2) a new antibiotic policy restricting the use of cephalosporins and quinolones	A retrospective interrupted time series analysis looking at antibiotic use and number of CDI cases was conducted, with the pre-intervention phase being January to December 2007 and the post-intervention phase being January 2008 to March 2009.	An 820-bed teaching hospital, United Kingdom	Although the number of CDI cases each month was falling before the intervention, there was a significant increase in the rate of reduction after the intervention from 3% to 8% per month (0.92, 95% CI, 0.86 to 0.99, p=0.03).	Not provided	A demonstration of a statistically robust change in CDI rates after the intervention supports the efficacy of enhanced isolation and antibiotic restriction in reducing CDI. The cohorting ward was specifically for patients with CDI. Patients testing positive for CDI who still had ongoing diarrhea were transferred to the cohort ward on the same day. The ward had its own nursing staff and all patients admitted to the ward were transferred to the care of the infectious diseases team. All staff working on the ward wore scrubs and put on a new apron and gloves between each patient contact. The new antibiotic policy replaced cephalosporin and quinolone antibiotics with aminopenicillin or antipseudomonal penicillins.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, moderate, Low)	Comments
Salgado et al., 2009[15]	Multicomponent intervention "enhanced infection control measures" (EICM), including placing patients with diarrhea into empiric contact precautions, cleaning with a bleach product in areas with CDI patients, and requiring soap and water hand hygiene. Memos describing EICM were sent to all patient care areas of the hospital and detailed in-services were conducted in areas with high CDI rates just prior to full implementation. (Historically, patients with diarrhea were routinely placed into contact precautions once they were diagnosed with CDI; hand hygiene and environmental cleaning not discussed or monitored.)	Pre/post-intervention measurements of CDI rates, amount of antibiotics prescribed, cleaning in areas with CDI patients, and trends in hand hygiene, i.e., washing with soap and water. Time series methodology was used to examine the association between CDI and antibiotic use.	A 610-bed, tertiary care, academic institution, South Carolina	During the outbreak (October 2004 to May 2005), the authors observed 144 excess cases of CDI. The CDI rate decreased after EICM were implemented ($p<0.0001$) and maintained for 36 months beyond the outbreak. The CDI rate decreased significantly over the subsequent 6 months after EICM were implemented ($p <.0001$). The greatest absolute as well as relative decrease in CDI rates occurred over the first 3 months after implementing EICM (a 2.50 per 1,000 patient-days rate decrease and 45.3% decrease, respectively). Measured antibiotic use increased. Multivariate analysis revealed positive associations between CDI rates and cefazolin use ($p=0.008$) and levofloxacin/gatifloxacin use ($p=0.015$).	Not provided	Without instituting a targeted antibiotic control program or any formulary changes, in this case an outbreak of nosocomial CDI was controlled with the use of EICM as recommended by the CDC. This finding may indicate that interruption of patient-to-patient spread can be an effective control measure for CDI. EICM were implemented early in the outbreak. Environmental services employees used a daily checklist to ensure proper cleaning techniques and use of proper products for patients with epidemiologically important organisms (such as *C. difficile*). To encourage the use of soap and water, signs were posted over the alcohol gel dispensers.	Low to moderate	Only nosocomial CDI rates were measured. Environmental hand hygiene compliance ranges from 62% to 80%. The results of this study would suggest a positive association between hospitalwide CDI rates and use of some antimicrobials.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, moderate, Low)	Comments
Weiss et al., 2009[7]	Dedicated housekeeping for CDI rooms; increase in housekeeping hours, 1:50 mixture of bleach to water, dedicated ward for CDI patients, contact isolation, hand washing out of rooms, limit of one visitor at a time, gloves, patient hand hygiene, prescribing guidelines, rapid enzyme immunoassay for each patient at first liquid stool, hiring of four infection prevention and control experts, staff education, 85 new sinks, no ABHRs when working with CDI patients, surveillance	Five-year (2002 to 2006) prospective observational study; most interventions occurred between years 3 and 4.	A 554-bed acute-care tertiary teaching hospital, Canada	From 2003 to 2004, there were 762 cases of CDI (mean annual rate, 37.28 cases per 1,000 admissions) recorded in the study, compared with the 292 cases of CDI (14.48 cases per 1,000 admissions) from 2006 to 2007 (odds ratio, 0.379, 95% CI, 0.331 to 0.435; p<0.001), a 61% reduction. This finding was comparable to the decreasing rates observed in other Quebec institutions once the provincial government started investing in infection control measures and forced institutions to implement them. Since the implementation of all the measures, there was a plateau, with monthly rates usually oscillating between 9 and 14 cases per 1,000 admissions. From 2002-2003 to 2006-2007, there was also a 26.2% increase in the number of hours dedicated to housekeeping, compared with 2003-2004.	Not provided	Outbreak situation. It is difficult to pinpoint a single intervention as the most effective. Simple, low-technology measures such as hand washing with soap and water, environmental cleaning with bleach, and rapid contact isolation of infected patients in a dedicated ward seemed to have an impact on number of CDI cases. With a decreasing number of CDI cases, physicians who were following published evidence-based guidelines started prescribing fluoroquinolones again. The authors report that antibiotic use seems to act more as a triggering factor.	Low	Massive CDI outbreak that affected the province of Quebec mainly from 2002 to 2005.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, moderate, Low)	Comments
Yakob et al., 2014[2]	Four control methods were explored in this analysis: (1) improved hand hygiene and sanitation; (2) stricter antimicrobial stewardship; (3) reduced length of stay for inpatients; and (4) expedited gut microbiota recovery, which can be achieved either through administering probiotics or through intestinal microbiota transplantation.	Simulation: A biological model of *C. difficile* used to simulate the modern epidemiology of the pathogen; and analysis of control combination. Number of patients in the model is not provided.	Simulated acute healthcare facility	The only combination of methods that provided significant gains in ameliorating CDI incidence was the simultaneous reduction in length of stay and the transmission coefficient. All control methods generated marked improvements in reducing the colonized ratio. Reducing the transmission coefficient through improvements to hygiene and sanitation had a comparatively large effect in decreasing the incidence of disease. Antimicrobial stewardship yielded meager benefits in terms of reducing the incidence of CDI, regardless of combination with other methods.	Not provided	The simulation output agrees in that it also demonstrates an inability to eliminate *C. difficile* from the hospital simply through cessation of within-hospital transmission. However, simulations indicate that under this highly idealized scenario of no within-hospital transmission, closer to 60% of infections can be controlled. More research is needed on different combinations of interventions. The next phase of development for this research is the conversion of the general, strategic framework presented here into a more tactical (idiosyncratic) tool for exploring control options for CDI in a specified healthcare setting.	Moderate	None

Table B.29: Clostridioides *difficile,* Multicomponent Interventions–Systematic Review

Note: Full references are available in the Section 4.6 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Barker et al., 2017[1]	*C. difficile* prevention bundles	Inpatient/ hospitals in a variety of contexts	Systematic review to examine the components of CDI bundles, their implementation processes, and their impact on CDI rates. Twenty-six studies met inclusion criteria. Despite different settings and the variety of bundle components used, all studies reported an improvement in CDI rates. Implementation and adherence factors to interventions were variably and incompletely reported, making study reproducibility and replicability challenging. Authors noted a lack of randomized controlled trials in the literature, making it unclear if CDI reduction can be attributed to a similar mechanism across all studies. The most common bundle components were: hand hygiene and environmental cleaning—both were included in 88.5% (23/26) of the studies. These were followed by isolation and/or cohorting (77%, 20/26). Contact precautions, antibiotic stewardship, and staff education were each included in 73% (19/26) of studies. System and workflow changes were in 54% (14/26), dedicated equipment, 27% (7/26), patient education, 19% (5/26), and proton pump inhibitor stewardship, 12% (3/26). (Within each category, the interventions were multifaceted.) The improvement was significant at the 0.05 level for the 15 studies reporting p-values (60%, 15/25). Authors concluded that, given the lack of randomized controlled trials in the literature, assessing a causal relationship between bundled interventions and CDI rates is currently impossible. Almost all articles reported measuring adherence for at least one component in the bundle (96.2%, 25/26) and 46.2% measured adherence for each component (12/26). However, most studies only stated that they had evaluated adherence to a bundle component, without reporting compliance results.	In all studies reviewed, bundle implementation was associated with a decline in CDI rates. There was considerable variation among the choice of bundle elements, making it hard to determine which components to implement. Despite the effectiveness of bundles, the authors conclude that there are three potential reasons for a lack of decline in CDI rates in certain hospitals: First, compliance with interventions may be below the threshold necessary to be effective. If adherence to bundle elements was low in the reviewed studies, the potential impact of *C. difficile* bundles may be underestimated. Second is the lack of infection control strategies focusing on asymptomatic carriers. Finally, since ABHRs do not kill CDI spores, hand hygiene compliance data that include the use of pure ABHRs may provide hospitals with an inaccurate assessment of CDI prevention efforts.	Article explores bundles' effectiveness in reducing CDI, issues with studies about bundles, and a discussion of the problem of healthcare workers' implementation of and compliance with bundles. Re: setting: This review draws from a wide range of hospital types, locations, and infection control contexts. Authors state that, since CDI rates improved across all studies despite contextual differences and the variety of bundle components, a tailored bundle approach may be effective.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Louh et al., 2017[13]	Review of interventions to reduce CDI, including bundles	Acute care hospitals	Systematic search for controlled trials of interventions to reduce the rate of CDI in acute care. Review of articles published between January 1, 2009, and August 1, 2015. Overall, 14 studies described the implementation of multiple interventions either simultaneously or sequentially. All found significant reductions in CDI from baseline. However, there was substantial heterogeneity among the studies, with some using concurrent environmental cleaning, which may have affected the results. Most common bundles incorporate two or more of the following: cleaning, isolation, checklists, education, antimicrobial stewardship programs (ASPs), contact precautions and hand hygiene. Bundled interventions with environmental efforts appeared to be more effective than those without them. Several interventions, including disposable thermometers, hand hygiene, universal gloving, and chlorhexidine gluconate bathing, do not need further evaluation and have sufficient evidence to make firm recommendations regarding managing CDI in acute care hospitals. In contrast, there is still much to learn about ASPs given the heterogeneity of study results.	Institutions with few resources should strive to improve environmental practices, with implementation of bleach-based cleaning. Institutions with more resources should consider bundled interventions that incorporate environmental cleaning, restrictive ASPs, and checklists.	Authors found that, in prevention studies performed in acute care hospitals, bleach-based environmental disinfection and bundled interventions appeared to have the most effect in preventing CDI.
Yakob et al., 2014[2]	*C. difficile* control bundles	Healthcare facilities	Search for articles published up to March 2014. Studies eligible for inclusion were those describing patient levels of symptomatic *C. difficile* infection before and after the implementation of multiple, overlapping infection transmission interventions. The relatively few studies detailing a bundle approach to *C. difficile* control indicate substantial reductions in disease incidence in healthcare settings from 33% to 61%. Assessments of these multicomponent interventions cannot partition the level of infection reduction to the individual control methods. Disentangling the efficacies of the different controls when they are used in conjunction is impossible, as is the precise estimation of any synergistic effect between control methods.	Multicomponent interventions appear to be effective. Research into strategic infection control combinations for healthcare-acquired pathogens is underdeveloped and needed to better understand the impact of different combinations of interventions.	None

Table B.30: MDRO, Chlorhexidine Bathing—Systematic Reviews

Note: Full references are available in Section 5.1 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Denny and Munro, 2017[5]	Bathing with chlorhexidine gluconate (2%-4%)	General healthcare settings, various countries (including the United States)	A literature search was conducted to identify peer-reviewed studies and meta-analyses that examined the impact of chlorhexidine bathing on HAIs. Generally found good evidence to support incorporating a chlorhexidine bathing regimen to reduce the incidence of CLABSIs, SSIs, and VRE and MRSA infections. MRSA: Several reviewed studies showed a decrease in MRSA transmission or colonization, although not always statistically significant compared with other treatment. VRE: Reduction of colonization on patients' skin and contamination of healthcare workers' hands and environment. Device- and procedure-associated infections (SSI, CLABSI, CAUTI, VAP): Mixed results of success in preventing SSI. Statistically significant reductions in CLABSIs. Reduction in CAUTIs and VAPs as well.	Chlorhexidine gluconate washcloths are more expensive than liquid but require less bathing time. Rinsing is not recommended, to maximize residual contact with skin. Adverse events consist of skin irritation. Accidental or intentional exposure to sensitive areas (eye, esophagus, intestinal lining, inner ear) has caused injury to those areas. Severe anaphylaxis is possible but rare. Future research should include randomized, controlled trials with specific bathing durations/ frequencies; studies of chlorhexidine resistance; and studies of compliance.	Organisms/Outcomes: VRE, MRSA CLABSIs, SSIs, VAPs, CAUTIs Compares level of evidence for studies.
Derde et al., 2012[6]	Bathing with chlorhexidine gluconate	ICUs, geographic locations not specified	Data from 16 studies were extracted. Chlorhexidine bathing statistically significantly reduced MRSA acquisition in 3 studies; significant reduction in MRSA infection was only observed in 1 of 5 studies. Carriage and bacteremia rates of VRE both significantly declined. Few studies had data on antibiotic-resistant Gram-negative bacteria.	Studies of chlorhexidine bathing also included other prevention practices, such as active surveillance or intranasal mupirocin, and did not control for the impact of these practices when evaluating the effectiveness of bathing.	Organisms/Outcomes: VRE, MRSA Review of seven studies; low risk of bias in individual studies, but also marked difference between the interventions in each study.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Sidler et al., 2014[7]	Chlorhexidine bathing	General healthcare setting, various countries (including the United States)	Swiss literature review on general infection prevention and control practices. Mixed results: one cluster-randomized trial showed a significant reduction (28%) in hospital-acquired BSIs in nine U.S. ICUs with daily washing, but not for MRSA- or VRE-related infections. Another meta-analysis showed significantly reduced MRSA/VRE colonization and infection densities in patients treated with daily washing compared with patients without (incidence rate ratio [IRR] 0.51; 95% CI 0.36–0.73; and IRR 0.57; 95% CI 0.33–0.97 for VRE colonization and VRE infection, respectively). Few studies have addressed the effect of chlorhexidine on extended-spectrum beta-lactamase producing Gram-negative bacteria (ESBL-GNB).	This review found mixed results for VRE and MRSA. Only a few studies addressed the effect of chlorhexidine body washing on ESBL-GNB and *C. difficile.*	Organisms/Outcomes: VRE, MRSA, ESBL-GNB Brief section in a larger literature review on MDR Enterococci.
Tacconelli et al., 2014[24]	Decolonization with chlorhexidine for MDR-GNB	Healthcare, various countries (including the United States)	European guidelines and systematic review that studied decolonization with chlorhexidine as part of a larger review on managing MDR-GNB. Decolonization with chlorhexidine is well studied and well supported for MRSA. However, for ESBL-producing Enterobacteriaceae, decolonization is short lived. The available evidence for efficacy against MDR-GNB does not support chlorhexidine use for decolonization. Reduced susceptibility to chlorhexidine has been reported among GNB, so sustained use should ideally be accompanied by surveillance for resistance over time.	The authors concluded that the available evidence did not support chlorhedixine use for MDR-GNB, although it is an effective part of decolonization regimens for MRSA, VRE, Gram-positive bacteria, and (temporarily) for ESBL-producing Enterobacteriaceae.	Organisms/Outcomes: VRE, MRSA, MDR GNB

Table B.31: MDRO, Chlorhexidine Bathing—Single Studies

Note: Full references are available in Section 5.1 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Abboud et al., 2016[16]	Enhanced control measures for ICU patients: providing alcohol gel at the bedside, daily bathing with no-rinse 2% chlorhexidine-impregnated washcloths, and disinfection of surfaces around the patient three times per day (provided in addition to the usual measures of screening and cohort nursing)	Observational pre-post cohort study; 543 patients; 1,120 cultures collected, 239 in the pre-intervention period and 881 in the post-intervention period.	40-bed post-operative adult cardiac surgery intensive care unit (ICU), Brazil	For carbapenem-resistant Enterobacteriaceae (CRE) isolation, 64 of 239 (26.8%) positive cultures were found in the pre-intervention period compared with 82 of 881 (9.3%) in the post-intervention period (p<0.001). The median time from CRE infection to colonization increased from 8 days to 14 days (statistical significance not assessed). The incidence of central line-associated bloodstream infections (CLABSIs) with CRE fell from 2.07 per 1,000 central-line-days in the pre-intervention period to 0.23 per 1,000 central-line-days in the post-intervention period (p<0.002). The rate of surgical site infections (SSIs) from CRE decreased from 2.4% in the pre-intervention period to 0.8% in the post-	A statistically significant increase in multidrug resistant (MDR) *P. aeruginosa* was observed post-intervention (p=0.0348).	The study demonstrated that the enhanced control measures—alcohol-based hand rub and chlorhexidine bathing (CHB)—were associated with a significant decrease in SSIs, CLABSIs, and CRE colonization. This finding is consistent with other studies showing the efficacy of using alcohol-based hand rub and CHB for reducing patient and environmental MDR organisms' rates. Due to study design, the relative effects of hand hygiene vs. CHB could not be assessed.	Moderate Compliance with hand hygiene using alcohol-based hand rub was not assessed, and the study did not include a control group of patients not receiving CHB.	Organisms/ Outcomes: CRE, *P. aeruginosa* Colonization, CLABSI, SSI, VAP and UTI rates, mean time to colonization

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
				intervention period (p<0.003). Other CRE infections such as ventilator-associated pneumonia (VAP) and urinary tract infections (UTIs) decreased, but the decreases were not statistically significant.				
Alotaibi et al., 2017[41]	In vitro evaluation of vancomycin-resistant *Enterococcus faecium* (VRE) resistance to benzalkonium chloride, chlorhexidine and hydrogen peroxide biocides	In vitro study of VRE and vancomycin-susceptible *Enterococcus* (VSE) isolates' susceptibility. 12 VSE *faecium* and 37 VRE *faecium* isolates obtained from Danish patients and chosen to represent an extended time period and cover major subtypes.	Isolations collected from hospitals, Denmark	Both VRE and VSE *faecium* strains displayed equal susceptibility to hydrogen peroxide, but a higher minimal bactericidal concentration (MBC, the lowest concentration required to kill a bacterium over 48 hours) was found for the former: 75% of VRE *faecium* showed MBC values of 70 mg/L or higher compared with only 25% of VSE *faecium.* (The difference was statistically significant, but p-values were not reported for this measure.)	For benzalkonium chloride, 89% of VRE *faecium* strains had a minimal inhibitory concentration (MIC) of 8 mg/L (the highest level reported in the article) whereas for VSE *faecium* strains, only 25% of the strains had an MIC of 8 mg/L. Almost all VRE strains (97%) showed a higher MBC of 8 mg/L or higher. Both the higher MIC and MBC of VRE strains compared with VSE strains were statistically significant (p<0.0001; chi-square test). For chlorhexidine, the MIC of 95% of VRE *faecium* strains was 4 mg/L or higher, while only	VRE *faecium* strains isolated from Danish hospitals demonstrated decreased susceptibility toward benzalkonium chloride and chlorhexidine compared with VSE strains, where the use of chlorhexidine is particularly heavy in hospitals. The enhanced tolerance of VRE strains to benzalkonium chloride and chlorhexidine was also reflected in reduced biocidal killing compared with VSE strains. The researchers suggest that these results imply that survival of VRE strains is superior to that of VSE strains with regard to two key	Low to moderate	*Organisms/ Outcomes VRE, VSE Bactericidal susceptibility of benzalkonium chloride, chlorhexidine, and hydrogen peroxide* Study uses Danish isolates. Well-designed study but tested in vitro only, not in a patient care setting.

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					33% of VSE *faecium* strains displayed MIC values at the same level (p=0.0003; chi-square test). The MBC for 95% of VRE strains was 4 mg/L or higher, compared with 50% of VSE strains (p=0.0013; chi-square test).	cleaning and disinfection agents commonly used in hospitals; and that the selective advantage in the presence of these agents may increase the prevalence of VRE *faecium* strains in hospitals.		
Boonyasiri et al., 2016[19]	Once-daily bathing with 2% chlorhexidine-impregnated wipes, without rinsing, compared with bathing with non-antimicrobial soap	Randomized, open-label controlled trial of 481 patients in 4 Thai ICUs. Patients were randomly assigned either to the control group (bathing with non-antimicrobial soap, n=241) or the chlorhexidine group (n=240).	Intensive care setting, Thailand	Once-daily cleansing of ICU patients with no-rinse 2% chlorhexidine-impregnated washcloths did not prevent or delay MDR Gram-negative bacteria colonization compared with routine twice-daily cleansing with nonantimicrobial soap. Favorable events (all samples negative throughout ICU admission, or initially positive samples with subsequent negative samples) at day 14 were observed in 34.8% of patients in the control group and 28.6% in the chlorhexidine group (p=0.79; not statistically significant).	A 2.5% incidence rate of mild skin reactions.	Use of 2% chlorhexidine-impregnated washcloths was not associated with fewer colonization events or infections by MDR Gram-negative organisms than twice-daily bathing with nonantimicrobial soap. Researchers also found that the time spent using the washcloths was much less than with the soap and it was also low cost and easy to implement, despite not producing desired outcomes.	Low	Organisms/ Outcomes MDR Gram-negative bacteria: extended spectrum beta-lactamase (ESBL) producing *Escherichia coli,* ESBL-producing *Klebsiella pneumoniae,* MDR *P. aeruginosa,* MDR *A. baumannii,* VRE No colonization event or confirmed decolonization; target MDR bacteria colonization-free time; VAP, CLABSI, CAUTI rates; length of

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				No statistically significant reduction in VAP rates (5.0% in control group vs. 5.8% in CHB group; p=0.69), CLABSI rates (2.0% vs 1.1%, p=0.74), or catheter-associated urinary tract infection (CAUTI) rates (7.0% vs. 8.5%, p=0.17). Mean length of ICU stay (16.5 days in control group vs. 14.6 days in CHB group, p=0.42) and mean length of total hospital stay (35.9 days vs. 31.8 days, statistical test not reported) did not differ.				ICU stay and length of hospital stay; and adverse skin reactions.
Camus et al., 2014[20]	Twice-daily bathing with 4% chlorhexidine solution (with rinsing) and 0.5% chlorhexidine mouthwash (4 times daily), as part of a decontamination protocol that also included:	Nonrandomized, pre-post study (1 year before and 1 year after intervention) with placebo control. The control group had 925 patients and the intervention group had	21-bed hospital ICU, France	The pre- and post-period groups were similar, except for a statistically significant difference in the distribution of the main diagnosis,[u] a lower Glasgow coma score (p=0.005), and a lower proportion of healthcare-associated infections at admission (p=0.02). All-cause infection rates were lower in	According to the article, the main concern with selective digestive decontamination (SDD) is the potential induction of antibiotic resistance, especially increased MRSA and VRE acquisition rates. The authors did not observe this occurrence in their study but noted that the number of	The intervention was associated with a reduction in acquired infections in all ICU patients, for all types of infections (including those related to MDR organisms.)	Low to moderate CHB was also combined with a chlor-hexidine mouthwash and with antibiotic treatment. The effect of each component	Organisms/ Outcomes Methicillin-susceptible *Staphylococcus aureus* (MSSA) Methicillin-resistant *S. aureus* (MRSA) MDR Gram-negative rod bacteria, including: *Enterobacter* species, *P.*

[u]The authors provide a *p*-value of 0.009, but it is not clear how it was calculated for the distribution of diagnoses.

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	1. Mupirocin (applied to nostrils 3 times daily); and 2. A mixture of polymyxin/ tobramycin/ amphotericin B administered to oropharynx and through gastric tube.	1,022 patients.		the intervention group, with adjusted odds ratios of 0.45 (0.31 to 0.63) in all patients; 0.43 (0.30 to 0.61) in those with a length of stay ≥48 hours; and 0.35 (0.2 to 0.54) in those intubated for ≥48 hours (all p< 0.001). Those in the intervention group with a shorter intubation period were also less likely to have an infection, but this difference was not statistically significant (adjusted odds ratio = 0.77, 0.35 to 1.71; p=0.52). The intervention group had lower rates of all acquired infections (9.4 vs. 23.6 per 1,000 patient-days; p<0.001), intubation-related pneumonia (5.1 vs 17.1 per 1,000 ventilator-days; p<0.001), and catheter-related BSIs (1.0 vs. 3.5 per 1,000 catheter-days; p=0.03). Fewer patients acquired infections due to MDR aerobic Gram-negative bacteria (p=0.008). Time to	acquired MRSA infections was too small from which to draw conclusions about any change in rates.		was not assessed. Rates for specific healthcare-associated infections (HAIs) caused by MDR Gram-negative bacteria were not provided.	*aeruginosa,* and ESBL-producing *K. pneumoniae*

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				first acquired infection was the same in both groups, as was length of stay. Antibiotic consumption was reduced in the intervention group, however.				
Camus et al., 2016[28]	Twice-daily bathing with 4% chlorhexidine solution (with rinsing) and 0.5% chlorhexidine mouthwash (4 times daily), as part of a decontamination bundle that also included: 1. Mupirocin (applied to nostrils 3 times daily); and 2. A mixture of polymyxin/ tobramycin/ amphotericin B administered to oropharynx and through gastric tube.	Observational time series: prospective, single-center study of ICU patients admitted over 5 years. 5,250 patients in intervention group over a 4-year period. Long-term assessment of impact of intervention on acquired infections from MDR aerobic Gram-negative bacilli (GNB) and acquired episodes of ESBL-producing Enterobacteri-aceae rectal carriage (see Camus et al., 2014)	Hospital ICU, France	The incidence rate of infections from MDR aerobic GNB was 5.43% during the 1-year pre-intervention period. It was significantly lower during the entire 5-year study period (1.59%, p<0.0001) and during each study year (2.02% [2008]; 2.50% [2009]; 2.13% [2010]; 0.77% [2011]; 0.50% [2012]; all p<0.01). The proportion of those who acquired rectal carriage of ESBL-producing Enterobacteriaceae during their ICU stays gradually declined with time (trend test using the Cox regression model: odds ratio = 0.92 [0.86 to 0.99], p=0.03).	No harms observed (no additional resistance or colonization with resistant organisms).	A multiple decontamination regimen did not lead to the emergence of MDR aerobic GNB. Infection and colonization rates declined with time.	Low to moderate Well-designed study but unable to speak to efficacy of only the chlor-hexidine bathing and mouthwash components of the regimen.	Organisms/ Outcomes Methicillin-susceptible *Staphylococcus aureus* (MSSA) Methicillin-resistant *S. aureus* (MRSA) MDR Gram-negative rod bacteria, including: *Enterobacter* species, *P. aeruginosa,* and ESBL-producing *K. pneumoniae*

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Cho et al., 2018[43]	Evaluation of chlorhexidine tolerance genes among MRSA isolates in a surgical intensive care unit (ICU) where MRSA-colonized patients are decolonized via CHB	Retrospective, genetic study of chlorhexidine and mupirocin resistance in MRSA isolates (n=119) from 135 ICU patients	Hospital ICU, South Korea	None assessed.	Among the isolates, 39 (32.8%) carried the quaternary ammonium compound (QAC) A/B genes, and 23 (19.3%) exhibited mupirocin resistance. Patients with QAC A/B-positive isolates were more likely to have ICU-acquired MRSA (p<0.001), longer ICU stays (p=0.030), and long hospital stays (p<0.001) than did patients with QAC A/B-negative isolates. QAC A/B-positive isolates were more likely than were QAC A/B-negative isolates to exhibit mupirocin resistance (p<0.001), a chlorhexidine MIC greater than 8mg/L (p=0.005), and the vancomycin-intermediate *S. aureus* phenotype (p<0.001).	QAC A/B-positive strains will require higher concentrations of chlorhexidine for successful environmental cleaning and have implications for decolonization strategies using CHB and mupirocin.	Low Based on isolates from a single Korean hospital; may not be applicable to the United States. Researchers did not evaluate the epidemio-logic link between MRSA-colonized patients and subsequent infection.	*Organisms/ Outcomes: MRSA Chlorhexidine resistance*
Climo et al., 2013[8]	Daily bathing with no-rinse 2% chlorhexidine-impregnated washcloths	Multicenter, cluster-randomized, nonblinded crossover trial of 7,727 patients	Nine intensive care and bone marrow transplant units in six	MDRO acquisition (MRSA, VRE): 23% lower rate of MDRO acquisition for chlorhexidine bathing: 5.10 cases per 1,000 patient-days with	No serious skin reactions related to bathing noted during either study period.	Daily 2% chlorhexidine bathing reduced MRSA and VRE acquisition rates, without indications of increased	Low to moderate Two ICUs with low compliance with study protocol were	Organisms/ Outcomes: Hospital-acquired bloodstream infections Chlorhexidine resistance

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		randomly assigned bath with no-rinse 2% chlorhexidine-impregnated washcloths or with nonantimicrobial washcloths for a 6-month period, exchanged for the alternate product during the subsequent 6 months. Susceptibility testing on 1,106 isolates (713 MRSA and 393 VRE).	hospitals, United States	chlorhexidine bathing versus 6.60 cases per 1,000 patient-days with nonantimicrobial washcloths (p=0.03). CLABSI: 28% lower rate with chlorhexidine bathing: 4.78 cases per 1,000 patient-days with chlorhexidine bathing versus 6.60 cases per 1,000 patient-days with nonantimicrobial washcloths (p=0.007). In vitro tests of susceptibility showed chlorhexidine was more active against MRSA isolates (4 micrograms/mL) compared with VRE isolates (8 micrograms/mL). Chlorhexidine was slightly more active against MRSA isolates, with a minimum inhibitory concentration required to inhibit the growth of 90% of organisms of 4 µg/mL, compared with 8 µg/mL for VRE isolates.		chlorhexidine resistance over a 6-month period.	excluded from the analysis.	

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DeBaun, 2008[46]	Bathing with alcohol-free 2% chlorhexidine gluconate solution	In vitro study of MDR *A. baumannii* and *S. aureus* strains	Laboratory, United States	The alcohol-free 2% chlorhexidine solution reduced bacterial counts of drug-resistant *A. baumannii* and MRSA by 99.9% and within 3 minutes of exposure. This effectiveness was maintained even with significant dilutions (between 1:2,048 and 1:8,192).	None assessed.	The 2% chlorhexidine bathing solution was effective in vitro at 3 minutes exposure in inhibiting MDR *A. baumannii*, and *S. aureus* strains, even when diluted.	Low to moderate Did not evaluate in vivo.	Organisms/ Outcomes: MDR *A. baumannii* MDR *S. aureus*
Duszynska et al., 2017[21]	Daily bathing with 2% chlorhexidine-impregnated washcloths. No rinsing after application. One cloth used per each of six body areas: neck, thorax, and abdomen; both upper extremities from armpits to hands; hips, followed by groin area; both lower extremities from thighs to toes; back of the body from neck to the waist; buttocks	Observational study of 272 patients; three time periods (3 months each): pre-intervention, intervention, post-intervention	16-bed ICU, Poland	During the intervention, the general incidence rates of infections (p=0.04) and of catheter-related infections (p=0.005) were significantly lower compared with pre-intervention. Reductions in intubation-associated pneumonia and UTIs were not statistically significant. Half of the infections in the study were caused by MDROs, which decreased by 32% in the intervention and post-intervention periods, but this decrease was not statistically significant.	No redness, rash, or other adverse side effects observed. Nursing personal rated chlorhexidine bathing intervention positively.	The intervention was associated with reduced HAIs, was well accepted by nursing staff, and had few adverse and rare effects.	Moderate Excluded anyone with hypersensitivity or a skin reaction (during study) to chlorhexi-dine	Organisms/ Outcomes: MDR *A. baumannii,* ESBL-producing *K. pneumoniae,* MRSA HAIs (catheter-related infection, urinary tract infection, intubation-associated pneumonia)

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Ekizoglu et al., 2016[31]	Chlorhexidine digluconate solution (2% and 4% concentration) for use in environmental cleaning and patient bathing	In vitro study of chlorhexidine resistance among MDROs—120 hospital isolated strains of 7 bacterial genera	Hospital setting, Turkey	A solution of 4% chlorhexidine digluconate was effective against antibiotic-resistant and susceptible bacteria after 5 minutes of contact time. Only MRSA showed a resistance to 2% chlorhexidine digluconate solution. However, many of the *S. aureus* strains (both methicillin resistant and methicillin susceptible) and *P. aeruginosa* strains were resistant to 0.5% solution.	Concentrations below 4% showed decrease in bactericidal activity, especially for *S. aureus* and *P. aeruginosa.*	The authors state that it is important to use biocides at appropriate concentrations and to perform surveillance studies to trace resistance or low susceptibility patterns of *S. aureus*, *P. aeruginosa*, and other hospital isolates.	Low As an in vitro study, there is limited applicability to use in patient bathing.	Organisms/ Outcomes: *S. aureus* (methicillin susceptible and resistant strains), MDR *A. baumannii,* MDR *A. lowoffii,* MDR *P. aeruginosa,* MDR *K. pneumoniae,* MDR *K. oxytoca, Enterobacter* sp*.,* and *Enterococcus* sp*.* Chlorhexidine resistance
Fritz et al., 2012[47]	Five-day *S. aureus* decolonization protocol consisting of hand hygiene, twice-daily intranasal 2% mupirocin, and daily 4% chlorhexidine body washing, performed by all household members (not just index patient). In addition, all participants were instructed	Open-label randomized trial of *S. aureus* decolonization in 183 index pediatric patients with a skin or soft tissue infection (SSTI), 92 in the index patient-only decolonization group, 91 in the household decolonization group	Community setting, United States	At 1 month after decolonization, 50% of index patient cases and 51% of household cases had eradicated all *S. aureus* (p=1.00). At 3 months, however, the household group had a higher rate of *S. aureus* eradication (72% vs. 54%, p=0.05). Eradication did not differ between groups at 3 and 6 months. Moreover, when stratified by baseline MRSA colonization, eradication rates	No serious adverse events were reported; 22% of cases reported side effects, including dry skin (14%), rash (6%), and hives (2%).	Decolonization of household members of index patients with an SSTI caused by *S. aureus* was well accepted, even if it did not statistically significantly reduce index patients' recurrent SSTIs or result in sustained eradication. The authors did not expect to find significantly lower SSTIs in the household members as well as lower rates of recurrent SSTIs in index	Low to moderate Compliance with decolonization and hygiene protocols was self-reported.	Organisms/ Outcomes: *S. aureus,* including MRSA *S. aureus* eradication at 1, 3, 6, and 12-months; adherence to decolonization measures; SSTIs

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	to avoid sharing personal hygiene items (razors, brushes, towels, bar soap, jars of lotion), launder linens in hot water at least weekly, and launder towels and washcloths in hot water after each use.	Study included 1-month, 3-month, 6-month and 12-month analyses; not all cases completed all 12 months of followup.		between groups did not differ significantly. Recurrent SSTI in the index patient was reported in 15% of the household group and 26% in the index patient-only group (p=0.12). The household members in the household decolonization group were less likely to report an SSTI than household members in the index patient-only group, at 1 month (2% vs. 7%, p=0.005), 3 months (4% vs. 10%, p=0.01), and 6 months (9% vs 16%, p=0.04). At 12 months, the trend continued but not statistically significantly (16% vs. 22%, p=0.10).		patients despite a lack of long-term eradication. The authors hypothesize that acquisition of a new *S. aureus* strain may result in infection; 20% of index patients were not initially colonized with *S. aureus.* The hygiene protocols may have reduced the acquisition of new *S. aureus* strains.		

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Grare et al., 2010[45]	Preliminary evaluation of para-guanidinoethylcalix [4] arene or Cx1 (an alternative to chlorhexidine) for patient bathing	In vitro study of an alternative cationic compound to chlorhexidine	General healthcare setting, France	MICs were determined for 69 clinical isolates including MRSA, MSSA, coagulase-negative *Staphylococci* (CoNS), VRE, beta-lactamase-producing Enterobacteriaceae, and nonfermenting bacilli (*P. aeruginosa, A. baumannii, Stenotrophomonas maltophilia*). Cx1 showed comparable bactericidal activity to chlorhexidine and hexamidine against all isolates except for nonfermenting bacilli.	Although previous studies have shown Cx1 to be less cytotoxic than chlorhexidine, Cx1 was also less effective against certain types of bacteria.	Emerging compounds such as Cx1 may, in the future, present alternatives for disinfection with reduced potential harms. Past in vitro studies cited by Grare et al. show that chlorhexidine is cytotoxic over long periods (>24 hours) of exposure or to certain cell types (such as osteoblastic cells). However, Cx1 also showed reduced activity compared with chlorhexidine or hexamidine, showing the importance of balancing potential harms against efficacy.	Low	Organisms/ Outcomes: MRSA, MSSA, coagulase-negative *Staphylococci* (CoNS), VRE, beta-lactamase-producing Enterobacteriaceae*, P. aeruginosa, A. baumannii, Stenotrophomonas maltophilia*

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Hayashi et al., 2017[42]	Use of 0.1% chlorhexidine gluconate solution, compared with 0.1% benzothium chloride for bathing	In vitro study of MICs of chlorhexidine and benzothium chloride for 137 MDR *A. baumannii* isolates, 99 non-MDR *A. baumannii* isolates, and 69 non-*baumannii* isolates	Laboratory, Japan	None assessed.	The authors investigated whether a specific MDR *A. baumannii* strain (international clone 2) was more or less susceptible to chlorhexidine or benzothium chloride than other *A. baumannii* strains or other types of bacteria. The distribution of MICs of MDR-AB was higher than non-MDR-AB as well as non-*baumannii* isolates, and this difference was statistically significant for both MICs of chlorhexidine and benzothium chloride.	Despite higher MICs for MDR-AB compared with non-MDR-AB and non-*baumannii* isolates, all MICs were below concentrations in typical use. Although some studies have shown resistance to chlorhexidine among other MDROs (*Pseudomonas* and *Klebsiella* species), MDR-AB strains are still susceptible to the concentrations typically used in skin disinfection, as long as appropriate contact times are used.	Low In vitro study, with limited applications for patient use	*Organisms/ Outcomes: MDR-AB Chlorhexidine resistance*
Hijazi et al., 2016[34]	Chlorhexidine gluconate solution (various concentrations, from 0.125 to 64 mg/L), ethidium bromide (positive control, various concentrations from 4-1,024 mg/L)	In vitro study of chlorhexidine susceptibility of *Staphylococcus* strains (including MRSA) in a setting where chlorhexidine is used for cleaning and patient bathing	Intensive therapy unit in hospital, Scotland	None assessed.	Of the bacteraemia isolate strains that were found positive for the QAC A/B gene, 20 strains were *S. epidermis* and 2 strains were *S. aureus.* These accounted for 80% and 13%, respectively, of the total *S. epidermidis* and *S. aureus* strains isolated from blood samples. Only 1 of	This study found no indication of decreased efficacy of chlorhexidine-based infection control measures against *S. aureus* infections in the setting. The researchers expressed concern over the high proportion of QAC A/B gene carriage in *S. epidermidis*, which in this study was	Moderate Statistical figures for higher MICs not available in this publication	Organisms/ Outcomes: MRSA, other *S. aureus, S. epidermis* This study informs future directions for chlorhexidine bathing (continuing to monitor resistance).

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		Isolates were collected over a period of 7 years. Forty strains of MRSA were randomly selected from intensive treatment patients screened at multiple body sites on admission. Forty-one *Staphylococcus* strains were obtained from blood cultures: 16 strains of S. *aureus* and 25 strains of *S. epidermidis.*			40 (2%) MRSA strains isolated from screening samples was found positive for the QAC A/B gene. Chlorhexidine and mupirocin susceptibility among *S. aureus* strains (methicillin susceptible and methicillin resistant) was reduced in strains carrying QAC A/B genes, but there was no evidence of decreased susceptibility over the 7-year data collection period. However, *S. epidermis* strains showed a higher prevalence of QAC A/B genes compared with MRSA isolates (74% vs. 2%).	associated with higher chlorhexidine and mupirocin resistance.		
Huang et al., 2019[9]	Daily bathing with chlorhexidine (and targeted nasal mupirocin) for MDRO decolonization.	Cluster-randomized trial comparing routine bathing and daily chlorhexidine bathing (with targeted nasal mupirocin)	Hospital, non-critical care units, United States	No differences were seen in the relative hazard ratio (HR) for MRSA- or VRE-positive clinical cultures: HR for the intervention period versus the baseline period was 0.79 (95% CI 0.73 to 0·87) in the decolonization group versus 0.87 (95% CI	Fewer than 1% of patients experienced an adverse event, related only to the chlorhexidine use.	This study did not find significant improvements in non-critical care patients. In a subgroup of high-risk patients (those with medical devices), chlorhexidine bathing offered reduced risk of MRSA- or VRE-positive cultures or	Low Very large study	Organisms/ Outcomes: MRSA, VRE, CRE, EBSL-producing Gram-negative bacteria, *Acinetobacter* and *Pseudomonas* species resistant to 3rd and 4th

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		12-month baseline period, followed by 2-month phase-in and 21-month intervention period 53 hospitals, including 189,081 patients in the baseline period and 339,902 patients in the intervention period (156,889 in routine care, 183,013 in the decolonization group)		0.79 to 0.95) in the routine care group; p=0.17. HRs for secondary outcomes were also not statistically significant: for MDR Gram-negative clinical cultures, routine care HR was 0.81 (95% CI 0.72 to 0.91) and decolonization HR was 0.91 (0.82 to 1.00; p=0.16); and HRs for all-pathogen BSIs were 0.96 for routine care (95% CI 0.85 to 1.08) and 0.90 for decolonization (0.80 to 1.01; p=0.43). For high-risk patients (those with medical devices), however, the differences were statistically significant: The HR for the decolonization was 0.8 (95% CI 0.69 to 0.96) compared with the routine care group's HR of 1.17 (95% CI 1.00 to 1.37) for MRSA- or VRE-positive culture (p=0.0004). Similarly, the all-cause BSI HR for the decolonization group was 0.81 (95% CI 0.70 to 0.94) compared with 1.13		all-cause BSI. The authors note that this finding is consistent with findings among ICU patients with devices and suggest further study of targeted decolonization protocols among non-critical care patients with medical devices.		generation cephalosporins Clinical cultures, BSIs (all-pathogen), *C. difficile* infections, UTIs, 30-day infectious readmissions, chlorhexidine or mupirocin resistance

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				(95% CI 0.96 to 1.33) for the routine care group (p=0.0032).				
Huang et al., 2013[10]	5-day MRSA decolonization day regimen of 2% nasal mupirocin and daily bathing with 2% chlorhexidine-impregnated washcloths	Cluster-randomized trial of three approaches for preventing MRSA in 43 hospitals, with a total of 74 ICUs and 74,256 patients Three strategies: group 1, MRSA screening and isolation; group 2, targeted decolonization (i.e., screening, isolation, and decolonization of MRSA carriers); and group 3, universal decolonization (i.e., no screening, and decolonization of all patients) 12-month baseline period; 4-	Hospital, ICU, United States	Universal decolonization resulted in a significantly greater reduction in the rate of all BSIs than either targeted decolonization or screening and isolation. Reductions in rates of MRSA-related BSIs were similar to those of all BSIs, but the difference was not significant. In the intervention period versus the baseline period, modeled hazard ratios for MRSA clinical isolates were 0.92 for screening and isolation (crude rate, 3.2 vs. 3.4 isolates per 1,000 days), 0.75 for targeted decolonization (3.2 vs. 4.3 isolates per 1,000 days), and 0.63 for universal decolonization (2.1 vs. 3.4 isolates per 1,000 days) (p=0.01 for test of all groups being equal).	Seven patients experienced mild pruritus or rash after chlorhexidine bathing that resolved on discontinuation of the use of chlorhexidine-impregnated cloths.	Universal decolonization resulted in the greatest reduction of BSIs by reducing environmental burden and by being implemented quickly (without needing to wait for screening results). Decolonization (both targeted and universal) had a high compliance rate (over 80%). If universal decolonization is implemented, it should be accompanied with surveillance for resistance.	Low Unable to separate the effectiveness of chlorhexidine bathing alone (always combined with mupirocin use)	Organisms/ Outcomes: MRSA MRSA colonization, MRSA-related BSIs, all BSIs

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		month phase-in period; and 18-month intervention period		In the intervention versus baseline periods, hazard ratios for bloodstream infection with any pathogen in the three groups were 0.99 (crude rate, 4.1 vs. 4.2 infections per 1,000 days), 0.78 (3.7 vs. 4.8 infections per 1,000 days), and 0.56 (3.6 vs. 6.1 infections per 1,000 days), respectively ($p<0.0001$ for test of all groups being equal).				

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Kengen et al., 2018[18]	Daily washing with 2% chlorhexidine-impregnated cloths	Single-site retrospective, open-label, sequential period, nonrandomized interrupted time series analysis in a 31-bed ICU, enrolling a total of 6,634 patients. Two periods—baseline: 32 months, intervention: 26 months	ICU, Australia	The incidence of clinically significant positive blood cultures during the chlorhexidine period compared with the water and soap period was 3.6 vs. 4.7 per 1,000 patient-days (p=0.37). Blood culture contamination rates were 11.8 vs. 9.5 (p=0.56); incidence rates of new ICU-associated MDRO acquisitions were 3.22 vs. 3.69 (p=0.27); incidence rates of new CDIs were 2.01 vs. 0.79 (p=0.16). Outcomes after adjustment for confounders were similar.	Although the rate of new ICU-associated CDI cases was observed to be higher after implementation of chlorhexidine washing compared with water and soap, it was not statistically significant. Potential confounders such as changes in surveillance may have impacted results. Compliance not measured.	Compared with washing with soap and water, daily washing with chlorhexidine-impregnated cloths was not associated with a statistically significant reduction in rates of ICU-associated clinically significant positive blood cultures, blood culture contamination, newly acquired MDRO isolates, or CDIs.	Low to moderate Nursing staff compliance was not measured, and the study included no patient-level data on the extent of application.	Organisms/ Outcomes: MRSA, VRE, MDR Gram-negative bacteria, *C. difficile* Clinically significant positive blood cultures attributable to the ICU stay; contaminated blood cultures; newly acquired MDROs attributable to ICU from clinical and screening cultures; and newly acquired C. difficile infections

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Marolf et al., 2017[40]	Regular hospitalwide bathing with 4% chlorhexidine solution (frequency not specified)	In vitro study of chlorhexidine susceptibility of *S. aureus* strains before and after periodic use of chlorhexidine bathing in a 689-bed teaching hospital. Of 122 *S. aureus* strains meeting the study's nosocomial criteria, 104 were available for testing.	689-bed academic medical center, United States	Of the isolates from the four testing periods (before bathing, after a period of bathing, after bathing had been stopped, and after a second period of bathing), more strains in the period before bathing showed higher MICs (>0.25 µg/mL) than in any of the following periods. The mean MIC for isolates collected before bathing was introduced was greater than for those collected after bathing was introduced at Time 1 and Time 2 (p=0.048 and p=0.024, respectively).	None assessed.	Low-level resistance to chlorhexidine is known, but the study found no evidence over a 7.5-year period of increasing resistance nor any evidence that would suggest 4% chlorhexidine was no longer effective.	Low	Organisms/ Outcomes: *S. aureus* (methicillin susceptibility not specified)

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Maxwell et al., 2017[26]	Daily chlorhexidine bath with twice-daily application of mupirocin ointment on nares for 5 days	Prospective, randomized control trial on 90 trauma patients admitted to the ICU at a Level I trauma center	Intensive care hospital setting, United States	Compared to a protocol of soap and water baths plus placebo ointment, there was no statistically significant difference in all-cause Gram-negative or positive infections for chlorhexidine vs. soap, 12 (54.5%) vs. 7 (70%), p=0.467. The days to the onset of first MRSA infection was 2.5 for the treatment group and 4.0 for the placebo group. This difference was not significant.	Subsequent invasive MRSA infections were typically caused by the endogenous colonization strain, which chlorhexidine plus mupirocin did not eradicate. No mupirocin resistance was identified by polymerase chain reaction testing in patients with both colonization and infection by the same strain, but seven tested positive for *smr*, a gene that can confer chlorhexidine resistance.	Although the study did not show a statistically significant difference in MRSA colonization and infection between the treatment and control groups, the authors noted that the study was underpowered for the planned objectives. The authors also speculated that a single 5-day treatment may not be sufficient for successful and sustained decolonization.	Moderate The study was terminated before reaching the number of enrolled patients needed for sufficient predictive power. Study patients may be sicker, given the requirement for a >5-day ICU stay to complete intervention treatment.	Organisms/ Outcomes: MRSA MRSA-related infections

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
McNeil et al., 2014[37]	Topical antiseptics in general use for prevention and treatment of skin and soft tissue infections caused by MRSA: retapamulin, mupirocin, chlorhexidine	In vitro study of resistance in *S. aureus.* Two hundred isolates from patients with a single skin and/or soft tissue infection and 200 isolates from patients with >3 previous episodes from the years 2010 to 2012 were selected from an *S. aureus* surveillance study.	*S. aureus* isolates from a pediatric hospital setting, United States	*Smr*-positive *S. aureus* accounted for 14% of isolates. The proportion of *smr*-positive organisms increased during the study ($p<0.005$). MICs were twice as high for *smr*-positive *S. aureus*, and MBCs were 8 to 16 times higher for bactericidal effect in 50% and 90% of isolates, respectively.	In the study, the prevalence of resistant *S. aureus* increased over time.	While the reasons for the relatively high prevalence of *smr*-positive *S. aureus* in the study population are unclear, the researchers suggest it may reflect the dissemination of drug-resistant strains into the community from the healthcare setting.	Low to moderate	Organisms/ Outcomes: MRSA and other *S. aureus* strains

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Mendes et al., 2016[15]	Daily bathing with 2% chlorhexidine gluconate and use of 2% chlorhexidine gluconate antisepsis for central venous catheter insertion, surgery, biopsies	Quasi-experimental observational study of VRE colonization/ infection and in vitro study of chlorhexidine resistance after an intervention The pre-intervention period (2005-2009) included 870 patients, and the intervention period (2009-2013) included 523.	Hemato-poietic stem cell transplant unit in a hospital, Brazil	The VRE colonization and infection rates were significantly reduced among unit patients post-intervention: colonization change in trend: Beta-3=–0.040, p=0.001; infection change in trend: Beta-3= –0.086, p=0.001.	MDR Gram-negative bacteria infection and colonization rates in the unit increased in the last years of the study. The chlorhexidine MICs for VRE increased during the exposure period to the antiseptic (by 2 dilutions for MIC_{50}). A higher MIC at baseline period was observed in MDR Gram-negative strains. A monoclonal *P. aeruginosa* clone emerged in the second period.	Chlorhexidine bathing was associated with decreased incidence of VRE colonization and infection; no similar results were found with MDR Gram-negative bacteria.	Low	Organisms/ Outcomes: MDR Gram-negative bacteria, including *A. baumannii, K. pneumoniae,* and *P. aeruginosa,* VRE MDRO colonization and infection rates

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Musuuza et al., 2017a[11]	Daily bathing with 2% chlorhexidine gluconate-impregnated washcloths	Pre-post-implementation test study of 619 patients with a total of 6,490 patient-days	24-bed intensive care unit, United States	Prevalence decreased in the immediate aftermath of daily chlorhexidine bathing implementation and generally remained at that level throughout the observation period. The authors observed low rates of incidence of MDRO colonization with VRE, MRSA, and fluoroquinolone-resistant Gram-negative bacilli (FQR-GNB). Monthly prevalence of colonization and incidence for the composite of MRSA, VRE, and FQR-GNB was 1.9%-27.9% and 0-1.1 per 100 patient-days, respectively. Prevalence of VRE and FQR-GNB was significantly reduced; MRSA prevalence was reduced, but not significantly.	Rare but potentially serious chlorhexidine reactions were not encountered in this study, but the authors recommend eliciting in patient history when implementing bathing.	The authors observed an immediate drop in MDRO prevalence and incidence (except MRSA) once bathing was implemented. Initial enthusiasm for daily chlorhexidine bathing was high but waned over time, posing a barrier to long-term implementation.	Low to moderate The study did not include a control group, and fidelity to daily chlorhexidine bathing was not assessed.	Organisms/ Outcomes: VRE, MRSA, fluoroquinolone-resistant Gram-negative bacilli MDRO colonization

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Musuuza et al., 2017b[25]	Daily bathing with 2% chlorhexidine gluconate-impregnated washcloths	In vitro study of chlorhexidine gluconate susceptibility following a daily bathing intervention among 619 patients with a total of 6,490 patient-days	24-bed intensive care unit, United States	Both admission and discharge median MICs for MRSA and FQR-GNB did not differ between the pre- and post-implementation periods. For paired samples, the median MIC for MRSA did not significantly change between admission and discharge. The highest overall MIC was 0.5 µg/mL, and none of the MICs reached the threshold that defines reduced susceptibility to chlorhexidine.	None assessed.	Daily chlorhexidine bathing interventions do not appear to reduce the effectiveness of chlorhexidine, but this study only observed 9.5 months of time.	Low	Organisms/ Outcomes: VRE, MRSA, FQR-GNB

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Naparstek et al., 2012[32]	Chlorhexidine digluconate solutions ranging from 0 to 256 mg/mL	In vitro study of susceptibility of extremely drug-resistant *K. pneumoniae* to chlorhexidine	Hospital setting, Israel	Extremely drug-resistant *K. pneumoniae* is still susceptible to the concentrations used in hospitals for skin preparation, bathing, handwashing, and environmental cleaning.	*K. pneumoniae* appears to be able to survive the residual effects of chlorhexidine.	Although chlorhexidine-resistant *K. pneumoniae* strains in this study were not resistant to the full concentration typically used for skin antisepsis and disinfection, these organisms appear to be resistant to the residual antimicrobial effect of chlorhexidine on skin. The authors theorize this situation could create an opportunity for recolonization with resistant bacteria.	Low	Organisms/ Outcomes: *K. pneumoniae*

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Noto et al., 2015[17]	Daily bathing with 2% chlorhexidine gluconate-impregnated washcloths	Pragmatic, cluster-randomized, crossover study of 9,340 patients in 5 ICUs	Hospital setting, United States	After adjusting for baseline variables, no statistically significant difference was detected between groups in the rates of CLABSI, CAUTI, VAP, and CDI. Chlorhexidine bathing did not change rates of infection-related secondary outcomes, including hospital-acquired BSIs, blood culture contamination, or clinical cultures yielding MDROs. In a prespecified subgroup analysis, no statistically significant difference in CLABSI, CAUTI, VAP, or CDI was detected in any individual ICU.	None assessed.	Daily chlorhexidine bathing over a 10-week period did not appear to reduce device-associated HAIs or CDI rates, in contrast to Climo and colleagues' (2013) 24-week intervention. However, this study did not conduct active surveillance for MDRO colonization, only observed in clinical cultures.	Low to moderate	Organisms/ Outcomes: Organisms not specified (beyond *C. difficile*) CLABSI, CAUTI, VAP, CDI, MDRO-positive cultures, hospital-acquired BSI

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Otter et al., 2013[38]	Decolonization protocol of 1%-4% chlorhexidine bathing and nasal mupirocin	In vitro study of susceptibility of MRSA to chlorhexidine after implementation of a chlorhexidine-based decolonization protocol	Intensive care unit, United Kingdom	None assessed.	Typing identified two dominant clones: CC22 (n=224) and CC30 (n=197). Annual MRSA BSI rates declined from 2004 (the start of the chlorhexidine bathing program) to 2009, although the rate of decline for CC22 was slower than for CC30. Carriage of QAC A/B and *smr* genes and having a chlorhexidine MIC ≥2 mg/L did not increase overall among MRSA BSI isolates; however, QAC A/B gene carriage increased in CC22 compared with CC30 (OR, 7.21; 95% CI, 1.32 to 39.17). Also, QAC A/B+ CC22 isolates were more likely to have a chlorhexidine MIC ≥2 mg/L than QAC A/B+ CC30 isolates (OR, 21.67; CI, 2.54 to 185.20).	A successful infection control program was associated with the selection of genes linked to higher chlorhexidine MICs in one dominant endemic MRSA clone (CC22), but not another (CC30). The slower reduction in the CC22 MRSA BSI rate suggests that carriage of the QAC A/B gene confers a selective advantage, with potential implications for the sustainability of decolonization practice.	Low	Organisms/ Outcomes: MRSA MRSA-related bloodstream infections

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Pedreira et al., 2009[27]	Oral care (toothbrushing) twice daily with 0.12% chlorhexidine digluconate	Randomized controlled study of 56 patients	Pediatric ICU, Brazil	A total of 26 samples contained pathogenic bacteria, and 24 (92%) of the 26 were antibiotic resistant, such as *K. pneumoniae* strains resistant to beta-lactamase, MRSA, carbapenem-resistant *P. aeruginosa* and *A baumannii,* and cephalosporin-resistant *Enterobacter* species. The number of children with an increase in the number of samples positive for pathogenic flora was greater in the control group than in the experimental group, but the difference was not statistically significant. Similarly, the colonization of the oral cavity by normal flora did not differ between the two groups of children.	None assessed.	In children in a PICU, the effects of mechanical oral care plus chlorhexidine did not differ from the effects of mechanical oral care alone.	Low to moderate Small number of patients in study.	Organisms/ Outcomes: MRSA, ESBL-producing *K. pneumoniae,* carbapenem-resistant *P. aeruginosa*, *A baumannii,* cephalosporin-resistant *Enterobacter* species MDR-positive cultures, MDRO colonization
Peterson et al., 2016[12]	Decolonization with 4% chlorhexidine body wash and nasal mupirocin, for 5 days	Prospective, cluster-randomized study in 12 units at 3 long-term care facilities (LTCFs).	Three LTCFs, United States	The overall rate of MRSA infections significantly decreased between the baseline and Year 2, a 65% reduction of MRSA clinical infection (reduced by	Costs of running this intervention include cost per decolonization ($10), MRSA testing (as high as $50), and expense of healthcare worker	The authors concluded that this study demonstrates a successful proof of concept that, with chlorhexidine bathing, it is possible to reduce MRSA	Low to moderate The cluster-randomized approach failed to perform adequately in	Organisms/ Outcomes: MRSA MRSA colonization (nasal), MRSA-related clinical infections

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	Initial decolonization followed by screening and second decolonization as needed Second decolonization: 4% chlorhexidine body wash for 2 weeks, 2% mupirocin ointment twice daily for 5 days, and 100 mg of minocycline and 600 mg of rifampin (both orally) for 5 days	274 long-term and 115 short-term beds in intervention units; 299 long-term and 174 short-term beds in control units.		0.78 infections per 10,000 patient-days; p<0.001). A significant reduction (p≤0.022) in MRSA clinical infection also was observed at each of the three LTCFs. Mupirocin resistance rates were significantly different between the LTCFs in March 2011 (chi-square, 2 df=12.7, p=0.002). There was a significant downward trend in resistance between March 2011 and March 2013 (chi-square, 1 df=4.1, p=0.042), and this trend was not significantly different between LTCFs (interaction chi-square, 2 df=3.9, p=0.145). The authors hypothesize that use of oral antibiotics in the second decolonization reduced all strains of MRSA, including mupirocin-resistant ones.	time to apply mupirocin. (Bathing is done routinely, and the substitution of chlorhexidine for soap has negligible impact on cost.)	infections without isolation and other contact precautions in the LTC setting.	this study: the amount of resident intermingling during daily gathering made it too difficult to separate treatment and control units within a single facility.	

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Roode and Bütow, 2018[30]	Single application of chlorhexidine rinse solution for 2 minutes	Observational study of 50 cleft palate surgical patients	Hospital setting, China	Over half of pathogens isolated (61 of 113, 54%) survived after 2 minutes of disinfecting the surgical and surrounding area with chlorhexidine. In addition, two-thirds (76 of 113, 67.3%) showed resistance to different antimicrobials in vitro. *K. pneumoniae* (n=13), *H. influenza* (n=11), and *S. aureus* (n=9) were the most prevalent pathogens after disinfection.	None assessed.	This small study demonstrated significant resistance to preoperative chlorhexidine disinfection, with implications for preventing surgical site infections, as well as chlorhexidine's effectiveness as a decolonization agent.	Moderate Small number of patients in this study.	Organisms/ Outcomes: *K. pneumoniae, H. influenza*, *S. aureus*

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Ruiz et al., 2017[13]	Daily bathing with 2% chlorhexidine gluconate-impregnated wipes	Prospective cohort study with an intervention of 11 months 1,657 patients admitted during observation period, 430 (25.7%) bathed with chlorhexidine wipes	ICU in hospital setting, Spain	A significant decrease was observed in the incidence of MDRO colonization over the intervention period ($\beta=-0.209$; $r^2=0.549$; p=0.027), and in the number of patients colonized compared with the equivalent period of the previous year (22.0% vs. 18.4%; p=0.01). No statistically significant decrease was observed in the incidence of nosocomial infection (whether or not they were caused by MDROs) between the two periods (4.11% vs. 4.57%; p=0.355).	No dermatologic problems were observed in treated patients.	While the use of chlorhexidine wipes reduced MDRO colonization, it did not lead to a statistically significant reduction in the rate of HAIs (whether or not they were caused by MDROs). The authors concluded chlorhexidine could be helpful as part of a strategy but may not be sufficient on its own, especially for critically ill patients with extended ICU stays.	Low to moderate No environmental sampling was performed, which could have identified MDRO reservoirs. Chlorhexidine resistance was also not studied.	Organisms/ Outcomes: *K. pneumoniae, P. aeruginosa, A. baumannii, E. cloacae,* MRSA*, E. coli* MDRO colonization, HAIs (catheter-related bacteremia, mechanical VAP, mechanical ventilator-associated tracheobronchitis, UTIs)

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Smith et al., 2013[39]	Oral care with mouthwashes containing one of the following active components: aloe vera and tea tree oil; cetylpyridium chloride (concentration not specified); 0.2% chlorhexidine gluconate; 1% chlorhexidine gluconate; 1.5% hydrogen peroxide; 0.03% triclosan	In vitro study of effectiveness of commercial, over-the-counter chlorhexidine mouthwashes against MRSA isolates. Oral isolates were collected from dental hospital patients and bloodstream isolates from a reference laboratory	Laboratory, Scotland	None of the biofilm isolates were completely eradicated by the compounds tested, with a maximal killing of only approximately 70% (shown by two mouthwashes). Maximum activity of all compounds tested was observed after 30 seconds.	None assessed.	MRSA biofilms are more prevalent in older and long-term patients. Over-the-counter mouthwashes have limited effect on MRSA biofilms, making oral colonization an infection reservoir.	Moderate/ Low This study did not assess actual mouthwash use by people, so unclear of the efficacy of mouthwashes when used as directed.	Organisms/ Outcomes: MRSA and other *S. aureus*
Suwantarat et al., 2014[35]	Daily bathing with 2% chlorhexidine gluconate-impregnated cloth	Observational, in vitro study of chlorhexidine susceptibility of MDROs in a single hospital, 8 ICUs MDROs cultured from CLABSIs 122 isolates tested for chlorhexidine susceptibility, 28 from patients in units with daily chlorhexidine	ICUs, United States	None assessed.	*Enterococcus* species were the most common organisms causing CLABSIs (n=30) and had a high prevalence of reduced chlorhexidine susceptibility (90%). Other organisms with a high prevalence of reduced susceptibility included coagulase-negative *Staphylococcus* species (51%), *K. pneumoniae* (88%), and *P. aeruginosa*	Units that bathed patients with chlorhexidine daily were more likely to have CLABSIs caused by organisms with chlorhexidine resistance, compared to CLABSIs in units that did not conduct daily bathing. In this study, the data do not suggest that chlorhexidine bathing is changing the microbial ecology of which organisms cause CLABSIs (that is, the percentage of	Low Relatively small number of isolates, and no isolates were available for chlorhexidine bathing units from the period before bathing began.	Organisms/ Outcomes: MRSA, *K. pneumoniae* (including ESBL-producing), *P. aeruginosa,* VRE CLABSIs

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		bathing and 96 from units with no chlorhexidine bathing			(100%). Patients with daily chlorhexidine bathing were more likely to have an organism with reduced susceptibility (86% vs. 64%; p=0.028) and to have infection with Gram-positive bacterial isolates (81% vs 52%; p=0.036) than patients with no bathing. Of 30 Enterococcal isolates, 10 were VRE. All VRE isolates (100%) and 17 vancomycin-susceptible Enterococci (85%) had reduced susceptibility. Reduced chlorhexidine susceptibilities were found in 15 isolates of methicillin-resistant coagulase-negative *Staphylococcus* species (60%), 3 ESBL- producing *K. pneumoniae* isolates (100%), and 1 MRSA isolate (33%).	CLABSI caused by each organism), although those organisms are showing more chlorhexidine resistance in units where regular chlorhexidine bathing occurred.		

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Taheri et al., 2016[33]	Benzalkonium chloride, benzethonium chloride, and chlorhexidine digluconate for surface and skin disinfection (patients and healthcare workers)	In vitro study of chlorhexidine resistance in isolates from a hospital setting. Three biocides were tested in dilutions ranging from 0.25 to 128 µg/mL.	Laboratory, Iran	None assessed.	Chlorhexidine was more effective than benzalkonium chloride and benzethonium chloride, with an MIC_{50} of 1 µg/mL, and MIC_{90} = 2 µg/mL against MRSA, and MIC_{50} = 0.5 µg/mL to MIC_{90} = 1 µg/mL against both MSSA and coagulase-negative Staphylococci.	When used at the directed concentrations, the biocides should kill 100% of bacteria. However, persistent effects on skin and environmental surface are at lower concentrations, and theoretically could be a selective pressure for resistant strains. Previous studies have also shown that biofilms on surfaces can provide a 10- to 1,000-fold higher tolerance, although this is more of a consideration for environmental cleaning.	Low	Organisms/ Outcomes: MRSA, MSSA, coagulase-negative Staphylococci Chlorhexidine resistance

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Urbanic et al., 2018[23]	Daily bathing with 2% chlorhexidine-impregnated wipes, compared to daily bathing with 1% triclosan	Sequential, before-and-after observational study of 4,262 ICU admissions, 2,117 before and 2,145 after chlorhexidine bathing implementation	ICU, Australia	Aside from a reduction in MRSA acquisitions, there were no statistically significant changes in the measurements before and after the intervention. There were no significant changes in the rates of CLABSI (from 1.69 per 1,000 catheter-days [95% CI, 0.68 to 3.48] to 1.33 [95% CI, 0.49 to 2.90]; p=0.68), or ICU-acquired positive blood cultures (from 5.14 per 1,000 patient-days [95% CI, 3.45 to 7.39] to 4.45 [95% CI, 3.00 to 6.36]; p=0.58). MRSA acquisition incidence was lower during the chlorhexidine-bathing period (mean difference, –2.13 [95% CI, –3.65 to –0.60] per 1,000 patient-days; p=0.007). No statistically significant difference was seen in the rate of isolates involving other pathogens, including VRE.	None assessed.	Chlorhexidine bathing is no worse than use of triclosan in this study and may be more effective at reducing MRSA acquisition. However, effects on infection may only be seen with a large number of patients due to the high number needed to treat HAIs such as CLABSI.	Moderate Single-site study	Organisms/ Outcomes: MRSA, VRE ICU-acquired CLABSIs

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Warren et al., 2016[36]	Daily bathing with 4% chlorhexidine aqueous solution (final dilution 1,250 µg/mL)	Retrospective cohort in vitro study of chlorhexidine susceptibility of MRSA isolates from an ICU with daily chlorhexidine bathing	ICU, United States	None assessed.	A nonlinear change in prevalence of QAC A/B genes associated with chlorhexidine tolerance changed in MRSA nasal isolates over the 8-year study period of daily patient bathing with chlorhexidine soap (an increase in years 5 and 6 of the study, then decrease in the remaining 2 years). Increase trends were significant for QAC A/B genes (p=0.02; highest prevalence, 16.9% in 2009 and 2010) and Staphylococcal cassette chromosome *mec* type IV (p<0.001; highest prevalence, 52.4% in 2012). The latter is associated with community-acquired MRSA strains.	In this study, long-term daily chlorhexidine bathing at the concentration used did not result in sustained, widespread dissemination of chlorhexidine-resistance genes; however, pre-exposure during previous admissions may result in patients having hospital-acquired, chlorhexidine-resistant strains present on readmission. A cited study on chlorhexidine-resistance gene prevalence among community-dwelling individuals showed a prevalence rate similar to what was found in this study, suggesting that chlorhexidine-resistance genes are circulating in community-acquired MRSA strains.	Low to moderate Single-site study; MIC testing of the MRSA isolates was not conducted.	Organisms/ Outcomes: MRSA Chlorhexidine resistance

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Wesgate et al., 2016[44]	Worst-case dilutions of biocidal solutions under typical use (1% and 0.001% hydrogen peroxide-based solutions, 0.0004% triclosan solution, and 0.00005% chlorhexidine gluconate solution)	In vitro study of resistance of *S. aureus* and *E. coli* to low concentrations of antimicrobials (including chlorhexidine)	Laboratory, United Kingdom	None assessed.	Exposure to triclosan (0.0004%) was associated with a high risk of developing microbicide resistance and antibiotic cross-resistance in *S. aureus* and *E. coli*. Neither exposure to chlorhexidine (0.00005%) nor a hydrogen peroxide-based biocidal product were associated with developing resistance. Persistent exposure to a low concentration of hydrogen peroxide (0.001%) carried a risk of emerging resistance to antibiotics. Unstable clinical resistances to antibiotics occurred after exposure to the cationic biocide and oxidizing agents, specifically tobramycin and ticarcillin–clavulanic acid.	These data suggest that persistent low concentrations of some types of antimicrobials on skin and other surfaces have potential to select for increasingly resistant MDROs. Chlorhexidine was not one of them in this study, but some common alternatives to chlorhexidine have resistance concerns.	Low In vitro study only; did not examine effects in actual clinical practice.	Organisms/ Outcomes: *S. aureus, E. coli* Chlorhexidine resistance, antibiotic resistance

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Whitman et al., 2010[29]	Daily bathing with 2% chlorhexidine gluconate-impregnated cloths	Cluster-randomized, double-blind, controlled effectiveness trial of chlorhexidine bathing for MRSA decolonization in 1,562 healthy military recruits	Community setting, United States	The compliance rate (defined as application of 50% or more of wipes) at 2 weeks was similar in both groups (chlorhexidine group, 63%; control group, 67%) and decreased over the 6-week period. The estimated difference in soft skin and tissue infection rate between the chlorhexidine group and the control group was 0.025 (±0.016, p=0.14). Rates of colonization were lower in the chlorhexidine group than in the control group at followup (0% to 2% lower for MRSA and 8% to 12% lower for MSSA across sampling visits). The mean incidence of colonization was also significantly lower in the chlorhexidine group, compared to the control group: MSSA, 49.9% vs. 60.8% (p=0.03); MRSA, 2.6% vs. 6.0% (p=0.03).[v]	Chlorhexidine bathing caused no serious adverse reactions in the treatment cohort but did cause infrequent, mild, self-limited skin irritation.	Daily bathing with 2% chlorhexidine cloths was ineffective in reducing soft skin and tissue infection in a healthy population, supporting only targeted use of chlorhexidine bathing.	Low	Organisms/ Outcomes: MRSA, MSSA *S. aureus* colonization, infection Not a healthcare setting but may have implications for long-term care setting where common areas are shared.

[v]No confidence interval was provided for these statistical tests.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Wittekamp et al., 2018[22]	Oral care with 2% chlorhexidine mouthwash (applied 4 times daily, until end of mechanical ventilation)	Randomized trial of effectiveness of chlorhexidine mouthwash, selective oropharyngeal decontam-ination (SOD), and selective digestive tract decontam-ination (SDD) on BSI from MDR-GNB. 8,665 ICU patients receiving mechanical ventilation	ICU, Nether-lands	ICU-acquired BSI with MDR-GNB occurred among 144 patients (154 episodes) in 2.1%, 1.8%, 1.5%, and 1.2% of included patients during the baseline, chlorhexidine, SOD, and SDD periods, respectively. Absolute risk reductions were 0.3% (95% CI, −0.6% to 1.1%), 0.6% (95% CI, −0.2% to 1.4%), and 0.8% (95% CI, 0.1% to 1.6%) for chlorhexidine, SOD, and SDD, respectively, compared with baseline. Adjusted hazard ratios were 1.13 (95% CI, 0.68 to 1.88), 0.89 (95% CI, 0.55 to 1.45), and 0.70 (95% CI, 0.43 to 1.14) during the chlorhexidine, SOD, and SDD periods, respectively, versus baseline.	Oromucosal lesions in a total of 29 (9.8%) of 295 patients treated with 2% chlorhexidine in two of the centers. No serious adverse events.	Among ICU patients receiving mechanical ventilation in settings with moderate to high MDRO prevalence, use of chlorhexidine mouthwash, SOD, or SDD did not reduce BSIs caused by MDR-GNB (compared to usual care).	Low Study may have been under-powered to detect difference in BSIs.	Organisms/ Outcomes: ESBL-producing Enterobacteriaceae, MDR Gram-negative bacteria ICU-acquired BSI, 28-day mortality

Table B.32: MDRO, Hand Hygiene—Systematic Reviews

Note: Full references are available in Section 5.2 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Ellingson et al., 2014[16]	General hand hygiene guidelines: what to use, in which circumstances, and how to incentivize hand hygiene compliance	General healthcare settings Multiple countries included in reviewed studies and policies	Opportunities for hand hygiene include: before touching the patient, before a clean/aseptic procedure, after body fluid exposure, after touching the patient, and after touching patient surroundings. Many studies and policies compress this list to two moments: entry and exit of a patient room. The main method for measuring hand hygiene compliance is direct (overt or covert) observation, but using multiple methods (such as product volume, technological systems for automatic monitoring, or even self-report) can strengthen measurement against any single mode's limitations. Alcohol-based hand rubs are generally superior to soap and water, with the major exception being spore-forming organisms such as *C. difficile*. The main drawback of hand rubs is contact dermatitis, which is positively associated with the number of hand hygiene events. For *C. difficile* and other spore-forming organisms, soap and water is the preferred method. Hot water, which can irritate skin, should be avoided. Artificial and long nails are recommended against, on the basis of microbial carriage and risk of glove puncture.	Recommendations for increasing hand hygiene compliance include: 1. Choose the appropriate products: alcohol-based hand rub with at least 62% alcohol, antimicrobial and nonantimicrobial soak, and antisepsic solutions specifically formulated for surgical use. 2. Provide convenient access to hand hygiene equipment and ensure it is refilled routinely. 3. Involve healthcare personnel in choosing products. 4. Perform hand hygiene at the five moments mentioned above (before touching the patient, before a clean/aseptic procedure, after body fluid exposure, after touching the patient, and after touching patient surroundings). 5. Perform hand hygiene when hands are visibly soiled. 6. Assess unit- or institution-specific barriers to hand hygiene. 7. Implement multimodal ("bundle") approaches to address those barriers. 8. Educate, motivate, and ensure competency of healthcare personnel. 9. Measure hand hygiene by direct observation and one other method (product volume, automatic monitoring). 10. Provide feedback to healthcare personnel on hand hygiene compliance.	Organisms/ Outcomes General bacteria and viruses, with specific instructions for *C. difficile*

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Graveto et al., 2018[8]	Cell phone use and hand hygiene	Hospitals, ICUs, operating theaters, dialysis units, burn centers Multiple countries included in reviewed studies	An integrative review of the literature was carried out following the PICOD Method. Thirteen studies met the defined criteria for this review. Cell phones from health care personnel working in ICUs showed a higher rate of bacterial contamination than those working in other units. Cell phones used by doctors posed the highest risk of contamination and of infection rates, compared with nurses or other health technicians, but one study showed that administrative/clerical professionals had higher contamination rates than those of personnel involved in patient care. One study found that 96.7% of health care professionals never disinfected their phone. Another found that 45% of professionals "never" washed their hands before and after using their cell phones, 38% "occasionally" and only 17% said "consistently," and (from a third study) 97% never washed their hands after using their phone. The most common organisms isolated in the reviewed studies were coagulase-negative *Staphylococcus* species (from 48.7% to 95.6% of all samples tested), *S. aureus* species (from 6.7% to 66.7% of all samples), and *Acinetobacter* species (1% to 33% of all samples). Between 9.5% and 52% of *S. aureus* samples across studies were resistant to methicillin, and a high percentage of Gram-negative bacteria (31.3%) was resistant to ceftazidime. Larger phones were associated with a larger number of colonies and a higher probability of pathogenic organism colonies. However, there is a lack of data about the connection between contaminated phones and health care-associated infections (HAIs).	Cell phone use represents a threat to successful hand hygiene, but the ubiquity and utility of cell phones does not support their ban in health care settings. (There is also limited data on the connection between cell phone contamination and HAIs.) Instead, the authors recommend that cell phone use be incorporated into hand hygiene promotion, including handwashing before and after use and regular, standardized disinfection of cell phones. Technological innovation can be a strong ally for healthcare personnel and organizations by creating new equipment such as antibacterial covers and films or ultraviolet light for sanitary purposes.	Organisms/ Outcomes *Staphylococcus aureus, Acinetobacter* species, multidrug-resistant Gram-negative bacteria (MDR-GNB) Hand hygiene compliance after using cell phones, HAIs

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Luangasanatip et al., 2015[26]	Hand hygiene compliance	Hospitals Multiple countries included in reviewed studies	Search of databases for studies published between 2009 and February 2014. Included studies were studies implementing an intervention to improve compliance with hand hygiene among healthcare workers in hospital settings and measuring compliance or appropriate proxies that met predefined quality inclusion criteria. Forty-one met the inclusion criteria (6 randomized controlled trials, 32 interrupted time series, one nonrandomized trial, and two controlled before-and-after studies). Meta-analysis of two randomized controlled trials showed the addition of goal setting to WHO "5 Moments" was associated with improved compliance (pooled odds ratio 1.35, 95% confidence interval 1.04 to 1.76; I2=81%). Nineteen studies reported clinical outcomes; data from these were consistent with clinically important reductions in rates of infection resulting from improved hand hygiene for some but not all important hospital pathogens. Reported costs of interventions ranged from $225 to $4,669 (£146-£3,035; €204- €4,229) per 1,000 bed-days. There is strong evidence supporting the efficacy of the WHO "5 Moments" multicomponent intervention. The clinical outcomes of hand hygiene interventions are not always consistent across all MDROs, and the authors hypothesize that this variation is due to the epidemiology of the organisms and whether strains are acquired outside or inside the care setting. To further increase compliance, the authors also suggest adding supplemental elements such as goal setting, reward incentives, and ways to increase staff accountability (e.g., direct observation).	The WHO "5 Moments" campaign effectively increases hand hygiene compliance among health care workers. Specifically, goal setting, incentives, and accountability can increase compliance and support it over time.	Organisms/ Outcomes: Hand hygiene compliance

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Tacconelli et al., 2014[6]	Contact precautions, environmental cleaning, hand hygiene, antimicrobial stewardship	General healthcare setting Multiple countries included in reviewed studies	Articles presenting data pertaining to the control of the spread, in hospitalized patients, of MDR-*Pseudomonas aeruginosa*, *A. baumannii*, and Enterobacteriaceae and organisms intrinsically resistant to broad-spectrum antimicrobial agents, such as *Stenotrophomonas maltophilia* and *Burkholderia cepacia*, were identified through computerized literature searches. The search was restricted to full articles published in English up to November 2011 and including adult patients (>16 years of age). Hands of any healthcare worker are vulnerable to colonization, although the type and count of MDR Gram-negative bacteria (MDR-GNB) are related to exposure from patients and their environment, as well as the ability of the microbe to successfully colonize on transient contact. Many MDR-GNB can also survive several hours on healthcare workers' hands, depending on the species. Both soap and water as well as alcohol-based hand rubs are equally effective in reducing carriage of MDR-GNB. However, alcohol-based hand rubs are less effective at removing MDR-GNB from artificial nails compared to natural nails. The use of gloves in place of hand hygiene is not sufficient, as one study found contamination of a sizable percentage (29.3% for MDR-*A. baumannii* and 17.4% for MDR-*P. aeruginosa*) after glove removal but before hand hygiene.	Correct hand hygiene before and after patient contact, as well as before and after contact with patient environment (regardless of gown and glove use), is strongly recommended for preventing MDR-GNB transmission in both epidemic and endemic settings.	Organisms/ Outcomes MDR-GNB MDR-GNB carriage

Table B.33: MDRO, Hand Hygiene—Single Studies

Note: Full references are available in Section 5.2 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Barnes et al., 2014[17]	Handwashing on entrance to and exit from patient room (details not specified in the model, just whether or not handwashing was done at both opportunities)	Mathematical model (agent-based modeling) Simulation of the transmission of *A. baumannii,* methicillin-resistant *S. aureus* (MRSA), and vancomycin-resistant Enterococci (VRE) for 1 year using data from the literature and observed data to inform model input parameters compared the effects of hand hygiene and environmental cleaning on rates of MDRO acquisition.	Model based on 20-patient hospital ICU, United States	Baseline rates for hand hygiene compliance of nurses were set at 70% and 85% on entry and exit, respectively, and at 57% and 67% on entry and exit for physicians, respectively, based on observation data from a single facility in the mid-Atlantic region. The mathematical simulation model found that MDR- *A. baumannii* (MDR-AB), MRSA, and VRE acquisition rates increase substantially more if hand hygiene compliance falls than if cleaning thoroughness decreases. In general, a 2:1 improvement in thoroughness of terminal cleaning compared to hand hygiene compliance is required to achieve an equal reduction in MDRO acquisition rates.	None assessed.	This model found hand hygiene to be a more efficient strategy for preventing transmission of MDROs than terminal cleaning. However, if terminal cleaning is easier to improve than hand hygiene, then improving thoroughness may be the more effective strategy in that facility.	Low to moderate Mathematical model only, based on rates at a single hospital. Does not account for other facilities' baselines.	Organisms/ Outcomes: MDR-AB, MRSA, VRE Transmission of MDROs
Cheng et al., 2015[20]	Strict contact precautions (including single-room isolation) for MDR-AB-colonized	Pre-post study of 5,058 patients cultured positive with MDR-AB	A university-affiliated hospital and three extended-	The first case of multiple-drug- resistant MDR-AB bacteremia emerged in 2009, with an incidence that increased from 0.27 (1 case) in 2009 to 1.86	None assessed.	This study presents a novel hand hygiene approach—reducing MDR-AB bacteremia through patient hand	Moderate Single site study; other parts of the multicompon ent	Organisms/ Outcomes: MDR-AB MDR-AB-related bacteremia

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	patients and directly observed hand hygiene in conscious patients immediately before they received meals and medications	between January 1, 2004, and June 30, 2014	care hospitals, with a total of 3,200 beds, Hong Kong	(14 cases) per 100,000 patient-days in 2013 (p<0.001). Following implementation, in July 2013, the incidence of MDR-AB bacteremia decreased from 14 cases in 2013 to 1 case in the first 6 months of 2014 (p<0.001). Nonbacteremic MDR-AB also decreased from 106 to 34 cases over that same period (p<0.001). Patients from long-term care facilities for older adults (odds ratio [OR] 18.6, confidence interval [CI] 2.1 to 162.4, p=0.008) and history of carbapenem (OR 7.0, CI 1.7 to 28.0, p=0.006) and beta-lactam/ betalactamase use (OR 5.6, CI 1.1 to 28.7, p=0.038) 90 days prior to admission were independent risk factors for MDR-AB bacteremia by logistic regression compared with carbapenem-susceptible *A. baumannii* bacteremia. The overall compliance of hand hygiene of healthcare workers has gradually increased from 23% in 2007 (baseline) and maintained at 75% to 79% between 2011 and 2013.		hygiene. Despite increases in staff hand hygiene, direct observation of patient hand hygiene and patient isolation were followed by a reduction in MDR-AB bacteremia. This MDRO is known for widespread environmental contamination, and hand hygiene of patients may protect against MDR-AB acquisition and subsequent bacteremia.	intervention (increased staff hand hygiene, contact precautions) may have contributed to results.	

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Cheng et al., 2018[21]	Direct observation of hand hygiene with alcohol-based hand rub (ABHR) performed at 2-hourly intervals during daytime, before meals and medication rounds by a trained nurse in each intervention site. The hand hygiene ambassador delivered 3 mL ABHR to the hands of residents per occurrence of observed hand hygiene, either at the communal areas or at the bedside. A pocket-sized 60 mL ABHR container was used by the research nurse, and standard-sized 500-mL ABHR containers were placed in the cubicle, corridor, and communal areas of sites for	One month, cluster-randomized controlled study of 10 (five intervention, five control) long-term care facilities in Hong Kong	Ten residential care homes for older adults, Hong Kong	After implementation, the number of organism-positive environmental cultures showed a significant reduction in MRSA (79 of 600 [13.2%] vs. 197 of 600 [32.8%]; p<0.001) and carbapenem-resistant *A. baumannii* (CR-AB) (56 of 600 [9.3%] vs. 94 of 600 [15.7%]; p=0.001) contamination in the intervention arm compared with the nonintervention arm during the study period. The volume of hand rub consumed per resident per week was three times as high in the intervention arm compared with the baseline (59.3 ± 12.9 mL vs. 19.7 ± 12.6 mL; p<0.001) and was significantly higher than the nonintervention arm (59.3 ± 12.9 mL vs. 23.3 ± 17.2 mL; p=0.006).	None assessed.	Observed resident hand hygiene before meals and promotion of use of ABHRs reduced environmental contamination with MRSA and CR-AB and was well received by residents.	Low	Organisms/ Outcomes: MRSA, carbapenem-*resistant Acinetobacter* species, extended-spectrum beta-lactamase (EBSL)-producing Enterobacteriaceae MDRO colonization, MDRO environmental contamination

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	the residents, staff, and visitors.							
D'Agata et al., 2012[9]	Mathematical model of infection control approach, including hand hygiene decolonization, contact precautions, active surveillance, and screening (for VRE and MRSA)	Mathematical model extending data from clinical individual-level studies to quantify the impact of hand hygiene, contact precautions, reduction of antimicrobial exposure, and screening of surveillance cultures in decreasing the prevalence of MDRO colonization and infection	Model based on a 600-bed tertiary care hospital, United States	Improving compliance with hand hygiene from 60% to 80% and from 80% to 100% decreases the colonization prevalence by 12% and 8%, respectively. Each improvement interval decreased MDRO infections by 8%. Comparatively, similar improvement in compliance with contact precautions (from 60% to 80% and from 80% to 100%) decreases the prevalence of colonization by 10% and 6% respectively, and decreases MDRO infections by 6% and 4%, respectively. Screening patients for asymptomatic colonization also reduces MDRO prevalence, but only among patients receiving antimicrobials.	None assessed.	Improving hand hygiene is essential because it prevents transmission regardless of whether the patient's colonization status is known and requires fewer supplies and processes to consistently implement than contact precautions.	Moderate Not a real-world test, but the methodology for the model is based on epidemiologic results of a 600-bed teaching hospital over 1 year.	Organisms/ Outcomes: MRSA, VRE MDRO colonization, MDRO-related infections

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
De la Rosa-Zamboni et al., 2018[11]	A multimodal, hospitalwide hand hygiene program with alcohol-based hand rubs, periodic education, leadership support, and monthly feedback "Let's Go for 100" involved all healthcare workers and encompassed education, awareness, visual reminders, feedback, and innovative strategies. Monthly hand hygiene monitoring and active health care-associated infection (HAI) surveillance were performed in every ward.	Prospective time series analysis. Intervention implemented in 2013. Baseline period: (January-August 2013); intervention and followup period (September 2013 through October 2016). Population: between January 2013 and October 2016, 27,975 patients were discharged from the hospital, yielding a total of 266,524 patient-days, 111,642 central line-days, 30,218 ventilator-days, and 26,327 urinary catheter-days.	349-bed public teaching and referral pediatric hospital, Mexico	Baseline hand hygiene adherence was 34.9% (SD 3.52) and increased significantly (p<0.0001) over the study period to 80.6% (SD 6.3) during the last 3 months. The increase was statistically significant for use of alcohol-based products (z=2.78 and p=0.005) but not for washing hands (z=0.32 and p=0.745). Adherence increased across all healthcare staff groups. The HAI rate decreased from 7.54/1,000 patient-days (SD 1.82) to 6.46/1,000 patient-days (p=0.004)). The authors observed a negative correlation between hand hygiene adherence and attack rate for: • MRSA (coef. -17.10, 95% CI -30.67 to -3.53, p=0.019) • VRE (coef. -54.87, 95% CI -73.28 to -36.46, p=0.001) • *Enterobacter* species (coef. -33.04, 95% CI -51.14 to -14.94, p=0.002) • Overall MDR-ESKAPE[w] group (-7.76, 95% CI -15.08 to 0.37, p=0.059)	N/A	This study shows the impact of a sustained hand hygiene promotion campaign that was associated with reductions in all studied MDROs (MRSA, VRE, and MDR-ESKAPE). The authors note that there are few hand hygiene studies in pediatric settings. Some of the innovative approaches to hand hygiene included messaging for pediatric patients and siblings using a mascot and holding contests among healthcare staff for the most innovative ways to improve hand hygiene compliance.	Low to moderate Single study, but long study period. No other policy changes during study period.	Organisms/ Outcomes: MRSA, VRE, MDR-ESKAPE group HAIs

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Harris et al., 2017[18]	Mathematical model based on an infection control intervention that included directly-observed hand hygiene on entry/exit of patient room (method not specified) and gown and glove use with patients known to be colonized with MDROs	Mathematical model of the relative effects of hand hygiene, glove and gown use, and dedicated staff on MRSA and VRE acquisition rates.	Hospital ICU, United States	This model was based on a previous study that looked at gown and glove use for MRSA and VRE acquisition, which found no effect on VRE acquisition rates but a large effect on MRSA acquisition rates. This study also found that ICUs in the glove and gown intervention had higher hand hygiene compliance rates than control ICUs (78.3% vs. 62.9%). Based on the model, the authors estimate that 44% of the decrease in MRSA acquisition was due to universal glove and gown use, 38.1% was due to improved hand hygiene, and 14.5% was due to the reduction in contact rates (a known side effect of contact precautions).	N/A	This model was able to break down a multicomponent intervention and assess the relative impact of hand hygiene in a multicomponent study. In a separate universal gown and gloving study, hand hygiene had almost as much impact as gown and glove use.	Low to moderate Mathematical model study but based on the data from a "real world" implementa-tion in several ICUs.	Organisms/ Outcomes: MRSA, VRE MDRO acquisition rates

[w] *Enterococcus faecium, S. aureus*, *Klebsiella pneumoniae, A. baumannii, P. aeruginosa*, and *Enterobacter* species.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
McLaws et al., 2009[15]	Regional hand hygiene promotion campaign, "Clean hands save lives" Campaign consisted of placing alcohol-based hand rub dispensers at the point of care (near patient locations), observing hand hygiene compliance, using promotional campaign posters for all audiences, and distributing brochures to encourage patients to confirm hand hygiene compliance.	Pre-post study of a hand hygiene promotion campaign to stop MRSA infections. Sample size not provided. Campaign included all public hospitals in the New South Wales State of Australia.	11 hospital, general wards, and ICUs, Australia	Between the pre- and post-campaign periods, there was a 25% fall in MRSA-related non-ICU sterile site infections, from 0.60/10,000 bed-days to 0.45/10,000 bed-days (p= 0.027), and a 16% fall in MRSA-related ICU non-sterile site infections, from 36.36/10,000 bed-days to 30.43/10,000 bed-days (p=0.037). The pre- and post-campaign rates of MRSA infection from ICU sterile sites (5.28/10,000 bed-days vs. 4.80/10,000 bed-days; p=0.664) and non-ICU, non-sterile sites (5.92/10,000 bed-days vs. 5.66/10,000 bed-days; p=0.207) remained stable. Australia-wide MRSA data reported to the Australian Council on Healthcare Standards showed a 45% decline in infections from ICU non-sterile sites, from 25.89/10,000 bed-days to 14.30/10,000 bed-days (p<0.001), and a 46% decline in infections from non-ICU non-sterile sites, from 3.70/10,000 bed-days to 1.99/10,000 bed-days (p<0.001) over the period 2005–2006.	None assessed, beyond failure to reduce MDROs in certain sites.	Although hand hygiene increased markedly in the intervention hospitals, there was no consistent reduction in all MDROs and in all observation sites. However, focusing only on clinical outcomes with hand hygiene does not reflect potential environmental or systemic factors that need to change (e.g., environmental contamination or a workflow at odds with hand hygiene).	Low Large sample size, and control group available (all other public hospitals outside New South Wales). May have unobserved differences between NSW hospitals and those in other areas.	Organisms/ Outcomes: MRSA Hand hygiene compliance rates, MRSA infections

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Pires dos Santos et al., 2011[13]	Alcohol-based hand rub use (coincidental with antibiotic stewardship initiatives)	Pre-post study of association between CR-*P. aeruginosa* (CR-PA) infection rates and alcohol-based hand rubs through three study periods: period 1, before ertapenem use (17 months); period 2, during ertapenem use (33 months); and period 3, after exclusion of ertapenem (15 months). Sample size not provided.	749-bed hospital, Brazil	CR-PA decreased over the period of ertapenem use as well as during the period of ertapenem restriction. The mean incidence of CR-PA infections per 1,000 patient-days was 0.51 (95% CI, 0.41 to 0.60) in period 1; 0.43 (95% CI 0.36 to 0.49; p=0.33) in period 2; and 0.33 (95% CI 0.26 to 0.41; p=0.34) in period 3. Between period 1 and period 3, this decrease was statistically significant (p=0.04). There was no significant correlation between CR-PA infection and ertapenem use throughout the study periods. However, by multiple regression analysis, the reduction in the rate of CR-PA infection correlated significantly with the increase in the volume of alcohol used as hand sanitizer (p<0.01; Spearman correlation r=-0.40), which increased from 660.7 mL per 100 patient-days in period 1 to 2,955.1 mL per 100 patient-days in period 3.	None assessed.	The natural experiment in this study (increased hand hygiene due to the H1N1 influenza pandemic) allowed the author to evaluate the relative impact of increased hand hygiene (as measured through hand rub consumption) on CR-PA. In this study, the association between alcohol-based hand rub use and increased CR-PA cases was stronger than the association with ertapenem (a type of carbapenem) restriction.	Moderate Single-setting study that initially sought to evaluate the impact of antibiotic stewardship; the hand hygiene component was an incidental finding.	Organisms/ Outcomes: CR-PA CR-PA-related infections

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Rupp et al., 2008[22]	Alcohol-based hand rub (62% ethyl alcohol and 0.3% triclosan) in the intervention group, compared to soap and water (antimicrobial soap with 0.3% chloroxylenol). Hand rub dispensers were installed inside and outside patient rooms in the first unit, with the same in the second unit during the crossover period.	Prospective crossover controlled trial Hand hygiene was covertly observed every 60 days by trained individuals; hand hygiene adequacy not assessed, only performance/nonperformance. Trial included 17,994 minutes of observation, which included 3,678 opportunities for hand hygiene between August 2001 and September 2003.	Two 12-bed ICUs in a single hospital, United States	Hand hygiene adherence rates improved dramatically after the introduction of alcohol-based hand rubs, from 37% to 68% in one unit and from 38% to 69% in the other unit ($p<0.001$). Hand hygiene rates were also better at higher workloads when the hand rub was available in the unit ($p=0.02$). However, no significant changes in MDRO, *C. difficile*, or device-associated infection rates were observed. (The authors noted that the infection rates were generally low during the study periods.)	Having fingernails longer than 2 mm, wearing rings, and lacking access to hand gel were associated with increased microbial carriage.	This study demonstrates that hand hygiene compliance can improve dramatically when the equipment is provided in the right place. When this study was conducted, the recommendations against alcohol-based hand rub for CDI had not yet been made, which likely accounts for the lack of effect on CDI rates. In addition, the authors note that active surveillance for MRSA was not done; given dramatic spread of MRSA throughout healthcare facilities and the community, colonization from outside the units may have been the cause of unchanged MRSA rates.	Low to moderate Process outcome focus	Organisms/ Outcomes: MRSA, VRE, MDR-PA, *C. difficile* Hand hygiene compliance, *C. difficile*-associated diarrhea, MDRO-associated infections, device-associated infections (central venous catheter–related bacteremia, urinary catheter–associated urinary tract infection, and ventilator-associated pneumonia)

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Sickbert-Bennett et al., 2016[23]	Hand hygiene upon entering and exiting patient rooms, observation and immediate feedback from all staff members, and covert observation from trained infection prevention and nursing staff Other PSPs: HAI surveillance	Longitudinal observational study; over 140,000 observations made over a 17-month period	A single 853-bed acute care hospital, United States	Hand hygiene compliance increased significantly by 10% (p<0.001) and HAIs (including those caused by MDROs) decreased significantly by 14% (p=0.0066). This decrease is estimated to have prevented 22 deaths and saved approximately $5 million. The association between hand hygiene compliance and health care associated-*C. difficile* infection, adjusting for unit-level data, showed a 10% improvement in hand hygiene, associated with a 14% infection reduction (p=0.070).	No association was noted between hand hygiene compliance and MDRO infections (p=0.7492).	Although an improvement in hand hygiene was associated with reduction in overall HAIs and produced cost savings, the authors found that this decrease was mostly driven by *C. difficile* infection and was not seen in MDROs. While hand hygiene was helpful in cost saving and is necessary to support other infection prevention practices, it alone may not be sufficient to control MDROs.	Low to moderate Single-site study. No other specific hospitalwide infection prevention goals were adopted during the period of analysis.	Organisms/ Outcomes: MDROs, *C. difficile* Hand hygiene compliance, HAIs, HAIs related to MDROs
Sopirala et al., 2014[12]	Hand hygiene promotion campaign using nurse liaisons to observe and give feedback on compliance with alcohol-based hand rub or soap and water washing on entry and exit of patient rooms Staff nurses were trained to be liaisons to infection prevention personnel. "Link nurses" would	Pre-post quality improvement study at a single 1,191-bed hospital Baseline period: January 1, 2006– March 31, 2008 Intervention period: April 1, 2008– September 30, 2009	Hospital, United States	Hand hygiene gradually increased from 30% in 6 months prior to the intervention to 93% in the 6 months after starting the intervention. Healthcare-associated MRSA incidence rates dropped by 28% from 0.92 cases per 1,000 patient-days to 0.67 (IRR=0.72 [95% CI 0.62 to 0.83], p<0.001). Overall MRSA rates dropped from 4.83 to 4.25 per 1,000 patient-days. Overall MRSA bacteremia decreased from 0.49 to 0.34 per 1,000 patient-days (IRR=0.59 [95% CI 0.42 to 0.84], p=0.003)	None assessed.	Hand hygiene promotion and feedback on compliance audits resulted in very high compliance rates that successfully reduced both health care-associated infections and total MRSA cases and bacteremia.	Moderate Single-site study, and other components were not controlled for in estimating clinical outcomes.	Organisms/ Outcomes: MRSA Hand hygiene compliance, health care-associated (HCA) and non-HCA MRSA incidence (infection or colonization), HCA and non-HCA MRSA bacteremia

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	observe hand hygiene, give immediate feedback to staff, identify and report on infection prevention issues in their units, and conduct hand hygiene education with staff. Independent audits were done by graduate students, and compliant units would receive recognition (e.g., plaque, celebratory lunch or dinner).			and health care-associated MRSA bacteremia from 0.18 to 0.10 per 1,000 patient-days (IRR=0.68 [95% CI 0.56 to 0.84], p<0.001).				

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Vernaz et al., 2008[14]	Two hand hygiene promotion campaigns using alcohol-based hand rubs: "VigiGerme®" in spring 2003 and "Clean care is safer care" in autumn 2005 (including hand hygiene observations of healthcare personnel). Other protocols included universal MRSA on-admission screening from January to August 2003 in the entire hospital, and from October 2004 to May 2006 in selected surgical wards.	Interventional time series analysis of the temporal relationship between increased use of alcohol-based hand rubs, antibiotic use, and MRSA and *C. difficile* rates. All hospital patients between February 2000 and September 2006; mean hospitalization days, 51,524 per month	2,200-bed primary and tertiary care teaching hospital, Switzerland	Over the study period, the average monthly MRSA incidence was 0.15 clinical isolates per 100 patient-days, varying from 0.09 to 0.21 with no overall trend (p=0.71). The monthly incidence of *C. difficile* was 0.027 isolates per 100 patient-days, varying from 0.004 to 0.054, without any trend (p=0.82). Consumption of hand rubs increased over the study period, from an average of 1.303 L per 100 patient-days in 2001 to 2.016 L per 100 patient-days in 2006, and the effect of the education intervention on increased hand rub use was statistically significant. Only MRSA showed a temporal association between the increase in hand rub use and a decrease in MRSA rates.	The campaign had no significant effect on MRSA reduction in the multivariable analysis.	This study demonstrated a temporal association between increased hand rub use and MRSA, although a multivariable analysis showed no effect of the hand hygiene promotion campaign on MRSA rates. As confirmed by later studies, alcohol-based hand rubs are less effective for reducing *C. difficile* transmission. The average antimicrobial use over the study period was 33 defined daily dose/100 patient-days and did not change over time (p=0.29).	Low to Moderate	Organisms/ Outcomes: MRSA, *C. difficile* Consumption of alcohol-based hand rubs

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Wares et al., 2016[19]	Mathematical modeling of the role of hand hygiene in reducing environmental contamination by MDROs and MDRO transmission	Mathematical simulation model looking at antimicrobial use and environmental contamination and other strategies	Modeled on a hospital dialysis unit serving 120 patients, United States	In this model, when hand hygiene compliance was at 0%, the estimated rate of MDRO acquisition almost doubled, from 14.5% at baseline to 23.1%.	Even with 100% compliance, 13.4% of patients still remained colonized.	In the dialysis setting, MDRO colonization is caused by many factors, although hand hygiene is an important one. Simultaneous improvements in hand hygiene, judicious antimicrobial use, and environmental decontamination are needed to reduce MDRO colonization.	Moderate	Organisms/ Outcomes: Hand hygiene, MDRO transmission Mathematical model—will need validation in actual dialysis setting

Table B.34: MDRO, Surveillance—Systematic Reviews

Note: Full references are available in the Section 5.3 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
McKinnel et al., 2013[18]	Active surveillance using risk-based screening for methicillin-resistant *Staphylococcus aureus* (MRSA)	Hospitals	Factors associated with MRSA colonization at admission screening include: • History of MRSA carriage, especially in the last 6 months. • History of hospitalization in last 12 months. • Transfer from a nursing home. • History of CDI, or VRE carriage. • Any infection in past 3 months. • Antibiotic use in past 3 months. • Comorbidities (congestive heart failure, diabetes, chronic obstructive pulmonary disease, renal failure, immunosuppression). Factors *not* associated with MRSA colonization at admission screening include: • Transfer from another hospital. • HIV infection. • Use of intravenous drugs. • Cirrhosis. • ICU admission.	By knowing risk factors associated with MRSA colonization, hospitals and other facilities can develop risk-based testing approaches for screening on admission, reducing costs in time and materials.	Organisms/ Outcomes: MRSA MRSA colonization

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Siegel et al. and the Healthcare Infection Control Practices Advisory Committee, 2006[33]	Active surveillance, including both cultures and testing, for multidrug-resistant organism (MDRO) prevention	General healthcare settings, United States	More research is needed on when it is most beneficial to implement active surveillance for MDRO prevention, but it should be considered when other control methods have failed. Implementing active surveillance requires personnel to collect cultures, adequate laboratory facilities for processing cultures, a mechanism for communicating results to caregivers, decisions or policies for additional measures triggered by culture results, and mechanisms for ensuring measure adherence. Decisions about which populations to screen and which MDROs to screen for vary based on the facility and patient risk factors (e.g., overall patient health, average length of stay, prevalence at other institutions from which the facility receives patients). Recommendations for screening sites: • MRSA: Cultures of the nares identify most patients with MRSA and perirectal and wound cultures can identify additional carriers. • VRE: Stool, rectal, or perirectal swabs are generally considered a sensitive method for detection of VRE. While one study suggested that rectal swabs may identify only 60% of individuals harboring VRE, and may be affected by VRE stool density, this observation has not been reported elsewhere in the literature. • MDR-GNBs: Several methods for detection of MDR-GNBs have been used, including use of perirectal or rectal swabs alone or in combination with oropharyngeal, endotracheal, inguinal, or wound cultures. Rapid detection methods allow facilities to quicker implement contact precautions, if that implementation is pending surveillance culture results. Chromogenic enzyme substrates (CHROMagar) have been shown to have high sensitivity and specificity for identification of MRSA as early as 16 hours after inoculation. In addition, real-time polymerase chain reaction (PCR)-based tests for rapid detection of MRSA directly from culture swabs (<1-2 hours) are commercially available.	Using surveillance to successfully prevent MDRO infection and colonization requires: 1. Obtaining the needed resources for that facility (personnel to collect samples, laboratory capabilities for rapid detection, policies for other practices based on culture results, mechanisms for ensuring adherence to other practices) 2. Understanding the risk factors for the facility and its patients to determine which organisms should be screened for and choose the correct sampling method for the organisms.	Organisms: MRSA, vancomycin-resistant Enterobacteriaceae (VRE), multidrug-resistant Gram-negative bacteria (MDR-GNB)

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Tacconelli et al., 2014[4]	Active surveillance, including both cultures and testing, for MDR-GNB Molecular testing using PCR	Hospital, ICUs, various countries included in review	The search was restricted to full articles published in English up to November 2011 and including adult patients (>16 years of age). Active screening for MDR-GNB is recommended in epidemic settings only. Surveillance of clinical samples will undercount MDR-GNB. The proportion of clinically evidence-based cases also varies by organism and susceptibility of the patient population. PCR-based methods are still in development for MDR-GNB, so culture-based tests are still the "gold standard." Rectal swabs, urine, or respiratory secretions are sufficient for almost all MDR-GNB, with rectal swabs being the most sensitive and groin being most specific (best for confirming negative results). However, one study showed that sensitivity of screening is low (29%) even when six body sites are included. No consensus exists on frequency of screening or timing, although several observational studies of outbreaks have used weekly screening until no cases of colonization/infection or cross-transmission were observed. Mean colonization times for MDR-GNB are 144 days (range, 41 to 349 days), so this period represents a significant time. The efficacy of screening is linked to the level of compliance, so screening must be maintained over time. There are no recommendations for screening for MDR-GNB in a nonoutbreak setting. In epidemic settings, targeted screening on admission for high-risk patients is recommended. Screening can also be used to reinforce other prevention practices in the outbreak response. In the endemic setting, surveillance should be used as an additional measure to control the spread of MDR-GNB, not a basic one.	"One size fits all" approaches do not apply to MDR-GNB. There is a strong link between the efficacy of screening and the level of compliance with screening, meaning that screening fatigue has implications for successfully detecting and preventing MDR-GNB colonization and infection. This situation is easiest to avoid in an epidemic situation yet less so in an endemic situation or where MDR-GNB are not prevalent.	Organisms: MDR-GNB

Table B.35: MDRO, Surveillance—Single Studies

Note: Full references are available in the Section 5.3 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Ahern & Alston, 2009[58]	Longitudinal surveillance data to assess the impact of infection control interventions and antibiotic use. Implementation of a resistance index. The surveillance system was used to measure associations of multiple interventions on health care-associated infection (HAI) rates. Only isolates recovered more than 48 hours after hospital admission are included.	Descriptive implementation case study that examined two 4-year periods before and after implementation of the interventions. The resistance index (a measure of nosocomial infection and colonization) and the rate of antimicrobial use were compared using the Poisson distribution. Two-sided p values of less than 0.05 were considered to be statistically significant.	562-bed academic medical center, United States Hospital with a 26-bed surgical ICU (SICU) and 22-bed medical ICU (MICU), each with a five-bed open ward, and a four-bed pediatric ICU in the SICU	The resistance index was developed to quantify nosocomial infection and colonization. The index, calculated monthly, consists of a numerator of the number of nosocomial isolates and a denominator of the number of patient-days for each nursing unit and for the hospital. Surveillance data suggest that infection control initiatives successfully reversed an upward trend in the six study MDROs, despite increasing antibiotic use. During the pre-intervention period, the resistance index was increasing in both units. The overall resistance index decreased in both units during the post-intervention period. The overall rate of antimicrobial use in the SICU was higher during the post-intervention period than during the pre-intervention period (366 vs. 352 defined daily doses per 1,000 patient-days; $p<0.01$). The overall rate of antimicrobial use in the MICU was higher during the post-intervention period than during the pre-intervention period (603 vs. 436 defined daily doses per 1,000 patient-days).	None assessed.	The paper describes a surveillance method to measure associations between multicomponent intervention and HAI rates. Keeping track of MDRO isolates over time and between different units allows hospitals to evaluate the effectiveness of their infection control protocols and to show reduction in MDROs despite increased rates of antibiotic prescription.	Moderate to high Authors did not differentiate between infection and colonization. Also, unable to determine which infection control strategy was most effective. The resistance index database required 8–12 hours of maintenance per month.	Organisms/ Outcomes MRSA, *C. difficile,* VRE*, P. aeruginosa,* MDR-GNB *Stentro-phomonas matlophilia Infections related to these six pathogens*

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Almyroudis et al., 2016[21]	Discontinuation of systematic surveillance (weekly perianal swabs) for VRE and contact isolation of colonized patients on the incidence of VRE bacteremia	Pre-post study (comparing two 3-year periods) to assess the incidence of VRE bacteremia and the incidence of bacteremia due to MRSA and *C. difficile*	125-bed hospital hematology/ oncology unit with high prevalence of VRE coloniza-tion, United States	The incidence of VRE bacteremia remained stable after discontinuation of VRE surveillance and contact precautions (reduction of 2.32 to 1.87 per 1,000 patient-days; p>0.05). The use of levofloxacin prophylaxis during neutropenia and daily chlorhexidine bathing had no effect on the incidence of VRE bacteremia (p>0.05). The incidence of MRSA bacteremia and *C. difficile* infection for which the facility continued contact precautions also remained stable. Aggregated antibiotic utilization and nursing hours per patient-days were similar between the two study periods. Antibiotic use also remained stable during the two periods (p>0.05, not significant). Nursing hours per patient per day decreased from 13.99 during the control period to 12.86 during the second period (p>0.05, not significant).	None assessed.	The authors found that MRSA bacteremia, *C. difficile* infection, and VRE bacteremia rates remained stable after discontinuation of an active surveillance and contact isolation protocol. Active surveillance and contact precautions for VRE colonization did not appear to prevent VRE bacteremia in patients with hematologic malignancies and recipients of hematopoietic stem cell transplantation with high prevalence of VRE. Based on the inefficiency of the contact isolation and the molecular epidemiology data, a decision was made to discontinue the systematic surveillance for VRE and contact isolation of colonized patients.	Moderate	Organism/ Outcomes: VRE, MRSA, *C. difficile* Colonization, bacteremia due to MRSA or VRE, *C. difficile* infection (CDI)

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Banach et al., 2014[23]	Active surveillance for carbapenem-resistant Enterobacteriaceae (CRE) using stool samples collected for CDI	Pre-post study for two hospitals. Before the study period, hospital A performed active surveillance for CRE among patients on high-risk units using perianal swab sampling at admission and weekly thereafter. There was no active surveillance program at hospital B prior to the intervention. Nested case-control study design was used to identify risk factors for CRE.	Two large academic hospitals, United States	CRE was isolated from 27 (2.6%) of 1,047 specimens. CRE prevalence was 2.9% (25/854 unique patients), with 4.0% (11/272 patients) at hospital A and 2.4% (14/582 patients) at hospital B (p=0.18). Among patients with CRE-positive samples, 10 (40%) had been previously identified as carriers (64% at hospital A, 21% at hospital B). CRE isolates included *Klebsiella pneumoniae* (n=23), *K. oxytoca* (n=1), and *Enterobacter cloacae* (n = 1). The KPC gene was detected in 21 (84%) isolates and 21 (91%) *K. pneumoniae* isolates. CRE-colonized patients were older (median age, 66 vs. 59 years; p=0.05). Rates of CRE positivity did not differ by negative and positive *C. difficile* tests (2/90 [2.2%] and 25/955 [2.6%], respectively; p=0.82) or by patient sex (p=0.97). Bivariate analyses of case-control study data identified characteristics associated with colonization: length of stay >1 week (p=0.04), admission from a skilled nursing facility (p=0.01), percutaneous tube feeding (p<0.01), prior ICU admission (p<0.01), and mechanical ventilation (p=0.01).	This intervention may not be as cost-effective in hospitals with lower prevalence of CRE (more testing required to identify an unrecognized case). Also does not include patients who are not displaying signs of CDI (and thus would not have a stool sample collected).	CRE colonization and CDI share risk factors. In this study, active surveillance for CRE using stool specimens submitted for *C. difficile* testing detected previously unrecognized CRE carriage. Although not comprehensive, this active surveillance strategy may be of value because of its convenience and relative low cost. The estimated average cost of surveillance testing was $8.53 per specimen, including technical support and supplies but not molecular testing. At the study prevalence, 76 and 68 specimens had to be tested at hospitals A and B, respectively, in order to identify one previously undetected CRE carrier. Total cost of detecting one CRE-colonized patient ranged from $580 (hospital B) to $649 (hospital A).	Low to moderate	Organisms/ Outcomes: CRE, *C. difficile* (as a risk factor)

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Barbadoro et al., 2017[11]	Active surveillance to identify patients colonized/infected with MDROs for isolation. Skin, blood, respiratory, and urine samples were taken, and compared for relative efficacy in identifying MDRO colonization/ infection. Feedback: Reporting MDRO incidence (number of isolates/ 1,000 days of stay). Other components of the intervention included: operational planning on contact precaution strategies; educational/training initiative on infection prevention practices; checklist for contact precautions; routine surveillance; and	Time series analysis before and after a multicomponent infection prevention intervention at a single, 900-bed teaching hospital in Italy 149,251 patients totaling 909,706 patient-days included in 2011-2013 study period	Hospital, Italy	Sampling from skin (β=0.08, p=0.001, 95% CI 0.06 to 0.10), blood (β=0.05, p=0.001, 95% CI 0.03 to 0.07), and respiratory samples (β=0.02, p=0.031, 95% CI 0.02 to 0.06) were significantly likely to initially identify MDRO-positive status; sampling from urine was not (β=-0.01, p=0.413, 95% CI -0.03 to -0.01). Overall, the study period after the implementation of a multicomponent intervention showed a month-over-month decrease in MDRO rates.	The authors speculate that results may be more pronounced (i.e., a greater reduction) in hospitals with high transmission rates, compared to hospitals where transmission rates are already low.	In widespread surveillance, skin, blood, and respiratory samples performed better at initially identifying the presence of an MDRO than did urine samples.	Moderate One study site, limited detail about the surveillance methods or how feedback was conducted. Patient case mix over the course of the study was not assessed.	Organisms/ Outcomes: *K. pneumoniae* *K. pneumoniae* infection/ colonization

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	reporting of incidence rates.							
Beneson et al., 2013[35]	Active surveillance: Weekly fecal cultures for extended-spectrum beta-lactamase-producing *K. pneumoniae* (ESBL-KP). Rectal swab if stool sample not available. Molecular typing of samples performed to identify strains.	Observational study of 1,763 neonate admissions (7 days or longer) during the 4-year study period across two neonatal ICUs (10-bed and 25-bed) in two academic hospitals	Hospital neonatal ICU, Israel	Surveillance cultures were obtained from 1,482/1,763 (84%) neonates over 4 years. ESBL-KP acquisition decreased continuously from 94/397 (24%) neonates in 2006 to 33/304 (11%) in 2009 ($p<0.001$, hazard ratio 0.75, 95% CI 0.66 to 0.85, $p<0.001$ for comparison of years). Hospitalwide ESBL-KP acquisition did not decrease outside the NICU. Pulsed-field gel electrophoresis identified identical ESBL-KP strains from multiple neonates on six occasions and different strains from single neonates on seven occasions. Continuous long-term surveillance with cohorting of neonates with positive cultures was associated with a significant decrease in ESBL-KP acquisition within the NICU.	Weekly screening would not include neonates whose admissions were <7 days, and so may miss some patients who are colonized (either before or after admission).	Neonates with positive cultures were managed with contact precautions by dedicated nurses separately from other neonates. ESBL-KP acquisition among neonates staying 17 days was compared for the consecutive years. In addition to demonstrating the impact of surveillance on MDRO acquisition, this study shows the importance of molecular testing to identify whether the MDROs identified are being spread within a unit or imported from outside.	Low to moderate Only two sites; no control group. The study did control for the effects of current infection control practices by adding active surveillance to an already established infection prevention protocol.	Organisms/ Outcomes: ESBL-KP ESBL-KP acquisition

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Bryce et al., 2015[38]	Risk-based, active weekly screening of patients (and contact precautions) in high-risk units for VRE (as opposed to VRE screening in *all* units at baseline) to make screening more cost-neutral. Risk-based surveillance was added to a horizontal implementation of environmental cleaning (decluttering) and antimicrobial stewardship program.	Pre-post study and economic analysis of targeted screening and contact precautions for VRE in a 728-bed adult acute care facility, starting in the 2012–2013 year	728-bed adult tertiary care hospital, Canada	In high-risk units, VRE bacteremia decreased significantly the first year after a spike in VRE infection cases in 2013 (p=0.009), as did facilitywide *C. difficile* and MRSA infection cases (by 46% [p<0.001] and 25% [p=0.02], respectively). VRE bacteremia rates outside the high-risk units remained unchanged after switching to risk-management surveillance approach. Cost avoidance for targeted surveillance comes in the form of reduction in VRE isolations (costs for gloves and gowns and hospital linen, as well as lost revenue due to reserving private rooms) and decreased laboratory reagent consumption. Although the project experienced net costs in the first 2 years of implementation (2012–2013 and 2013–2014), by the third year (2014–2015), the project had saved an estimated $14,655.	None assessed.	Risk-management surveillance can be as effective in reducing the target MDRO (as well as others) although it was unclear what the unique impact was of each intervention: risk management surveillance, antimicrobial stewardship, and environmental cleaning.	Low to moderate Single-site study; efficacy results may differ depending on VRE prevalence and risk factors.	Organisms/ Outcomes: VRE, MRSA, *C. difficile* VRE prevalence and bacteremia, CDI, MRSA infection

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
D'Agata et al., 2012[39]	Active surveillance: screening for asymptomatic MRSA and VRE colonization Other PSPs included in model: hand hygiene, contact precautions, reducing antimicrobial exposure	Mathematical model simulation Modeled on a 600-bed tertiary care hospital	Hospital	Screening patients for asymptomatic colonization reduces the overall prevalence of MDRO, but only among patients already receiving antimicrobials. Improving screening has less effect on the prevalence of MDRO compared to improving compliance with hand hygiene or contact precautions, since a smaller population size is targeted. In addition, the model only incorporates screening for VRE and MRSA.	This model also highlights the importance of vulnerability to infection: even modest increases (5-10%) in MDRO infection rate among colonized patients can negate all the beneficial effects of infection prevention interventions.	Universal screening for asymptomatic colonization of MRSA and VRE did not reduce MDROs in this model; however, targeted screening for MRSA and VRE for patients already receiving antimicrobials (a known risk factor for MDRO acquisition) should theoretically reduce MDRO acquisition in the clinical setting.	Moderate Mathematical study, not in situ; only included screening for MRSA and VRE (other MDROs may have different results).	Organisms/ Outcomes: MRSA, VRE, MDR Gram-negative bacteria (MDR-GNB) MDRO colonization
Friere et al., 2017[10]	Screening cultures from inguinal-rectal area, axilla, and throat swabs immediately before liver transplant, and weekly thereafter for carbapenem-resistant *P. aeruginosa* (CR-PA), carbapenem-resistant *A. baumannii* (CR-AB), ESBL-producing *K. pneumoniae.*	Sensitivity study of different methods for collecting surveillance cultures Prospective cohort study of all patients who underwent liver transplant from November 2009 through November 2011 (n=181); 4,110 samples collected	Hospital transplant ward, Brazil	The MDRO positivity rate was highest among the inguinal-rectal collection site samples. However, if only samples collected from this area were considered, surveillance would fail to identify 34.9% of the cases of CR-AB colonization. The sensitivity of active surveillance for EBSL-KP was 92.5%. The performance of screening cultures was poorest for CR-AB (sensitivity, 80.6%).	Routine screening has costs associated with materials, time, and patient isolation (once carriage is identified).	The sensitivity and specificity of a sample collection site or type varies by type of MDRO. Given the costs associated with surveillance and subsequent patient isolation, universal surveillance may make the most sense in facilities where the incidence of MDROs is moderate to high, and for patients for whom the rate of conversion from colonization to infection is high (e.g., transplant patients).	Moderate Single study, observational study design	Organisms/ Outcomes: CR-PA, CR-AB, ESBL-producing *K. pneumoniae,* and EBSL-producing *Escherichia coli* MDRO colonization, MDRO infection, health care-associated infections

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Fujitani et al., 2011[20]	Active surveillance of VRE colonization in patient stool samples positive for *C. difficile* colonization	Prospective laboratory analysis of stool samples from all inpatients with CDI in a single hospital from July 2006–October 2006, comprising 158 CDI cases.	Hospital, United States	Of the 158 cases of CDI evaluated, 88 (55.7%) involved VRE colonization. Independent risk factors for VRE colonization were admission from long-term care facilities (p<0.013), dementia (p=0.001), and hospitalization in the previous 2 months (p=0.002). No statistically significant difference between CDI cases with and without VRE colonization in terms of previous receipt (within 1 month) of antibiotics, including metronidazole and vancomycin, was found on multivariate analysis. CDI cases with VRE colonization had a higher prevalence of coinfection with MRSA (p=0.002) and *Acinetobacter* species (p=0.006).	None assessed.	Given the high rate of CDI associated with VRE colonization, active surveillance of VRE in patients with CDI is reasonable in high-risk settings.	Moderate	Organisms/ Outcomes: VRE, *C. difficile,* MRSA, *Acinetobacter* species VRE colonization

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Huskins et al., 2011[22]	Active surveillance for MRSA (nasal swabs) and VRE (perianal swabs and stool cultures) within 2 days of admission to ICU and 2 days before or after discharge Control ICUs used existing hospital procedures (not specified) to identify MRSA and VRE. Results were reported to health care personnel in the intervention ICUs, but not the control ICUs.	Cluster-randomized trial of an active surveillance and reporting intervention in 10 intervention ICUs (5,434 admissions) and 8 control ICUs (3,705 admissions)	Hospital ICUs, United States	Patients who were colonized or infected with MRSA or VRE were assigned to contact precautions more frequently in intervention ICUs than control ICUs (median of 92% of ICU days with either contact precautions or universal gloving [51% with contact precautions and 43% with universal gloving] in intervention ICUs vs. a median of 38% of ICU days with contact precautions in control ICUs, p<0.001). The change in incidence of MDRO colonization varied widely between ICUs, but mean ICU incidence (of events of MDRO colonization/infection per 1,000 patient-days at risk), adjusted for baseline incidence, did not differ significantly between intervention and control ICUs (40.4 ± 3.3 and 35.6 ± 3.7, respectively; p=0.35). MDRO colonization/infection incidence was not significantly associated with the percentage of patient-days of contact precautions for colonized/ infected patients (p=0.26) or correct hand hygiene compliance (including gloves when recommended) (p=0.61).	In intervention ICUs, health care providers used clean gloves (82% of the time), gowns (77%), and hand hygiene (69%) less frequently than required for contacts with patients assigned to barrier precautions.	Although active surveillance identified a number of colonized patients who had previously been missed, the intervention did not reduce MRSA and VRE colonization or infection compared to usual care. The authors hypothesize that this unexpected result may be due to the lag between culture results and assignment to contact precautions, and the gaps in compliance with the required components of contact precautions and universal gloving. "Identify and isolate" approaches alone may not be enough, since closing one gap in surveillance did not close the gap in compliance.	Low	Organisms/ Outcomes: MRSA, VRE MRSA and/or VRE colonization or infection

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Jones et al., 2015[17]	Active screening at hospital admission for MDR-GNB: nasal screening, screening of clinical cultures Cultures tested for relatedness using PCR	Retrospective cohort study of all patients with both a nasal screen and clinical culture, admitted to a Veterans Affairs (VA) facility between January 2009 and December 2012 (759,759 total). Assessed how often patients with MDR-GNB in clinical cultures obtained within 30 days following admission would have been in contact precautions because of a positive MRSA admission screen	All VA acute care medical facilities, United States	Of patients with MDR-GNB-positive cultures within 30 days following admission, up to 44.3% (dependent on bacterial species) would have been in contact precautions because of a clinical positive admission MRSA nasal screen. Admissions with a positive MRSA screen had odds for MDR-GNB in a culture 2.5 times greater than those with a negative screen (95% confidence interval [CI], 2.4 to 2.6). Odds ratios were 2.4 (95% CI, 2.3 to 2.5) for MDR Enterobacteriaceae, 2.7 (95% CI, 2.5 to 2.9) for MDR *P. aeruginosa*, and 4.3 (95% CI, 3.8 to 4.8) for MDR *Acinetobacter* species.	None assessed.	Evidence supports an association between MRSA status at admission and later discovery of MDRO colonization. This association was strongest for *Acinetobacter* species. Therefore, when patients are placed in contact precautions because of a positive MRSA screen, there may be a collateral benefit of isolating patients at increased risk for transmitting MDR-GNB to others within the hospital. However, it is not clear from this study if the MDR-GNB were present on admission or acquired in the facility. Still, in places where universal MRSA screening is already in place, a positive result may be considered a risk factor for other MDROs.	Moderate VA population may not be representative of general population (more likely to be older, male); unable to determine if MDR-GNB were present on admission or acquired.	Organisms/ Outcomes: MDR-GNB (Enterobacter-iaceae*, P. aeruginosa, Acinetobacter* species), MRSA Positive screening for any of the above organisms

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Karampatakis et al., 2018[24]	Active surveillance was added to an infection prevention study also consisting of hand hygiene; contact precautions, patient and staff cohorting; environmental cleaning; antimicrobial stewardship; staff education; compliance monitoring audits and feedback. Active surveillance consisted of (1) weekly rectal swabs; and (2) environmental surface samples.	Quasi-experimental study of all patients (300 total) in a 9-bed ICU with CR-GNB infection (n=34, retrospectively studied for 6 months) and those in an active surveillance program (n=266, prospectively studied for 22 months)	Hospital ICUs, Greece	The downward trend of average incidence, prevalence, and colonization pressure for all CR-GNB during the active surveillance program mostly occurred due to the reduction of CR-*K. pneumoniae* (CR-KP) and CR-*P. aerguinosa* (CR-PA) infections and resistance rates. Despite enhanced infection control, CR-*A. baumannii* infections were not reduced. Total CR-GNB infections decreased from 29.9 to 25.2 infections per 1,000 bed-days (p>0.05). CR-KP infections decreased from 19.6 to 8.1 per 1,000 bed-days (p=0.001), and CR-PA infections decreased from 5.1 to 1.8 per 1,000 bed-days (p=0.043).	None assessed.	A multicomponent intervention including active surveillance successfully reduced certain rates of CR-GNB (*K. pneumoniae* and *P. aeruginosa*) but not others (*A. baumannii).*	Low to moderate Single-site study but quasi-experimental design with case mix analyzed	Organisms/ Outcomes CR-KP, CR-PA, CR-AB CR-GNB infection and colonization
Lin et al., 2018[16]	Active surveillance for MRSA (nasal and inguinal swabs, pulsed-field gel electrophoresis to distinguish community-associated strains from others) followed by contact precautions for	Observational study of 25 hospitals, including 51 ICUs and 3,909 patients in point prevalence surveys; 5-year study period	Hospital ICUs, United States	In this study, 93% of patients in received active surveillance for MRSA on hospital admission. The overall admission prevalence of MRSA colonization as reported was 9.7% (95% CI, 8.8% to 10.8%) and did not change over time (p=0.95 for trend). The number of hospitals using daily chlorhexidine bathing in at least one ICU grew from 5 to 17 over the study period. The	Only 54% of patients with MRSA-positive cultures during the point prevalence surveys (n=184) were on contact precautions. Fifteen (8%) were not	Despite high compliance with mandatory active surveillance, almost 4 of 10 patients identified as MRSA-colonized by the point prevalence survey were not on contact precautions. In addition, few hospitals were using recommended decolonization	Low No control group, as the legislation affected all hospitals in the State of Illinois	Organisms/ Outcomes: MRSA MRSA colonization

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	any patients whose culture tested positive, as mandated by Illinois legislation at the start of the study period. Hospitals also reported if daily chlorhexidine bathing and mupirocin were used.			percentage of study patients who were in an ICU using chlorhexidine bathing grew from 28% to a peak of 59% by year 3 (p<0.001 for trend). No hospital ICUs routinely used mupirocin for decolonization. No significant change in MRSA colonization (as measured by the point prevalence survey) was observed after legislation of mandatory active MRSA. MRSA colonization prevalence was unchanged during the study period: year-over-year relative risk for colonization was 0.97 (95% CI, 0.89 to 1.05; p=0.48). This trend remained nonsignificant after adjusting for chlorhexidine bathing and rapid results testing use over time.	screened at admission; 16 (9%) had a positive admission MRSA screen but contact precautions had not yet been initiated; 27 (15%) had a pending admission culture that eventually became MRSA positive; and 126 (69%) had a negative admission MRSA culture, representing either admission MRSA screen insensitivity or ICU acquisition.	protocols (chlorhexidine bathing and nasal mupirocin) at the start of the study, limiting the effectiveness of active surveillance to reduce MRSA colonization. For patients with results available for both nose and groin sites, nasal culturing alone identified 84% (327/ 388) of MRSA-positive patients; 61 patients (16%) were nasal culture negative and groin culture positive. Nasal MRSA screening had a negative predictive value of 98% (95% CI, 97.6% to 98.5%).		

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Mawdsley et al., 2010[42]	Active surveillance: process surveillance for compliance with contact precautions for MDRO-flagged patients Infection preventionists conducted weekly rounding to identify whether patients whose electronic medical record (EMR) had electronically flagged them as MDRO-positive (i.e., positive clinical cultures for MRSA, VRE, and MDR-GNB) were put on appropriate contact precautions.	Case study: Surveillance rounding project for a 22-week period	500-bed academic medical center, United States	The program significantly improved the percentage of patients with appropriate isolation (p<0.001). Overall point prevalence of appropriate implementation of precautions was 70% on the first day of the program rollout period, 74% for the first month, and 82% overall for the entire period. The percentage of patients isolated at the first surveillance encounter ranged from 40% to 77%. For those patients still hospitalized 1 week later (for a second surveillance encounter), 97% were appropriately isolated. Patients with MDR-GNB were significantly less likely to be isolated appropriately at the first surveillance encounter than those with MRSA or VRE (p=0.03), with VRE patients having the highest percentage appropriately isolated (66%). Non-ICU patients were less likely to be isolated (p<0.001).	None assessed.	Weekly surveillance rounding alone was successful in improving compliance with contact isolation initiation and required minimal resources (two person-hours of work per week, split among six infection preventionists). However, this approach does not ensure that contact precautions will be consistently followed, and MDROs may require surveillance apart from measure compliance.	Moderate Single-site case study	Organisms/ Outcomes: MRSA, VRE, MDR-GNB Compliance with contact precautions based on EMR flagging

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Mayer et al., 2016[26]	Mandatory surveillance reporting, which was initiated in New York State in July 2013	Retrospective validation of CRE cases reported to the National Healthcare Safety Network using retrospective laboratory report audit of all CRE infections between July 2013 and December 2014 in acute care hospitals in New York State; 1,151 CRE laboratory reports were audited.	178 acute care hospitals, New York, United States	None assessed.	Of CRE laboratory reports audited, 13.6% were not reported (as required by New York State law) and 4.6% were reported in error. Some underreporting was due to lapses in surveillance. Other, systematic underreporting was due to misinterpretation of surveillance definitions.	Lapses in surveillance, misunderstanding or misinterpretation of surveillance definitions can result in under- or overreporting of CRE cases. In this study, underreporting was far more frequent than overreporting. Cases of misinterpretation of surveillance definitions included: not reporting community-onset cases, not reporting specimens from all body sites, not reporting intermediate susceptibilities, changing overall carbapenem susceptibility interpretation based on ertapenem results, and only reporting carbapenemase-producers.	Low to moderate Retrospective study	Organisms/ Outcomes: CRE Mandatory surveillance reporting rates

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Palmore et al., 2011[43]	Infection control adherence monitors were placed in MDR-AB cohort areas to observe and correct staff infection control behavior. Surveillance reporting was done in weekly stakeholder meetings. Other PSPs in outbreak response included active surveillance cultures, hand hygiene, enhanced contact isolation, patient cohorting with dedicated staff, and enhanced environmental cleaning.	Outbreak response (two outbreaks) in an 18-bed medical-surgical ICU	Hospital, ICU, United States	All but two of the patients included in the outbreak had overlapping stays with other MDR-AB patients. Nearly all (90%) of case patients were infected or colonized with outbreak strains. Post-ICU-discharge screenings had low yield rates, and thus were discontinued in the second outbreak. Few of the environmental samples in either outbreak (three and five, respectively) had positive culture results, and all but one were from patient rooms. Based on the evidence from environmental sampling and adherence monitoring, the authors concluded that MDR-AB in these outbreaks were spread by transmission from health care worker to patient (due to insufficient adherence to contact precautions). Collaborative team meetings were critical to halting the outbreak.	Physicians were responsible for more infection control violations than other staff categories, although most all-staff observations showed compliance (95.7% of 4,781 observations) .	Extensive surveillance of patients and environment, combined with adherence monitoring, can home in on the transmission patterns of MDR-GNB and expose areas for improvement (in this case, hand hygiene and gown and glove compliance among physicians).	Moderate Single-site outbreak response. Unable to assess the relative effectiveness of each of the components.	Organisms/ Outcomes: MDR-AB Infection prevention practice adherence

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Quan et al., 2015[53]	Automatic surveillance system for flagging patients for contact precautions, with physician-ordered discontinuation.	Case study of a single hospital The system automatically reviewed daily positive laboratory results for 110,212 patient-days involving 20,000 historical admissions.	410-bed academic hospital, United States	In this case study, an automated system surveyed microbiology results for positive cultures for MRSA, VRE, CRE, ESBL pathogens, MDR-AB, and *C. difficile.* Physicians could order discontinuation of contact precautions as appropriate (e.g., negative cultures). Automation saved 43 infection preventionist hours per 1,000 admissions, as well as unmeasured hours spent reviewing MDRO history for each admission.	Discontinuation protocols were too complex to be fully automated.	Automated systems can support enforcement of contact precautions and save considerable infection preventionist time in identifying MDROs. Point prevalence assessment showed that all precautions were appropriate.	Moderate Single-site case study; time savings may vary at other sites.	Organisms/ Outcomes: MRSA, VRE, CRE, ESBL-producing pathogens, MDR-AB, *C. difficile.* Appropriateness of automatic flagging for initiating and discontinuing contact precautions
Rosenman et al., 2014[54]	Active surveillance using EMR evidence of positive culture for MRSA, VRE, CRE, ESBL-producing Enterobacteriaceae, or other MDR-GNB	Retrospective analysis of 80,180 patients (in 12 hospital systems) with microbiology data between October 1, 2013, and December 31, 2013; includes subsequent healthcare encounters (through February 6, 2014).	Hospitals in a shared geographic region, United States	This project created standardized data collection across 12 hospital systems that used clinical data to create MDRO alerts (based on a pre-existing MRSA/VRE alert system). For infection preventionists, the most important alerts were ones at other facilities (identifying which patients may be colonized with organisms and then transferred to other institutions).	Here, 2% of alerts were internally inconsistent (alert email titles did not match the results in the body of the email).	The authors created a regional surveillance system for MDROs, through which they observed several transmissions between institutions.	Moderate Single case series	Organisms/ Outcomes: MRSA, VRE, CRE, ESBL-producing Enterobacteriaceae, MDR-GNB (*P. aeruginosa, A. baumannii,* and others) Accurate MDRO alerts using positive culture results captured in EMRs

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Silwedel et al., 2016[32]	Routine microbiological screening, including: examination of ear swabs and gastric fluid immediately after birth. Surveillance of intestinal colonization of preterm infants comprised the weekly microbiological examination of anorectal swabs or stool samples in all infants. Infants admitted from external NICUs were screened on admission and isolated until receipt of results. Other PSPs in outbreak response: hand hygiene; glove, gown, and apron use; shared equipment disinfection; patient isolation; dedicated staff.	Retrospective case study. All infants in a single neonatal ICU during a 35-day outbreak. Outbreak affected 13 infants.	Two neonatal ICUs at 113-bed children's hospital, Germany	Routine stool sampling revealed MDR-*E. coli* detected in a total of 35 infants using active surveillance of anorectal or stool samples. Despite infection prevention precautions, ongoing transmission occurred in the NICU. Control was ultimately achieved by relocating all preterm infants from NICU-1 to NICU-2 and moving NICU-1 into a temporary ward. NICU-1 was reopened at the beginning of 2015 after thorough disinfection and extensive reconstruction work.	Although environmental surveillance revealed no MDR-*E. coli,* the outbreak only ended after closure of the original NICU for extensive decontamination and construction of isolation rooms.	Although the environmental sampling turned up no MDR-*E. coli*, the change of environment was what was needed to eventually end the outbreak. Relocation and reconstruction improved the NICU's structural layout, focusing on isolation capacities.	Moderate Outbreak study, single site.	Organisms/ Outcomes: MDR-*E. coli* MDR-*E. coli colonization*
Zarpellon et al., 2018[45]	Active surveillance	Prospective study; all patients in a	Hospital, Brazil	The study found significant decreases in infections from MDROs after implementing a	Implementing surveillance programs can	This implementation was successful, but the authors note that	Moderate	Organisms/ Outcomes:

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	protocol consisting of: (1) Rectal swab on admission for VRE/CP-*K. pneumonia* in adult and pediatric patients hospitalized for >48 hours in preceding 30 days, had stayed in ICU in preceding 6 months, or were on dialysis; (2) Nasal swabs for MRSA for pediatric patients; (3) Nasal and rectal swabs for all admitted neonates; and (4) Weekly rectal swabs for all adults and nasal swabs for MRSA in pediatric and neonatal patients. PCR molecular testing Other PSPs: patient isolation, contact precautions, two terminal cleanings	123-bed teaching hospital		multicomponent infection prevention program, including routine surveillance on admission. The overall hospital infection rate in the pre-intervention period (2005–2010) was 5.35% (range: 4.58% to 6.12%). The same rate in the post-intervention period (2011–2016) was 3.62% (range: 3.0% to 4.24%). The overall rate of HAIs decreased by 1.73%. Statistically significant differences in the HAIs rate were observed between the pre- and post-intervention periods (p=0.00198).	be costly in both labor and materials, and the cost-benefit comparison of implementation should be considered.	this may not always be the case. Cost-effectiveness of surveillance interventions depends on how many infections are reduced (or are likely to be reduced) by the intervention, which varies by facility and even within facilities. For example: in this hospital, MRSA is considered endemic (except in pediatric and neonatal wards). Accordingly, the authors only screened for MRSA in patients where the MDRO was not yet endemic (and thus could be prevented from establishing).	Single site, observational study design	VRE, MRSA, *K. pneumoniae* carbapenemase-producing bacteria All hospital infections, all health care-associated infections

Table B.36: MDRO, Environmental Cleaning—Systematic Reviews

Note: Full references are available in the Section 5.4 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Marra et al., 2018[29]	Use of no-touch disinfection methods, including: ultraviolet light (UVL), hydrogen peroxide mist, hydrogen peroxide vapor (HPV), and traditional environmental cleaning methods	Healthcare settings, multidrug-resistant organism (MDRO) healthcare-associated infections (HAIs), United States and United Kingdom	When the results of the UVL studies were pooled, statistically significant reduction in *C. difficile* infection (CDI) (pooled risk ratio, 0.64; 95% confidence interval [CI], 0.49 to 0.84) and vancomycin-resistant *Enterococci* (VRE) infection rates (pooled risk ratio, 0.42; 95% CI 0.28 to 0.65) were observed. No differences were found in rates of methicillin-resistant *Staphylococcus aureus* (MRSA), or Gram-negative multidrug-resistant pathogens. UVL and hydrogen peroxide mist or vapor should be used to augment traditional cleaning methods. Using UVL no-touch technology to enhance environmental hygiene can decrease HAIs for specific pathogens, specifically CDIs and VRE infections. For CDI prevention, there seems to be a benefit for hospitals with high baseline CDI rates. There was some evidence of a decrease in VRE infection with HPV disinfection, but more studies are needed to confirm these results.	Two studies on UVL performed a cost-effectiveness evaluation of using no-touch technology after terminal cleaning, with annual costs for the first year estimated to be nearly $300,000 (including personnel and equipment acquisition), and approximately $200,000 for the next year. The authors determined that randomized trials and cost-effectiveness studies are needed.	Organisms/Outcomes: *C. difficile,* MRSA, VRE, other MDROs Systematic review included many studies that were before-and-after quasi-experimental studies, which are subject to multiple biases.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Nikitovic-Jokic et al., 2018[61]	Use of no-touch disinfection method: portable UVL surface-disinfecting devices	Hospitals, United States	The researchers were not certain of the effectiveness of UVL disinfection in reducing HAIs, given the very low to low quality of evidence, using the GRADE rating system. The intervention was effective in reducing the rate of the composite outcome of HAIs (combined) and colonization (but quality of evidence was low). The authors estimated that the typical cost for a hospital that purchased two portable devices would be $586,023 over 5 years for devices that use pulsed xenon technology and $634,255 over 5 years for devices that use mercury technology.	More rigorous evidence is needed to support the use of portable UVL surface disinfecting technologies in reducing HAIs and environmental MDRO contamination to justify the high cost.	Organisms/Outcomes: *C. difficile* and "combined HAIs" that varied per reviewed article but included MRSA, carbapenem-resistant Enterobacteriaceae (CRE), VRE, multidrug-resistant *Acinetobacter* (MDR-A), *Acinetobacter baumannii, Klebsiella pneumonia*e, MDR Gram-negative bacteria, extended-spectrum beta lactamase-producing Enterobacteriaceae (ESBL-E), MDR *Pseudomonas aerigunosa,* and *Stenotrophomonas maltophilia*

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Tacconelli et al., 2014[1]	Use of environmental screening during outbreaks, use of education, monitoring (e.g., fluorescent gel markers), feedback to improve quality of environmental cleaning, use of antimicrobial surfaces, reduction of shared equipment, and use of disinfectants versus detergents	Hospitalized patients, International	Environmental cleaning is often assessed as a bundle of interventions in an endemic situation and thus does not have strong studies assessing its efficacy. The authors recommend environmental screening when infection control practices fail to stem an outbreak. Cleaning inspections, education, monitoring and feedback, and observation of staff can also improve performance and thoroughness. Bacteria within biofilms may display greater capacity for antimicrobial resistance and can tolerate chlorine and other disinfectants. Disinfectants are more effective at killing pathogens than detergents, but some hospital pathogens can resist the bactericidal effect of particular agents. Disinfectant solutions themselves can become contaminated with bacteria, so containers used should also be cleaned. There is ambiguous support for antimicrobial surfaces (i.e., silver surfaces). Epidemic settings: Vacate rooms and monitor cleaning and adherence to policies; reduce sharing of equipment if a patient is colonized or infected. Endemic settings: Have cleaning procedures and policies; reduce sharing of equipment if a patient is colonized or infected.	Methods for assessing cleanliness are needed, both for scientific studies and to reassure staff and patients. Such methods can be defined within two main categories: process evaluation, where the cleaning process is monitored by visual inspection or with a fluorescent gel marker; and outcome evaluation, where cleanliness is evaluated with the use of adenosine triphosphate (ATP) bioluminescence systems or microbial cultures.	Organisms/Outcomes: MDR Gram-negative bacteria

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Teerawattana-pong et al., 2017[47]	Multicomponent interventions including environmental cleaning, antimicrobial stewardship, decolonization methods, source control, and combinations of the above	Adult ICU patients, Belgium, Brazil, Canada, China, Europe, France, Germany, Hungary, Israel, Italy, Netherlands, Spain, South Korea, Thailand, Vietnam, United States	Of 3,805 publications retrieved, 42 met inclusion criteria (5 randomized controlled trials and 37 observational studies). These 42 studies included 62,068 patients (median age, 58.8 years). Environmental cleaning bundled with antimicrobial stewardship, evaluation of standard care, and source control was the most effective intervention for reducing MDR *A. baumanii* (MDR-AB), ESBL-E, and CRE acquisitions. Compared with standard care, a four-component strategy composed of the same standard care combined with antimicrobial stewardship, environmental cleaning, and source control was the most effective intervention (rate ratio [RR], 0.05; [95% CI, 0.01 to 0.38]). When environmental cleaning was added to a program of standard care with antimicrobial stewardship, or when source control was added to standard care with environmental cleaning, there was a significant reduction in the acquisition of MDR-AB (RR, 0.28 [95% CI 0.18 to 0.43] and 0.48 [95% CI 0.35 to 0.66], respectively).	Environmental cleaning bundled with antimicrobial stewardship, evaluation of standard care, and source control was the most effective intervention for reducing MDR-AB, ESBL, and CRE acquisitions.	Organisms/Outcomes: MDR-AB, CRE, and ESBL-Enterobacteriaceae

Table B.37: Environmental Cleaning—Single Studies

Note: Full references are available in the Section 5.4 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Adams et al., 2011[14]	Multicomponent intervention including unannounced decontamination audits and monitoring using an ATP luminometer, twice-daily cleaning and terminal cleaning with 1,000 ppm hypochlorite or 70% alcohol wipes, replacement of hard-to-clean equipment, cleaning of ICU ventilation with biocide fog, and disinfection of ICU with hydrogen peroxide vaporization.	Outbreak intervention study, three cases (ICU patients)	12-bed ICU, small acute hospital in the United Kingdom	The Infection Control Nurses Association (ICNA) audit (2004) demonstrated 96% compliance (pass rate defined as 85%); issues noted were largely attributable to dusty ventilation grills, ward clutter, and poor documentation. A score between 0 and 66 relative light units (RLUs) was reported on the first assessment following confirmation of MDR-AB. A score of 0 to 45 RLUs was recorded before environmental disinfection with HPV. Both sets of results were acceptable against the risk assessment undertaken for these items of equipment. No more cases after second phase of decontamination.	Phase 2 of the decontamination strategy required that ICU be relocated to recovery room for 1 week, which required relocating 12-bed ICU, reviewing surgical admissions, reviewing staffing levels, informing staff/patients/ family of changes, and putting up new signs.	Initial environmental audit using the ICNA audit tool, and cleanliness monitoring using an ATP luminometer, unannounced weekly audit, required pass rate of 90% for 3 consecutive weeks to stop audit, and identification of dirty equipment resulted in a failed audit. A general declutter of the environment was undertaken and twice-daily environmental and equipment decontamination was initiated with either 1,000 ppm hypochlorite or 70% alcohol wipes. The facility replaced hard-to-disinfect equipment (i.e., exposed equipment placed into single-use sealable bags, new trolleys with sealed door system, new binders), cleaned ICU ventilation system by “fogging” with Klercide-CR Biocide B, performed HPV of	High	Organisms/ Outcomes: MDR-AB outbreak

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
						ICU, used ATP luminometer to find and clean any contaminated surfaces, and performed terminal cleaning with wall washing and curtain changes.		

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Alotaibi et al., 2017[23]	Use of benzalkonium chloride 10 mg/L, chlorhexidine 20 mg/L, and hydrogen peroxide 30 mg/L for environmental disinfection	Cross-sectional study, 12 vancomycin-susceptible (VS) *E. faecium* and 37 vancomycin-resistant (VR) *E. faecium* isolates, Danish patients	Statens Serum Institute Hospital, Denmark	For benzalkonium chloride, 89% of VR *E. faecium* strains had a minimal inhibitory concentration (MIC) of 8 mg/L whereas for VS *E. faecium*, only 25% of the strains had an MIC of 8 mg/L. For chlorhexidine, the MIC of 95% of VR *E. faecium* strains was 4 mg/L or higher, while only 33% of VS *E. faecium* strains displayed MIC values at the same level. In contrast, both VR and VS *E. faecium* displayed equal susceptibility to hydrogen peroxide, but a higher minimal bactericidal concentration (MBC) was found for the former. The efflux activity was also assessed and was generally higher for VR strains than for VS strains.	VR *E. faecium* was found to have decreased susceptibility toward benzalkonium chloride and chlorhexidine compared with VS *E. faecium.*	VR *E. faecium* from Danish hospitals demonstrated decreased susceptibility toward benzalkonium chloride and chlorhexidine compared with VS *E. faecium*. Biocide tolerance may be common in these settings.	Moderate to high Samples were taken over an undefined period.	Organisms/ Outcomes: VR and VS *E. faecium* strains

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Anderson et al., 2017[18]	Terminal cleaning interventions with either quaternary ammonium compound (QAC) disinfectant, UVL, bleach, or bleach and UVL	Cluster-randomized crossover study, 21,395 patients, patients infected or colonized with target organism	Nine hospitals in south-eastern United States	Strategies were implemented at every hospital for 4 consecutive 7-month periods. The primary outcome was not statistically lower with bleach (n=101; 41.6 cases per 10,000 exposure-days; RR 0.85, 95% CI 0.69 to 1.04; p=0.116), or bleach and UVL (n=131; 45.6 cases per 10,000 exposure-days; RR 0.91, 95% CI 0.76 to 1.09; p=0.303) among exposed patients. Incidence of CDI among exposed patients was not changed after hospitals added UV to cleaning with bleach (n=38 vs. 36; 30.4 cases vs. 31.6 cases per 10,000 exposure-days; RR 1.0, 95% CI 0.57 to 1.75; p=0.997).	None assessed.	The incidence of target organisms (MRSA, VRE, *C. difficile*, and MDR-AB) among exposed patients was significantly lower after hospitals added UVL to standard cleaning strategies (n=76; 33.9 cases per 10,000 exposure-days; RR 0.70, 95% CI 0.50 to 0.98; p=0.036). The quaternary ammonium-containing disinfectant in this study was delivered with microfiber cloths, which the authors found removed more bacteria than cotton and synthetic fiber cloths.	Low to moderate	Organisms/ Outcomes: MRSA, VRE, MDR-AB, *C. difficile*

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Apisarn-thanarak et al., 2008[16]	Multicomponent intervention including contact isolation, hand hygiene, active surveillance, cohorting, and environmental cleaning with 1:100 sodium hypochlorite. In Phase 3, environmental cleaning was instead done with detergent and phenolic agents.	Three-year prospective, controlled, quasi-experimental study, n=4,071 patients admitted to three ICUs during study period: medical ICU (MICU), surgical ICU (SICU), and coronary care unit (CCU)	Thammasat University Hospital's three ICUs (MICU, SICU, CCU), each of which has 8 beds, Thailand	Before the intervention, the rate of pan-drug-resistant *A. baumannii* colonization or infection was 3.6 cases per 1,000 patient-days. After the intervention, the rate of pandrug-resistant *A. baumannii* colonization or infection decreased by 66% in period 2 (to 1.2 cases per 1,000 patient-days; p<0.001) and by 76% in period 3 (0.85 cases per 1,000 patient-days; p<0.001). The monthly hospital antibiotic cost of treating pandrug-resistant *A. baumannii* colonization or infection and the hospitalization cost for each patient in the intervention units were reduced by 36% to 42% (p<0.001) and 25% to 36% (p<0.001), respectively, during periods 2 and 3.	None assessed.	Phase 3 was the most effective in reducing colonization and infection rates. Overall, the intervention resulted in sustained reductions in colonization and infection, reduced cost of antibiotic therapy, and reduced cost of hospitalization among ICU patients.	Moderate During the study period, hand hygiene and contact precautions were standard practice.	*Organisms/ Outcomes:* Pan-drug-resistant *A. baumannii* (PDR-AB) PDR-AB colonization, infection

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Apisarn-thanarak et al., 2014[8]	Twice-daily environmental cleaning with detergent-disinfectant (Phase 1) or sodium hypochlorite (Phase 2), preceded by a deep environmental cleaning with bleach after flooding of the MICU	Before-and-after study (multiphase), 1,365 patients, all patients admitted to MICU	MICU (8 beds) in a university hospital, Thailand	Compared with Phase 1 (11.1 cases per 1,000 patient-days), the rate of extensively drug-resistant (XDR) *A. baumannii* clinical isolates declined in Phase 2 (1.74 cases per 1,000 patient-days; p<0.001) and further in Phase 3 (0.69 cases per 1,000 patient-days; p<.0.001). Compared with Phase 1 (12.15 cases per 1,000 patient-days), the rate of XDR *A baumannii* surveillance isolates also declined in Phase 2 (2.11 cases per 1,000 patient-days; p<0.001) and Phase 3 (0.98 cases per 1,000 patient-days; p<0.001). Incidence of nosocomial infections remained stable.	None assessed.	Phase 1: Intervention included twice-daily environmental cleaning with detergent-disinfectant. Phase 2: Sodium hypochlorite was substituted for detergent-disinfectant. All interventions except cleaning with sodium hypochlorite were continued during the 12.5-month followup period.	Moderate	Organisms/ Outcomes: XDR *A. baumannii* (XDR-AB) Clinical isolates of XDR-AB, XDR-AB infections Authors suggest that bleach was only necessary when infection rates and colonization rates were high.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Apisarn-thanarak et al., 2017[5]	Facility-level compliance with a MRSA prevention bundle, use of HPV for MDR-AB prevention, environmental cleaning of patient room and surroundings, and presence of a facilities maintenance division and microbiology laboratory	Cross-sectional survey, n=212 hospitals	Hospitals with ICUs and ≥250 beds, Thailand	Most hospitals regularly used environmental cleaning of patient room and surroundings (85.4%). HPV for MDR-AB was used by 21.2%. Facilities with ≥75% compliance with the MRSA prevention bundle experienced a 17.4% reduction in MRSA rates (p =0.03). Although the presence of environmental cleaning services department (41.3% reduction, p=0.01) was among characteristics associated with decreases in MDR-AB rates, greater compliance with the MDR-AB prevention bundle did not lead to reductions in MDR-AB rates.	None assessed.	Hospitals reporting high compliance with the prevention bundle for MRSA were more successful at reducing MRSA but not MDR-AB, which may be better controlled though enhanced environmental cleaning practices. Hospitals better equipped to limit transmission routes due to better facility infrastructure and resources (e.g., having a facilities maintenance department division and microbiology laboratory) will likely achieve better infection control for MDR-AB than hospitals with limited resources.	High	Organisms/ Outcomes: MRSA and MDR-AB MRSA and MDR-AB rates

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Bagattini et al., 2015[43]	Use of an overheated dry-saturated steam vapor disinfection system compared with 5% sodium hypochlorite	In vitro lab tests on glass surfaces	Micro-biology laboratory, Italy	To reduce *Candida parapsilosis* and *Aspergillus fumigatus* counts (from 107 colony-forming unit [CFU]/mL), a longer contact time was necessary (7 minutes). In vitro tests with sodium hypochlorite at 5% in the absence of an organic substance resulted in an overall reduction in bacterial counts (from 109 CFU/mL) after 5 minutes of treatment. In the presence of an organic substance, after 5 minutes, the hypochlorite reduced the viable count from 109 to 105 CFU/mL for all bacterial strains except *Enterococcus faecalis.* That organism showed a reduction of 2 log units (109 to 107 CFU/mL). For *C. parapsilosis* and *A. fumigatus*, a 2-log unit reduction was observed after 7 minutes.	None assessed	Testing was done using glass surfaces, which are easy to contaminate and highly resistant to chemical products and heat. A portable vapor disinfection system is a viable alternative to available chemical disinfectants, including chloride derivatives, for the disinfection of hospital environmental surfaces.	Moderate to high	Organisms/ Outcomes: XDR-AB*, P. aeruginosa,* carbapenemase-producing *K. pneumonia,* MRSA, high-level amino-glycoside-resistant *E. faecalis, C. parapsilosis,* and *A. fumigatus* Colony-forming units in vitro

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Barnes et al., 2014[58]	Improved terminal cleaning thoroughness and compliance and improved hand hygiene compliance	Simulated before-and-after intervention study, 20 ICU patients	Simulated 20-patient ICU, United States	From the baseline, a 2:1 improvement in terminal cleaning compared with hand hygiene was required to match an equal reduction in acquisition rates (e.g., a 20% improvement in terminal cleaning reduced infections comparably to a 10% improvement in hand hygiene compliance).	None assessed.	The baseline level for thoroughness of terminal cleaning (i.e., surfaces being appropriately cleaned) was set at 40%. Increasing hand hygiene compliance was a more efficient intervention than increased terminal cleaning efficiency by a 2:1 ratio for reducing MDRO acquisition.	Moderate to high	Organisms/ Outcomes: VRE, MRSA, *A. baumannii* Hand hygiene, MDRO acquisition The study used existing literature for parameters.
Bernstein et al., 2016[56]	Environmental service workers (ESW) knowledge, practice, and attitude toward environmental cleaning and other infection prevention strategies	Cross-sectional online survey, n=327 ESWs at 5 hospitals in New York	Two large, tertiary-care academic hospitals, a free-standing academic pediatric and women's hospital, and two community hospitals within a single hospital network in New York, United States	ESWs who reported being trained to properly perform daily cleaning (90%) and discharge cleaning (93%) and were "very confident" in their abilities to do so (72% and 86%, respectively). Reported "often" or "always" using the hospital-approved cleaner-disinfectant to clean surfaces around the patient bed during daily (91%) and discharge (95%) cleaning.	Sixty percent reported "always" knowing the type of isolation precautions to be followed when entering a room to perform discharge cleaning, and 45% reported that it was "always" easy to identify the type of precautions required for a room without a sign posted at the time of discharge cleaning. Twenty-seven percent of respondents reported "often" or "always" worrying that	Systemic issues can impair the effectiveness of ESWs: 43% reported "never" or "sometimes" receiving useful feedback about their work and 28% reported "never" or "sometimes" knowing when to use ultraviolet light (UVL) disinfection. Some ESWs reported "never" or "sometimes" having enough time to perform daily cleaning (30%) and discharge cleaning (20%) properly, and 26% reported "often" or "always" being interrupted to assist with another task. Thirty-seven percent reported that it was	Moderate to high	Organisms/ Outcomes: ESWs' knowledge, training, and opportunities to carry out environmental cleaning

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					cleaning products may be harmful to them, while 20% reported "often" or "always" worrying that they might get sick due to exposure to patients while cleaning.	"always" clear what items ESWs were responsible for cleaning. Thirty-nine percent reported "often" or "always" avoiding cleaning near patients to avoid disturbing them, and 40% reported that the over-bed table was "often" or "always" too cluttered for daily cleaning. Most respondents (86%) agreed that their work was "very important" to keep patients safe, and 54% reported that clinicians "never" or "sometimes" showed appreciation for their work.		

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Blazejewski et al., 2015[40]	Use of hydrogen peroxide disinfection following routine terminal cleaning, and comparison of an HPV device with a hydrogen peroxide and paracetic acid aerosolizer (aHPP)	Cluster-randomized crossover study; 182 ICU rooms disinfected (51% disinfected with HPV and 49% with aHPP system)	Five medical and surgical ICUs in a university hospital in France. The units included three 10-bed, one 12-bed, and one 4-bed unit. All units were single bed.	Routine terminal cleaning reduced environmental bacterial load ($p<0.001$) without effect on MDROs (15/182 [8%] rooms at T0 vs. 11/182 [6%] at T1; p=0.371). Hydrogen peroxide technologies were effective for environmental MDRO decontamination (6% of rooms contaminated with MDRO at T1 versus 0.5% at T2, p=0.004). No significant difference was found between aHPP and HPV regarding the rate of rooms contaminated with MDRO at T2 (p=0.313).	Hydrogen peroxide decontamination devices are associated with a longer waiting time between two subsequent admissions in the same room, approximately 1 hour 40 minutes for HPV and three hours for aHPP. They are also associated with increased hospital costs.	No difference was found in the reduction of MDRO room contamination with aHPP versus HPV. Both hydrogen peroxide methods reduced the rate of rooms contaminated with MDROs.	Moderate	Organisms/ Outcomes: MDROs, including ESBL-Gram-negative bacteria, imipenem-resistant *A. baumannii* (IR-AB), MRSA, and MDR *P. aeruginosa* (MDR-PA) Environmental bacterial load Future studies are needed to determine cost-efficiency and toxicity of aHPP techniques.

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Butler, 2018[46]	Use of copper-oxide impregnated woven linens (e.g., gowns, pillowcase, blankets)	Before-and-after study, all patients admitted to hospital	Six hospitals, United States	Compared with the three before periods, there was a 61.2% ($p<0.05$), 41.1% ($p<0.05$), and 42.9% ($p<0.01$) reductions in *C. difficile*-related HAIs per 10,000 patient-days in periods B1, B2, and B3, respectively. There was also a 48.3% ($p>0.05$), 36.4% ($p>0.05$), and 19.2% ($p>0.05$) reductions in all HAIs caused by MDROs per 1,000 patient-days. Finally, the decreases in the combined total of MDRO- and *C.* difficile-*related* HAIS per 1,000 patient-days were 59.8% ($p<0.01$), 39.9% ($p<0.05$), and 37.2% ($p<0.05$) for periods B1, B2, and B3.	None assessed.	Linens included patient gowns, pillowcases, fitted and flat sheets, washcloths, bath towels, bath blankets, and thermal blankets. The use of biocidal copper oxide-impregnated linens resulted in significant reduction in both HAIs caused by *C. difficile*, and the combined metric of *C. difficile* or MDRO infection.	Moderate Study did not control for continuous education efforts undertaken to reinforce best practices for disinfection, which may have also contributed to the reduction of the HAI rates.	Organisms/ Outcomes: *C. difficile* and MDROs, which included MRSA, VRE, ESBL-E, MDR-AB, and CRE *C. difficile*-related HAIs

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Cadnum et al., 2018[32]	Mobile ultraviolet-C (UV-C) light room decontamination at a 10-minute exposure time and 5 feet of distance	Laboratory experiment, four different organisms	Laboratory, United States	Generally, larger surface areas were decontaminated more effectively (lower density of pathogens). The reduction in MRSA was significantly greater than the reduction in each of the *Candida* species and *C. difficile* spores (P <0.001). For each of the *Candida* species and for *C. difficile* spores, increasing the cycle time to 20 or 30 minutes resulted in significantly greater reductions in recovery (p<0.001).	None assessed	UV-C room decontamination reduced MRSA contamination at a statistically significant greater rate than *Candida* and *C. difficile* spores. For the latter two organisms, increased cycle time resulted in increased deactivation of the organisms. Larger surface areas with lower densities of pathogens were decontaminated more effectively with all other factors remaining equal.	Moderate to high	Organisms/ Outcomes: *Candida auris, C. albicans, C. glabrata, C. difficile,* MRSA Surface decontamina-tion Further studies are needed to evaluate efficacy of UV-C devices in patients' rooms.
Carling et al., 2010[57]	A fluorescent targeting method was used to objectively evaluate the thoroughness of terminal room cleaning and provide feedback and education to environmental cleaning workers.	Before-and-after study, n=3,532 environmental surfaces	260 ICU rooms in 27 acute care hospitals, ranging from 25 beds to 709 beds (mean: 206 beds), United States	Only 49.5% (1,748) of surfaces were cleaned at baseline (95% CI 42% to 57%). After intervention and multiple cycles of objective performance feedback to environmental services staff, thoroughness of cleaning improved to 82% (95% CI, 78% to 86%).	None assessed.	Thoroughness of cleaning at baseline did not correlate with hospital size, patient volume, case-mix index, geographic location, or teaching status. After initial analysis of the thoroughness of cleaning, identical structured educational programs were developed for the environmental services staff of each hospital. Subsequently, the thoroughness of cleaning was	Moderate	Organisms/ Outcomes: General MDROs (organisms not specified) Fluorescent targets used to measure cleaning thoroughness

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						reevaluated and the results were used to direct further programmatic and educational interventions (referred to as a feedback cycle). High-risk objects include floors, walls, and other surfaces not regularly cleaned by housekeeping. Additional interventions took place in some facilities, such as addition of staff, education of environmental staff, and personnel resource allocation.		

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Casini et al., 2017[19]	Use of chlorine sodium hypochlorite (1,400 mg/L) with reusable cotton cloths or chlorhexidine—60% isopropyl alcohol with disposable cloths, standard cleaning, and twice-daily cleaning of high-touch surfaces with disposable cloths moistened with a ready-for-use solution of 0.5% chlorhexidine-60% isopropyl alcohol	Before-and-after intervention study, n=103 surfaces	Burn ICU with seven beds in a tertiary care teaching hospital, Italy	During the standard cleaning regimen, 3 of 23 samples (13%) gave results over the AFNOR (French standard that classifies four zones based on the level of risk of infection to which a patient is exposed) limit, and 5 (21.7%) showed unacceptable ATP levels with 100 relative light units/100 cm^2 as the benchmark limit (sensitivity 86.4%, specificity 92.2%). Following improvement of the cleaning procedure, only 2 samples of 50 (4%) did not satisfy the microbiological criteria and 7 (14%) exceeded the ATP limit. In a successive phase, 8 of 30 samples collected showed unacceptable results (27%).	None assessed.	The addition of disinfection with a chlorhexidine solution to the standard sodium hypochlorite solution reduced environmental contamination, infection, and colonization rates, as well as ATP assay detection (a monitoring method).	High	Organisms/ Outcomes: Carbapenem—resistant *A. baumannii (CR-AB)* Microbial growth

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Cheon et al., 2016[11]	Multicomponent intervention including environmental cleaning and disinfection policy enforcement, cleaning of contaminated medical equipment and infected/ colonized patient environments three times per day with bleach or quaternary ammonia, monthly environmental cultures followed by targeted cleaning, antimicrobial stewardship, staff education, contact precautions, staff education, and hand hygiene promotion	Before-and-after intervention study with a 1-month baseline period, a 9-month intervention phase, and a 1-month followup phase, ICU patients	South Korean university teaching hospital ICUs: MICU (19 bed), SICU (20 bed), and a second SICU (7 bed)	The incidence density rate of hospital-onset MDR-AB decreased from 22.82 cases per 1,000 patient-days to 2.68 cases per 1,000 patient-days after the interventions were implemented (odds ratio [OR], 0.12; 95% CI 0.03 to 0.4; p<0.001).	None assessed	Contaminated medical equipment was meticulously disinfected. The nursing staff wiped the environments surrounding colonized or infected patients at least three times per day, with a cloth that was soaked with 1:100 diluted bleach or quaternary ammonium chloride wipes. Monthly environmental cultures were in the ICUs, followed by targeted cleaning focused on any near-patient hand-touch sites and sites that tested positive for MDR-AB.	Moderate to high	Organism: MDR-AB MDR-AB cases, environmental cultures

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Choi et al., 2010[27]	Multicomponent intervention including terminal and environmental cleaning with sodium dichloro-isocyanurate, environmental culturing before new admissions to room, and introduction of closed-suctioning system for ventilators	Outbreak intervention study, 57 ICU outbreak cases (42 MICU patients and 15 SICU patients), 135 environmental samples of patients, 65 samples of hands of HCWs	Korean university hospital ICUs (18-bed MICU and 18-bed SICU)	The number of newly diagnosed cases per month increased to a maximum of 17 in March 2008 and began to decrease after the introduction of outbreak control measures. By August 2008, there were no new cases of CR-AB colonization or infection in either ICU.	None assessed.	Terminal cleaning followed by environmental sampling. New admissions were allowed only if cultures were negative. The environment of the ICU and the surrounding areas was cleaned thoroughly with 100 ppm sodium dichloroisocyan-urate. A higher concentration (200 ppm) was used to clean the environment in which the CR-AB patients were hospitalized. A closed-suctioning system was introduced for all patients receiving mechanical ventilation, and for those who did not receive mechanical ventilation, aseptic techniques were implemented. Strict contact precautions, massive environmental decontamination, and a closed-suctioning system can be effective for controlling CR-AB outbreaks.	Moderate to high	Organisms: CR-AB CR-AB cases, environmental samples, HCW hand samples

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Chojecka et al, 2015[28]	Use of glucoprotamin (GP) for environmental disinfection	Laboratory minimum inhibitory concentrations (MICs) of GP and minimum bactericidal concentrations (MBCs) against tested strains evaluated by serial broth-dilution technique	Laboratory, Poland	Gram-negative strains were more tolerant to GP than Gram-positive strains among tested strains. MRSA and methicillin-susceptible *S. aureus* exhibited similar susceptibility to GP. Tetracycline-resistant *P. aeruginosa* (PAO-LAC) had significantly lower susceptibility to GP than *P. aeruginosa* ($p \leq 0.05$). There were no differences in GP efficiency against these strains based on GP phenol coefficient (GP-PC).	None assessed.	The researchers found that variation in susceptibility of reference strains and antibiotic-resistant standard strains to GP had no meaning at clinically used concentrations, which were higher than concentrations causing bactericidal activity of GP.	Moderate	Organisms/ Outcomes: MRSA and PAO-LAC In vitro bacterial growth

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Ciobataro et al., 2011[10]	Multicomponent intervention including retraining of environmental cleaning staff, inspection of rooms after cleaning by nurse, cleaning of stations that had been used for cases or carriers, guidelines for patient isolation, cohorting, environmental cleaning, and a computerized notification system that flagged of carbapenem-resistant *K. pneumoniae* (CR-KP) carriers and provided instructions	Before-and-after study; facility level	Acute-care university hospital (553-bed hospital and 230-bed rehabilitation facility), Israel	The incidence of CR-KP decreased by 16-fold ($p<0.001$), and this decrease was sustained for 30 months. The rate of cross-infection decreased from 6% during 2007-2008 to 2.7% in 2009-2010 ($p<0.05$). This period saw an increased rate of active surveillance for carriers, from 20% to 89%.	None assessed.	Detailed instructions for cleaning and disinfecting CR-KP-positive patients' units during the hospital stay and after discharge, emphasizing the use of hypochlorite 1,000 ppm, were provided to all housekeeping staff. Vacated rooms had to be certified for reuse by the infection control nurse. The same cleaning procedure was applied to any station that had been used by CR-KP cases/carriers.	Moderate to high	Organisms/ Outcomes: CR-KP CR-KP case, CR-KP carriage

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De Giglio et al., 2014[25]	Hydrogen peroxide (5%) and silver ion (0.1%) disinfection via direct surface application	Laboratory study	Laboratory, Italy	The disinfecting action of hydrogen peroxide and silver ions was effective after 5 minutes for ATCC® (drug sensitive) strains and after 10 minutes for multidrug-resistant isolates. In the presence of 0.3 g/L bovine serum albumin (BSA; organic matter), the disinfectant appears effective after 5 minutes of contact with ATCC strains, and after 10 minutes with multidrug-resistant isolates. Moreover, it was more effective when used in the absence or in presence of a low concentration of biological materials. In the presence of 3 g/L of BSA, the required contact time became 10 minutes for the ATCC strains and 20 minutes for multidrug-resistant isolates.	None assessed.	There were no differences in the effectiveness of these disinfectants for the two organisms studied. Hydrogen peroxide and silver ions may be a quick and easy disinfectant for occasionally contaminated small surfaces.	Moderate	Organisms/ Outcomes: *S. aureus* ATCC 6538, *P. aeruginosa* ATCC 15442 Surface disinfection

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Galvin et al., 2013[42]	Use of helium and helium air plasma for room decontamination	Laboratory	Laboratory, Ireland	Both plasma types exhibited bactericidal effects on *S. aureus* (log3.6 to >log7), with increased activity against methicillin-resistant strains but had a negligible effect on *C. difficile* spores (<1 log).	None assessed.	A glass surface was used for study.	Moderate to high	Organisms/ Outcomes: *S. aureus* and *C. difficile* Bactericidal effects on glass surface
Gan et al., 2017[45]	Multicomponent intervention including patient zone cleaning with a single microfiber cloth, patient zone cleaning with three microfiber cloths, and audit and feedback using ATP assay and fluorescent markers	Before-and-after intervention study, ICU surfaces	General ICU (25 bed), China	The study comprised a baseline period (period 1) and four sequential tiered interventions: daily wiping of patient zone (high-touch surfaces) with a single clean microfiber cloth (period 2), fluorescent markers and ATP assay to monitor and provide feedback on the effectiveness of cleaning (period 3), daily wiping of a single-patient zone with three clean microfiber cloths (period 4), and withdrawal of the feedback (period 5). The first cloth was used for the bedside table and supply cart rail. The second cloth was used for high-touch surfaces such as buttons and touch screens of ventilators.	None assessed.	Use of three cleaning cloths for one patient zone was more effective compared with a single cloth.	Moderate	Organisms/ Outcomes: MDROs *(*not specified further) Fluorescent markers, and bio-luminescent ATP markers

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				The third cloth was used for high-touch surfaces in direct contact with patients, such as bed rails. Compared with period 1, the cultures of MDROs from high-touch surfaces were reduced by 41.0% (prevalence ratio [OR]=0.59, p<0.001), 70.8% (OR=0.29, p<0.001), 82.6% (OR=0.17, p<0.001), and 70.8% (OR=0.29, p<0.0001) in the subsequent sequential interventions, respectively.				

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Gavalda et al., 2016[44]	Implementation of a microfiber cleaning system that involves cleaning high-touch surfaces six times a day, using one wipe per room, and soaking clean cloths in 0.1% chlorine	Four-year quasi-experimental, before-and-after study, 1,058 rectal swabs, ICU patients during screening periods	ICUs in teaching hospital (800 bed), Spain	The percentage of carriers at admission was significantly lower during the second screening period (8.9% vs. 0.8%, respectively; p<0.001), after the intervention bundle was implemented.	None assessed.	By only using one wipe per room, the hospital reduced cross-contamination during environmental cleaning as measured by ICU XDR-AB incidence. The authors also attributed the reduction in cases to a one-time in depth cleaning and prompt isolation of cases. Improved cleaning techniques were equally as important as a good organizational strategy to determine the regularity with which certain items and equipment needed to be disinfected.	Moderate to high	Organisms/ Outcomes: XDR-AB Positive XDR-AB screening

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Gupta et al., 2016[9]	Multicomponent intervention including daily high-touch point cleaning, terminal cleaning, ventilator cleaning, environmental cleaning, disposable microfiber cloths, bleach, and environmental auditing twice a day of cleaning processes using a luminometer and ATP testing prior to admitting a patient to a room	Before-and-after study, 26 cases during study period, SICU patients	Surgical ICU (14-bed unit) in tertiary care hospital (1,170 bed), United States	During the 5-month period before the intervention, there were 17 MDRO infections in 16 patients in the SICU at a rate of 9.09 per 1,000 patient-days. During the 7-month period after protocol implementation, there were 9 MDRO infections in 9 patients. The SICU MDRO infection rate decreased by 65% to 3.27 per 1,000 patient-days (p=0.02). In addition to MDROs, during the pre-intervention period, there were 15 cases of *Burkholderia cepacia complex* (BCC) infection. Following the protocol implementation, the number of BCC infection cases fell to 2 cases during the first month and then remained undetectable (p=0.0008) for the remaining 6 months.	None assessed.	A prolonged reduction in infection rates was seen after the intervention and throughout the 6-month followup period. The authors attribute the multifaceted approach to the success of the intervention, including the focus on environmental cleaning and incorporation of dry and wet mopping to reduce organic material, additional disinfection with UV while the ICU was closed, and ongoing monitoring using ATP markers.	Moderate to high Limitation: Lack of true controls	Organisms/ Outcomes: MDROs and BCC MDRO and BCC infections
Haas et al., 2014[54]	Ultraviolet environmental disinfection (UVD) for patient rooms	Retrospective before-and-after study; UVD performed 11,389 times	Tertiary care hospital (643 bed),	UVD was used 11,389 times; 3,833 (34%) uses were for contact precaution discharges. UVD was	Staff are not primarily budgeted to run UVD; rather, this task is added	Labor cost and availability must be considered in the budget and implementation plan	Low to moderate The study did not evaluate antibiotic use,	Organisms/ Outcomes: MDROs*, C. difficile*

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			United States	completed for 76% of contact precaution discharges. UVD was used after end of day cleaning in the operating rooms, weekly in the dialysis unit, and for all burn unit discharges. UVD could be requested for rooms of long-stay patients or for discharges in units with high prevalence of MDRO or *C. difficile*. In rooms with more than one occupant, UVD was deferred until the room was no longer occupied. There was a significant 20% decrease in hospital-acquired MDRO plus *C. difficile* rates during the 22-month UVD period compared with the 30-month pre-UVD period (2.14 cases/1,000 patient-days vs. 2.67 cases per 1,000 patient-days, respectively; rate ratio, 0.80; 95% confidence interval 0.73 to 0.88, p<0.001).	onto the existing role of the staff or supervisor and may divert staff from other essential functions.	for UVD. Missed contact precaution discharges were discussed weekly to assess flaws.	which can clearly affect acquisition rates of MDROs and *C. difficile*. In addition, many components occurred simultaneously.	MDRO and *C. difficile* rates A cost-benefit analysis of UVD use that includes labor costs is also needed.

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Hess et al., 2013[22]	Multicomponent intervention including enhanced daily cleaning with QAC of ICU room surfaces frequently touched by HCWs, and feedback on intervention implementation using fluorescent gel markers	Cluster-randomized controlled trial, 4,444 cultures collected from 132 rooms with patients colonized by MRSA or MDR-AB	Four ICUs (one 29-bed medical ICU and three 12-bed surgical ICUs) in a 757-bed tertiary care teaching hospital, United States All ICUs with single-bed, single-occupant rooms	The mean proportion of contaminated HCW gowns and gloves following routine care provision and before leaving the rooms of patients with MDR-AB was 16% among control rooms and 12% among experimental rooms (RR: 0.77, 95% CI 0.28 to 2.11, p=0.230). For MRSA, the mean proportions were 22% and 19%, respectively (RR: 0.89, 95% CI 0.5 to 1.53, p=0.158).	None assessed.	Intervention was a single, supplementary cleaning of high-touch surfaces using quaternary ammonium. Surfaces were chosen based on a Centers for Disease Control and Prevention (CDC) list. Implementation of the intervention was verified using an invisible fluorescent gel, which was done in 10% of rooms. Enhanced cleaning was associated with a nonsignificant reduction in HCW gown and glove contamination.	Low to moderate	Organisms/ Outcomes: MRSA and MDR-AB Contamina-tion of HCW gowns and gloves

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La Forgia et al., 2010[4]	Flooding of drainage system with sodium hypochlorite to disinfect sinks	Outbreak intervention study, 16 cases, ICU patients with MDR-AB	Twenty-four ICUs in a university hospital (476 beds), United States	Ten gallons of water were run into each plugged sink in every location in the ICU, followed by slowly pouring 1 gallon of bleach into the water, avoiding splashing. Once all the sinks were filled, the plugs of all sinks were pulled simultaneously, thereby flushing the sink drain piping with the bleach solution. This protocol was continued weekly throughout the observation period. Before this intervention, 18 patients over 10 months had MDR-AB. After the intervention, this rate decreased to 19 patients over 28 months, a statistically significant reduction in infection rate ($p<0.01$).	None assessed.	The authors determined that this one-time comprehensive disinfection of the entire plumbing system was crucial to eliminating all underlying sources of contamination. If they had disinfected each sink individually in a staggered manner, the contamination issue would have persisted. Flooding 100% of the system ensured that bacterial colonization was eliminated and could not return unless from an external source. The weekly repetition of this strategy and the reduction of splashing on surfaces around the sink also contributed to the success of this technique.	Moderate to high No comparison group	Organisms/ Outcomes: MDR-AB MDR-AB cases
Lee et al., 2017[21]	Use of Bio-Kil (3-(Trimethoxysilyl) propyloctadecyl-dimethyl ammonium chloride, a QAC) for environmental cleaning and	Prospective before-and-after study, n=77 patients, patients in four study rooms in ICU (two study rooms, two control rooms)	Medical and surgical ICUs in 750-bed Thai teaching hospital	Environmental samples were collected from room surfaces and patients twice weekly during pre-intervention period. The room walls, ceilings, and air-conditioning filters, surfaces of	None assessed.	The use of Bio-Kil to disinfect and provide ongoing microbial activity reduced environmental bacterial contamination and sepsis incidence in the ICU compared with manual surface	Moderate to high	Organisms/ Outcomes: MRSA, VRE, CRE, carbapenem-resistant *P. aeruginosa* (CR-PA), and CR-AB

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	use of Bio-Kil objects for ongoing antimicrobial action			instruments, textiles, and nurses' clothing were all decontaminated or replaced with Bio-Kil products. Sampling was repeated. After application of Bio-Kil, the bacterial burden declined in both groups, although the reduction was greater in the study rooms compared with the control rooms ($p<0.001$). During the pre-intervention period, 16 patients were admitted to control rooms and 18 patients to study rooms. After the intervention, 22 patients were admitted to control rooms and 21 patients to study rooms. The number of cases of new-onset sepsis declined in the intervention group (from 33% to 23.8%) but increased in the control group (from 25% to 40.9%); however, there was no significant difference in incidence of new-onset sepsis between		cleaning with 500 ppm sodium hypochlorite. Bio-Kil has little to no toxicity to humans and therefore may be a useful disinfectant for textiles and other items that are regularly in direct contact with humans and at high risk of carrying fomites.		Environmental bacterial samples, new-onset sepsis cases

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				the study and control rooms after intervention.				
Lemmen et al., 2015[35]	Use of HPV room decontamination for common MDROs and spores	Before-and-after study, 4 cultures (2 representative MDR Gram-positive and 2 MDR Gram-negative bacteria) and 7 spore indicators (times three trials)	Operating rooms, Germany	Stainless steel and cotton carriers containing viable organism cultures were placed around. HPV was then used to decontaminate the operating room. This process was repeated three times. HPV inactivated all spore biological indicators and no MRSA, VRE, or MDR-AB were recovered from the stainless steel and cotton carriers. HPV was equally effective at all carrier locations.	None assessed.	No identified difference in efficacy for microbes dried onto stainless steel or cotton surfaces, indicating that HPV may have a role in the decontamination of both porous and nonporous surfaces.	Moderate	Organisms/ Outcomes: MRSA, VRE, MDR-AB Spore biological indicator
Levin et al., 2009[52]	Educational intervention on radiograph machine decontamination and hand hygiene education	Before-and-after trial of decontamin-ation protocol, radiographs during observation (173), intervention (112), and followup periods (120).	Academic tertiary care hospital ICU, Israel	The radiology technicians were told that infection control performance was inadequate, that multidrug-resistant bacteria were being cultured from the radiograph machine, and that this situation could be detrimental to patient safety. They were requested to improve infection control measures using alcohol hand	The researchers observed a statistically significant decrease in the use of adequate infection control during radiographs in the followup period compared with the intervention period. Positive cultures were	The intervention was heavily focused on the education of radiologist technicians and hand hygiene compliance, while the outcome of interest was environmental contamination of the radiograph machines. Short-term results were shown, but long-term infection control practices resulted in continuing	Moderate	Organisms/ Outcomes: Gram-negative bacteria resistant to ceftazidime, ceftriaxone, or imipenem; MRSA, VRE Surface sample cultures

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				rub and changing gloves before and after each contact with the patient or radiograph machine. Adequate infection control was practiced during 2/173 observation period radiographs (1%), 48/113 intervention period radiographs (42%; p<0.001), and 12/120 followup period radiographs (10%; (p<0.001). Radiograph machine surface culture samples yielded positives on 12/30 occasions (40%), 0 of 29 occasions, and 7 of 14 occasions (50%) for the respective periods.	highest in the followup period.	contamination of the machines. The authors recognized that their study was the first study to focus on contaminated radiology equipment, which is very likely to contribute to cross-contamination and transmission of bacteria. However, further studies will be needed to assess which types of interventions can maintain more long-term results.		

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Liu et al., 2014[7]	Multicomponent intervention including hypochlorite disinfection, environmental sampling, contact precautions, patient isolation, and hand hygiene education	Outbreak intervention study, 22 patients colonized with imipenem-resistant *A. baumannii* (IR-AB) and 18 infected with IR-AB, outbreak cases	Regional hospital, 16-bed medical ICU, Taiwan	Nine environmental specimens, including five specimens collected after terminal disinfection, were positive for IR-AB. The low-concentration 0.08% sodium hypochlorite was inadequate. After the facility corrected the environmental cleansing methods, the surveillance study showed no further IR-AB isolates on the control panel surfaces of the medical equipment or in patients in the ICU. In vitro study showed that 0.5% sodium hypochlorite eradicates IR-AB after 30 seconds of inoculation, but 0.08% sodium hypochlorite only reduces the bacterial load.	None assessed.	A correction to the preparation of disinfectant solutions was found to eradicate IR-AB, whereas the more diluted 0.08% hypochlorite was only somewhat reducing the bacterial load. The study demonstrates that education of environmental cleaning staff and auditing of environmental disinfection practices can be crucial for reducing environmental contamination and subsequent disease transmission.	Moderate to high	Organisms/ Outcomes: IR-AB Environmental sample cultures

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Manian et al., 2011[36]	Use of routine terminal cleaning and disinfection (C/D) with quaternary ammonium and sodium hypochlorite compared with HPV room disinfection	Before-and-after study, approximately 20 sample sites per room for 483 rooms, newly vacated by multidrug-resistant *Acinetobacter baumannii* complex (MDR-ABC)- and MRSA-positive patients. ABC and MRSA samples collected from 312 rooms following four rounds of C/D, 37 rooms following one round of C/D before and after HPV treatment, and 134 rooms following one round of C/D and HPV treatment.	900-bed tertiary care teaching hospital, United States	Following four rounds of C/D, 83 (26.6%) rooms had one or more culture-positive sites. Following one round of C/D and HPV treatment, six (4.5%) rooms were culture positive for ABC, MRSA, or both. The addition of HPV treatment to one round of C/D resulted in a significant drop in ABC- and MRSA-positive room sites (odds ratio, 0 [95% CI 0 to 0.8]; for both organisms, p=0.04).	Several culture-negative sites became culture positive after C/D, indicating potential recontamination of surfaces during the C/D process. This change was not found after HPV treatment.	The addition of HPV to multiple rounds of cleaning and disinfection was shown to reduce positive environmental cultures. Even four rounds of routine cleaning and disinfection were insufficient in eradicating environmental cultures. The authors attributed the insufficiency of routine environmental cleaning to the suboptimal cleaning and not to the ineffectiveness of the sodium hypochlorite. Thus, the use of HPV to supplement routine C/D may be a useful alternative or supplement to staff education and monitoring of cleaning and disinfection practices.	Moderate	Organisms/ Outcomes: ABC, MRSA Environmental sample cultures

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Mathew et al., 2016[33]	Use of enclosed UV-C radiation for decontamination of mobile handheld devices (MHDs)	Laboratory, 50 MHDs of healthcare staff	Laboratory, United States	An enclosed UV-C device designed for decontamination of MHDs was effective in rapidly reducing MRSA, and to a lesser degree, *C. difficile* spores, in a laboratory setting. Presence of organic matter reduced the efficacy of the decontamination.	None assessed.	There was no significantly different result between species. Time required for disinfection of MHDs was 15 to 77 seconds for cell phones and 50 to 147 seconds for a tablet.	Moderate Study did not compare effectiveness of the UV-C device with other methods that have been shown to be effective for decontami-nation of MHDs.	Organisms/ Outcomes: MRSA and C. difficile
Munoz-Price et al., 2010a[49]	Multicomponent intervention including enhanced environmental cleaning, daily 2% chlorhexidine gluconate baths for patients, surveillance cultures at admission, serial point prevalence surveillance (PPS), isolation precautions, and training of personnel.	Before-and-after study, n=213 patients screened, patients admitted to the facility	Long-term acute care hospital (LTACH), United States	Baseline PPS performed on June 17, 2008, showed a prevalence of colonization with *K. pneumoniae* carbapenemase (KPC)-producing isolates of 21% (8 of 39 patients screened). After implementation of the intervention, monthly PPS was performed five times, which showed prevalence rates of colonization with KPC-producing isolates at 12%, 5%, 3%, 0%, and 0% ($p<0.001$).	None assessed.	Spray bottles replaced buckets to avoid contamination, assigned cleaning responsibilities were changed due to confusion over previous policies, new curtains were installed, and several additional objects and surfaces were included in disinfection procedures. Staff education included hemodialysis cleaning training and avoidance of cross-contamination with personal objects.	Moderate	Organisms/ Outcomes: KPC-producing *K. pneumoniae* (KPC-KP) KPC colonization

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Munoz-Price et al., 2010b[60]	Multicomponent intervention including environmental cleaning assessments and feedback using UV-detectable powder on high-touch surfaces, cleaning of KPC-patient rooms' high-touch surfaces and ventilators every shift, daily baths with 2% chlorhexidine, PPS, isolation precautions, and staff education	Outbreak intervention study, nine cases, SICU patients with KPC-KP	20-bed surgical ICU in public teaching hospital, United States	Environmental cleaning assessments were done by applying UV-detectable powder to high-touch surfaces and surveying the presence of the powder after 48 hours. Environmental cultures were also done. One staff member per shift was assigned to clean KPC-patient rooms. Bleach-impregnated cloths were used for cleaning. A respiratory therapist cleaned high-touch ventilator surfaces using UV-powder detection; researchers found that nobody was cleaning bed rails or mechanical ventilators and subsequently provided assignments for these tasks. No further spread of the organism or additional cases were seen.	None assessed.	The multicomponent intervention successfully reduced KPC-KP horizontal transmission even with the ongoing admission of colonized patients. While it is difficult to attribute success to any one component, the authors hypothesized that an increased focus on environmental cleaning may have reduced environmental contamination and subsequent contamination of healthcare workers' hands, contributing to the reduction of horizontal transmission.	High	Organisms/ Outcomes: KPC-KP KPC-KP cases

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Munoz-Price et al., 2014[50]	Weekly electronic communication providing feedback on environmental decontamina-tion, environmental cultures, and other factors	Before-and-after study, 1,103,900 patient-days, all admitted patients during 42-month period	1,500-bed public teaching hospital, United States	Hospitalwide, the rate of CR-AB acquisition decreased from 5.13 +/-0.39 to 1.93+/-0.23 per 10,000 patient-days, during the baseline and post-intervention periods, respectively (p<0.0001). This effect was also observed in the medical and trauma ICUs, with decreased rates from 67.15+/-10.56 to 17.4+/-4.6 (p<0.0001) and from 55.9+/-8.95 to 14.71+/-4.45 (p=0.0004), respectively.	None assessed.	Bundled intervention originally failed to reduce CR-AB acquisition rates, so email updates were implemented. Email recipients included the C-suite of the hospital, the Quality and Patient Safety Division, and the nursing and medical directors of inpatient units. Emails included graphic description and interpretation of environmental findings (cultures and UV markers), maps of positive cultures, and action plans.	Moderate	Organisms/ Outcomes: CR-AB CR-AB acquisition

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O'Connor et al., 2015[6]	Multicomponent intervention including prohibited prescription and use of linezolid, adherence to infection prevention and control practices, enhanced environmental cleaning, isolation of affected patients, and hospitalwide education programs	Outbreak intervention study, nine affected patients	Tertiary care teaching hospital (483 inpatient beds) and ICU, England	Enhanced cleaning of the ICU was instigated in parallel with increased auditing. This process involved twice-daily cleaning of affected areas with detergent, in addition to a deep clean with sodium hypochlorite to decontaminate the area on discharge. The adopted infection prevention intervention was effective, and the outbreak was limited to the affected ICU.	None assessed	Due to the multicomponent nature of the intervention, it is difficult to attribute the halt of the outbreak to any one component. The authors cited lack of resources as a reason for not implementing environmental and staff screening.	High	Organisms/ Outcomes: Linezolid-resistant *S. epidermidis* *S. epidermidis* cases
Otter et al., 2010[37]	HPV decontamination of ICU rooms	Outbreak intervention study, 12-bed spaces covering all hand-contact areas adjacent to bed and mattress	12-bed ICU, Nether-lands	Ten of 21 areas cultured after cleaning but before HPV (47.6%) yielded Gram-negative rods (GNRs). No GNRs were cultured from the 63 sites sampled after HPV, including areas adjacent to the 21 sites sampled before HPV. All 40 biological indicators were inactivated by the process.	None assessed.	HPV decontamination of the unit took approximately 12 hours, including an overnight aeration, and was completed without incident or damage to the materials and equipment in the ICU.	Moderate to high	Organisms/ Outcomes: MDR GNRs Environmental sample cultures

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Park et al., 2015[41]	Use of argon gas-feeding dielectric barrier discharge (Ar-DBD) and nanosecond pulsed plasma (NPP) for disinfection	Laboratory	Laboratory, South Korea	Both plasma sources inactivated both sensitive and resistant bacteria.	None assessed.	No discussion of clinical applications. Paper mostly assessed the mechanisms of plasma inactivation of bacteria.	High	Organisms/ Outcomes: Drug-sensitive *S. aureus,* MDR *S. aureus*
Passaretti et al., 2013[55]	Use of standard cleaning practices with quaternary ammonium and hydrogen peroxide compared with HPV for room decontamination	Prospective cohort intervention study, 6,350 admissions, patients admitted to rooms previously occupied by MDRO-infected patients	994-bed tertiary care teaching hospital, 6 high-risk units, including ICUs and surgical units, United States	Standard cleaning practices included QAC for surfaces and floors and a hydrogen-peroxide-based cleaner for *C. difficile* patients' rooms. Periodic monitoring of cleaning policy compliance was performed (period was not defined). HPV decontamination was performed in common areas of the surgical ICU and terminal cleaning of rooms was performed after colonized patients were discharged. Shared equipment was also decontaminated with HPV. Biological indicators were also used during decontamination. Patients admitted to HPV-decontaminated were 64% less likely	One brand of paint used on the walls of one of the HPV units showed some incompatibility with the process; once this paint was replaced, there were no reports of damage to materials or equipment. Individual risk of MRSA, MDR-GNR, or *C. difficile* were not reduced by HPV use.	The use of HPV compared with disinfection with quaternary ammonium and hydrogen peroxide was found to reduce environmental contamination and patient acquisition of MDROs. The use of HPV even reduced acquisition of MDROs in patients without neighbors who were infected. The authors attributed the lack of HPV's effect on MRSA, MDR-GNR, and *C. difficile* to their overall low incidence before and during the intervention.	Moderate	Organisms/ Outcomes: VRE, MRSA, *C. difficile,* MDR-GNB, and general MDROs MDRO acquisition Multiple infection prevention initiatives ongoing during study period, including daily chlorhexidine bathing of patients

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
				to acquire any MDRO (incidence rate ratio [IRR], 0.36; 95% CI 0.19 to 0.70; p<0.001) and 80% less likely to acquire VRE (IRR, 0.20; 95% CI 0.08 to 0.52; p<0.001). The risk of acquiring *C. difficile*, MRSA, and MDR-GNB individually was reduced but not statistically significantly. The proportion of rooms contaminated with MDROs was reduced significantly only on the HPV units (relative risk, 0.65, p=0.03).				

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Peterson et al., 2016[13]	Intensive bleach disinfection (bundle), intranasal mupirocin, and chlorhexidine bath, hand hygiene education in addition to active surveillance	Cluster-randomized nonblinded trial, 16,773 tests, all long-term care facility (LTCF) admissions	Three LTCFs, United States	The MRSA infection rate decreased 65% between the baseline (44 infections during 365,809 patient-days) and Year 2 (12 during 287,847 patient-days; p<0.001); significant reduction was observed at each LTCF (p<0.03). Due to the intervention, 23 MRSA infections were avoided when baseline data were compared with the final year of the program, which translates to a saved expense of $552,000.	None assessed.	The researchers implemented the multicomponent intervention without decreasing socialization or activities of daily living for the residents. Active surveillance, targeted decontamination, and environmental cleaning resulted in a decreased infection rate of MRSA in multiple LTCFs.	Low to moderate	Organisms/ Outcomes: MRSA MRSA infections

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Ratnayake et al., 2011[12]	Enhanced terminal and daily cleaning with hypochlorite and staff education	Outbreak intervention study, nine cases, patients in vascular surgery ward	24-bed vascular unit on an acute surgical ward, United Kingdom	Hypochlorite terminal cleaning was done to reduce spore contamination. Cleaning of equipment and high-contact areas was performed daily. Staff were educated on environmental cleaning practices. Outbreak was stopped, and MRSA acquisitions fell as well (no statistical report).	None assessed.	Both *C. difficile* transmission and MRSA acquisitions were reduced by this multicomponent intervention. It is difficult to attribute success to one component of the intervention, as they were implemented simultaneously. The authors do not describe in detail an environmental audit but claim that one was performed and did not identify any issues that could have contributed to the outbreak. However, the authors do restate the importance of hypochlorite disinfection to eradicate the environmental reservoir of *C. difficile* spores.	High	Organisms/ Outcomes: Clindamycin-resistant *C. difficile,* MRSA MRSA and *C. difficile* acquisitions

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Ray et al., 2010[38]	Use of HPV for room disinfection with terminal cleaning	Before-and-after case-control study (outbreak), 13 patients infected or colonized with MDR-AB and 27 control subjects	54-bed LTACH affiliated with a tertiary care hospital, United States	Case patients were more likely to have wounds (odds ratio [OR], 12.92; p=0.01), have tracheostomy tubes (OR, 9.60; p=0.03), and have received intravenous antibiotics on admission to the LTACH (OR, 6.86; p=0.04). Terminal cleaning was performed to remove organic and porous materials. HPV was performed at least once in each room in the facility and chemical and biological indicators were used for quality assurance. After the completion of HPV room decontamination in the LTACH wards, no further cases of nosocomial acquisition of MDR-AB colonization or infection were detected.	None assessed.	The authors also mentioned that "HPV is favorable in part because of its portability, low vapor temperature, and lack of harmful residue."	Moderate to high This is primarily a case study.	Organisms Outcomes: MDR-AB MDR-AB cases

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Rhodes et al., 2016[34]	Use of violet 405 nm light for room decontamination	Laboratory	Laboratory, United States	Here, 405 nm light-emitting diodes were used to treat varying concentrations of a common laboratory *E. coli* K-12 strain transformed with the pCIG mammalian expression vector, which conferred ampicillin resistance via expression of the beta-lactamase gene. Treatment time was 120 minutes at varying intensities. Study showed a statistically significant log_{10} reduction in bacterial concentration ($p<0.001$).	None assessed.	The researchers found that visible light therapy with 405 nm violet light significantly reduced concentration of beta-lactamase-producing *E. coli* on plated growth media. This process has not yet been applied in clinical settings, but the authors hypothesize that it could be used as a novel sterilization method.	High	Organisms/ Outcomes: Ampicillin-resistant *E. coli* Bacterial concentration in plate samples

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Robustillo-Rodela et al., 2017[39]	Intensive chlorine decontamination and HPV decontamination, preceded by an indepth cleaning with a 0.05% chlorine solution	Outbreak intervention study, n=31, ICU patients and outbreak cases	1,200-bed university hospital, ICU, Spain	The cumulative incidence of OXA-48 carbapenemase-producing Enterobacteriaceae (OXA-48-PE) and MDR-AB was 3.48% and 4.81%, respectively. In the period after the intervention, they were 0.8% and 0%, respectively ($p<0.001$). Before the HPV decontamination, 4.5% of environmental samples were positive for OXA-48-PE and none for MDR-AB. After decontamination, 1.4% of samples were positive for OXA-48-PE.	Conventional cleaning by manually applying a disinfectant is difficult to standardize and has a high risk of error. If wipes and dusters are not correctly used, they can be contaminated and allow the spread of pathogens from one surface to another.	Environmental samples were taken before and after HPV. Indepth ICU cleaning was done with a 500 ppm chlorine solution. Air conditioning grilles were covered, and sink drains were left uncovered. Chemical and biological indicators were used for quality assurance.	High	Organisms/ Outcomes: OXA-48-PE and MDR-AB OXA-48-PE and MDR-AB cases, environmental sample cultures

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Rock et al., 2018[48]	UV-C light room decontamination	Cross-sectional survey, n=100, hospital healthcare workers and patients	Teaching hospital, United States	None assessed.	None assessed.	Eighty-four percent of the patients said the purpose of the UV-C light was well explained. Sixty-four percent let staff know when their room was available for UV-C disinfection. Ninety-three percent felt comfortable with the UV-C light operating in the bathroom while they were in the room. Also, 93% reported that the UV-C light did not interfere with their daily schedule. Finally, 39% had at some time refused UV-C light disinfection in their room or bathroom; reasons included not feeling well (25%), wanting to sleep (13%), not wanting to be bothered (11%), and not liking the smell (5%).	High	Organisms/ Outcomes: No organisms specified. Patient attitudes and experiences with UV-C room decontamina-tion. This study was done 8 months after implementa-tion of a UV-C study.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Rodriguez-Bano et al., 2009[51]	Multicomponent intervention: strict environmental cleaning policy, limited sharing of medical devices, ongoing staff education, promotion of hand hygiene, strict contact and isolation precautions, environmental cleaning, and targeted active surveillance in high-risk areas during periods of likely transmission and contamination	Before-and-after study, 971 cases, all patients in 21 wards	Acute care university hospital with 30-bed ICU, Spain	Device sharing was limited between patients. Environmental sampling was performed in each of the three intervention periods. A strict environmental cleaning policy following CDC recommendations for rooms and any object that might have come into contact with colonized patients was implemented. Before the bundle was instituted, the rate of colonization/infection was 0.82 cases per 100 admissions (1994–1995). Colonization and infection rates showed a sustained decrease after implementation of the control program in 1995 to 0.46 in 1996–1997 and to 0.21 in 1998–2003 ($p<0.001$). The rate of bacteremia due to MDR-AB decreased sixfold during the 8-year observation period.	Rate of positivity of environmental samples did not change over the intervention period.	Decreased incidence of MDR-AB, decreased incidence in bloodstream infections, and decreased clonal diversity of MDR-AB were attributed to this multifaceted intervention. However, no decrease in positivity of environmental cultures was found. In total, several important clinical outcomes improved as a result of this multicomponent intervention and stemmed this multiyear outbreak. The authors also added that the active surveillance component was costly and time consuming, and the presence of the infection control practitioner alone may have improved compliance.	High	Organism: MDR-AB MDR-AB colonization/ infection, MDR-AB bacteremia

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Rutala et al., 2012[3]	Use of an improved hydrogen peroxide disinfectant, standard hydrogen peroxide, and quaternary ammonium	Laboratory	Laboratory, United States	The improved hydrogen peroxide disinfectant was superior to all three concentrations of the standard hydrogen peroxide and similar or superior to the quaternary ammonium product in its effectiveness in log_{10} bacterial reduction.	Hydrogen peroxide is a category IV in the Environmental Protection Agency (EPA) toxicity categories (very low toxicity).	Improved hydrogen peroxide disinfectant includes anionic and nonionic surfactants in an acidic product to augment microbicidal activity. The authors indicate that this product has the lowest EPA toxicity categorization. Also, the improved hydrogen peroxide has a lower contact time than most EPA low-level disinfectants.	Moderate to high	Organisms/ Outcomes: MRSA, MDR-AB Bacterial reduction
Shaikh et al., 2016[31]	Use of low-intensity UV-C radiation for keyboard decontamination	Before-and-after study, n=25, decontamin-ation of in-use keyboards	Hospital rooms, United States	Keyboards were cultured before and after a 6-minute UV-C cycle. The UV-C device significantly reduced total aerobic bacterial counts on in-use keyboards (p=0.0006). In addition, there was a significant reduction in recovery of potential pathogens after use of the device.	Device required four or five cycles to achieve a <1 log reduction in *C. difficile.*	The UV-C significantly reduced total aerobic bacterial counts on in-use keyboards. The device was less effective against *C. difficile* and required four or five cycles to achieve a <1 log reduction.	Moderate	Organisms/ Outcomes: Gram-negative bacilli, *C. difficile, S. aureus,* and *Enterococcus* spp. Bacterial counts
Strassle et al., 2012[20]	Terminal cleaning with QAC, disposable wipes, and mops	Before-and-after study, patients with known history of colonization or infection with organism	University teaching hospital, medical, surgical, and cardiac surgery ICUs,	Environmental sampling was done before and after terminal cleaning. Samples were taken from sinks, floors around patient bed, and high-touch areas. Curtains, infusion	None assessed.	Culturing was performed to isolate areas that were missed during routine terminal cleaning. The rooms were emptied to ensure all hard-to-reach areas were disinfected. There was	Moderate to high Molecular typing was not completed; it cannot be proven that the strain of *A. baumannii* is	Organisms/ Outcomes: MDR-AB Environmental sample cultures

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
			United States	pumps, and respiratory equipment were removed from the room. Wipes saturated with quaternary ammonium were used to clean all surfaces. A new wipe was used on each surface to avoid cross-contamination. The floor was mopped from back to front with the same disinfectant solution with an 8- to 10-minute dwell time. Fifteen rooms (46.9%) and 41 sites (n=268, 15.3%) were found positive pre-terminal cleaning. Eight rooms (25.0%) were found positive post-terminal cleaning. Overall, a significant reduction in the number of contaminated rooms (p=0.01) and sites (p>0.01) was observed. Twelve sites (n=219, 5.5%) were found positive post-cleaning.		a focus on replacing cleaning wipes to reduce cross-contamination, as well as adhering to recommended dwell times for the used disinfectants. Cleaning methods and staff were not observed, potential poor cleaning technique or practice may have occurred, and post-cleaning contamination rates may be improved with education and feedback to environmental services.	identical between patient and environmental isolates.	

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Ushizawa et al., 2016[15]	Multicomponent intervention including: Enhanced environmental cleaning with bleach and QAC, closure of the emergency room and interruption of admission to the CCC, and isolation of patients with MDR-AB colonization or infection within a single room	Outbreak intervention study, 15 cases, outbreak cases and other hospital patients	Tertiary care hospital, critical care center, Japan	Medical equipment was disinfected three times per day. A QAC, followed by 0.01% sodium hypochlorite, was used for environmental cleaning in the ER and the ward where the MDR-AB strains were isolated. This bundle of intervention led to a decreased isolation rate of MDR-AB and a halt to the outbreak.	ER was temporarily closed during the outbreak response.	The ER was temporarily closed to prevent ongoing transmission. Shared medical equipment was determined to be a common source of contamination, and so environmental cleaning policies were enacted to increase their disinfection.	High	Organisms/ Outcomes: MDR-AB MDR-AB cases

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Wendel et al., 2015[53]	Multicomponent intervention including sink trap replacement and a reduction in washbasin use	Outbreak intervention study, 29 cases, outbreak cases	Tertiary care hospital, 40-bed surgical ICU, Germany	Environmental sampling revealed colonization of the wastewater system, several sinks, and a reusable hair washbasin. Use of washbasin was restricted. Sink traps were also replaced. Continued surveillance over a period of 2 years revealed no further case of this outbreak strain GIM-1e carrying *P. aeruginosa.*	None assessed.	Due to the difficulty in cleaning and disinfecting sink traps with biofilms, the researchers opted for replacement of the sink trap systems and an ongoing focus on their cleaning and disinfection. As it is a high-risk area for biofilm growth and bacterial contamination, researchers opted to limit washbasin use entirely to prevent cross-contamination. A 2-year followup period reiterated the success of this intervention in halting the spread of the outbreak strain.	High Colonization or infection status was difficult to assess in the retrospective part of the data analysis.	Organisms/ Outcomes: GIM-1-producing *P. aeruginosa* ST111 GIM-1-producing-PA cases, environmental sample cultures

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Zarpellon et al., 2018[62]	Multicomponent intervention: enhanced terminal cleaning, twice-daily room disinfection, establishment of prevention guidelines, hand-hygiene promotion, isolation of patients colonized or infected by such organisms, and enforced contact precautions	Before-and-after study, all hospitalized patients	123-bed public teaching hospital, Brazil	This intervention included terminal cleaning and disinfection of the rooms, performed twice by different teams on separate days in its bundle. Statistically significant differences were observed between the pre- and post-intervention periods (p=0.00198). Control measures were effective in halting a previously endemic clone of *A. baumannii*. The incidence of VRE, *K. pneumoniae*, and *P. aeruginosa* during the surveillance period was low.	None assessed.	While a policy change and focus on monitoring environmental cleaning was part of this multicomponent intervention, the authors primarily attributed success to an active surveillance program.	High Low incidence of some target MDROs.	Organisms/ Outcomes: *A. baumannii, K. pneumoniae, P. aeruginosa* MDRO incidence

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Zarrilli et al., 2012[26]	Multicomponent intervention: environmental cleaning with 500 ppm chloride derivatives, disinfection of incubators with 4% chlorhexidine, sterilization of ventilation equipment with low-temperature hydrogen peroxide gas plasma, and ongoing monitoring with environmental sampling	Outbreak intervention case-control study, 22 cases, neonates in NICU	Neonatal ICU in university hospital, Italy	The intervention included environmental cleaning procedures with chloride derivatives at 500 ppm and disinfection of incubators with 4% chlorhexidine. All reusable assisted ventilation equipment was sterilized with low-temperature hydrogen peroxide gas plasma technology. Environmental sampling identified several contaminated sites. After intervention, these sites never cultured positive.	None assessed.	The multicomponent intervention successfully stemmed the outbreak, although it is difficult to attribute success to any one component. Extensive environmental investigation and screening were done to identify any ongoing sources of contamination, which was especially crucial due to the sensitivity of the population. Ongoing environmental screening was performed throughout the outbreak.	High	Organisms/ Outcomes: XRD-AB XRD-AB cases, environmental sample cultures

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Zoutman et al., 2014[59]	Environmental services department activities including auditing, training, supply availability, and resource allocation	Cross-sectional survey, n=96 from 103 hospitals, environmental services managers	Hospitals, Canada	Here, 86.3% (82/95) of managers responsible for environmental services reported their staff were adequately trained, and 76.0% (73/96) said supplies and equipment budgets were sufficient.	Here, 36.8% (35/95) of environmental services departments did not audit the cleaning of medical-surgical patient rooms on at least a monthly basis. Cleaning audits of medical-surgical patient rooms frequently included environmental marking methods in only one-third (33.3%, 31/93) of hospitals and frequently included the measurement of residual bioburden in only 13.8% (13/94).	Researchers concluded there is a general need for increased and improved auditing of environmental cleaning in Canadian hospitals, and most hospitals had environmental services staffing deficits.	High	Organisms/ Outcomes: MDROs (not specified) Environmental staff knowledge and self-report of resources for cleaning

Table B.38: MDROs, Minimizing Catheter Use and Reducing Harm—Systematic Reviews

Note: Full references are available in the Section 5.5 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Bermingham et al., 2013[18]	The use of various materials and practices for urinary catheters including clean versus sterile noncoated intermittent self-catheterization, hydrophilic catheters, gel reservoir catheters, and clean noncoated catheters	Eight studies of long-term (>28 days) intermittent self-catheterization in community or primary care settings, mostly men with spinal cord injuries; International setting	For the systematic review, the researchers searched MEDLINE, Embase, and Cochrane and CINAHL databases from 2002 to April 18, 2011. Clinical outcomes of interest included symptomatic urinary tract infection (UTI), bacteremia, mortality, patient preference or comfort, and number of catheters used. An economic model was created to determine cost-effectiveness (incremental cost per quality-adjusted life year [QALY] gained) of various interventions and included costs associated with downstream complications of UTI. The final review included eight studies. Most were conducted of patients with spinal cord injuries, and most of the included patients were men. People using gel reservoir and hydrophilic catheters were significantly less likely to report one or more UTIs compared with sterile noncoated catheters (absolute effect for gel reservoir = 149 fewer per 1,000 (95% confidence interval [CI] −7 to 198, p=0.04); absolute effect for hydrophilic = 153 fewer per 1,000 (95% CI −8 to 268, p=0.04). The authors also concluded that there was no difference in the mean monthly number of UTIs (mean difference −0.01; (95% CI −0.11 to 0.09, p=0.84), total number of UTIs at 1 year (mean difference 0.18 (95% CI −0.50 to 0.86, p=0.60), or total antibiotic treatment episodes at 1 year (mean difference −0.88 (95% CI −1.58 to −0.18, p=0.01) for people using hydrophilic coated catheters compared with those using noncoated catheters. There was no statistically significant difference in the incidence of one or more UTIs for people using clean versus sterile noncoated catheters (p=0.86). Although the most effective at reducing UTIs, gel reservoir catheters cost >£54,350 per QALY gained.	The type of catheter used for intermittent self-catheterization seems to make little difference to the risk of symptomatic UTI. The authors concluded that patients should be offered a choice between hydrophilic and gel reservoir catheters due to the limitations and gaps in evidence supporting one over the other. The authors determined that despite the lowered risk of UTI for patients using gel reservoir catheters, these catheters were not cost-effective compared with their counterparts, clear noncoated catheters.	Organisms/ Outcomes: Symptomatic UTI and bacteremia

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Doyle et al., 2011[11]	Multiple patient safety practices: staff education, subclavian central venous catheter (CVC) insertion, alcoholic chlorhexidine gluconate skin antisepsis at insertion site, maximal barrier precautions during CVC care, anti-infective and antimicrobial-impregnated CVC, needleless connectors, biopatch disk, decontamination of the oropharynx for patients on ventilators, selective decontamination of the digestive tract for patients on ventilators, and semirecumbent positioning during ventilation.	113 ICU outbreak studies from multiple countries, including the United States	Using surveillance data collected in the United States and internationally, article describes contemporary rates, sites, and pathogens responsible for common ICU-acquired infections. Emerging pathogens are outlined, including a systematic review of published ICU infection outbreaks from 2005 to 2010. Multiple PSPs associated with controlling ICU outbreaks are reviewed (see "Description of PSP"). PSPs with mixed evidence: Minocycline-rifampicin and silver or chlorhexidine-silver sulfadiazine-impregnated catheters, and needleless connectors. PSP with supporting evidence: Educating physicians and nurses on central line insertion and care, subclavian insertions versus jugular or femoral sites, maximal barrier precautions at the time of catheter insertion, elevation of beds to 30-45 degrees for patients receiving ventilation, selective decontamination of the digestive tract to prevent ventilator-associated pneumonia, chlorhexidine to decontaminate the oropharynx, application of alcoholic chlorhexidine gluconate versus aqueous-based solutions for skin antisepsis at the time of insertion.	The authors identified evidence supporting the use of several PSPs for the control of ICU outbreaks, including those caused by pathogens commonly associated with drug resistance.	Organisms/ Outcomes: Common ICU pathogens, including some commonly associated with drug resistance (e.g., *Staphylococcus aureus, Candida,* and Enterobacteria-ceae species) ICU-acquired infections

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Kidd et al., 2015[9]	Use of urethral (indwelling or intermittent) or suprapubic routes for short-term urinary catheterization	38 studies of hospitalized adults; International setting	This systematic review was conducted by performing a review of trials identified from the Cochrane Central Register of Controlled Trials, and by manually searching journals and conference proceedings. The interventions considered were urethral (indwelling or intermittent) or suprapubic catheterization. Fourteen trials compared indwelling urethral catheterization with intermittent catheterization. Two trials had data for symptomatic UTI and were included in the meta-analysis. Results were not pooled due to inconclusive, poor quality of evidence and clinical and statistical heterogeneity. Suprapubic catheters reduced the number of participants with asymptomatic bacteriuria, recatheterization, and pain compared with indwelling UTI and asymptomatic bacteriuria. The evidence for symptomatic UTI was inconclusive. The evidence was inconclusive for suprapubic versus intermittent urethral catheterization.	The authors determined that adequately powered trials comparing all catheters are required, particularly suprapubic and intermittent urethral catheterization. Some low-quality studies reported increased risk of catheter-associated pain in patients with indwelling urethral catheters compared with suprapubic catheters. The authors could not conclusively determine any increased risk of UTI when comparing indwelling and intermittent urethral catheterization.	Organisms/ Outcomes: No specified organisms Urinary tract infection, adverse events, replacement, duration of use, participant satisfaction, and cost-effectiveness
Meddings et al., 2015[10]	Use of the RAND/UCLA Appropriateness Method to determine the criteria for appropriate use of Foley-catheters, intermittent straight catheters (ISCs), and external condom catheters	30 studies of hospitalized adults and reviews of international guidelines; International setting	The panel rated 105 Foley scenarios (43 appropriate, 48 inappropriate, 14 uncertain), 97 ISC scenarios (15 appropriate, 66 inappropriate, 16 uncertain), and 97 external catheter scenarios (30 appropriate, 51 inappropriate, 16 uncertain). The refined criteria clarify that Foley catheters are appropriate for measuring and collecting urine only when fluid status or urine cannot be assessed by other means; specify that patients in ICUs need specific medical indications for catheters because ICU location alone is not an appropriate indication; and recognize that Foley and external catheters may be pragmatically appropriate to manage urinary incontinence in select patients.	The recommendations and criteria created by this review should be used to inform large-scale collaborative and bedside efforts to reduce inappropriate urinary catheter use.	Organisms/ Outcomes: No specified organisms Any inappropriate use of various types of urinary catheters

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Meddings et al., 2017[8]	Single- or multicomponent intervention including improving appropriate use of urinary catheters, performing aseptic placement, providing maintenance care, and prompting removal of unnecessary catheters, as well as hand hygiene, barrier precautions, infection control strategies, infection surveillance, use of standardized infection definitions, and interventions to improve antibiotic use	20 studies of nursing homes, rehabilitation centers, and spinal cord injury programs, included studies reporting at least one outcome for catheter-associated UTI (CAUTI), UTIs not identified as catheter associated, bacteriuria, or urinary catheter use; International setting	Nineteen studies were included. Many studies were underpowered for the review's outcomes of interest and did not demonstrate any statistically significant change. The only intervention that demonstrated a statistically significant reduction in CAUTI in chronically catheterized patients used a comprehensive program to improve antimicrobial use, hand hygiene (including hand hygiene and gloves for catheter care), and preemptive precautions for patients with devices, along with promotion of standardized CAUTI definitions and active multidrug resistant organism (MDRO) surveillance.	The strength of evidence to motivate catheter avoidance and removal in nursing homes is low compared with other settings. A multicomponent intervention involving antimicrobial use, hand hygiene, and preemptive precautions for patients with devices was the only intervention that statistically significantly reduced CAUTI rates.	Organism/ Outcome: MDROs (general, not specified) Any CAUTI, non-catheter-associated UTI, bacteriuria, or urinary catheter use not associated with an infection

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Patel et al., 2018[5]	For urinary catheters and CVCs, interventions were categorized using a conceptual model, with stages applicable to both CAUTI and CLABSI prevention: avoid catheter if possible (stage 0), ensure aseptic placement (stage 1), maintain awareness and proper care of catheters in place (stage 2), and promptly remove unnecessary catheters (stage 3).	102 randomized and nonrandomized studies that implemented at least one intervention to prevent CLABSI or CAUTI in an adult ICU setting. Review did not include general ward, outpatient/ ambulatory, and neonatal/ pediatric settings. International setting.	The studies that demonstrated the greatest success in preventing CLABSI and CAUTI had several features in common. They often addressed multiple steps within the lifecycle of catheter use (avoidance, insertion, maintenance, and removal). They used auditing to ensure compliance. For CLABSI, they used a checklist as a central quality improvement tool. For CAUTI, engaging a multidisciplinary team including nurse leadership seemed critical to optimize implementation and sustainability efforts. In addition, a focus on stage 3 (removal), including protocols to remove by default, was associated with success in CAUTI studies.	Successful interventions to reduce CAUTI and CLABSI often included multicomponent interventions that addressed all stages of device use, checklists, auditing and monitoring, multidisciplinary teams and nurse leadership, and focus on removal of devices (for CAUTI).	Organisms/ Outcomes: No organisms specified Any CAUTI or CLABSI Studies with interventions that are no longer standard of care in the United States were excluded.

Table B.39: MDROs, Minimizing Catheter Use and Reducing Harm—Single Studies

Note: Full references are available in the Section 5.5 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Ansari et al., 2014[15]	Use of gum arabic capped-silver nanoparticles (GA-AgNPs), as an antimicrobial surface coating material for surgical implants and instruments	Laboratory experiment to assess antimicrobial properties, n=55 isolates	Laboratory, India	The lowest minimum inhibitory concentration (MIC) for extended spectrum beta-lactamase (ESBL), non-ESBL, and metallo-beta-lactamase (MBL) *P. aeruginosa* was determined to be 11.25 µg/mL, demonstrating strong bacteriostatic activity. The minimum bactericidal concentration (MBC) was found to be in the range of 11.25–45 µg/mL, demonstrating bactericidal activity of GA-AgNPs. At a concentration of 30 µg/mL, biofilm formation stopped without affecting the cell viability, whereas at a concentration of 60 µg/mL, the biofilm formation and bacterial growth were stopped.	None assessed.	Results demonstrated that the GA-AgNPs can easily penetrate the biofilm, reduce its formation, and reduce the surface coverage and bacterial colonization.	Low to moderate	Organisms/ Outcomes: Biofilm-forming MDROs (specifically *Pseudomonas aeruginosa*) Bacterial inhibition/ bactericide

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Bayston et al., 2009[16]	Impregnation of continuous peritoneal dialysis catheters using rifampicin, triclosan, and trimethoprim	Laboratory testing of medical-grade silicone sheets and tubing	Laboratory, United Kingdom	The authors concluded that the duration of antimicrobial activity would have lasted longer than 280 days. Bacterial growth was stopped and there were no signs of resistance toward any of the agents for 30 days. Test catheters after 72 hours did not show bacterial migration down the track.	The toxicity of triclosan for anything other than topical use is not well studied, and it may cause inflammation of the peritoneal membrane, leading to adhesions and loss of absorptive capacity. However, this study did not demonstrate any adverse reactions in mice after 7 days or 30 days.	The authors concluded that the antimicrobial substances had a long-lasting ability to kill ~99% of pathogens associated with infection in patients on continuous ambulatory peritoneal dialysis, even after very large challenge doses and that the tested catheters with the tested antimicrobials could resist colonization in flow conditions for prolonged periods.	Moderate to high	Organisms/ Outcomes: Methicillin-resistant/ methicillin susceptible *S. aureus* MRSA/MSSA), *S. epidermidis,* and *E. coli* Bacterial growth

Camus et al., 2014[22]	Administration of polymyxin/ tobramycin/ amphotericin B in the oropharynx and the gastric tube plus a mupirocin/ chlorhexidine body wash regimen in intubated patients and standard care in the other patients	Before-and-after study in ICU patients during two 1-year periods, N=925 before and 1,022 after, ICU patients	21-bed medical ICU at a university-affiliated hospital, France	The comparison of acquired infection rates between groups was adjusted for differences at baseline. Infection rates were lower in the study group compared with the control group (5.3% vs. 11.0%; p <0.001), as were the incidence rates of total acquired infections (9.4 vs. 23.6 per 1,000 patient-days; p<0.001), intubation-related pneumonia (5.1 vs. 17.1 per 1,000 ventilator-days; p<0.001), and catheter-related bloodstream infections (1.0 vs. 3.5 per 1,000 catheter-days; p= 0.03). In the patients who required intubation for less than 48 hours or who were not intubated, infection rates did not decline significantly in the study group (adjusted odds ratio = 0.77, 95% CI 0.35–1.71, p=0.52). Compared with the control group, the study group experienced fewer acquired infections caused by ceftazidime-resistant Enterobacteriaceae (0.8‰ vs. 3.6‰; p<0.001), ciprofloxacin-resistant Enterobacteriaceae (0.8‰ vs. 2.5‰; p=0.02), ciprofloxacin-resistant *P. aeruginosa* (0.5‰ vs. 1.6‰; p=0.05), and colistin-resistant Gram-negative bacilli (0.7‰ vs. 1.9‰; p=0.04). Fewer patients acquired infections due to multidrug-resistant aerobic Gram-negative bacilli (AGNB) (p=0.008 The median length of stay in the ICU was	Other literature suggests there is some increased risk of MRSA with the use of selective digestive decontamination.	In intubated patients, the use of topical polymyxin/ tobramycin/ amphotericin B plus mupirocin/chlorhexidine was associated with the reduction of all-cause ICU-acquired infections. The authors report that the use of selective digestive decontamination (SDD) is still reluctantly accepted due to concerns over the potential induction of antibiotic resistance, which the authors stated is not backed by current evidence. The authors also admitted concerns over the increased risk of MRSA with the use of SDD and over increase in the AGNB tobramycin resistance rate, especially for Enterobacteriaceae and *P. aeruginos*a.	Low to moderate The study controlled for patient characteristics but not antibiotics use.	Organisms/ Outcomes: Ceftazidime-resistant Enterobacteriaceae, ciprofloxacin-resistant Enterobacteriaceae, ciprofloxacin-resistant *P. aeruginosa,* colistin-resistant GNB, and multidrug-resistant AGNB General device-related infections,

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
				similar in the control and study groups (p=0.63).				
Damas et al., 2015[21]	Subglottic suctioning for patients undergoing ventilation	Randomized control trial, n=252, adult patients intubated with a tracheal tube	Five ICUs in a French hospital	Group 1 underwent suction and group 2 was the control group. Ventilator-associated pneumonia occurred in 15 patients (8.8%) of group 1 and 32 patients (17.6%) of group 2 (p = 0.018). In terms of ventilatory days, ventilator-associated pneumonia rates were 9.6 of 1,000 ventilatory days and 19.8 of 1,000 ventilatory days, respectively (p = 0.0076). The total number of antibiotic days was 1,696 in group 1, representing 61.6% of the 2,754 ICU days, and 1,965 in group 2, representing 68.5% of the 2,868 ICU days (p < 0.0001).	None assessed.	Subglottic secretion suctioning resulted in a significant reduction of ventilator-associated pneumonia prevalence associated with a significant decrease in antibiotic use. By contrast, ventilator-associated condition occurrence did not differ between groups and appeared more related to other medical features than ventilator-associated pneumonia.	Low	Organisms/ Outcomes: Organisms not specified Ventilator-associated pneumonia, ICU length of stay, days of antibiotic use, days of ventilation

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Dixon et al., 2012[12]	Use of antimicrobial lock (AML) solutions with systemic antibiotics for patients with tunneled hemodialysis catheters	Retrospective cohort study, controls (n=265) and study group (n=662), all catheter-related blood stream infections (CR-BSI).	Renal and trans-plantation center and its five regional satellite units, United Kingdom	This study analyzed antibiotic sensitivity/ resistance profiles of MRSA, vancomycin-resistant *Enterococci* (VRE), resistant *Escherichia coli*, resistant *Pseudomonas* species, and resistant *Enterobacter* species, and changes in the incidence of infection (chi-square test) and resistant organisms (Fisher's exact test). The incidence of CR-BSI decreased from 8.50/1,000 catheter-days (controls) to 3.80 (study group; p<0.0001), and the incidence of relapses decreased from 13.2% to 6.8% (p=0.0027). The proportion of MRSA (p=0.87) and VRE (p=0.90) did not increase.	The proportion of gram-positive cultures increased (p<0.0001), including *S. aureus* (p=0.03). Gentamicin resistance (relative risk [RR] >15.29; p<0.0001) and ciprofloxacin resistance (RR = 6; p=0.007) increased in *Enterobacter* species, but not *Pseudomonas* or *E. coli* species.	Overall, the incidence of CR-BSI and CR-BSI relapses decreased statistically significantly in the study group compared with the control group. A statistically significant increase in Gram-positive cultures and an increase in gentamicin and ciprofloxacin resistance in *Enterobacter* species was also observed.	Moderate–low The study did not control for patient character-istics or antibiotic treatment.	Organisms/ Outcomes: MRSA, VRE, resistant *E. coli,* resistant *Pseudomonas* species, resistant *Enterobacter* species CR-BSI

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Mody et al., 2017[7]	Multicomponent intervention that included a technical bundle involving urinary catheter removal, aseptic insertion, regular assessments, training for catheter care, and incontinence care planning, as well as a socioadaptive bundle emphasizing leadership, resident and family engagement, and effective communication	Before-and-after study of 404 nursing homes	Community-based nursing homes across 48 States, DC, and Puerto Rico	The unadjusted catheter-associated UTI (CAUTI) rates decreased from 6.78 to 2.63 infections per 1,000 catheter-days. With use of the regression model and adjustment for facility characteristics, the rates decreased from 6.42 to 3.33 (incidence rate ratio [IRR], 0.46; 95% CI 0.36 to 0.58, p<0.001). Catheter utilization dropped from 4.5% at baseline to 4.9% at the end of the intervention. Catheter utilization remained unchanged (4.50 at baseline, 4.45 at conclusion of project; IRR, 0.95; 95% CI 0.88 to 1.03, p=0.26) in adjusted analyses. The number of urine cultures ordered for all residents decreased from 3.49 per 1,000 resident-days to 3.08 per 1,000 resident-days. Similarly, after adjustment, the rates were shown to decrease from 3.52 to 3.09 (IRR, 0.85; 95% CI 0.77 to 0.94; p=0.001).	None assessed.	The intervention, which combined technical and socioadaptive interventions, successfully reduced the incidence of CAUTIs but did not decrease catheter utilization in either the adjusted or unadjusted analysis. Possible explanations for this finding include that utilization rates were already low in the nursing homes at the start of this project. In addition, with catheter use being a CMS publicly reported measure since 1990, nursing homes have had several decades to improve their practice of discontinuing the use of clinically unnecessary catheters.	Low to moderate	Organisms/ Outcomes: Organisms not specified Any CAUTI

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Olthof et al., 2012[13]	Long-term taurolidine catheter locking use in patients on home parenteral nutrition	Retrospective cohort study, n=158, home parenteral nutrition patients	Patient homes, Netherlands	Between January 2009 and April 2011, 14 patients developed at least one CR-BSI episode during long-term taurolidine catheter locking (median [range] = 451 [78-1,394] days). Coagulase-negative *Staphylococcus* species or *S. aureus* were the most common CR-BSI-causing Gram-positive bacteria. Taurolidine MICs were 512 mg/L or less in 50% of these isolates (MIC_{50}). Taurolidine MIC_{50} among CR-BSI-causing *Candida albicans* was 2,048 mg/L.	The effectiveness of taurolidine on the development of biofilms, prevention of Gram-positive bacteria, and prevention of fungi has not been well studied.	Long-term use of taurolidine seems to be safe for up to 1,394 days of taurolidine catheter locking. Increased taurolidine resistance was most notably observed in *C. albicans*. The authors recommended additional research on the mechanism of the antiseptic effect of taurolidine on Gram-positive bacteria to provide insight on why patients who use taurolidine still occasionally develop CR-BSI.	Moderate	Organisms/ Outcomes: CR-BSI-causing Gram-positive bacteria and taurolidine resistance CR-BSI

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Raad et al., 2008[19]	The use of CVCs impregnated with: minocycline and rifampicin (M/R), silver-platinum and carbon (SPC), and chlorhexidine and silver sulfadiazine (CHX/SS)	Laboratory testing using "established biofilm colonization model"	Laboratory, United States	By measuring colony forming units (CFUs)/cm, the authors determined M/R catheters had superior antiadherence activity and more prolonged antimicrobial durability compared with CHX/SS-CVCs, SPC-CVCs, and uncoated control catheters for preventing biofilm formation of MDR and vancomycin-resistant *S. aureus* (p<0.02), MDR *S. maltophilia* (p<0.005), and MDR *A. baumannii/calcoaceticus* (p<0.002). M/R-CVCs and CHX/SS-CVCs did not vary statistically in their antiadherence properties or antimicrobial durability against MDR *E. agglomerans*. However, they were superior to SPC-CVCs and the uncoated control catheters (p<0.001).	None assessed.	M/R-CVCs were superior in antiadherence activity and prolonged antimicrobial durability for MDR and vancomycin-resistant *S. aureus*, MDR *S. maltophilia*, and MDR *A. baumannii/ calcoceticus.* For MDR *E. agglomerans*, M/R-CVCs and CHX/SS-CVCs were both statistically significantly superior to SPC-CVCs and uncoated control catheters.	Moderate to high	Organisms/ Outcomes: MDR *S. aureus* and MDR Gram-negative bacteria Bacterial adherence

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Raad et al., 201217	The use of second-generation CVCs impregnated with minocycline and rifampicin (M/R) + chlorohexidine (CHX)	Laboratory testing using "established biofilm colonization model"	Laboratory, United States	CHX-M/R CVCs were the only antimicrobial catheters that completely inhibited the biofilm colonization of all resistant bacterial and fungal organisms tested. In terms of CFUs/cm segment of the catheter, they were superior to uncoated catheters ($p<0.003$). CHX-M/R-coated CVCs had a significantly more effective and prolonged (up to 3 weeks) antimicrobial activity against MRSA and *P. aeruginosa* than M/R, CHX/SS, and uncoated CVCs ($p< 0.0001$). CHX-M/R-coated peripherally inserted central catheters (PICCs) also showed statistically significant reductions in biofilm formation compared with M/R-coated and CHX-coated PICCs for MRSA, VRE, *P. aeruginosa*, and *Candida* species ($p<0.003$).	M/R and CHX/SS CVCs both demonstrated limited effectiveness against MDR *P. aeruginosa* (in this study) and *Candida* (in other literature).	The authors concluded that CHX-M/R-coated catheters more effectively reduced biofilm colonization and had prolonged efficacy against colonization of MRSA, VRE, *P. aeruginosa*, and fungi in a manner superior to that of M/R- and chlorhexidine-treated catheters.	Moderate to high	Organisms/ Outcomes: MRSA, VRE*, P. aeruginosa, C. albicans,* and *C. glabrata* Biofilm colonization
Ramos et al., 2011[20]	Use of CVCs coated with minocycline and rifampicin (M/R)	Retrospective cohort study, n=8,009, all patients admitted between 1999 and 2006	Tertiary care university-affiliated hospital and ICU, United States	The incidence of central line-associated bloodstream infection (CLABSI) per 1,000 patient-days in the medical ICU significantly and gradually decreased from 8.3 in 1998 to 1.2 in 2006 ($p<0.001$). The resistance *of S. aureus* and coagulase negative *Staphylococci* clinical isolates to tetracycline or rifampin remained stable or decreased significantly during the same period.	None assessed.	There was a statistically significant decrease in CLABSIs over the 8-year study period after the introduction of CVCs coated with M/R. However, other interventions were occurring at the same time. Authors suggest a prospective study in the future.	Moderate	Organisms/ Outcomes: *Staphyloccoci*, *S. aureus* CLABSI and resistance to tetracycline and rifampin in clinically relevant *Staphylococcal* isolates

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Saint et al., 2016[24]	Use of the Comprehensive Unit-based Safety Program, which included education of sponsor organizations and hospitals, data collection, and education on technical and socioadaptive factors for CAUTI prevention.	Before-and-after study, 962 units in 603 hospitals, both ICU and non-ICU units	Hospital units in 32 of the United States, DC, and Puerto Rico	Program recommendations included assessing daily the presence and need for an indwelling urinary catheter, considering alternative urine-collection methods to avoid catheter use, emphasizing the importance of aseptic technique during insertion and proper maintenance after, providing units feedback regarding urinary catheter use and CAUTI rates, and addressing gaps in knowledge of urinary management processes. The unadjusted CAUTI rate decreased overall from 2.82 to 2.19 infections per 1,000 catheter-days. In an adjusted analysis, CAUTI rates decreased from 2.40 to 2.05 infections per 1,000 catheter-days (IRR, 0.86; 95% CI 0.76 to 0.96, p=0.009) Among non-ICUs, catheter use decreased from 20.1% to 18.8% (IRR, 0.93; 95% CI 0.90 to 0.96, p<0.001), and CAUTI rates decreased from 2.28 to 1.54 infections per 1,000 catheter-days (IRR, 0.68; 95% CI 0.56 to 0.82, p<0.001). Catheter use and CAUTI rates were largely unchanged in ICUs. Tests for heterogeneity (ICU vs. non-ICU) were significant for catheter use (p=0.004) and CAUTI rates (p=0.001).	None assessed.	The national prevention program reduced catheter use and CAUTI rates in non-ICUs. Similar effects were not seen in ICUs. One possible explanation is that patients who are ill enough to warrant admission to the ICU require close monitoring of urine output, which is an appropriate criterion for indwelling urinary catheters.	Low to moderate	Organisms/ Outcomes: Any CAUTI

Table B.40: MDRO, Status Communication—Systematic Reviews

Note: Full references are available in the Section 5.6 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Tacconelli, 2014[6]	Use of an alert code upon admission for carriers of multidrug-resistant Gram-negative bacteria (MDR-GNB)	Acute care facilities, Germany	These evidence-based guidelines were produced after a systematic review of published studies on infection prevention and control interventions aimed at reducing the transmission of MDR-GNB. Recommendations include an alert code for previously known positive patients/known carriers to perform screening and preemptive contact precautions (CPs) (for epidemic settings of MDR *Klebsiella*. There is also a moderate level of evidence to implement alert codes in endemic settings of MDR *Acinetobacter*. Before transferring patients to other healthcare facilities (acute and non-acute care), facilities should ensure communication of infection/colonization status.	Moderate evidence was defined as: We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.	Organisms/ Outcomes: MDR-GNB Includes guidelines and recommendations

Table B.41: MDRO, Status Communication—Single Studies

Note: Full references are available in the Section 5.6 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Andersen, 2013[4]	Multicomponent intervention: Bedpost sign, leaflet for front page of patient file, ordering procedures with prompt questions about isolation requirements, rapid involvement of infection control nurses with same-day visits of new extended-spectrum beta lactamase (EBSL) cases	Prospective, interrupted time series, all patients in hospital more than 3 years	510-bed Danish university hospital	Reported significant reduction in cefuroxime consumption (74.5%). Other results were not statistically significant: reductions such as ciprofloxacin (8.9%, p=.7); the rate of isolated EBSL *Klebsiella pneumoniae* (ESBL-KP), which decreased from 39.5% to 22.5%; and the incidence of infections with ESBL-KP, which showed a special cause pattern (nonrandom variation) indicative of a decrease. Reduced use of isolation precautions: number of isolated patients per 1,000 occupied bed-days (OBDs) declined from 0.94 (95% CI 0.74 to 1.14) to 0.65 (95% CI 0.43 to 0.87), p=0.021, for ESBL and did not change for non-ESBL causes. Isolation days per 1,000 OBDs decreased from 13.8 (95% CI 8.6 to 19.0) to 7.1 (95% CI 3.4 to 10.8) for ESBL, and from 42.8 (95% CI 30.8 to 54.7) to 28.6 (95% CI 22.0 to 35.3) for non-ESBL, p=0.0032.	None assessed.	Multidisciplinary discussion led to decision that isolation precaution policy and coordination with sections that provide transverse services needed to be improved. It also led to collective learning and collaboration and system thinking. Initial cross-sectional study in three wards determined carrier prevalence. Rollout of changes included informing staff and ward managers of new changes and their goals, newsletters and diagrams of resistance rates, and later CUSUM charts.	Low to moderate	Organisms/ Outcomes: ESBL-KP Cefuroxime consumption, ciproflaxin consumption, EBSL-KP infections

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Ariza-Heredia, 2012[10]	Interfacility communication for organ transplants from MDRO carriers. All interfacility communication occurred before organ transplantation into recipients and appropriate preventive strategies were implemented (contact isolation for those with positive cultures and preemptive pathogen-directed antibiotic treatment in all cases).	Case study on transplant recipients receiving organs/tissue from one donor with *Klebsiella pneumoniae* carbapenemase-producing *K. pneumoniae* (KPC-KP).	Four hospitals, United States	All transplant recipients had good short-term outcomes.	One-half (two of four) recipients developed KPC-KP infections.	Cases were promptly reported to Organ Procurement and Transplantation Network (OPTN) and there was prompt interinstitutional communication. OPTN/United Network for Organ Sharing (UNOS) has a policy requiring the prompt sharing of culture results between centers and organ procurement organizations, and potential donor-derived infections are tracked by the OPTN/UNOS through the Ad Hoc Disease Transmission Advisory Committee.	Moderate to high	Organisms/ Outcomes: KPC-KP KPC-KP infections
Buser, 2017[8]	Interfacility communication upon admission and transfer	Outbreak study, 21 cases, residents and patients in skilled nursing facilities (SNFs), long-term acute care hospitals (LTACHs), and acute care hospitals	Multi-facility outbreak in Oregon	Twenty-one cases were identified that were highly related by PFGE or healthcare facility exposure. Overall, 17 patients (81%) were admitted to either LTACH A (n = 8), or SNF A (n = 8), or both (n = 1) prior to XDR *A. baumannii* (XDR-AB) isolation. Interfacility communication of patient or resident XDR status was not	Outbreak attributed to lack of communication among facilities, despite Oregon Public Health Department recommendations.	An outbreak linked to SNF A was suspected, so they launched what became a multifacility investigation to determine the scope of the problem, identify a source, and intervene to prevent further spread. Index case was transferred to SNF A, status was not communicated, and	Moderate to high	Organism: XDR-AB XDR-AB cases

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
		(ACHs). Reviewed medical records and surveillance surveys and used pulsed-field gel electrophoresis (PFGE) and molecular analysis. Six large, hospital-based, clinical microbiology laboratories processing ~90% of OR clinical microbiology specimens.		performed during transfer between facilities.		eight more carriers were identified over 25 months. Other hospitalizations and transfers of other cases were associated with additional transmission. OPHD assisted facilities to develop a form and process for interfacility communication during admission and transfer. Outbreak was only detected because of a voluntary surveillance system. Recommend timely and transparent communication to allow rapid contact precautions. Inspired creation of Oregon Administrative Rule 333-019-0052, which mandates written communication of MDRO status for interfacility patient transfer, effective January 1, 2014.		
Chou, 2008[16]	Implementation of antimicrobial resistance (AMR) prevention and control strategies	Cross-sectional survey, 448 infection control professionals	Hospitals represented in the 2001 American Hospital Association Annual Survey	Formalization, standardization, centralization, institutional culture, provider–management communication, and information technology use were associated with optimal antibiotic use and enhanced implementation of strategies that prevent and control	None assessed.	Research found formalization and standardization may eliminate staff role conflict, whereas centralized authority may minimize ambiguity. Culture and communication likely promote internal trust, whereas information	Moderate	Organisms/ Outcomes: No organisms specified Self-reported hospital factors associated with implementa-

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
				antimicrobial resistance spread (all p<0.001). However, interdepartmental coordination for patient care was inversely related with antibiotic use in contrast to antimicrobial resistance spread prevention and control (p<0.0001). Multiple structural and process factors were associated with the implementation of AMR prevention and control strategies, including feedback on hand hygiene compliance (p<0.0001), distribution of copies of the policy to providers (p=0.03), use of forms to enhance infection control adherence (p=0.0008), administrator-directed infection control activities (p<0.0001), availability of decision support (p<0.0001), a culture of data-driven decision making (p<0.0001), communication of AMR trends to physicians (p<0.0001), and interdepartmental coordination of patient care (p<0.0001).		technology use helps integrate and support these organizational processes. These findings suggest concrete strategies for evaluating current capabilities to implement effective practices and foster and sustain a culture of patient safety.		tion of AMR prevention and control strategies
Miller et al., 2015[11]	Accurate and timely (<72 hours) communication of infections in donated organs	Retrospective cohort study, n=56 infection events (IEs), donor-derived transmission	United States organ donor centers, OPOs, and	None assessed.	Eighteen IEs (48 recipients) were associated with communication gaps, of which 12 resulted in adverse	Communication failures can occur at multiple levels in organ transplant processes. These failures often result in poor patient	Moderate to high	Organisms/ Outcomes: No organisms specified

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	from the donor center, to organ procurement organizations (OPOs), to the recipient center	events over 2 years	recipient centers, United States		effects in 69% of recipients (20/29), including 6 deaths. When IEs and test results were reported without delay, appropriate interventions were taken, subsequently minimizing or averting recipient infection (23 IEs, 72 recipients). Communication errors included: the transplant center delayed contacting the OPO or OPTN with a suspected donor-derived infection, the laboratory failed to relay donor results (including autopsy results) to the OPO and/or transplant center, an OPO delayed contacting OPTN or transplant centers, clerical errors occurred in reporting donor viral serologies, and the OPO provided incomplete communication of test results to transplant centers.	outcomes, including death. These results warrant education of all involved clinicians on existing communication policies and continuous evaluation of current failures in the communication process to refine the policies. The authors also recommend future actions to require expedited donor autopsies with reporting of findings to OPOs, as well as safeguards to prevent clerical errors in the reporting of donor serologies.		Transplant-related MDR infections

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Mularoni, 2015[13]	Communication of MDRO status during organ donation	Retrospective cohort study, 214 recipients and 170 deceased donors, all extraintestinal cultures from deceased donors whose organs were transplanted between January 1, 2012, and December 31, 2013; seven case studies	Italy	Transmission did not occur in high-risk recipients who received appropriate and prompt antibiotic therapy for at least 7 days.	In a 2-year period, 30/214 (14%) recipients received an organ from 18/170 (10.5%) deceased donors with infection or colonization caused by carbapenem-resistant gram-negative bacteria that was unknown at the time of transplantation. Among them, 14/30 recipients (47%) received a transplant from a donor with bacteremia or with infection/colonization of the transplanted organ and were considered at high risk of donor-derived infection at the time of transmission. Also, 16/30 (53%) recipients received an organ from a nonbacteremic donor with colonization of a nontransplanted organ and were considered at low	The safe use of organs from donors with multidrug-resistant bacteria requires intra- and interinstitutional communication to allow appropriate management and prompt treatment of recipients to avoid transmission of infection. The authors recommend that donor culture results always be reviewed in the first few days after transplantation to allow prompt antibiotic treatment. Another type of error that contributed to donor-derived infection transmission was the inappropriate treatment resulting from the underestimation of the risk of donor MDR transmission. A thorough review of donor cultures and uniform protocols of antibiotic treatment for recipients of organs from donors infected with MDR bacteria have now been implemented at the studied institution.	Low to moderate	Organisms/ Outcomes: Carbapenem-resistant Gram-negative bacteria Donor-derived infections Includes definitions of low and high risk of donor-derived infection transmission in text. Also discusses Italian guidelines for quality and safety of organs for transplanta-tion.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
					risk of infection transmission. Proven transmission occurred in 4 of the 14 high-risk recipients because donor infection was not recognized, was underestimated, or was not communicated. These recipients received late, short, or inappropriate post-transplant antibiotic therapy.			
Ong & Coiera, 2010[2]	Accurate use of transfer form and patient identity verification during transport	Prospective observational study, n=101, inpatient transfers to radiology unit over a 6-month period	Australian teaching hospital	None assessed.	No incidents of patient harm were recorded. Inadequate handover was the most common transfer error (43.1%), followed by failure to perform patient identification checks (41.9%). Inadequate infection control precautions also occurred 2.9% of the time.	Analysis of the transfer process revealed numerous redundancies that safeguard against transfer errors. However, they were relatively ineffective in preventing errors, due to the poor compliance rate. Thus, the authors advocate increasing compliance to existing redundant processes as an improvement strategy, before investing resources on new processes.	Moderate to high	Organisms/ Outcomes: No organisms specified Transfer process measures (handover, infection control practices, patient identification)

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Ong et al, 2013[3]	The use of a pretransfer checklist used by radiology porters to confirm a patient's infectious status or the use of a colored cue to highlight written infectious status information in the transfer form	Randomized crossover trial, 300 transfers over 4 months, inpatient transfers between wards and radiology	Australian teaching hospital	Compliance with infection control precautions in the intervention groups was significantly improved relative to the control group ($p<0.01$). Adherence rate in the control group was 38%. Applying the colored cue resulted in a compliance rate of 73%. The pretransfer checklist intervention achieved a comparable compliance rate of 71%. When the two methods were combined, a compliance rate of 74% was attained. Acceptability of the colored cue was high, but adherence to the checklist was low (40%).	The checklist was not well received by some porters, who rejected its use. The checklist was only implemented 40% of the time.	Both interventions demonstrated an improvement in infection control precautions compared with the control group. However, the colored cue was better received by staff, and the checklist was only implemented in 40% of the transfers.	Moderate to high	Organisms/ Outcomes: No organisms specified Rate of compliance with a pre-transfer checklist

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Palmore, 2013[5]	Communication of patient status during a carbapenem-resistant *Klebsiella pneumoniae* (CR-KP) outbreak as part of a multicomponent intervention, which also included surveillance, cohorting, hand hygiene, chlorhexidine baths, adherence monitoring, isolation precautions, and attention to the details of environmental decontamination	Outbreak study, n=17 infected or colonized, severely immuno-compromised patients	Clinical research center (NIH Clinical Center), Bethesda, Maryland	Temporal association between implementation of infection control interventions and mitigation of the outbreak.	The authors noted "unintended consequences of publication"—incomplete information was distributed to other NIH staff and the public that created fear and concerns. The strong reaction and "kitchen sink" approach to stemming this outbreak may have contributed to the heightened sense of fear among people who were largely not at risk.	Weekly, multidisciplinary meetings were held to discuss new developments, interventions, and investigative findings. The meetings allowed for comments/questions and education. Daily staff meetings were implemented to discuss outbreak investigation and control. Hospital epidemiologists and infection preventionists made dozens of presentations at a variety of events. Email notifications provided status updates, and infection control reminders were distributed to all clinical staff when new information was available and every few weeks. Information was distributed regarding enhanced contact precautions and active surveillance. An info sheet was included in admission materials about the risk of nosocomial MDROs.	High Small case series; study does not control for each component	Organisms/ Outcomes: CR-KP CR-KP cases
Pfeiffer, 2014[15]	Developing a statewide network for carbapenem-	Implementation case study. Cross-sectional	Oregon infection prevention and	The DROP-CRE working group, comprising representatives from academic institutions and	None assessed.	Needs assessment surveyed microlaboratories and infection preventionists	Moderate to high	Organisms/ Outcomes: CRE

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	resistant Enterobacteriaecea (CRE) prevention	surveys and guidance from interdisciplinary advisory committee, statewide	microbiology laboratory personnel, including 48 microbiology laboratories, 62 acute care facilities, and 140 long-term care facilities	public health, convened an interdisciplinary advisory committee to assist with planning and implementation of CRE epidemiology and control efforts. The working group established a statewide CRE definition and surveillance plan; increased the State laboratory capacity to perform the modified Hodge test and polymerase chain reaction for carbapenemases in real time; and administered surveys that assessed the needs and capabilities of Oregon infection prevention and laboratory personnel. Results of these inquiries informed CRE education and the response plan, the Oregon CRE Toolkit (a state specific CRE guide booklet). Of 60 CRE cases reported from November 2010 through April 2013, only 3 were identified as carbapenemase producers; the cases were not linked, and no secondary transmission was found. Microbiology laboratories, acute care facilities, and long-term care facilities reported lacking carbapenemase testing capability, reliable interfacility communication, and CRE awareness, respectively.		in acute care facilities, and LTCFs. 50% and 78% of laboratories "flagged" carbapenem-resistant organisms and ESBLs in the medical records, respectively; 68% of labs included MICs in the susceptibility report. Actions taken when MDR Enterobacteriaceae were encountered included notifying infection control (44%), notifying the nursing station (44%), generating an automated report on the medical record (42%), notifying the ordering physician (33%), and no further action (14%). For acute care facilities, only 58% of respondents agreed that their facility was made aware of patient MDRO status at admission to the hospital. In contrast, 82% believed that the receiving facility was made aware of patient MDRO status at discharge from the hospital. For LTCFs, 79% of respondents stated that their transfer documents indicated		Survey of CRE communica-tion practices

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
						MDRO infection or colonization status upon release to other levels of care, and 75% said MDRO status was documented for residents transferred into their facility.		
Trick, 2015[14]	Use of a statewide web-based registry of XDROs	Cross-sectional survey after implementation of statewide registry, 1,557 reports during the first year, 173 facilities	Illinois, ACHs, LTACHs, LTCFs, reference labs	Here, 55% of 21 hospitals and 43% of 7 LTACHs had queried the status of a CRE-unknown patient. Two (29%) of seven LTACHs queried all patients on admission.	Time-consuming manual queries and entry, no explicit consent required from patients.	Most ACHs did not routinely query (59%) or queried occasionally (32%); none queried every admitted patient. Nearly all (96%) hospitals expressed interest in automated CRE alerts.	Moderate to high	Organisms/ Outcomes: CRE CRE reporting and report review

Table B.42: Carbapenem-Resistant *Enterobacteriaceae*, Transmission-Based Precautions—Systematic Reviews

Note: Full references are available in the Section 6.1 reference list.

Author, Year	Description of Patient Safety Practice	Setting(s) Population(s)	Summary of SR Findings	Implementation Themes/Findings	Notes
French et al., 2017[23]	Multicomponent infection control measures, including: patient screening, personal protective equipment (PPE), hand hygiene, staff education or monitoring, environmental cleaning/ decontamination, patient and/or staff cohorting, and patient isolation	Carbapenemase-producing *Enterobacteriaceae* (CPE) outbreaks in acute care settings	Ninety-eight reports on CPE outbreaks were included, with 53 reports from Europe. The number of cases (CRE infection or colonization) involved in outbreaks varied widely, from 2 to 803. Although the risk of bias for selected reports was high, the literature suggests that CPE outbreaks can be controlled using multi-component interventions. Outbreak scenarios that were unsuccessful in controlling transmission may be underrepresented in literature.	Compliance may impact effectiveness, although it is often unmonitored or unreported in literature. The findings indicate that CRE outbreaks can be controlled using combinations of existing measures. However, the quality of the evidence base is weak, and further high-quality research is needed, particularly on the effectiveness of individual infection control measures.	Organism: CPE
Tomczyk et al., 2018[32]	Multimodal strategies comprising three or more components, including contact precautions (CP), active surveillance, patient isolation, audit, feedback, and monitoring	Healthcare facilities	Ninety percent of studies had implemented CP; 80% had monitoring, audit, and feedback of preventive measures; 70% had patient isolation or cohorting. Of the nine studies that reported implementing CP, eight reported patient isolation or cohorting, and eight found that monitoring and audits were associated with a significant reduction in slope and/or level. Study quality was low.	Multimodal infection prevention and control (IPC) strategies (>=3 components implemented in an integrated way) were found to be highly effective for CRE prevention and control. Active surveillance was found to be effective for identifying CRE carriers or infections, but varied in terms of policies from institution to institution, depending on definitions of high-risk populations. Because most studies reviewed were of multimodal IPC strategies, it was difficult to determine the effectiveness of individual interventions.	Organisms: CRE, Carbapenem-resistant *Acinetobacter baumannii* and Carbapenem-resistant *Pseudonomonas aeruginosa*

Author, Year	Description of Patient Safety Practice	Setting(s) Population(s)	Summary of SR Findings	Implementation Themes/Findings	Notes
Van Loon et al., 2017[8]	Use of physical barriers (PPE), patient cohorting, and other contact precautions	Hospitalized patients	Author searched for articles published up to 2017. One hundred sixty-two studies were included in the systematic review, of which 69 studies regarding risk factors for CRE acquisition were included in the random-effects meta-analysis studies. The meta-analyses regarding risk factors for CRE acquisition showed that the use of medical devices generated the highest pooled estimate (odds ratio [OR]=5.09; 95% confidence interval [CI], 3.38 to 7.67), followed by carbapenem use (OR=4.71; 95% CI, 3.54 to 6.26). Based on data from 95 studies, use of a physical barrier and/or CP were found to be most successful intervention (n=71), followed by patient cohorting (n=68).	To control hospital outbreaks, bundled interventions are needed, including the use of barrier/ contact precautions for patients colonized or infected with CRE, In addition, it is necessary to optimize the therapeutic approach, which is an important message to infectious disease specialists, who need to be actively involved in a timely manner in the treatment of patients with known CRE infections or suspected CRE carriage.	Organism: CRE

Table B.43: Carbapenem-Resistant *Enterobacteriaceae*, Transmission-Based Precautions—Single Studies

Note: Full references are available in the Section 6.1 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias	Comments
Arena et al., 2018[10]	Screening at admission, active surveillance and preemptive contact isolation, including contact precautions, single-bed rooms, and rehabilitation treatments inside the room	Pre-post intervention, 1,084 long-term acute care facility (LTACF) patients; included a 25-bed severe brain injury ward with patients who have extended lengths of stay; mean=97+/-72 days	LTACF with 100 beds (Italy)	The intervention was associated with a decline in the incidence of CRE colonization in the severe brain injury (SBI) ward (from 17.7 to 7.2 acquisitions/100 at-risk patient-weeks), but not in other wards. The decline was not statistically significant.	Not provided	The majority of CRE carriers were in the SBI (20/25). SBI admission screening positive results/in-hospital transmission/cross-transmission were all higher there than in other wards. The SBI ward experienced a decreasing trend in in-hospital colonization throughout the program (not significant), whereas the trend in other wards remained stable. Limitations: 1-year length, limited pre-intervention data, and no analysis of genetic variation in strains.	Moderate	Organism: *Klebsiella pneumoniae* carbapenemase-producing K. *pneumoniae* (KPC-KP)

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias	Comments
Ben-David et al., 2014[12]	Active surveillance and contact isolation for carriers, cross-sectional surveys to determine carrier prevalence, and periodic on-site assessments of facility infection control policies	Pre-post intervention study, hospitalized patients	Thirteen long-term acute care hospitals (LTACHs) in Israel (median, 209 beds; range, 104–320 beds)	Prevalence of carriage among those not known to be carriers decreased from 12.1% to 7.9% (p=0.008). Overall carrier prevalence decreased from 16.8% to 12.5% (p=0.013). The appropriate use of gloves was independently associated with lower new carrier prevalence.	Not provided	A multifaceted intervention was initiated between 2008 and 2011 as part of a national program involving all Israeli healthcare facilities. The intervention has included: Periodic on-site assessments of infection control policies and resources, using a score comprising 16 elements Assessment of risk factors for CRE colonization Development of national guidelines for CRE control in long-term acute care hospitals involving active surveillance and contact isolation of carriers Three cross-sectional surveys of rectal carriage of CRE that were conducted in representative wards.	Moderate	Organism: CRE

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias	Comments
Ben-David et al., 2019[13]	Implementation of a national real-time notification system for transfers and admission screenings, population-tailored contact precautions (CP), supervised inter-facility information exchange, and directed intervention at the institutional level during local outbreaks	Pre-post intervention study; 25,000 beds in over 300 institutions	Israeli Long-term care facility, including 15 LTACHs, 15 skilled nursing facilities (SNFs), and 300 nursing homes	The intervention included implementation of population-tailored CP and early detection of carriers. During the study period, incidence declined in all facility types, to approximately 50% of the baseline (p<.001). The number of SNFs and nursing homes experiencing ≥5 CRE acquisitions annually decreased from 35 to 11 during this period. The point prevalence of newly detected CRE carriage in long-term acute care hospitals decreased from 12.3% in in 2008 to 0.8% in 2015 (p<0.001).	Not provided	A key element was real-time notification of healthcare facilities upon detection of such cases (transfers/admission screenings), enabling timely contact tracing and local preventive measures. Uptake and implementation may have varied across institutions. There was implementation of population-tailored CP and early detection of carriers, a real-time repository of all CRE carriers and events of acquisition, supervised information exchange between healthcare facilities, and directed intervention at the institutional level during local outbreak.	High	This is a national-level real-time notification system and multi-facility intervention.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias	Comments
Borer et al., 2011[15]	Multicomponent intervention that included preemptive contact precautions for high-risk patients, improved signage for patients on contact precautions, dedicated staff and equipment (e.g., x-ray machines and monitors, visitor restriction and CP education, and assigned patient transport)	Pre-post intervention stud;, 8,376 patients	1,000-bed tertiary-care university teaching hospital, Israel	The CR-KP infection density was reduced from 5.26 to 0.18 per 10,000 patient-days ($p<0.001$), and no nosocomial infections were diagnosed.	Not provided	Researchers implemented "enforcement of CP compliance." Upon admission for high-risk patients: strict, preemptive CP; signage; 1:4 ratio of trained nurses to patients. In cohort ward: signage; strict isolation; dedicated nursing staff and equipment, including an x-ray machine and monitors. Visitors required patient permission and were educated about hand hygiene, use of gowns, gloves, etc. There was also assigned transport of patients.	Moderate to low	Organism: *Klebsiella pneumoniae* carbapenemase-producing K. *pneumoniae* (KPC-KP)

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias	Comments
DalBen et al., 2016[20]	Compliance monitoring and feedback for hand hygiene and contact precautions	Pre-post intervention with a 44-week baseline period and 24-week intervention period; 14 bed intensive care unit (ICU) (all patients admitted); mathematical model of intervention	ICU of a tertiary care teaching hospital; 14 beds; Brazil	During the baseline period, the calculated R_0 was 11; the median prevalence of patients colonized by CRE in the unit was 33%, and three times it exceeded 50%. In the intervention period, the median prevalence of colonized CRE patients went to 21%, with a median weekly R_0 of 0.42 (range, 0 to 2.1).	Not provided	Compliance was monitored using an audit and feedback routine with weekly meetings. During the baseline period, the ICU had to be closed three times as a measure to stop the spread of CRE. The prevalence of CRE-colonized patients on these occasions exceeded 50%. Each time the unit was reopened, prevalence rates soared rapidly. The goals for compliance with hand hygiene and CP were reached on the third week of the intervention period and were kept above target levels in all but weeks 6 and 8. Rates of compliance with CP went from 66% in the baseline period to a median of 84% in the intervention period.	Moderate	Organism: mainly KP, but study includes all CREs. Contact rates were assumed to be the same for every patient, which is generally not true and could bias the model.
Djibré et al., 2017[7]	Multicomponent intervention that included active surveillance and preemptive contact precautions for high-risk patients, improved CP signage, patient/visitor CP education, and use of personal protective equipment	Pre-post intervention study; Phase 1: n=413, Phase 2: n=368; medical and surgical ICU patients	20-bed medical and surgical ICU of a French university-affiliated hospital	The rate of acquired multidrug-resistant organisms (MDRO) (positive screening or clinical specimen) was similar during both periods (respectively, 10%, n=15 and 11.8%, n=15; p=0.66). The risk estimate of MDRO carriage using selected risk factors was feasible, and a zero-risk estimate	Not provided	Phase 1: admit screenings with preemptive additional CP; Phase 2: admit screenings with additional CP for patients with one or more risk factors. There was also weekly screening. Risk factors: exposure to antibiotics within the preceding 3 months, hospitalization within the preceding year, admission to another hospital department with a hospital stay of more than 5 days, immunosuppression, chronic dialysis, transfer from rehab,	High	

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias	Comments
	(PPE) (gowns and gloves)			had a very good negative predictive value, allowing a 19% reduction rate of the use of additional CP.		Long-term care unit, or nursing home, and travel abroad within 1 year. Standard precautions included hand hygiene, protective gowns and gloves in case of risk of contact with blood or bodily fluids, and gloves in case of lesions of the healthcare worker's hands. Additional CP included wearing gowns during contact with patient and bodily fluids, wearing gloves as part of standard precautions, door signs at the room entrance stating, "isolation screening" or "isolation confirmed," and oral education of the patients and relatives. Authors did not measure hand hygiene and CP compliance. Acquisition rates were estimated in 50% of population due to relatively short median length of stay and lack of follow-up or discharge sample.		

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias	Comments
Fedorowsky et al., 2015[26]	N/A	Cross-sectional study; self-administered questionnaires; 420 healthcare workers, including: registered/ academic nurses, practical nurses/ auxiliary staff, physicians, and paramedical staff	One acute care hospital and 1 LTACH in Israel (same HMO)	Staff engagement was negatively correlated with CRE acquisitions (r^2=0.25; p<0 .05), overwhelmed/ stress-chaos was positively correlated with CRE acquisitions (r^2=0.22; p<0.06), and hospital leadership showed no significant correlation with CRE acquisition (r^2=0.09; p>.05).	Not provided	When staff engagement was high, the probability of staff reporting compliance with patient isolation was 2x as high as the probability of their reporting noncompliance (p<0.01). High overwhelmed/stress-chaos scores also increased the probability of staff reporting not knowing what precautions to take before caring for a CRE carrier or the environment (p<0.05).	Moderate	Focuses on how work environment can affect CP compliance. Employees with <12 months on the job and students were excluded.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias	Comments
Jalalzaï et al., 2018[5]	Active surveillance in settings with universal contact precautions	Retrospective, uncontrolled pre-post intervention study; n=1,069; all patients admitted for 3 or more days during two consecutive 1-year periods with and without active surveillance cultures (ASC)	ICU of 1,100 bed French hospital	An ICU-acquired extended-spectrum beta lactamase *Enterobacteriaceae* (ESBL-E) infection occurred in 1.1% and 1.5% of patients admitted during the ASC and the no-ASC periods (p=0.64). An admission during the no-ASC period exerted no impact on the hazards of ESBL-E infections (adjusted OR 1.16, 95% CI, 0.38 to 3.50, p=0.79), in-ICU death (SHR 1.22, 95% CI, 0.93 to 1.59, p=0.15), and extended LOS (SHR for discharge 0.89, 95% CI, 0.79 to 1.01, p=0.08).	Not provided	Because universal CP are already in place in ICU settings, the study found active surveillance screening to be unnecessary and to have no effect on incidence of ICU-acquired infections. This study defined CP as single-use gloves and gowns in case of close contact with patients and potential exposure to body fluids during nursing, physiotherapy and other care not requiring full-barrier precautions.	Moderate to low	Organism: extended-spectrum beta-lactamase producing *Enterobacteriaceae*

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias	Comments
Kim et al., 2014[6]	Discontinuation of CP after three consecutive negative cultures taken 3 days apart, passive surveillance using only clinical samples, and strict CP with single-use gowns and gloves	Pre-post intervention study; n=5,790 isolates	Nine hundred-bed tertiary care university teaching hospital in South Korea	CRE incidence rates rose from 1.61 in 2008 to 5.49 in 2009; they rose further to 9.81 per 100,000 patient days in early 2010. After adoption of strict infection control measures, CRE frequency fell back in 2011 and remained at baseline afterward. Resistance rates began to decline, reaching baseline in 2011 ($p<0.001$), and remained at this level afterward.	Not provided	CP kept until three consecutive negative clinical cultures of the same specimen taken at least 3 days apart. Reduced incidence was accomplished without active surveillance. CP were implemented only with positive clinical samples (likely due to lower rates of CRE compared with in the United States). Hospital used strict individual CP with single-use gowns and gloves.	Moderate to low	Organisms: beta lactamase-producing CREs *(E. coli and K. pneumoniae)*

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias	Comments
Lowe et al., 2012[21]	Facility policies on CP discontinuation, risk factor-based screening, and patient isolation	Cross-sectional survey; 15 facilities (6 academic and 9 community hospitals)	Toronto, Canada	There was wide variation in the use of infection control practices for ESBL-E and CRE, respectively, including admission screening (53% and 53%), CP (53% and 100%), and isolation (60% and 100%). Of hospitals performing admission screening, 75% used risk factor-based screening for ESBL-E and CRE.	Not provided	One hundred percent of respondents' facilities use CP on all patients, 6.7% discontinue after one negative specimen, 26.7% discontinue after three negative specimens separated by 1 week, 53.3% continue until discharge, 13.3% have unknown practices, and 33.3% have written infection control policies. The study was conducted only shortly after Canadian guidance for CRE had been released, and hospitals may have been in the process of developing or modifying their practices with respect to CRE. Because of the low prevalence of CRE in Toronto, there is limited experience managing CRE infected/colonized patients from an infection control perspective.	High	Organism: CRE

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias	Comments
Molter et al., 2016[17]	Multicomponent intervention that included weekly staff education, an interdisciplinary outbreak response team, PPE use including facemasks and head protection, dedicated equipment, and patient cohorting with dedicated staff and equipment	Outbreak study, n=10	Tertiary care hospital with 18 bed medical intensive care unit and 18 bed surgical intensive care unit, Germany	There was no contamination of environmental surfaces or equipment, and no new cases, after 4 days of intervention.	Suspected breaches in infection control such as incomplete environmental cleaning and poor hand hygiene may have led to prolonged dissemination of carbapenem-resistant *Acinetobacter baumannii*.	Researchers implemented weekly educational sessions for all personnel. Crucial to the successful outbreak containment was the rapid establishment of an interdisciplinary outbreak intervention team, which instituted infection control measures, including closing the ICU for new admissions, and extended CP including hand hygiene, gowns, gloves, face masks, head protection, cohorted staff and patients and contact patients, individual supplies/ equipment, and separate communal facilities.	Moderate to high	Organism: Carbapenem-resistant *Acinetobacter baumannii*
Robustillo-Rodela et al., 2017[11]	Multicomponent intervention that included staff education, patient and staff cohorting, and in-depth environmental cleaning of the ICU	Outbreak study; ICU	Acute care hospital in Bolivia	Cumulative incidence of OXA-48 (a type of carbapenemase) decreased 77% ($p<0.05$), whereas multidrug-resistant *Acinetobacter baumannii* did not change.	Not provided	The ICU already had strict CP before the outbreak, including gowns and gloves for any contact with patient. During outbreak, CP training was given to staff, among other interventions.	Moderate to high	Organisms: OXA-48 *Enterobacteriaceae,* multidrug-resistant *Acinetobacter baumannii*

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias	Comments
Rossi Gonçalves et al., 2016[16]	Multicomponent intervention that included hand hygiene promotion and education, environmental cleaning monitoring, dedicated equipment, and active surveillance.	Outbreak study; n=111	University hospital in Brazil	Infection control measures were strengthened at the time of the first outbreak to include hand hygiene promotion and supervised cleaning of bed spaces and rooms. Sharing of patient equipment was limited as much as possible, and a program of structural repairs on the AICU was implemented.	Outbreak was not contained, and the ward was eventually closed to new admission.	CP were implemented during outbreak in addition to bedside alcohol gel and active screening. Poor CP/infection control compliance is implicated, but monitoring was not done. There was anecdotal observation of inappropriate use of gloves.	Moderate to high	Organism: KP-KPC
Schwaber et al., 2011[14]	National policy development that implemented intervention monitoring using active surveillance and daily feedback, patient isolation and cohorting, and dedicated staff and equipment	Pre-post intervention study; 1,275 cases; 27 acute care hospitals (ACHs) with 13,040 beds	Israeli ACHs	Pre-intervention, the monthly incidence of nosocomial CRE was 55.5 cases per 100,000 patient-days. During intervention the increase in incidence stopped, and eventually it reduced to 11.7 cases per 100,000 patient-days (p=0.001). There was a direct correlation between compliance with guidelines and success in containment of transmission (p=0.02).	Not provided	The Israeli Ministry of Health task force paid site visits at acute-care hospitals, evaluated infection control policies and laboratory methods, supervised adherence to the guidelines via daily census reports on carriers and their conditions of isolation, provided daily feedback on performance to hospital directors, and intervened additionally when necessary. There was also placement of patients in self-contained nursing units—either single rooms or cohorts—containing all materiel needed for their care and staffed by dedicated nurses on all shifts.	Moderate to low	Organism: CRE Author is consultant of MSD, Johnson & Johnson, and Intercell.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias	Comments
Sypsa et al., 2012[18]	Mathematical model that measured the effects of improved hand hygiene compliance, active surveillance, and patient isolation and cohorting	Prospective observational study and mathematical model of intervention; n=850 surgical unit patients	30-bed Greek tertiary care hospital	Simulation results: Hand hygiene alone did not decrease colonization prevalence in model. With 60-80% hand hygiene compliance there would be a 60-90% reduction in number of colonized admissions.	Not provided	The Ross-Macdonald model for vector-borne diseases was applied to obtain estimates for the basic reproduction number R_0 and assess the impact of infection control measures on CP-KP (Carbapenemase-producing *Klebsiella pneumoniae*) containment in endemic and hyperendemic settings.	Moderate to high	Organism: CP-KP
Toth et al., 2017[19]	Mathematical model that measured the effects of enhanced contact isolation and improved outbreak response time	Model-based intervention study	One LTACH, 6 nursing homes, 3 ACHs; Utah-based data	Model showed reductions in CRE transmissions by 79-93%.	Delaying intervention until the 20th case reduced transmissions by only 60-79%.	Model was for LTACH-focused intervention in a previously CRE-free region. The enhanced isolation model accounted for patients contributing 75% less to transmission rate compared with 50% for standard isolation.	High	Organism: CRE COI: Author received personal fees from Promise Hospital of Salt Lake.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias	Comments
Viale et al., 2015[28]	Multicomponent intervention that included active surveillance for high-risk units or roommates of CRE-positive patients, patient isolation/ cohorting with strict CP, and staff education on CP and hand hygiene	Pre-post intervention study; n=1,571 CRE-positive cultures	1,420-bed teaching hospital in Italy	Following the intervention, the incidence rate of CRE bloodstream infections (risk reduction 0.96, 95% CI, 0.92 to 0.99, p=0.03) and CRE colonization (risk reduction 0.96, 95% CI, 0.95 to 0.97, p<0.0001) significantly decreased over a period of 30 months.	Not provided	The intervention consisted of the following: (a) rectal swab cultures were performed in all patients admitted to high-risk units (ICUs, transplantation, and hematology) to screen for CRE carriage, or for any roommates of CRE-positive patients in other units; (b) cohorting of carriers, managed with strict CP; (c) intensification of education, cleaning, and handwashing programs; and (d) promotion of an antibiotic stewardship program (carbapenem-sparing regimen). Researchers stated that targeted screening of populations and units expected to be at high risk for serious CRE infection makes definitive calculation of CRE carrier incidence rates impossible, and that these rates are potentially underestimated.	Moderate	Organism: CRE

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias	Comments
Zimmerman et al., 2013[25]	N/A	Ambidirectional cohort study; 137 patients; adult hospitalized patients with at least one CRE-positive culture	700-bed teaching hospital in Israel	N/A	Not provided	Mean time to CRE negativity was 387 days (95% confidence interval: 312 to 463). Seventy-eight percent of patients (64/82) had a positive culture at 3 months, 65% (38/58) at 6 months, and 39% (12/30) at 1 year. Duration of carriage was affected by repeated hospitalization (p=0.001) and clinical, as opposed to surveillance, culture (p=0.002).	Moderate to low	Relevant to discontinuation of CP

Table B.44: Anticoagulants, Ambulatory Setting–Systematic Reviews

Note: Full references are located in the Section 7.1 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/ Findings	Notes
Canadian Agency for Drugs and Technologies in Health, 2011[1]	Specialized anticoagulation services that include patient self-testing or self-management, as compared with other specialized anticoagulation services or usual care (defined as dose adjustment managed by a non-hematologist physician who also treats other medical problems)	Adult patients receiving long-term warfarin treatment, most for atrial fibrillation but also including some patients with thromboembolism	One health technology assessment, 8 systematic reviews or meta-analyses, 6 randomized controlled trials (RCTs), and 12 non-RCT studies were included. Specialized anticoagulation services had significantly more favorable time to therapeutic range (TTR) compared with usual care. Improved TTR did not correlate with reduction in hemorrhage, thromboembolism, or need for additional medical care. Patient self-testing or patient self-management had mixed results, with some studies finding improved TTR and others finding no difference as compared with usual care. In most studies, patient self-testing/self-management resulted in lower mortality rates and reduced incidence of thromboembolism, but rate of bleeding events did not differ between specialized and usual care. Some evidence suggests that patient self-testing/self-management may improve quality of life.	Not provided	None

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/ Findings	Notes
Entezari-Maleki et al., 2016[2]	Pharmacist-managed warfarin therapy, usually in a primary care clinic using a protocol approved by physician specialists	Outpatient settings comparing pharmacist-managed warfarin therapy with "usual medical care"	Of 24 included studies, 4 were RCTs and 20 were observational studies. A total patient population of 11,607 was included. In non-RCT studies, pharmacist-managed patients had a significantly higher percentage of time in the therapeutic range (72.1% vs. 56.7%; p=0.013) and significantly fewer major bleeding events (0.6% vs. 1.7%, p<0.001), thromboembolic events (0.6% vs. 2.9%; p<0.001), instances of hospitalization (3% vs. 10%; p<0.001), and emergency department (ED) visits (7.9% vs. 23.9%; p<0.0001), as compared with patients managed with usual medical care. No cases of mortality were noted among the non-RCT studies. In RCT studies, pharmacist-managed and usual care groups did not significantly differ in the following outcomes: percentage of time in therapeutic range, major bleeding events, mortality, instances of hospitalization, and ED visits. No thromboembolic events were observed in the four included RCTs. One report on health-related quality of life did not find significant differences between pharmacist-managed and usual care. With the exception of one RCT, included studies indicated cost savings in the pharmacist-managed service as compared with usual care.	Not provided	None
Hou et al., 2017[3]	Pharmacist-managed warfarin therapy	Studies comparing pharmacist management of warfarin and any other model, e.g., physician-managed, nurse-managed	Of 17 included studies, 8 were RCTs and 9 were observational cohort studies. A total of 9,919 patients were included. Overall study quality was reported to be high, as evaluated by two independent reviewers using GRADE. In pooled results of the RCTs, the following outcomes were not significantly different between groups: TTR, hemorrhage events, thrombosis events, and mortality. In pooled results of the observational studies, TTR was significantly higher in the pharmacist-managed group, and risks of hemorrhage and thrombosis events were significantly lower in the pharmacist-managed group. Two included studies that reported on cost found that pharmacist management resulted in a significant decrease in cost.	Not provided	None

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/ Findings	Notes
Manzoor et al., 2017[5]	Pharmacist-managed outpatient warfarin clinics	Outpatient settings; patients receiving warfarin therapy for any reason	Of 25 included studies, 3 were RCTs and 22 were observational studies that included a comparison group of some kind. A total of 12,252 participants were included. In the majority of studies (23 out of 25), the pharmacist-managed group showed better quality of anticoagulation control as compared with regular medical care, as indicated by TTR. In 10 of 12 studies that reported on the outcome, the pharmacist-managed group also had lower or equal risk of major bleeding as compared with usual care. In 9 of 10 studies that reported on the outcome, the pharmacist-managed group had lower or equal risk of thromboembolic events as compared with usual care. In 9 of 9 studies that reported on the outcome, the pharmacist-managed group had decreased rates of hospitalization, shorter length of hospital stay, and fewer ED visits as compared with usual care. In 6 of 6 studies that reported on cost, the pharmacist-managed group had cost savings as compared with usual care.	Not provided	None
Satokaew et al., 2010[11]	Pharmacist-participated warfarin therapy management (PWTM)—may include dosage adjustment, medication/drug interaction review, and/or providing patient or provider education	Various—both acute and ambulatory; Three studies included only surgical patients; others included all patient groups	Of 24 included studies, 5 were RCTs, 9 were quasi-experimental studies, and 10 were cohort studies. A total of 728,377 patients were included in the meta-analysis. In RCTs, PWTM was significantly associated with a 49% reduction in total bleedings (relative risk [RR], 0.51; 95% confidence interval [CI], 0.28 to 0.94) compared with usual care without heterogeneity. In 19 non-RCTs, PWTM was significantly associated with a 29% reduction in total bleedings (RR, 0.71; 95% CI, 0.52 to 0.96; p=0.028) when compared to usual care. For major bleeding (4 RCTs), the RR for PWTM vs. usual care was 0.64 (95% CI, 0.81 to 2.36; p=0.507) without heterogeneity. In 11 non-RCTs, PWTM was significantly associated with a 51% reduction in major bleedings (RR, 0.49; 95% CI, 0.26 to 0.93; p=0.030). Out of four RCTs, the RR for PWTM vs. usual care on thromboembolic events was 0.79 (95% CI, 0.33 to 1.93; p=0.610) without heterogeneity. In 15 non-RCTs, PWTM was significantly associated with a 63% reduction in thromboembolic events (RR, 0.37; 95% CI, 0.26 to 0.53; p<0.001) without heterogeneity. There was no significant difference in mortality between PWTM and usual care in either RCTs or non-RCTs.	Not provided	None

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/ Findings	Notes
Zhou et al., 2016[4]	Pharmacist-managed warfarin therapy as compared with other models	Various	Eight randomized controlled trials with a total of 1,493 patients were included. In the pooled meta-analysis, pharmacist-managed models had significantly higher patient satisfaction and a higher percentage of time within the standard therapeutic range as compared with all other models. The models did not significantly differ on time within the expanded therapeutic range, mortality, and incidence of bleeding and thromboembolic events.	Not provided	None

Table B.45: Anticoagulants, Ambulatory Settings —Single Studies

Note: Full references are available in the Section 7.1 reference list.

Author, Year	Description of PSP	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Risk of Bias (High, Moderate, Low)
Duran-Parrondo et al., 2011[5]	Followup by a pharmacist within primary care, who provided patient education for 12 months—providers in primary care setting did not provide management of anticoagulation, only patient education	Controlled trial; 272 patients followed by pharmacist, 460 controls; patients receiving oral anticoagulation therapy under the care of a hematologist	Four primary care clinics in northwest Spain	Compared with the control group, the intervention group improved its proportion of individuals with international normalized ratio (INR) results within 0.5 units of the target range by 25% (relative risk [RR]=0.75; 95% confidence interval [CI] 0.69 to 0.82) and by 26% (RR=0.74; 95% CI, 0.67 to 0.81) for those within 0.75 units of the target range. Patients belonging to the intervention group additionally had a 75% reduction in bleeding (hazard ratio [HR]=0.25; 95% CI, 0.18 to 0.36). The intervention group had an 8% reduction (odds ratio 0.92; 95% CI, 0.88 to 0.96) in the number of medical consultations required to maintain individual patients' INR within the correct range. Additionally, the intervention group had a fivefold reduction (HR=0.20; 95% CI 0.13 to 0.32) in the need to use rescue medications. There was no significant difference between the two groups in incidence of thromboembolic events or in the number of times that the dose needed to be adjusted to maintain the correct range.	Low: not randomized
Hassan et al., 2013[9]	Telephone-based warfarin management by nurse practitioner—phlebotomist visited patients' homes to draw blood samples, and the nurse practitioner called the patient to communicate results and direct dosage adjustment	Observational; 448 homebound patients receiving warfarin therapy for at least 3 months from 2000 to 2011	Patients' homes	The mean percentage of INR values in range was 58.39%. The mean time of the INR in therapeutic range (TTR) was 62.75%. The percent of patients who were therapeutically controlled decreased as the number of medications increased. The complication rate was 4% per patient year, with an equal distribution between bleeding and clotting. The cost per visit at the anticoagulation clinic was found to be approximately $300, compared with $82 when using the homebound service.	Moderate: no control group

Author, Year	Description of PSP	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Risk of Bias (High, Moderate, Low)
Hawkins et al., 2018[6]	Management of stable, in-range warfarin by pharmacy technicians as opposed to pharmacists	Retrospective cohort; 2,956 patients—1,840 managed by pharmacy technicians and 1,116 receiving usual care (pharmacist-managed); patients receiving chronic warfarin therapy with INR within therapeutic range 100% of the time during the 3 months prior to the index date	One integrated healthcare delivery system with a centralized pharmacy team that provides anticoagulation management for > 10,000 patients	The technician group had a higher percentage of in-range INRs (mean difference=6.8%; 95% CI, 5.0% to 8.7%) and patients with 100% TTR (mean difference=10.5%; 95% CI, 7.0% to 14.0%) during followup. The propensity-weighted 6-month followup mean TTR was 83.3% (95% CI, 82.4% to 84.2%) in the technician group and 77.7% (95% CI, 76.4% to 78.9%) in the usual care group, with a mean difference of 5.7% (95% CI, 4.1% to 7.2%. The mean difference did not cross the noninferiority margin of -2.5%, indicating that technician management was noninferior to usual care. There was no significant difference between groups in incidence of thromboembolic events. Bleeding (HR=0.60; 95% CI, 0.39 to 0.94; p=0.026) and all-cause mortality (HR=0.44; 95% CI, 0.25 to 0.77; p=0.004) were lower in the technician group during followup.	Low-to-moderate: no random assignment, single health care system—findings may not be generalizable
Lee et al., 2018[7]	Telephone-based warfarin management using either local laboratory testing or patient self-testing, as compared with face-to-face management by a pharmacist	Retrospective cohort; 336 patients on established warfarin therapy, with those not living within a given proximity of the clinic eligible for either local laboratory or self-testing	Academic medical center providing outpatient care in both rural and urban settings across a single U.S. State	INR TTR for face-to-face management was significantly greater than for distance management using local laboratory testing (69.0% vs 60.5%, p=0.0032). No difference was observed between face-to-face management and patient self-testing (69.0% vs 68.0%, p=0.25). No significant difference in bleeding or thromboses was observed. Although increased clinician time was used during face-to-face encounters compared with telephone encounters (8.7-minute face-to-face, 5.5-minute local laboratory, and 5.4-minute patient self-testing), face-to-face encounters tended to be billable at lower levels, whereas telephone-based encounters were billable at higher levels.	Moderate: no random assignment; relatively small sample size; single health care system—findings may not be generalizable

Author, Year	Description of PSP	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Risk of Bias (High, Moderate, Low)
Philip et al., 2015[8]	Telephone-based anticoagulation management by clinical pharmacists	Quasi-experimental; 502 patients (301 pre-intervention and 201 post-intervention); randomly selected patients who had not been hospitalized in the past 12 months and had at least three consecutive INR readings within the target therapeutic range	Four ambulatory care centers within one health system	The mean number of visits per month for the clinical pharmacy service significantly differed between the pre-intervention group and the post-intervention group (270 vs. 313; p=0.011). The following outcomes were not significantly different between the two groups: percentage of clinical pharmacy visits for anticoagulation management, elapsed time to the third available clinic appointment, number of clinical pharmacy visits for anticoagulation management, percentage of INR values in the therapeutic range, proportion of hospitalizations due to thromboembolic or bleeding events, pharmacist work hours per prescription volume.	Moderate: no true control group; single health care system—findings may not be generalizable

Table B.46: Anticoagulants, Protocols for Newer Oral Anticoagulants—Single Studies

Note: Full references are located in the Section 7.2 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
Ansara et al., 2009[8]	Weight-based dosing nomogram for argatroban to treat Heparin-induced thrombocytopenia (HIT)—one nomogram for standard and one for hepatic/ critically ill	Observational, retrospective study; N=51 patients prospectively treated for suspected or documented HIT: n=34 patients treated with the standard nomogram, n=17 with the hepatic/critically ill nomogram	One community hospital	Mean time to activated partial thromboplastin time (aPTT) stabilization was 16.25 hours with the standard nomogram and 27.05 hours with the hepatic/critically ill nomogram. The percentages of patients with aPTTs within the therapeutic range at 6, 12, 24, 48, 72, and 96 hours were 82.4%, 82.4%, 88.2%, 96.4%, 100%, and 100% with the standard nomogram and 58.8%, 82.4%, 76.5%, 93.3%, 100%, and 90.9% with the hepatic/critically ill nomogram. No statistical significance examined.	Three cases of major bleeding occurred in patients dosed on hepatic/critically ill nomogram, although the authors asserted they were not attributable to argatroban. No bleeding events in the standard nomogram patients. There were no thrombotic events after the initiation of argatroban during hospital stay. One patient died during the observation, although this was attributed to other factors.	Not provided	High: no control group, small sample size, one health system—not generalizable

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
Burcham et al., 2013[14]	Simplified dosing nomogram for nurses to administer intravenous bivalirudin for heparin-induced thrombocytopenia, which specifies fixed adjustments (0.005 or 0.01 mg/kg/hr) according to the current aPTT value relative to aPTT goals	Observational, retrospective study n=65 patients who received continuous infusion of bivalirudin for suspected or confirmed HIT during 3-year period	One academic medical center intensive care unit	Mean time to aPTT stabilization was 11.0 hours (range, 5.0–31.8 hours). Nurse adherence to the nomogram was 100%, and no dosing errors occurred during a total of 487 dosage changes. Overall, 53.7% of the aPTT values were in the target range (30.5% of values were above target, and 15.8% were below target). The median bivalirudin dosage for all patients at steady state was 0.04 mg/kg/hr (range, 0.02–0.07 mg/kg/hr), the median length of bivalirudin treatment was 49 hours (range, 29.0–190.5 hours), and the median number of dosing changes per patient was 4.0 (range, 1.5–8.5 changes), with a median of 1.2 dosing changes per day. After the pilot study, the nomogram was adjusted for patients with creatinine clearance values of >30 mL/min. Provided more direction for initial dosing, too.	Bleeding occurred in 20 (30.8%) of the evaluated patients, with 7 (10.8%) meeting the criteria for a major bleed and 13 (20%) having a minor bleed. All-cause mortality was 41.5%, and the median hospital length of stay was 28 days (range, 2–104 days).	Not provided	High: no control group, small sample size, one health system—not generalizable

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
Draper et al., 2017[17]	Anticoagulation service to encourage adherence to novel oral anticoagulant prescribing protocols	Observational, retrospective study; N=1,518 total prescriptions; all initial prescriptions of apixaban, dabigatran, and rivaroxaban to adults 18 and older over 4-year period; 1,518 total initial prescriptions were issued: 247 for apixaban (16%), 537 for dabigatran (36%), and 734 for rivaroxaban (48%)	One large multicenter, multispecialty group practice	Seventy-two percent of apixaban, 52% of dabigatran, and 70% of rivaroxaban prescriptions were per protocol. Therefore, 24–45% of prescriptions were potentially inappropriately prescribed. The most common reasons for nonadherence to protocol for apixaban and rivaroxaban were off-label indications (11% and 13%, respectively) and dosage too low (11% and 11%, respectively). Age greater than 75 years (35%) and off-label indication (5%) were the most common reasons for not per protocol dabigatran prescriptions. A minority of patients enrolled in the anticoagulation service: 24% of patients receiving apixaban, 22% receiving dabigatran, and 27% receiving rivaroxaban. Enrollment in anticoagulation service was low across the direct acting oral anticoagulants (22–27%). Based on a test of significance, enrollment in the anticoagulation service was not associated with increased adherence to protocols.	Not provided	Not provided	Moderate-to-high: patients not randomly assigned to participate in anticoagulation service, one health system—not generalizable

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
Smythe et al., 2012[15]	HIT recognition and management protocol	Pre-post evaluation; N=49 patients started on direct thrombin inhibitors (DTI) post-protocol implementation; 4-month period before implementation compared with 4-month period after implementation	One academic medical center	Correct protocol-directed initial DTI dose ordered for 100% of patients, compared with only 31% of patients during the pre-implementation period. Prior to protocol implementation, the appropriate documentation of HIT in the medical record was lacking in >15% of cases. During the post-implementation period, documentation of HIT was found in the electronic medical record of 100% of patients with suspected or confirmed HIT at the time of discharge.	Not provided	The authors describe the establishment of a multidisciplinary HIT working group that conducted a needs assessment, developed and revised protocols, and conducted education on the protocols.	High, no control group, small sample size, one health system

Table B.47: Anticoagulants, Transitions Between Hospital or Emergency Department and Home —Single Studies

Note: Full references are located in the Section 7.3 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Risk of Bias (High, Moderate, Low)
Barbic et al., 2018[17]	Atrial fibrillation and flutter (AFF) pathway developed at the study site by emergency physicians, cardiologists, and pharmacists. The pathway consists of a care map, decision aids, medication orders, management suggestions, and electronic consultation or referral documents, all embedded into the computerized physician order entry and integrated electronic medical record program.	Pre-post; 301 (129 pre-pathway and 172 post-pathway); patients presenting in the emergency department (ED) with final diagnosis of AFF	Two EDs—one academic inner-city medical center, one community hospital; Vancouver, BC	The rates of new anticoagulation on discharge from the ED for patients who were incorrectly not on anticoagulation at ED arrival were 51/105 (48.6%, 95% confidence interval [CI] 42.1% to 55.1%) in the pre group and 97/138 (70.2%, 95% CI, 62.1% to 78.3%) in the post group, for an absolute difference of 20.6% (95% CI, 15.1% to 26.3%). The 30-day ED revisit rate for congestive heart failure decreased from 13.2% (pre) to 2.3% (post) (absolute difference of 10.9%; p<0.01 [95% CI, -8.1% to -13.7%]). Median ED length of stay decreased from 262 to 218 minutes (44 minutes [p<0.03; 36.2–51.8]). There were no significant differences between pre and post groups on the following outcomes: 30-day ED revisit for stroke, major bleeding, or AFF; death within 30 days; outpatient clinic referral.	Moderate-to-high: small sample size, no comparison group
Castelli et al., 2017[14]	Rivaroxaban Patient Assistance Kit (R-PAK)	Randomized controlled trial—patients randomized to receive either education by a pharmacist plus the R-PAK or education by pharmacist alone; 25 patients; patients newly diagnosed with acute venous thromboembolism(s) (VTE) and treated with rivaroxaban	Hospital discharge from one community teaching hospital	No difference in the baseline assessment of health literacy status was noted (p=1.00). Proper transition to daily administration on Day 22 was no different between the groups (p=0.891). Adherence was reported in 99.8% of R-PAK patients and 97.65% of control patients (p=0.074). There was no significant difference between the two groups on any of the following outcomes: percentage of patients who stopped rivaroxaban for any reason, patient understanding of correct timing and dose of medication, overall patient satisfaction, self-reported side effects, recurrent VTE, death.	High: very small sample; single site

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Risk of Bias (High, Moderate, Low)
Chu and Limberg, 2017[15]	Commercially available medication dose pack with counseling by ED pharmacist	Retrospective cohort; 75 patients (41 received intervention, 34 received usual care); patients discharged from ED on rivaroxaban with a discharge diagnosis of VTE	Discharge from ED in one urban community hospital	No statistically significant differences were found between the two groups on the following outcomes: medication adherence beyond the first month after discharge, 90-day readmission for recurrent VTE due to nonadherence or treatment failure, 90-day readmission due to bleeding or adverse event.	High: very small sample; single site
DiRenzo et al., 2018[16]	Pharmacist management of rivaroxaban, as compared with management by primary care provider	Prospective cohort; pharmacist-managed patients (n=17) were seen for low-risk VTE in the ED over a 5-month period in 2015; Comparison group (n=17) was selected from the outpatient pharmacy records and matched to patients in intervention group on month and year of rivaroxban initiation, age, and sex	One academic, safety-net medical center in a metropolitan city	There were no significant differences between groups 6 months after diagnosis in major bleeding, recurrent thromboembolism, fatal event due to either bleeding or thromboembolism, number of hospitalizations after diagnosis, adverse events, or Morisky medication adherence score. Only one complication (recurrent thromboembolism) occurred in each group. Only eight patients in the pharmacist group were assessed for medication adherence, compared with no patients in the comparison group.	Moderate-to-high: small sample size; no random assignment; one health system—not generalizable
Stafford et al., 2011[18]	Home-based post-discharge warfarin management service adapted from the Australian Home Medicines Review program—includes home visits for patients with INR monitoring and a summary of the patient's inpatient warfarin therapy sent to the patient's general practitioner, from which the general practitioner may make adjustments	Prospective cohort; 268 patients (129 intervention, 139 controls); adults being discharged from the hospital with an indication for ongoing warfarin therapy for at least 3 months	Eight hospitals across five metropolitan, rural, and remote regions of Australia	The intervention was associated with significantly decreased major and minor hemorrhagic events at 90-day followup post discharge (5.3% vs. 14.7%; p=0.03) and at 8-day followup (0.9% vs. 7.2%; p=0.01) as compared with usual care. The rate of combined hemorrhagic and thrombotic events at Day 90 also decreased (6.4% vs. 19.0%; p=0.008) and persistence with warfarin therapy improved (95.4% vs. 83.6%; p=0.004). No significant differences in readmission and death rates or time to therapeutic range or international normalized ratio control were demonstrated.	Low-to-moderate: moderately small sample size

Table B.48: Harms Due to Diabetic Agents, Insulin Protocols–Single Studies

Note: Full references are available in the Section 8.1 reference list.

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Cavalcanti et al., 2009[4]	Computer-assisted insulin protocol (CAIP) to maintain blood glucose levels between 100 and 130 mg/dL	The study compared three types of protocols used to obtain glucose control during an intensive care unit stay. The sample size was 165 patients.	Five intensive care units from five different Brazilian institutions	The mean of patients' median blood glucose was 125.0 (plus/minus 17.7) for CAIP, 127.1 (plus/minus 32.2) for Leuven, and 158.5 (plus/minus 49.6 mg/dL) for conventional treatment. The incidence of hypoglycemia was lower in the CAIP group than in the Leuven group, but higher in the CAIP than the conventional treatment. When episodes of hypoglycemia were considered in relation to the number of blood glucose (BG) measurements done, patients in CAIP protocol had a mean of 0.43 percent of glucose measurements below 40 mg/dL compared with 0.55 percent in Leuven group (P=04) and 0.03 percent in conventional group (P=.007).	Although the CAIP group when compared with Leuven had a lower risk of hypoglycemia, the risk was still considerable.	Acceptance of the insulin protocol by the nursing staff is critical for smooth implementation. The nurses who implemented the treatment judged it in terms of complexity and time spent to execute the protocol tasks: 11.7% found the CAIP difficult or very difficult as compared with 38.4% for Leuven protocol and 13.3% for conventional treatment.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Clergeu et al., 2017[5]	Use of a paper-based dynamic insulin infusion protocol (DP). The DP is a paper-based dynamic sliding-scale insulin protocol (SP).	One-year prospective study that compared two continuous intravenous insulin infusions—(1) dynamic insulin infusion protocol, (2) sliding scale static protocol—and the effects on glucose variability and hypoglycemia. One hundred thirty-one patients were included: SP (n=65), DP (n=66). Outcomes of interest included: mean BG (mmol/L), time spent in the target range (140-180 mg/dL to 7.7-9.9 mmol/L), time spent at greater and less than target range, and time before the first glucose value in the target range, low blood glucose (BG) episodes (<80 mg/dL-4.4 mmol/L), hypoglycemia (<60 mg/dL-3.3 mmol/L), and severe hypoglycemia (<40 mg/dL-2.2 mmol/L).	Intensive care unit (ICU) of French university hospital	Low BG (<4.4 mmol/L) and hypoglycemia (<3.3 mmol/L) were more frequent in the SP group than in the DP group. In cases of hypoglycemia, direct intravenous dextrose infusion (triggered by glucose values less than 3.3 and 4.1 mmol/L) occurred more frequently in the SP group than the DP group (0.17 plus/minus 0.49 and 0.03 plus/minus .17 dextrose injection per patient; P=0.03).	SP is not recommended because it was previously demonstrated to provide less control of parameters (blood glucose variability, hyperglycemia, and hypoglycemia).	Twenty-eight percent of nurses who completed the satisfaction survey felt that SP was suitable for ICU patients, compared with 66% of nurses who selected DP. The DP was also found to be more complex.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Donsa et al., 2017[11]	An algorithm-driven basal-bolus insulin regimen implemented through a computerized workflow and decision support system	A post-hoc analysis that used a before and after study design. The study included data from 70 type 2 diabetes patients. Diabetes management with a paper-based protocol for an algorithm-driven basal-bolus insulin therapy was compared to diabetes management with a computerized protocol for an algorithm-driven basal-bolus insulin therapy.	Division of Endocrinology and Metabolism at the Department of Internal Medicine at the Medical University of Graz, Austria.	Detection of Error Outcomes: Number of BG documentation errors and median absolute error were similar in both groups (p>0,2), 64.7% paper and 43.4% computer. Effect on Insulin Dose Outcomes: 11.1% of paper and 23.9% of computer of the BG documentation errors affected the results of bolus insulin dose calculations. Clinical Impact Outcomes: In the paper group, insulin dosing errors had a statistically significant influence on hypoglycemia. In the computer group, no statistically significant effects of insulin dosing errors on hypo or hyperglycemia were noted.	Not provide	Nurses performed 85% of all tasks and 80% of tasks including insulin dose calculations. The majority of errors affecting insulin dose calculations were from nurses when using the paper protocol. The relative frequency and absolute amount of insulin dosing errors were higher for physicians.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Dortch et al., 2008[9]	Automated nurse-driven computer-based protocol	A retrospective investigation of patients treated with a manual, paper-based, nurse-driven, glycemic control protocol compared to an automated nurse-driven computer-based protocol. Five hundred fifty-two patients were included in the study.	A 31-bed integrated acute and subacute ICU	The computerized protocol group was associated with lower rates of hypoglycemia. The absolute rate of hypoglycemic glucose levels was significantly lower in the computerized protocol group than with the manual protocol: 23 of 10,0003 (0.2%) vs. 60 of 11,175 (0.5%). Proportionately fewer patients among the computerized protocol group experienced 2 or more hypoglycemic events: 3 patients of 243 (1.2%) vs. 13 of 309 (4.2%), p=.04.	Computerized protocol group experienced a greater rate of nosocomial infections.	After implementation of the computerized protocol, the proportion of study glucose values in the ideal range improved in all patients, regardless of the need for insulin. It also worked with nursing workflows, and overall compliance was good.	Not provided	None
Doyle et al., 2014[10]	Implementation of pre-printed insulin orders to standardize insulin-prescribing practices, promote use of basal and mealtime insulin, reduce reliance on sliding-scale insulin as the only form of diabetes treatment, and standardize hypoglycemic management.	Two pilot phases involving two inpatient units (cardiology and nephrology) and the implementation of pre-printed insulin orders.	Bilingual Canadian multicampus tertiary care hospital with more than 1,100 beds and 47,000 patient admissions yearly	The rate of hypoglycemia was reduced after the implementation of the intervention. The number of high BG days (2 or more documented BG readings over 11 mmol/L in 24 hours) did not improve on either unit.	Small increase in the number of days with 2 BG readings over 11 mmol/L was observed	Utilization of the order forms increased with additional education, development, and dissemination of decision-support tools and improved access to forms. It went from 11% in nephrology and 38% in cardiology to 68% and 74%, respectively.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Jakoby et al., 2012[6]	Transition order set	Prospective study with a retrospective control group	Nine-bed medical ICU at Hadassah Hospital in Jerusalem Israel.	Hypoglycemia in the protocol group was rare. Of the 9,893 blood glucose measurements, only 11 measurements (0.11%) in six patients were less than 70 mg/dL.	Not provided	Protocol was more time consuming for nurses, but nurses reported protocol was useful and an instructive tool for glucose control.	Not provided	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Joyner Blair et al., 2018[13]	Utilization of evidence-based diabetic ketoacidosis order set	Purpose of study: whether utilization of an evidence-based diabetic ketoacidosis order set vs. an individualized provider approach decreases resolution time and occurrences of hypoglycemia and improves clinical outcomes. Design: retrospective chart review of demographic and outcome variables for nonpregnant patients admitted and treated for diabetic ketoacidosis during two periods (2/2016 to 7/2016 and 8/2016 to 12/2016). A team of hospital experts developed, implemented, and evaluated the evidence-based order set. The sample included 150 nonpregnant adults, 19 years or older, with type 1 or type 2 diabetes presenting to the emergency department and diagnosed with diabetic ketoacidosis during the data collection periods.	Level II trauma cent/ED and/or critical care unit of a 500-bed acute care academic medical center in West Central Georgia	Length of stay, arrival to intravenous fluid time, intravenous insulin initiation to discontinuation time, arrival to subcutaneous insulin administration time, time from initial to sequential laboratory testing, use of basal, prandial, and correction insulin approach, and the frequency of hypoglycemia. None of the t-tests were significant.	Not provided	Team members were expected to implement and follow the approved order set, but utilization was not required and the ability of providers to follow and adhere to protocol was not assessed.	Not provided	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Khalaila et al., 2011[8]	Nurse-led self-adjusting, standardized intravenous insulin protocol	Prospective study with a retrospective control group. There were 96 patients in the prospective study and 153 patients in the retrospective control group	Nine-bed medical intensive care unit	Hypoglycemia in the protocol group was rare. Of the 9,893 blood glucose measurements, only 11 measurements (0.11%) in six patients were less than 70 mg/dL (hypoglycemic). The mean blood glucose levels in these measurements was 57.0 (standard deviation, 11.5 mg/dL). Hypoglycemic events occurred less often in the protocol group than in the control group (7/10,000 measurements vs. 83/10,000 measurements), and fewer patients experienced one or more episodes of hypoglycemia (6% vs 30%, P<.001).	Not provided	Studies on tight glycemic control (80-110 mg/dL) in intensive care unit patients have shown conflicting results, with both improved outcomes and increased morbidity and mortality reported.	High	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Manders et al., 2016[14]	Nurse-driven diabetes in-hospital protocol (N-DIABIT)	Study population included adult patients with type 1 or type 2 diabetes admitted to 1 of the 11 participating wards at the hospital. Intervention group included 210 patients and the control group included 200 patients. Intervention group was exposed to the nurse-driven diabetes in-hospital protocol.	University Medical Centre in Amsterdam, Netherlands	In the total study population, no significant differences were found between the intervention group and control group in mean BG level, fasting BG level, the occurrence of severe hypoglycemia, consecutive hypoglycemia, or very severe hyperglycemia, and number of BG measurements.	Not provided	Nurses can successfully implement the protocol.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Perera et al., 2011[7]	Triple B (basal-bolus-booster [BBB]) subcutaneous insulin protocol	Study evaluated standardized subcutaneous insulin regimen throughout non-critical areas in hospital. Study included 57 patients who were recognized as significantly hyperglycemic. Results of study were compared with retrospective controls (n=45) treated with sliding-scale insulin.	Prince Alfred Hospital, Sydney, Australia	The mean BG level was lower in in the BBB group compare to the sliding-scale insulin group (11.7 plus/minus 2.6 vs. 13.6 plus/minus 2.4 mmol/L). The number of hyperglycemic episodes per patient was less with BBB (median 3 vs. 7). Patients who experienced hypoglycemic were less likely to have a repeat episode when managed using BBB compared to the sliding-scale insulin protocol (median 1 vs. 3). No severe hypoglycemic episode requiring intervention occurred while on the BBB protocol.	Not provided	Education about protocol was given to nursing and junior medical staff. Overall the protocol is user-friendly and can be implemented by staff who are not experts in managing diabetes. Staff was good at monitoring BGLs at scheduled times and administering basal/bolus insulin doses, but there was poor compliance with adding the booster dose insulin, especially with the bedtime booster dose.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Schroeder et al., 2012[3]	Intensive subcutaneous insulin protocol, which targeted fasting blood glucose of 110 mg/dL and postprandial glucose level of <180 mg/dL	All patients with previously diagnosed diabetes or suffering from recurrent hyperglycemia (2 or more measurements for blood glucose levels >180 mg/dL) who were admitted to the orthopedic surgery department via the emergency room were assigned to either ward A or ward B. Patients in ward A were treated with glycemic control intervention (n=35), and patients assigned to ward B were treated with standard sliding- scale insulin protocol (n=30). All patients had their blood glucose levels monitored four times a day.	Department of Orthopedic Surgery, Hebrew University Medical Center, Jerusalem Israel	No significant difference was noted in hypoglycemic rates between the two groups (p=0.6).	Protocol included staff training and the use of patient education from the diabetologist.	Low	Not provided	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Maynard et al., 2009[15]	Structured subcutaneous insulin order sets and insulin management protocols	Prospective observational research in parallel with performance improvement efforts. Study population included all adult inpatients on non-critical care units with electronically reported point of care glucose testing. Sample size: 9,314 patients were included in the study, and of those 5,530 were included in the secondary analysis of glycemic control and hypoglycemia.	Four hundred-bed academic center	The percent of patients' days that was uncontrolled (> than or equal to 180 mg/dL) was reduced over the three time periods (37.8% vs. 33.9% vs. 30.1%, P<.005). Percent of patients with uncontrolled patient stays (mean glucose > than or equal to 180 mg/dL) was also reduced over the three time periods (41.5% vs. 36.7% vs. 34.2%). The percent of patients who suffered one or more hypoglycemic event over the course of their inpatient stay was 11.8%, 9.7%, and 9.2% for time points (TPs) 1, 2, and 3, respectively. The rate ratio (RR) of patients suffering from a hypoglycemic event was significantly improved in the intervention time periods compared to baseline with RR of TP3:TP1=0.77 (confidence interval, 0.65-0.92). TP3 to TP2 did not have statistical significance (<0.05).	Not provided	Fear of hypoglycemia is the most significant barrier to glycemic control efforts.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Schnipper et al., 2009[12]	Glycemic management protocol	Prospective before-after trial. Sixty-three patients for preintervention and 106 patients for postintervention.	Brigham and Women's Hospital	The mean percent of glucose readings between 60 and 180 mg/dL per patient was 59.1% for preintervention and 64.7% postintervention (=0.13). There was no significant difference in percent of patient days with any hypoglycemia or severe hypoglycemia. There were also no significant differences in the mean number of hypoglycemic events per patient day or severe hypoglycemic events per patient day.	Not provided	Protocols should promote the continuous use of intravenous insulin infusions or scheduled basal-bolus subcutaneous insulin regimens.	Not provided	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Wong et al., 2017[2]	Computerized provider order entry with integrated insulin order sets	An interrupted time series design with 2,217 pre-implementation patient encounters and 2,330 post-implementation patient encounters.	A large tertiary and quaternary facility with 550 inpatient beds; non intensive care. unit patients	Introduction of computerized provider order entry-integrated insulin order sets did not lead to significant change in glycemic control. With respect to hypoglycemia, on average 2% of blood glucose measurements were considered hypoglycemic in pre and post interventions. There was no significant change in glycemic control with the intervention. It did improve adherence to evidence-based practices via an increase in basal-bolus-correctional insulin ordering behavior.	Lack of change in overall glycemic outcomes was most likely attributable to low order set uptake of only 51.5%. Prior study in 2012 did show change in outcomes.	Low	Not provided	None

Table B.49: Harms Due to Diabetic Agents, Teach-Back–Single Studies

Note: Full references are available in the Section 8.2 reference list.

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Coulter, 2018[4]	Educational intervention that uses the teach-back method to reduce HbA1c levels between baseline and 3 months among individuals receiving care for type 2 diabetes in a rural setting	Pre-test and post-test design. Data were collected over a 3-month period. Standard teaching was delivered at baseline during face-to-face office visits and intervention using a standardized survey, and teach- back method was delivered via phone dialogue. Dependent t-test compared the pre- and post-HbA1c mean scores. Patient sample, n=12.	Rural clinic in northern Illinois	The HbA1c levels decreased from pre-test (mean=9.26%, standard deviation=1.46) to post-test (mean=8.26% standard deviation=1.56). The mean difference of 1.00167 was statistically significant at t(11)=2.099, p<.05.	Not provided	Behavior modification and lifestyle changes are the mainstay treatment for people with diabetes.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Kandula et al., 2011[5]	Teach-back	Experiment 1 (n=113) included a pre-test and post-test. The evaluation was the Short Test of Functional Health Literacy in Adults. Experiment 2 (n=58) included pre-test and post-test, then another post-test. At the end the Short Test of Functional Health Literacy was administered. Two-sided test with a p value of .05 or less was used to determine statistical significance. The diabetes knowledge score was the main outcome of interest.	Federally Qualified Health Center and academic medical center outpatient clinic in Chicago	Experiment 1: Pre-test: median knowledge score, 5 points; post-test: 12 (p<.001). At the 2-week follow-up the median score was 9 (p<.001). There were no significant differences by literacy level in median knowledge gained from the pre-test to the post-test Experiment 2: Pre-test: median score was 4 points, post-test: 11. After teach-back, score was 16. Teach-back did not improve knowledge retention at the 2-week follow-up period.	Not provided	An individual with more education and more health background knowledge may have an easier time integrating new information into longer term memory.	Low	Lack of control groups, small sample size, and limited generalizability because patients were recruited from two clinics
Negarandeh et al., 2013[6]	Teach-back	Randomized controlled trial compared the impact of the teach-back method and pictorial image on diabetes-specific knowledge Intervention (pictorial), sample=45. Intervention group with teach-back had 45 patients, and the control group receiving the usual diabetes intervention had 45 patients.	Hospital in Kurdistan	The mean literacy scores for pictorial image, teach-back, and control group were 34.84, 34.71, and 33.58. Significant difference between baseline and follow-up measurement scores demonstrating differences in participants' diabetes-specific knowledge to self- management and patients' adherence to dietary regimen.	Not provided	Tailored strategies are needed for people with low health literacy levels to enhance treatment adherence and improve diabetes control.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design, Sample Size, Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Goessl et al., 2019[7]	DVD diabetes prevention intervention followed by a teach-back call	The small-group diabetes prevention class (120 minutes) focused on prevention objectives and the creation of an individualized action plan. The class was followed by a teach back call. The DVD diabetes prevention intervention was a 60 minute DVD designed to cover the same content presented in the small-group diabetes prevention class. After watching the DVD, participants also received a teach-back call. Participants also completed the Newest Vital Sign tool to assess health literacy.	Outpatient	Eighteen percent of participants had a low health literacy score, and 82 percent of participants had an adequate or high level adequacy score. Participants with low health literacy were older and significantly more likely to be African American (30%). There were significant differences in overall score performances between the two groups (the higher, the better). DVD: 15.4 plus/minus 2.5; class: 14.8 plus/minus 2.6. (p<0.001).	Not provided	Need for interventions that include strategies to address participants with varied levels of health literacy. Even when information is presented with the use of clear communication strategies, it may not be enough to ensure information uptake. Improved comprehension is achieved with multiple rounds f teach-back.	Low	None

Table B.50: Reducing Adverse Drug Events in Older Adults, Deprescribing to Reduce Polypharmacy-Single Studies

Note: Full references are available in the Section 9.2 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings
Ailabouni et al., 2019[2]	Pharmacist medication review with physician consult	Study Design: Feasibility study Sample: n=46 Patient Population: Adults 65 years and older living in residential care facilities and prescribed at least one anticholinergic or sedative medication	Residential care facilities in New Zealand	Primary Outcomes: Pharmacist-led intervention model led to implementation of 72% of deprescribing recommendations and a significant reduction in adverse drug reactions.	No change in cognition scores or reported quality of life	Reduction in drug burden index scores, numbers of falls, and adverse drug reactions 6 months post intervention.
Ocampo et al., 2015[1]	Pharmacist medication review with an 18-month followup	Study Design: Effectiveness-implementation hybrid design Sample: n=132 Patient Population: Community pharmacy patients, prescribed at least one medication, were offered the service when they sought advice, when a drug administration aid was required or when the provision of service was requested during the 18 month follow up period.	Community pharmacy in Spain	Primary Outcomes: Pharmacist-conducted medication review decreased the number of medications prescribed from 6.1 to 3.3, decreased observed hospitalizations, and decreased emergency department (ED) visits.	Not provided	Intervention led to a reduction in the number of medicines used, reduction in hospitalizations, reduction in ED visits, and improvement in physical and mental health.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings
Chan et al., 2014[12]	Use of medication safety review clinics, including a team of research assistants, pharmacist, and geriatric clinician for solving drug-related problems	Study Design: Intervention Sample: n=139 Patient Population: Outpatients age 65 or older who had been prescribed eight or more chronic medications (28 days or longer) or had visited more than three physicians at two participating hospitals	University hospital in Taiwan	Implementation of medication safety review clinics led to a reduction in chronic medication prescribed and led to the improvement of good health status from 22% to 38% in 24 weeks.	Not provided	Intervention led to a reduction in chronic medication and improvement of good health status rating.
Garfinkel and Mangin, 2010[5]	Good-Palliative-Geriatric Practice algorithm was used to recommend drug discontinuations	Study Design: Feasibility trial Sample: 70 intervention Patient Population: Community-dwelling adults referred by family physician or family for comprehensive geriatric assessments.	Day center for senior citizens and/or home care in Israel	Primary Outcome: Algorithm led to discontinuation recommendations for 58% of drugs.	Not provided	Protocol indicated that discontinuation was recommended for 311 medications in 64 patients.
Kojima et al., 2012[14]	Physician-led intervention using the Beers Criteria® and the Epocrates online drug-drug interaction program to reduce polypharmacy in long-term care residents	Design: Quality improvement cost study Sample: n=70 Patient Population: Patients age 65 years or older with polypharmacy	Skilled nursing facility and intermediate care facility in Hawaii	Primary Outcome: Physician-led, tool-assisted medication review led to a decrease in monthly medication costs by $22 per resident and a decrease in nursing medication administration costs.	Not provided	Intervention led to a decrease in monthly medication costs and nursing medication administration costs.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings
Lenander et al., 2014[9]	Pharmacist-led structured medication review involving a patient questionnaire and pharmacist consultation in primary care setting	Design: Randomized controlled trial (RCT) Sample: 209 total patients: 107 intervention group; 102 control group Patient Population: Patients age 65 or older with five or more prescribed medications	Primary care center in Sweden	Primary Outcome: Drug-related problems and number of drugs Secondary Outcome: Healthcare utilization and self-rated health during 12-month follow-up.	Not provided	1. Pharmacist-led medication review led to a decrease in the number of drug-related problems from 1.63 to 1.31 at followup and a decrease in the number of drugs prescribed. 2. No significant difference in healthcare utilization, but a significant change in self-rated health.
McKean et al., 2016[6]	Physician-led education intervention supported by listing clinical and medication data linked with clinical decision support tool	Design: Prospective pilot study Sample: n=50 Patient Population: General medicine patients 65 years or older receiving eight or more medications	Tertiary teaching hospital in Australia	Primary Outcome: Physician-led education intervention led to a decrease in the number of medications prescribed at discharge from 10 to 7.	Not provided	Intervention led to decrease in the number of medications per patient.
Martin et al., 2018[8]	Consumer based, pharmacist-led education intervention using an educational deprescribing brochure in parallel to sending the physicians an evidence-based pharmaceutical opinion	Design: Cluster RCT Sample: 489 patients: 219 intervention group; 218 control group Patient Population: Patients age 65 or older, prescribed at least one of four prescribed peer criteria medications (sedative-hypnotics, first-generation antihistamines, glyburide, or nonsteroidal anti-inflammatory drugs)	Community pharmacies in Canada	Primary Outcome: Pharmacist-led education intervention led to a reduction in the number of inappropriate medications prescribed by 43% in the intervention group.	Not provided	Intervention led to a decrease in number of inappropriate medications filled.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings
Petersen et al., 2018[4]	Use of a deprescribing intervention (Shed-Meds) to identify deprescribing targets and priorities, decide on appropriate deprescribing through patient interview, synthetize and communicate deprescribing recommendations to providers	Design: Single site feasibility study Sample: 40 total patients: 20 intervention group; 20 control group Patient Population: Medicare beneficiaries 65 years of age or older receiving five or more prescribed medications and admitted to hospital with intended discharge to a skilled nursing facility	Tertiary care hospital in Tennessee	Primary Outcome: Deprescribing protocol led to a reduction in medications at discharge from 11.6 to 9.1.	Not provided	Intervention decreased the mean number of medications prescribed at discharge and reduced medication burden in older adults.
Pope et al., 2011[3]	Intervention included medical assessment by a geriatrician and medication review by a multidisciplinary expert panel	Design: Prospective RCT Sample: 225 permanent patients: 110 intervention group; 115 control group Patient Population: Permanent patients on continuing care wards	Two residential continuing care hospitals in Ireland	Primary Outcome: Geriatric specialist medication review led to a reduction in the number of medications from 11.65 to 11.09 in the intervention group.	Intervention did not lead to a significant difference in mortality or acute hospitalization outcomes	Intervention led to a decrease in the total amount of medications in the intervention group.
Tamura et al., 2011[11]	Geriatric fellow and faculty medication review using the Beers Criteria® and Epocrates online drug interaction program	Design: Intervention study Sample: n=74 Patient Population: Residents with nine or more medications	Kuakini Geriatric Care, long-term care facility in Hawaii	Primary Outcome: Geriatrician-led medication review led to a decrease in the number of prescribed regular medications.	Not provided	Intervention led to a decrease in the number of regular prescribed medications, as-needed medications, and high-risk medications per patient.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings
Tannenbaum et al., 2014[7]	Direct-to-consumer education intervention using an 8-page booklet based on self-efficacy and a self-assessment of benzodiazepine use in community pharmacies	Design: Cluster RCT Sample: 303 total patients: 148 intervention; 155 control group Patient Population: Community pharmacy patients age 65 or older with a minimum of five active prescriptions, one being an active benzodiazepine prescription, dispensed for at least 3 consecutive months	Community pharmacies in Canada	Primary Outcome: Direct-to-consumer pharmacist-led intervention led to a significant decrease in benzodiazepine use in the intervention group.	Not provided	Intervention led to a significant decrease in benzodiazepine use in the intervention group.
Wouters et al., 2017[13]	Multidisciplinary Multistep Medication Review	Design: Pragmatic cluster RCT Sample: Total 426: 233 intervention group; 193 control group Patient Population: Nursing home residents	Nursing home wards for long-term care in the Netherlands	Primary Outcome: Pharmacist and clinician-led medication review led to a 39.1% reduction of inappropriate medications in the intervention group.	Intervention did not lead to a change in clinical outcomes between groups	Intervention led to a decrease in the number of inappropriate medications.

Table B.51: Reducing Adverse Events in Older Adults, Using STOPP (Screening Tool of Older Peron's Inappropriate Prescriptions)

Note: Full references are available in the Section 9.3 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Campins et al., 2017[1]	Clinical pharmacist-led review based on algorithm and STOPP/START criteria (Screening Tool of Older People's Prescriptions/Screening Tool to Alert to Right Treatment)	Design: Randomized controlled trial (RCT) Sample: 251 control group; 252 intervention group Patient Population: Community-dwelling older adults, aged 70 years and older, receiving six or more drugs and resident in municipalities of Martaro and Argentona, Spain.	Primary Health Care Centers in Spain	Primary Outcomes: About 26.5% of prescriptions were rated as potentially inappropriate and 21.5% were changed (9.1% discontinuation, 6.9% dose adjustment, 3.2% substitution, and 2.2% new prescription). The mean number of prescriptions per patient was significantly lower in the intervention group at 3- and 6-month followup.	Not provided	Not provided	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Cossette et al., 2017[15]	Use of a computer alert system-based pharmacist-physician intervention model to compare change in the use of potentially inappropriate medications (PIMs) with usual clinical care. A panel of experts used STOPP criteria to develop the model	Design: RCT with block randomization. Patients were randomly assigned to control and intervention groups with a 1:1 ratio using block sizes of 2, 4, and 6, and stratification by hospital site. Sample: 139 intervention (126 analyzed); 133 control group (128 analyzed). Patient Population: Older adults, 65 years and older. with at least one geriatric-explicit criterion for PIMs	University hospital in Canada	Primary outcome: Drug cessation or dosage decrease implemented in targeted PIMs. Secondary outcome: Length of stay, in-hospital death, ED visits, and readmissions within 30 days of discharge.	Not provided	1. Clinical relevance of the computer alert system alerts: 50% in control group and 30% in intervention group. 2. Significant drug cessation and dosage decreases in intervention compared with control group at 48 hours post alert: (30%) and hospital discharge (20.8%). Average time (means) to analyze a patient file and complete the interventions was about 44.25 minutes in intervention group. 3. No significant decrease in readmissions or inpatient death rates for intervention vs. control group.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
De Bock et al., 2018[16]	Medication review process that used STOPP to assess appropriateness of medication	Design: RCT Sample: 52 patients who were taking a median of 10 medications at the time of the study. Patient Population: Older adults, 70 years of age or older, with an unplanned admission to the geriatric ward; took at least five drugs chronically; not hospitalized in the preceding 3 months; and no documented cognitive impairments	University Hospital in Belgium (235 beds)	Primary Outcome: Reduction in number of drug discrepancies and potentially inappropriate prescriptions (PIPs). Secondary Outcome: Positive reports of satisfaction with services and opinions on interprofessional communication.	Medication reconciliation was time consuming and did not involve an integrated electronic patient file to record diagnoses, lab results, and medications	1. Time needed to review and make recommendations was considered reasonable. 2. Successes for medication review: full access to patient file; relatively fast screening; identification of significant amount of PIMs; improvement in prescribing appropriateness; 20% of recommendations accepted. 3. Barriers for medication review: scattered information; inefficient communication; lack of continuity of care. There were no service level agreements in place prior to intervention implementation.	Moderate
Frankenthal et al., 2017[7]	Review by study pharmacist using STOPP/START criteria at beginning of study and 6 months later	Design: Retrospective cohort study Sample: 160 intervention; 146 control group Patient Population: Older adults, 65 years and older	Chronic care geriatric facility in Israel	Primary Outcome: The prevalence of PIPs was significantly lower in the intervention group (33.3%) than the control group (48.4%) at 24-month followup (p=0.02).	Not provided	Between baseline and 24 months, there was a significant reduction in costs of medications in the intervention group (113 Israeli shekels [$29]] per patient per month, p<0.001) but not in the control group.	Low

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Gibert et al., 2018[2]	STOPP used during primary care general practitioner consultations on PIMs	Design: Intervention study Sample: 170 patients Patient Population: Older adults, 75 years and older	Primary care in Isere County, France	Primary Outcome: The number of PIMs decreased by 37.6% (n=170 vs. 106) with the application of STOPP criteria by general practitioners. This intervention reduced PIMs for 44.9% of patients (n=44, p<0.001).	Not provided	Not provided	High
Hannou et al., 2017[3]	Clinical pharmacist medication reviews to reduce potentially inappropriate drug prescriptions	Design: Prospective interventional study Sample: 102 intervention; no control group Patient Population: Older adults, 65 years and older, being admitted to an acute psychiatric geriatric facility	Geriatric psychiatry admission unit of a university hospital in Switzerland (16 beds)	Primary Outcome: Global pharmacist intervention acceptance rate was 68% (78% for standard pharmacist recommendations [recs], and 47% for STOPP/START recs). Of 186 STOPP recs, 82 were accepted (44%).	Not provided	Not provided	High

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Hill-Taylor et al., 2013[8]	Assessment of effectiveness of STOPP/START criteria on prescribing quality and clinical, humanistic, and economic outcomes in adults aged 65 and older (updating a 2013 review).	Design: Systematic review with meta-analysis of PIM rates, and narrative summary of other outcomes. Four studies were included in analysis. Sample: 1,925 adults. Patient Population: Adults age 65 years and older; one study restricted participants to 75 years and older	Acute care admission, long-term care	Primary Outcomes: All followup rates showed improvement in PIM rates in both the intervention and control groups. At every time point in every study, the intervention demonstrated some success, with the intervention PIM rates being lower than control rates. Three studies reported a significant and sustained drop in potential prescribing omissions (PPOs) in the intervention group. There was also a reduction in PPOs in all control groups on followup.	Not provided	Two studies reported cost outcomes and found cost efficiencies in medication choices in the intervention group compared with the control group.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Ilic et al., 2015[4]	Using START/STOPP criteria to assess the appropriateness of prescribing before and 6 months after the intervention implementation	Design: Pre- and post-observation trial that included a 3-month pre-phase; a 1-month intervention phase; a 6-month post-intervention phase; and a 3-month period of repeated recording and analysis of prescribing practices. Sample: 104 nursing home residents and 27 nursing home physicians; no control group. Patient Population: Older adults, 65 years and older, who resided in the nursing home. Average age was 83 years,	Twenty nursing home facilities in Serbia	Primary Outcome: Seventy PIPs prescribed pre intervention and 20 PIPs 6 months post intervention (median 3.5, range 1–20 pre intervention, and median 1.5, range 0–6 post). The decrease in PIPs was significant ($z=2.823$; $p<0.005$).	Not provided	Not provided	Moderate
Kiel and Phillips, 2017[12]	Clinical pharmacist comprehensive medication reviews using START/STOPP criteria	Design: Prospective cohort with post-hoc analysis Sample: 26 intervention and 26 control group participants Patient Population: Older adults, 65 years and older, taking at least five prescription medications	Primary care clinic in Michigan	Primary Outcome: Difference in number of medication-related problems, as defined by the START and STOPP criteria. The acceptance rate for recommendations on STOPP/START med problems was 35% (n=17).	Not provided	Not provided	High

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Kimura et al., 2017[14]	Clinical pharmacist medication reviews using STOPP-2 criteria to reduce PIMs	Design: Prospective observational study Sample: 822 in intervention group; no control group Patient Population: Older adults, 65 years and older, who were newly admitted into inpatient care and prescribed more than one prescription medication	University hospital in Japan	Primary outcomes: Number of PIMs was 651; of these, it was recommended to doctors that 310 (47.6%) be changed, and 292 (44.9%) were discontinued/ changed after the pharmacist's assessment. Acceptance rate of pharmacists' recommendations was 94.2%.	Not provided	The mean time for pharmacist's assessment was 6.2 +/- 3.1 minutes per patient.	High
O' Connor et al., 2016[6]	Using START/STOPP criteria to help attending physicians identify PIMs	Design: Single-blinded, clustered RCT Sample: 732 in intervention group; no control group Patient Population: Consecutively admitted adults aged 65 and older	Tertiary referral hospital in Ireland	Primary Outcome: When STOPP/START was applied, 451 recommendations were made on 233 participants (64.7%). Of these, 292 were STOPP recommendations; attending doctors accepted and implemented 237 STOPP recs (81.2%).	Not provided	Application of STOPP/START criteria resulted in significant reductions in adverse drug reaction incidence and medication costs in acutely ill older adults but did not affect median length of stay.	Low

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Price et al., 2017[14]	Using STOPP guidelines as part of an electronic medical records clinical decision support system to identify PIPs for older adults	Design: Mixed-method, pragmatic, cluster RCT Sample: 44,290 in intervention group; 37,615 in control group Patient Population: Consecutively admitted adults aged 65 and older	Primary care offices	Primary Outcome: Regression analysis showed no significant difference in change of recorded PIPs in control versus intervention group (p=0.80).	Not provided	Barriers to implementation: The STOPP rules were presented in a different location from simple drug alerts; the guideline tool did not have a clear way to support users in prioritizing suggestions and alerts as recommended.	Low
Unutmaz et al., 2018[5]	Comprehensive geriatric assessment (CGA) complemented by STOPP/START criteria	Design: Retrospective assessment of before and after intervention Sample: 1,579 patients Patient Population: Older adults, age 65 and older	Geriatrics outpatient clinic of tertiary hospital in Turkey	Primary Outcome: Mean number of drugs decreased from 5.3±3.4 before CGA to 4.6 ±2.5 (p<0.05).	Not provided	After CGA, monthly saved total per capita cost of PIMs was $12.8 and monthly increased total per capita cost of PPOs was $5.6.	Moderate

Table B.52: Opioids, Opioid Stewardship–Systematic Reviews

Note: Full references are available in the Section 10.1 reference list.

Author, Year (Reference)	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Starrels et al., 2010[1]	• Treatment agreement • Urine drug test (UDT)	• Pain clinics • Primary care	All studies were observational and rated as poor to fair quality. In four studies with comparison groups, opioid misuse was modestly reduced (7% to 23%) after treatment agreements with or without UDT. In seven studies, the proportion of patients with opioid misuse after treatment agreements, UDT, or both varied widely (3% to 43%).	Not provided	None

Table B.53: Opioids, Opioid Stewardship–Single Studies

Note: Full references are available in the Section 10.1 reference list.

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
Anderson et al., 2016[15]	Stepped Care Model for Pain Management (SCM-PM): provider continuing medical education (CME) related to opioid prescribing; opioid dashboard for patients receiving chronic opioid therapy (COT) that listed whether the patient had a signed treatment agreement, had a urine drug screening (UDS) within the past 6 months, had completed a pain interference assessment questionnaire within the past 3 months, and made at least one behavioral health visit in	• Treatment agreement • UDS • Pain interference • Behavioral health visit • Project ECHO	• Education • Dashboard • Policy • Electronic health record (EHR) templates	Pre/post intervention; Provider and patient surveys (3,357 pre-intervention and 4,385 post-intervention) No control group	Multisite Federally qualified health center (FQHC) in Connecticut 25 providers Primary care; FQHC	During the baseline period, only 360 (34%) of the 1,309 patients receiving COT had a documented treatment agreement in the chart and 680 (64%) had had a urine drug test (UDT) in the preceding year. After implementation, 778 (61%) out of 1,230 patients receiving COT had a treatment agreement and 1,103 (87%) had had a UDT in the preceding year (both differences significant at $p<0.05$). Documentation of the presence of pain and the source and/or cause of pain increased significantly,	Not provided	Not provided	Moderate: no control group; one health system—not generalizable

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
	the past year; onsite specialty care; virtual access to pain specialists; EHR templates for chronic pain; and chronic pain and opioid prescribing policy.					from 64% to 82% (p=0.001) and from 62% to 74% (p=0.025), respectively. There were also significant improvements in documentation of functional status from 5% to 19% (p=0.001), in a documented treatment plan from 92% to 98% (p=0.002), and in documentation of pain reassessment from 17% to 39% (p=0.001). Providers' pain knowledge scores increased to an average of 11% from baseline; self-rated confidence in ability to manage pain also increased. Use of opioid treatment agreements and UDSs increased significantly by 27.3% and 22.6%,			

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
						respectively. Significant improvements were also noted in documentation of pain, pain treatment, and pain followup. Referrals to behavioral health providers for patients with pain increased by 5.96%. Results demonstrate statistically significant increases in the percentage of patients with pain who had a visit with an onsite behavioral health provider. Referrals to chiropractors also increased significantly for both groups, while there was a significant decline in referrals to neurosurgery or orthopedic surgery and to pain specialists. There was no			

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
						significant decline in opioid prescribing.			
Anderson et al., 2015[11]	Opioid dashboard to increase adherence to guidelines	• Treatment agreement • UDT • Document functional status • Behavioral health visit	• Dashboard	Outcomes evaluation with pre/post design provider survey post implementation. One multisite community health center serving over 140,000 medically underserved patients No control group	Multisite FQHC in CT Primary care; FQHC	Post implementation, there was an increased proportion of COT patients with: a signed opioid treatment agreement (49% to 63%, p<0.001), UDT (66% to 86%, p<0.001)), documented assessment of functional status (33% to 46%, p<0.001)), and at least one visit with behavioral health (24% to 28%, p<0.03). Percentage of adult patients who received opioid prescriptions decreased (13% to 12.5%, p=0.036). The percentage of patients receiving COT also declined (3.4% to 3.1%, =0.057) (Anderson, 2015).	Not provided	54% of primary care provider (PCP) respondents felt that the missed opportunities report was helpful. 85% of respondents reported that the dashboard helps them identify patients on chronic opioids, and gaps in services for patients. 54% reported dashboard helps them to plan care for these patients and 69% felt that it was easy to use the dashboard to help collaborate with team. 77% felt dashboard was clinically useful.	Moderate: no control group; one health system—not generalizable

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
Dorflinger et al., 2014[18]	SCM-PM—increase safe opioid prescribing practices and bolstering nonopioid, multimodal pain care	• Treatment agreement • Shared decision making • Pain specialty care services • Use of nonpharmacological treatments • Referrals	• EHR templates	Cross-sectional/ pre-post; 2,261 patients who received at least 90 consecutive days of opioids prescribed by a U.S. Department of Veterans Affairs (VA) PCP from July 2008 to June 2012 No control group	VA Connecticut Healthcare System—serves 178,144 patients Primary care; VA	Over the 4-year study period, the proportion of patients receiving high-dose opioids decreased from 27.7% to 24.7%. Use of opioid risk mitigation strategies increased significantly. The mean pain intensity rating did not differ from year to year over the 4-year study. Proportion of patients with an opioid treatment agreement increased from 27.9% to 81.1% ($p<0.0001$) and the percentage receiving a UDS increased from 52.5% to 79.6% ($p<0.0001$). Referrals to physical therapy, pain management, and chiropractic increased significantly ($p<0.05$), but not for mental health.	Not provided	Use of EHR note templates likely increased uptake. Challenges with EHR capturing complementary health approaches (e.g., chiropractic).	Not provided

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
						Use of topical analgesics increased (p<0.05) but not use of nonsteroidal anti-inflammatory drugs (NSAIDs), antidepressants/ neuro, or anticonvulsants.			
Dublin et al., 2019[8]	Clinical leadership encouraging adherence to Washington (WA) state's 2007 COT guideline—periodic voluntary educational presentations and one mandatory CME course; Implementation of policy making PCPs responsible for overall management of COT patients; PCPs and medical directions received lists of their patients receiving high-dose COT;	• Dose reduction • Risk stratification • Increased monitoring • Opioid care plans • UDS • Pain specialist consultation	• Education • Dashboard • Audit and feedback	Interrupted time series; 31,142 patients (22,673 intervention, 8,469 control) receiving COT from 2006 to 2014 Control group	26 group practice primary care clinics in WA state Primary care; Integrated group practices	Among 21,853 people receiving COT in the integrated group practice and 8,260 in contracted care, there were 2,679 injuries during followup. The baseline injury rate was 1.0% per calendar quarter in the integrated group practice and 0.9% in contracted care. Risk reduction initiatives did not decrease injury rates: Within the integrated group practice, the relative risk in the dose reduction period was 1.01 (95%	Not provided	Not provided	Low-to-moderate: control of bias accounted for in analysis through comparing intervention and control groups; study took place within single health system and may not be generalizable

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
	supervisory guidance for those PCPs with large numbers of patients on high-dose COT; financial incentives for physicians completing COT care plans					confidence interval [CI], 0.95 to 1.07) and in the risk stratification and monitoring period, 0.99 (95% CI, 0.95 to 1.04). Injury trends did not differ between the two care settings.			
Jacobs et al., 2016[19]	Clinical pain pharmacist telephone-based risk assessment for COT renewals—two pharmacists provided monthly risk assessment for every patient requesting prescription renewal Pharmacist assessment of risk and VA guideline-concordant care	• Pharmacist telephonic monthly assessment of medication use and aberrant drug-related behaviors at prescription renewal • Informed consent • UDT • Prescription drug monitoring program (PDMP) • EKG monitoring	• EHR assessment and recommend-ations to provider	Pilot/ implementation study; 148 patients served by 5 PCPs; patients receiving COT in primary care, excluding MAT for substance-use disorder (SUD) No control group	Medical Practice Primary Care Clinic at San Francisco VA Health Care System, serving 10,000 patients Primary care; VA	After the pilot, the proportion of patients meeting the universal precautions measures increased significantly. The proportion of patients with an updated opioid informed consent increased from 4.7% to 64.8% (p<0.0001), the proportion of patients with a completed UDT within 1 year increased from 62.8% to 79.7% (p=0.002), and the proportion of patients with a completed PDMP report within 1 year	Not provided	Not provided	Moderate: small sample; no control group; implementa-tion at one VA system with only 5 PCPs

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
						increased from 30.4% to 100% (p<0.0001). There was also a nonsignificant increase in EKG monitoring for patients on methadone (47.4% vs. 73.6%; P D .187).			
Liebschutz et al., 2017[6]	Transforming Opioid Prescribing in Primary Care (TOPCARE): (1) nurse care management (assesses pain, addiction, misuse risk; prepares prescriptions; collects UDTs; conducts pill counts; checks PDMPs, assessing concerning patient issues; and collaborates with PCP), (2) electronic registry to facilitate population management, (3) one-on-one academic detailing, and	• Nurse care management • Assess pain, addiction, misuse • UDTs • Pill counts • PDMPs • Electronic registry	• EHR tools • Education • Academic detailing • Electronic decision tools (INT and Control)	Cluster-randomized trial; 93 PCPs and 985 patients; patients receiving long-term opioid therapy; one health center served the homeless population; individual PCPs were randomized across four sites. Control group	Four safety-net primary care practices in Boston, MA Primary care; Safety net	At 1-year followup, intervention patients were more likely than controls to receive guideline-concordant care (65.9% vs 37.8%; p<0.001; adjusted odds ratio (AOR), 6.0; 95% CI, 3.6 to 10.2), to have a treatment agreement (53.8% vs. 6.0%, p<0.001, AOR, 11.9; 95% CI, 4.4 to 32.2), to have received at least one UDT (74.6% vs. 57.9%, p<0.001, AOR, 3.0; 95% CI, 1.8 to 5.0), and to have either a 10%	Not provided	Not provided	Low: no data from outside the health system

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
	(4) orientation and access to electronic decision tools through online platform (e.g., Opioid Risk Tool), and interactive tools to assist with UDT ordering and interpretation. Control clinicians only received fourth component.					morphine equivalent daily dose reduction or opioid treatment discontinuation (AOR 1.6). Intervention patients had a mean morphine equivalent daily dose 6.6 (1.6) mg lower than controls ($p<0.001$). There was no difference between the two groups in early refills of opioids.			
Von Korff et al., 2016[9]	Clinical leadership encouraging adherence to WA state's 2007 COT guideline—periodic voluntary educational presentations and one mandatory CME course; Implementation of policy making PCPs responsible for overall management of COT patients;	• Dose reduction • Risk stratification • Increased monitoring • Opioid care plans • UDS • Pain specialist consultation	• Education • Dashboard • Audit and feedback	Interrupted time series; 31,142 patients (22,673 intervention, 8,469 control) receiving COT from 2006 to 2014 Control group	26 group-practice primary care clinics in WA state Primary care: integrated group practices	From 2006 through June 2014, the percentage of patients on COT receiving ≥120 mg morphine equivalent dose decreased from 16.8% to 6.3% in the intervention clinics (a 63% reduction) versus 20.6% to 13.6% among patients on COT of control clinics (a 34% reduction). From the first quarter	Not provided	Not provided	Low-to-moderate: control of bias accounted for in analysis through comparing overdose trends and other variables between intervention and control groups; study took place within single health system and may not be generalizable

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
	PCPs and medical directors received lists of their patients receiving high-dose COT; supervisory guidance for those PCPs with large numbers of patients on high-dose COT; financial incentives for physicians completing COT care plans					of 2006 to June 2014, the average daily MED decreased from 75.8 to 40.0 mg among all intervention clinic patients on COT (47% lower), compared with a decrease from 92.1 to 64.6 mg among patients on COT in the control clinics (30% lower). Among intervention clinic patients who used opioids regularly for 1 year, the percentage that received a UDT in a 1-year interval was >50% in 2011 through 2014, after being <20% in earlier years. In contrast, among control clinic patients who used opioids regularly for 1 year, the percentage that received a UDT within a 1-year			

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
						interval ranged from 15.2% in 2011 to 21.4% in 2014.			
Von Korff et al., 2019[10]	Clinical leadership encouraging adherence to WA state's 2007 COT guideline—periodic voluntary educational presentations and one mandatory CME course; implementation of policy making PCPs responsible for overall management of COT patients; PCPs and medical directions received lists of their patients receiving high-dose COT; supervisory guidance for those PCPs with large numbers of patients on high-dose COT; financial incentives for physicians	• Dose reduction • Risk stratification • Increased monitoring • Opioid care plans • UDS • Pain specialist consultation	• Education • Dashboard • Audit and feedback	Interrupted time series; 31,142 patients (22,673 intervention—integrated group practices, 8,469 control—contracted practices) receiving COT from 2006 to 2014 Control group	26 group practice primary care clinics in WA state Primary care; integrated group practices	Authors compared patients on COT in settings that implemented a COT dose reduction initiative and then a COT risk stratification/ monitoring initiative to similar patients on COT from control settings. From 2006 to 2014, 31,142 patients on COT (22,673 intervention, 8,469 control) experienced 311 fatal or nonfatal opioid overdoses. In primary analyses, changes in opioid overdose rates among patients on COT did not differ significantly between intervention and control settings with the	Not provided	Not provided	Low-to-moderate: control of bias accounted for in analysis through comparing intervention and control groups; study took place within single health system and may not be generalizable

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
	completing COT care plans					implementation of either dose reduction or risk stratification/ monitoring. In planned secondary analyses, overdose rates decreased significantly (17% per year) during the dose reduction initiative among patients on COT in intervention settings (relative annual change, 0.83; 95% CI, 0.70 to 0.99), but not in control settings (0.98. 95% CI, 0.70 to 1.39). We conclude that overdose rates among patients on COT were not decreased by risk stratification and monitoring initiatives. Results were inconsistent for COT dose reduction, with no significant difference between			

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
						intervention and control settings (primary hypothesis test), but a significant decrease in overdose rates within the intervention setting during dose reduction (secondary hypothesis test).			
Weimer et al., 2016[17]	Provider education and dose limitation policy (120 mg morphine milligram equivalents [MME]/day)	• Pain task force • Dose limitation • Initiate taper for >120 MEDs • Patient list of patients with high dosage	• Education • Policy	Retrospective cohort; 116 patients—41 tapered to safe dose following intervention, 71 not tapered; primary care patents prescribed opioids for more than 90 consecutive days No control group	One academic primary care clinic Primary care	Statistically significant change in MED per day during the post-intervention period. Among the 112 patients prescribed high-dose opioids, the average total MED declined from 263 to 199 mg MED in the post-intervention period (average change of 64 mg MED [95% CI, 32 to 96]; p<0.001). As shown in Figure 2, among the 41 TSD patients, the average dose declined from 207 to 85	Not provided	Not provided	Moderate-to-high: single clinic—may not be generalizable; followup period limited to 8 months; no control group; did not control for other interventions or increased visibility of opioid epidemic that may have happened during the same time

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
						mg MED (average change of 122 mg MED [95% CI,: 165 to 250]; p<0.001).			
Weiner et al., 2019[16]	Multicomponent program: inter-departmental Prescribing Task Force to develop safe prescribing guidelines for the health system; multidisciplinary Addiction Task Force, which proposed creation of a Bridge Clinic for patients with opioid use disorder (OUD) being discharged from hospital or emergency department (ED); provider education through Opioid Grand Rounds every 2 months; opioid take-back program advertised to patients; creation of curriculum on	• Opioid Stewardship Committee • Prescribing, addiction, education task forces • Nonpharma-cologic treatments • Referral for OUD treatment • Naloxone	• Education • Patient education • EHR template • Integrated PDMP in EHR • Autopopulate patient discharge instructions • Connection to ED information exchange • Dashboard • Audit and feedback • Monitoring with opioid-related metrics	Cross-sectional/pre-post intervention; program began in Feb 2016 and data were gathered for July 2015 through April 2018; size of patient population for the health system not given in article No control group	One health system in Boston, consisting of 160 ambulatory care clinics, 15 primary care practices, and 2 hospitals Health system-wide	Schedule II opioid prescribing decreased from 8,941 prescriptions in July 2015 (the first year for which data are available) to 6,148 in April 2018 (-73.5 prescriptions per month; p<0.001). Mean MME per prescription (-0.4 MME per month; p<0.001). The number of unique patients receiving an opioid prescription each month also decreased, from 6,863 in July 2015 to 4,894 in April 2018, a 28.7% decrease (-52.6 patients per month; p<0.001). Prescriptions	Not provided	Determining metrics and gaining access to data was important to guide the effort. Tensions between primary care and pain specialists because of mismatch of expectations of who was responsible for prescribing opioids and taking care of patients. Increased access to SUD, but outpatient practices believed had inadequate access. Helpful to convene stakeholders to address the challenges encountered.	Moderate: patients may have had prescription outside the system; no control; one health system—limited generaliz-ability

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
	Clinical Opiate Withdrawal Scale for providers to access on demand; creation of opioid prescribing SmartForm in EHR to alert providers on best practices for prescribing opioids; integrate state PDMP into the EHR; join statewide ED information exchange to detect patients seeking opioids at multiple EDs; benchmarking reports for each provider's opioid prescribing, which lets them see how they compare with unidentified peers; autopopulating opioid education information in patients' discharge instructions; creation of					containing a total of ≥90 MME also decreased (-48.1 prescriptions/ month; p<0.001). The number of prescriptions (+ 6.0 prescriptions/mo nth; p<0.001) and prescribers (+ 0.4 providers/month ; p<0.001) for the film version of buprenorphine/ naloxone, indicated for treatment of OUD, increased. Overdose trend was downward, but not significant. The number of overdoses fluctuates markedly by month, and although the overall linear trend is downward, it does not reach statistical significance (-			

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
	internal opioid-related metrics					0.2 overdoses/ month; p=0.29).			
Kahler et al., 2017[12]	Protocol to transfer "superusers" from ED to outpatient chronic pain program—following referral to the program, an EMR alert would appear when patients arrived in ED	• Transfer "superusers" of ED to outpatient chronic pain	• EHR alert of superusers	Crossover patients served as their own controls in the year prior to referral to the chronic pain program; 243 patients with at least 6 visits/ year to the ED, with 1 visit primarily driven by opioid-seeking behavior; adults age 18–67, cancer and sickle cell disease excluded Control group (crossover)	One ED in Indianapolis, IN, serving 102,000 patients/year ED	ED visits decreased from 14 to 4 (58% decrease, 95% CI, 50 to 66). We also found statistically significant decreases for these patients' state PDMP opioid prescriptions (30% decrease, 95% CI, 24 to 37), total unique controlled-substance prescribers from 11 to 7 (31% decrease, 95% CI, 23 to 38), computed tomography imaging (2 to 0), radiographs (5 to 1), electro-cardiograms (12 to 4), and labs run (47 to 13).	Not provided	Administrative support is critical EHR alerts were key component	Moderate: no control group; national attention on opioid prescribing at the time of the intervention, which may have introduced confounding; no measure of MME; no control for whether improvements were due to passage of time
Neven et al., 2016[7]	City-wide care coordination program that provides real-time ED treatment plans through a case manager for	• Citywide care coordination with EDs for patients opioid-seeking behavior	• Information exchange across systems	Randomized controlled trial; 165 patients; patients with 5 or more ED visits in the previous 12 months, at least	Three EDs in same metropolitan area of Spokane, WA—combined annual total	The intervention arm experienced a 34% decrease (incidence rate ratio = 0.66, p<0.001; 95% CI, 0.57 to 0.78)	Not provided	Providers reported being more empowered to say "no" in prescribing opioids.	Low to moderate: relatively small sample; did not assess for opioids prescribed

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
	patients at risk of obtaining opioids for inappropriate use			half of which were attributed to pain and/or drug-seeking behavior Control group	of 112,000 visits ED	in ED visits and an 80% decrease (OR=0.21, p=0.001) in the odds of receiving an opioid prescription from the ED relative to the control group. Declines of 43.7%, 53.1%, 52.9%, and 53.1% were observed in the treatment group for MMEs, controlled substance pills, prescriptions, and prescribers. At 1 year following study enrollment, patients receiving the intervention were 33% less likely to visit the ED compared with the control group, visited the ED fewer times on average than the control group, and received a smaller mean			outside the ED or illicitly obtained

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
						number of prescription at discharge. There were 23 unique prescribers in the treatment group as compared with 40 in the control group over the study year. Number of pills dispensed and MME prescribed in the intervention group was nearly half that of the control group.			
Hartford et al., 2018[14]	"Pain care bundle"—promoting co-analgesia during surgery, reduced opioid prescriptions post-surgery (provider education), patient education around expectations for postoperative pain management	• Intra- and postoperative pain care bundle • Opioid reduction strategies	• Education • Patient education	Pre-post intervention; 224 patients (pre) to 192 (post); patients undergoing open hernia repair or laparoscopic cholecystec-tomy No control group	Three hospitals in Ontario that perform general outpatient surgery Hospital, outpatient surgery	The median total MMEs for prescriptions filled in the post-intervention group were significantly less (100; interquartile range 75 to 116 pre-intervention vs 50; interquartile range 50 to 50 post-intervention; p<0.001). Only 78 of 172 (45%) patients filled their opioid	Not provided	Division-wide buy-in from nurses, surgeons, and anesthesiologists was a strength	Low to-moderate: includes control group but differences between two groups are not compared; conducted at one health system and may not be generalizable.

Author, Year	Description of Patient Safety Practice	Opioid Stewardship Interventions or Strategies	Implementation Strategies	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)
						prescription in the post-intervention group (p<0.001), with no significant difference in prescription renewals (3.5% pre-intervention vs 2.6% post-intervention; p = 0.62).			
Young et al., 2018[13]	Provider education on CDC guideline; clinic guidelines implemented that required checking PDMP before prescribing and limiting all opioids to 7 days' supply.		• Education • Guideline • Monitoring	Cross-sectional/ pre-post intervention; clinic sees 2.75 patients per provider per hour; patients of all ages, pediatric through geriatric (95% adults); outcomes assessed via PDMP eight weeks before and after implementation. No control group	Four privately owned urgent care centers in Rhode Island, with a total of 14 providers Urgent care	Opioid prescribing before and after adoption of the guideline, and in this manner, a statistically significant (P < 0.05) decline in the rate of opioid prescribing was revealed. On average, 2.43 fewer opioid prescriptions were written, per provider, per week, in weeks five through eight after promulgation (5.21, SD =4.37) than in the eight weeks before promulgation (7.64, SD =7.73).	Not provided	Not provided	Moderate to high: no control; one health system—limited generali-zability; short followup period; small sample size

Table B.54: Opioids, Medication-Assisted Treatment–Single Studies

Note: Full references are available in the Section 10.2 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Busch et al., 2017[28]	Initiation of buprenorphine/ naloxone in the emergency department (ED) as compared to screening/referral/brief intervention only	Cost-effectiveness study; 244 patients (subset of larger randomized controlled trial [RCT] [D'Onofrio 2015], limited to those who completed 30-day follow-up; ED patients with a DSM-IV diagnosis of opioid dependence	Emergency department	At all positive willingness-to-pay values, ED-initiated buprenorphine treatment was more cost-effective than brief intervention or referral.	Not provided	Not provided	Low-to-moderate: single site—findings may not be generalizable	None
D'Onofrio et al., 2017[7]	Initiation of buprenorphine/ naloxone in the ED as compared to screening/ referral/brief intervention only	RCT with three arms: screening for opioid dependence and referral; screening, brief intervention, and referral; initiation of treatment in ED with 10-week follow-up in primary care; 290 patients (subset of larger RCT [D'Onofrio 2015]; opioid-dependent patients treated at an urban teaching hospital ED from 2009-2013	Emergency department	Six- and 12-month followup to 2015 RCT: a greater number of patients in the buprenorphine group were engaged in addiction treatment at two months [68/92 (74%), 95% confidence interval (CI) 65–83] compared with referral [42/79 (53%), 95% CI 42–64] and brief intervention [39/83 (47%), 95% CI 37–58; $p < 0.001$]. The differences were not significant at six months [51/92 (55%), 95% CI 45–65; 46/70 (66%) 95% CI 54–76; 43/76 (57%) 95% CI 45–67; p	Not provided	Not provided	Low-to-moderate: single site—findings may not be generalizable	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
				= 0.37] or 12 months [42/86 (49%) 95% CI 39–59; 37/73 (51%) 95% CI 39–62; 49/78 (63%) 95% CI 52–73; p = 0.16]. At two months, the buprenorphine group reported fewer days of illicit opioid use [1.1 (95% CI 0.6–1.6)] vs. referral [1.8 (95% CI 1.2–2.3)] and brief intervention [2.0 (95% CI 1.5–2.6), p = 0.04]. No significant differences in illicit opioid use were observed at six or 12 months. There were no significant differences in HIV risk or rates of opioid-negative urine results at any time.				
D'Onofrio et al., 2015[6]	Initiation of buprenorphine/ naloxone in the ED as compared to screening/ referral/brief intervention only	RCT with three arms: screening for opioid dependence and referral; screening, brief intervention, and referral; initiation of treatment in ED with 10-week follow up in primary care; 329 patients; opioid-dependent patients treated at an urban teaching	Emergency department	Seventy-eight percent of patients in the buprenorphine group (89 of 114 [95% CI, 70%-85%]) vs. 37% in the referral group (38 of 102 [95% CI, 28%-47%]) and 45% in the brief intervention group (50 of 111 [95% CI, 36%-54%]) were engaged in addiction treatment on the 30th day after randomization (P < .001). The buprenorphine group reduced the number of	Not provided	Not provided	Low-to-moderate: single site—findings may not be generalizable	At 30-day follow-up, rates of positive urine drug tests did not differ among the groups.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
		hospital ED from 2009-2013		days of illicit opioid use per week from 5.4 days (95% CI, 5.1-5.7) to 0.9 days (95% CI, 0.5-1.3) vs. a reduction from 5.4 days (95% CI, 5.1-5.7) to 2.3 days (95% CI, 1.7-3.0) in the referral group and from 5.6 days (95% CI, 5.3-5.9) to 2.4 days (95% CI, 1.8-3.0) in the brief intervention group (P < .001 for both time and intervention effects; P = .02 for the interaction effect). Eleven percent of patients in the buprenorphine group (95% CI, 6%-19%) used inpatient addiction treatment services, whereas 37% in the referral group (95% CI, 27%-48%) and 35% in the brief intervention group (95% CI, 25%-37%) used inpatient addiction treatment services (P < .001). Patients who received medication-assisted treatment (MAT) initiation while in the ED were less likely to use inpatient treatment for opioid use disorder (OUD) in the 30 days following the ED visit. This suggests that initiation of treatment in				

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
				the ED may result in more efficient use of resources.				
Doolittle & Becker, 2011[25]	Buprenorphine/ naloxone treatment	Case series; 228 patients with opioid use disorder over four-year period	Community practice with two primary care provider prescribers	One out of 228 experienced precipitated withdrawal during induction. Of the convenience subsample analyzed (n = 28), 82% (+/−10%) had negative urine drug tests for opioids; 92% (+/−11%) were negative for cocaine; 88% (+/−12%) were positive for buprenorphine. Authors concluded that treatment of OUD using buprenorphine in primary care was both feasible and safe.	Not provided	Not provided	Moderate: single site, no comparison group	None
Doorley et al., 2017[21]	Shared medical appointments for buprenorphine maintenance	Retrospective chart review; 77 opioid-dependent patients; 61% of patients currently homeless, 92% were unemployed, 81% had an Axis I psychiatric diagnosis, and 53% had recent polysubstance use	Clinic providing health care for homeless individuals in San Jose, CA	Of the 77 patients, 95% attended at least one shared medical appointment. Treatment retention at 12 and 24 weeks was 86% and 70%, respectively.	Not provided	Not provided	High: single site, no comparison group, small sample size	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Fiellin et al., 2014[4]	Maintaining MAT indefinitely, as opposed to tapering following stabilization	RCT—participants randomized to either a three-week buprenorphine taper following six weeks of stabilization vs. ongoing buprenorphine maintenance therapy; 113 patients with prescription opioid dependence	One primary care clinic at a large, urban, academically-affiliated hospital in New Haven, CT	Patients in the taper group reported more days per week of illicit opioid use than those in the maintenance group once they were no longer receiving buprenorphine (mean use, 1.27 [95% CI, 0.60–1.94] vs. 0.47 [95% CI, 0.19–0.74] days). Patients in the taper group had fewer maximum consecutive weeks of opioid abstinence compared with those in the maintenance group (mean abstinence, 2.70 [95% CI, 1.72–3.75] vs. 5.20 [95% CI, 4.16–6.20] weeks). Patients in the taper group were less likely to complete the trial (6 of 57 [11%] vs. 37 of 56 [66%]; P < .001). Sixteen patients in the taper group reinitiated buprenorphine treatment after the taper owing to relapse.	Not provided	Not provided	Low-to-moderate: single site—findings may not be generalizable; patients were receiving nurse counseling during study period about their drug use, potentially overestimating effects.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Fiellin et al., 2013[10]	Cognitive behavioral therapy (CBT)	RCT—Participants randomized to receive physician management or physician management plus 12 weeks of CBT; 141 adult patients with opioid dependence receiving buprenorphine, enrolled from 2006–2009	One primary care clinic at a large, urban, academically-affiliated hospital in New Haven, CT	Both groups experienced a significant reduction in opioid use during treatment, but the findings do not support addition of CBT to standard physician management for MAT treatment.	Not provided	Not provided	Low-to-moderate: single site—findings may not be generalizable	At 12 weeks follow-up post-treatment, the two groups did not significantly differ in frequency of illicit opioid use.
Fiellin et al., 2008[13]	Long-term treatment with buprenorphine/ naloxone in primary care: Results at 2–5 years	Observational (no control group); 53 opioid-dependent patients who had initiated MAT through a previous RCT	One primary care clinic at a large, urban, academically-affiliated hospital in the U.S.	Thirty-eight percent of enrolled subjects were retained for two years. Ninety-one percent of urine samples had no evidence of opioid use, and patient satisfaction was high. No serious adverse events related to treatment occurred. Authors summarize that this is a "moderate" level of retention two years after initiation of MAT in primary care.	Not provided	Not provided	High: single site, no comparison group, small sample size	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Kowalczyk et al., 2017[8]	Clonidine as an adjunct to buprenorphine to decrease stress from craving	RCT—clonidine vs. placebo for 18 weeks of buprenorphine treatment; 118 participants seeking treatment for opioid dependence (108 included in this analysis due to 10 participants dropping out)	Outpatient substance-use disorder (SUD) treatment center in Baltimore, MD	Participants who received buprenorphine plus clonidine reported longer streaks of abstinence when they had unstructured time, as compared to the buprenorphine-only group. This indicates that addition of clonidine may help reduce cravings.	Not provided	Not provided	Low-to-moderate: single site—findings may not be generalizable	There was no statistically significant difference in average length of longest abstinence between the two groups.
Lagisetty et al., 2017[3]	MAT in primary care—buprenorphine or methadone	Systematic review; 35 included studies (10 RCTs and 25 quasi-experimental designs); included studies across eight countries	Adult outpatient primary care	Successful programs tended to integrate clinical teams with support staff such as nurses and pharmacists to serve as clinical care managers, utilize patient agreements, and offer treatment induction at the patient's home. More research is needed to determine the optimal level of provider training needed to provide behavioral counseling to this population.	Not provided	Not provided	Not provided	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Lee et al., 2012[15]	Buprenorphine/ naloxone maintenance in primary care vs. community referral	Observational—patients induced to buprenorphine in jail vs. those seeking buprenorphine induction post-release; 252 patients from 2007–2008	Individuals released from jail—primary care maintenance vs. community referral	Treatment retention rates for post-release (37%) vs. community (30%) referrals were similar at 48 weeks. Rates of opioid positive urines and self-reported opioid misuse were also similar between groups. Post-release patients in primary care buprenorphine treatment had equal treatment retention and rates of opioid abstinence vs. community-referred patients.	Not provided	Not provided	Not provided	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Lee et al., 2009[24]	Home buprenorphine/ naloxone induction, after prescription in primary care setting; the initial physician visit included assessment, education, induction telephone support instructions, an illustrated home induction pamphlet, and a one-week buprenorphine/ naloxone prescription. Patients initiated dosing off-site at a later time.	Pilot study (observational, no control group); 103 patients—predominantly heroin users (68%) but also prescription opioid misusers (18%) and methadone maintenance patients (14%).	Patient home/ primary care	At the end of week 1, 73% of patients were retained in treatment, 17% provided induction data but did not return to the clinic, and 11% were lost to follow-up with no induction data available. No cases of severe precipitated withdrawal and no serious adverse events were observed. Home buprenorphine induction was thus considered feasible and "appeared safe."	Not provided	Not provided	Low-to-moderate: small sample size, but this was feasibility not outcomes study	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Liebschultz et al., 2014[5]	Linkage to hospital-based outpatient buprenorphine treatment following hospitalization; as compared to detoxification using buprenorphine taper	RCT; 139 patients; medically hospitalized opioid-dependent patients in general medical wards of one urban safety-net hospital between 2009–2012	Inpatient hospital	Participants who received linkage to buprenorphine treatment in primary care were more likely to enter outpatient buprenorphine treatment (52 [72.2%] vs. eight [11.9%], P < .001) as well as to stay in treatment at six-month follow-up (12 [16.7%] vs. two [3.0%], P = .007). Participants receiving the linkage intervention were also less likely to report illicit opioid use in the past month at six- month follow-up (incidence rate ratio, 0.60; 95% CI, 0.46-0.73; P < .01).	Not provided	Not provided	Moderate: small sample size; one study site—limited generalizability; underlying medical condition and severity of opioid dependence were not controlled for	Participants were expected to have lower rates of linkage to MAT compared to the general outpatient population of OUD patients, due to the medical illness that resulted in their hospitalization.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Lucas et al., 2010[14]	Buprenorphine treatment in an HIV clinic, as opposed to referral to an OUD treatment program	RCT; 93 participants; HIV-infected, opioid-dependent patients	Outpatient HIV clinic in Baltimore, MD	Initiation of opioid agonist therapy was substantially more rapid in the clinic-based buprenorphine (BUP) group than in the referred-treatment arm: at two weeks, 84% (95% CI 72%–93%) in clinic-based BUP had initiated opioid agonist therapy compared to 11% (5%–24%) in referred-treatment ($p<0.001$). The average estimated percentages of opioid positive and cocaine positive urine drug tests were significantly lower in clinic-based BUP than referred-treatment (44% [32%–58%] vs. 65% [95% CI, 52%–76%] for opioids, $p=0.015$, and 51% [39%–61%] vs. 66% [54%–76%] for cocaine, $p=0.012$). Subjects in clinic-based BUP had significantly more visits with their primary HIV providers during the study than subjects in referred-treatment (median 3.5 [interquartile range (IQR) 2–4] vs. 3.0 [IQR 1–3] visits, respectively, $p=0.047$).	Not provided	Not provided	Low-to-moderate: small sample size; single center—limited generalizability; authors did assess for the effect of loss to follow up on the results.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Miotto et al., 2012[18]	Buprenorphine therapy delivered in three distinct treatment settings: an opioid-treatment program (OTP) offering individual counseling; a group counseling program utilizing the manualized Matrix Model (MMM) of cognitive-behavioral treatment; and a private clinic setting mirroring standard medical management for buprenorphine treatment provided specifically at a psychiatrist's private practice (PCS).	Randomized trial: 94 participants—28 in OTP, 33 in PCS, and 33 in MMM; patients meeting opioid dependence criteria based on DSM-IIIR, recruited in the community through advertising.	Three settings: (1) a typical OTP is a structured clinical setting where the administration of methadone is observed, (2) a psychiatrist's private practice, and (3) a cognitive behavioral group therapy program, which had not offered physician services on-site in the past.	The proportion of participants who stayed in the study through Week 20 was significantly associated with treatment site (chi square= 6.12; p = 0.05) with the MMM site associated with the highest percentage of participants retained through week 20 (51.5%). For participants who remained in the study past nine weeks, OTP participants had a four times higher drop-out rate compared to MMM participants (p = 0.01) and a six times higher drop-out rate compared to PCS participants (p = 0.01).	Not provided	Initial education of the staff in all three settings about the utility of buprenorphine was crucial. This was particularly true at the MMM program where the staff advocated an abstinence approach to treatment. In addition to a shift in attitude, modifications of practice management were necessary, such as implementing a monitored induction protocol, on-site drug testing and random pill callback checks. The study staff all indicated that they would have made additional refinements in patient management practices had they not been confined by a research protocol.	Moderate: small sample size	No difference in opioid use by treatment site was found.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Mitchell et al., 2013[11]	Intensive outpatient counseling vs. standard outpatient counseling for buprenorphine patients	Randomized trial; 300 participants; African American adults newly admitted to buprenorphine treatment from March 2010–March 2011	Two outpatient SUD clinics	Not provided	Controlling for number of days in treatment, greater counseling exposure was associated with significantly less improvement for three outcomes—days of heroin use, days of cocaine use, and days of criminal activity (all ps < .01).	Not provided	Moderate: no control; two sites—limited generalizability	There was no statistically significant difference between groups receiving standard counseling vs. intensive counseling, and there was no comparison group that received buprenorphine and no counseling.
Neumann et al., 2013[20]	Buprenorphine treatment	Retrospective cohort (chart review); 356 patients receiving buprenorphine for opioid addiction	Outpatient primary care	Of the 356 patients, 127 (35.7%) completed six-month buprenorphine treatment. Completion of treatment was associated with counseling attendance and having had a past injury.	Not provided	Not provided	Low-to-moderate: no comparison group; single center	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Ober et al., 2018[19]	Behavioral therapy based on motivational interviewing and cognitive behavioral therapy; MAT in form of either injectable naltrexone or buprenorphine/ naloxone	Secondary analysis of RCT; 392 total RCT participants—23% received behavioral therapy and 13% received MAT; patients screening positive for substance use (either opioid abuse or alcohol abuse)	Federally qualified health center in Los Angeles, CA	Individuals who initiated behavioral therapy were more likely to have greater self-stigma (odds ratio [OR]=1.60, CI=1.06, 2.42), receive MAT (OR=5.52, CI=2.34, 12.98), and have received the study intervention of collaborative care management (OR=12.95, CI=5.91, 28.37). Individuals more likely to initiate MAT tend to be older age (OR=1.07, CI=1.03, 1.11), female gender (OR=3.05, CI=1.25, 7.46), having a diagnosis of heroin abuse or dependence (with or without alcohol abuse or dependence compared with have a diagnosis of alcohol dependence only (OR=3.03, CI=1.17, 7.86), and having received at least one session of BT (OR=6.42, CI=2.59,15.94),	Not provided	Not provided	Low-to-moderate: no comparison group; single center	Not sure whether the RCT results were ever published; the citation in the reference list has no title.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Pade et al., 2012[23]	Buprenorphine/ naloxone in primary care (BUP/NLX)	Retrospective cohort (chart review); 143 patients induced with buprenorphine/ naloxone between 2009–2011	Co-occurring Disorders Clinic for patients with both chronic pain and opioid dependence (within outpatient primary care)	Sixty (65%) of those 93 patients were on BUP/NLX for more than six months, 19 (21%) were on BUP/NLX for greater than 12 months, and five (6%) for greater than 18 months. Pain scores showed a modest but statistically significant improvement on buprenorphine/ naloxone.	Not provided	Not provided	Moderate: no comparison group; single center; small sample size	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Polsky et al., 2010[27]	Buprenorphine-naloxone detoxification (DETOX) vs. 12-week course of buprenorphine-naloxone (BUP)	Cost-effectiveness study based on randomized trial; 152 patients ages 15-21 years recruited from 2003–2006	Six community outpatient treatment programs	Treatment cost was $1,514 ($p<0.001$) higher for BUP relative to DETOX. One-year total direct medical cost was only $83 higher for BUP ($p=0.97$). The cost-effectiveness ratio of BUP relative to DETOX was $1,376 in terms of one-year direct medical cost per quality-adjusted life year (QALY) and $25,049 in terms of outpatient treatment program cost per QALY. The acceptability curve suggests that the cost-effectiveness ratio of BUP relative to DETOX has an 86% chance of being accepted as cost-effective for a threshold of $100,000 per QALY. Therefore, extended buprenorphine-naloxone treatment relative to brief detoxification was found to be cost effective.	Not provided	Not provided	Low-to-moderate: multisite but small sample	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Polydorou et al., 2017[9]	Integration of buprenorphine maintenance treatment into an established hospital-based opioid treatment program	Case study; 735 opioid-dependent patients treated with buprenorphine from 2006–2013	Hospital-based outpatient opioid treatment program in New York City	During the initial 20 months of implementation, patients enrolled in OTP demonstrated lower rates of positive urine toxicology results for opioids compared with patients in primary care and outpatient psychiatry.	Not provided	Main barriers to implementation were regulations, clinical logistics of dispensing medications, internal cost and reimbursement issues, and professional and cultural resistance.	Moderate: single site but fairly large sample size; implementation themes were identified based on authors' personal experience	None
Schackman et al., 2011[26]	Long-term buprenorphine-naloxone treatment in primary care	Cost-effectiveness study; hypothetical data	Primary care	Office-based buprenorphine/naloxone for clinically-stable patients may be a cost-effective alternative to no maintenance treatment at a threshold of $100,000 QALY.	Not provided	Not provided	Unsure how to assess for a cost-effectiveness study with hypothetical data	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Stein et al., 2015[12]	Distress tolerance (DT) intervention during buprenorphine initiation—behavioral exposure to opioid craving and skills training based in Acceptance and Commitment therapy (based on intervention developed for smokers, *Brown, 2008*).	RCT; 49 participants—24 assigned to DT intervention, 25 assigned to standard of care, which included health education; Individuals age 18–65 seeking buprenorphine treatment, excluding those requiring opioid treatment for chronic pain	Ambulatory care	Participants receiving the DT intervention had lower rates of opioid use at each of the three monthly follow-up points. At three months post-initiation of buprenorphine treatment, 72% of the health education participants were opioid positive compared with 62.5% of DT intervention participants. However, this difference was not statistically significant. No difference existed in drop-out rates between the two conditions.	Not provided	Buprenorphine initiators were targeted because they are at high risk for treatment drop-out and relapse.	Moderate: small sample size, possibility for selection bias as participants responded to study advertisements; study not blinded; no placebo control	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Sullivan et al., 2008[22]	Buprenorphine/ naloxone treatment in primary care	Longitudinal; 166 opioid dependent patients receiving buprenorphine/ naloxone in primary care; outcomes assessed HIV risk behaviors at baseline, 12 weeks, and 24 weeks after treatment initiation	Primary care	Buprenorphine/naloxone treatment was associated with significant reductions in overall and drug-related AIDS/HIV Risk Inventory scores from baseline to 12 and 24 weeks. Intravenous drug use in the past three months was endorsed by 37%, 12%, and 7% of patients at baseline, 12 weeks, and 24 weeks, respectively; $p < 0.001$. Sex while you or your partner was "high" was endorsed by 64%, 13%, and 15% of patients at baseline, 12 weeks and 24 weeks, respectively; $p<0.001$. Inconsistent condom use during sex with a steady partner was high at baseline and did not change over time.	Not provided	Not provided	Not provided	None
Suzuki, 2016[17]	Initiation of buprenorphine during hospitalization	Case series; 29 patients; hospitalized with intravenous-drug-use related infective endocarditis	Inpatient; one urban medical center in Boston, MA	Overall, nine patients (31.0%) successfully initiated buprenorphine maintenance during the hospitalization, and nine (31.0%) accepted a referral to methadone maintenance following discharge. Eleven (37.9%) declined MAT altogether.	Not provided	Not provided	High: single site, no comparison group, small sample size	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting:	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (high, moderate, low)	Comments
Suzuki et al., 2015[16]	Initiation of buprenorphine during hospitalization	Case series; 47 patients; hospitalized for reasons other than treatment of opioid dependence	Inpatient; one urban medical center in Boston, MA	Twenty-two (46.8%) patients successfully initiated buprenorphine treatment within two months of discharge. Those patients obtaining a referral to a specific program were more successful in continuing treatment, but this difference did not reach statistical significance (59.1% vs. 39.1%, p = 0.18).	Not provided	Not provided	High: single site, no comparison group, small sample size	None

Table B.55: Patient Identification Errors in the Operating Room–Single Studies

Note: Full references are available in the Section 11.1 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Bergal et al., 2010[6]	Patient participation in preoperative site-marking procedure	Study involved 200 patients scheduled to undergo orthopedic surgery. On the day of their surgery, patients were assessed as to their compliance with the instructions. The Fischer exact test for categorical data and the standard t test for continuous data were used to test differences in patient characteristics between those who did and did not mark their surgical site. The level of significance was 0.05.	Preoperative room/ operating room	Out of the 200 patients in the study, 135 patients (68%) were compliant with marking before the surgery. Of the 135 patients who completed a mark, 133 patients (67.2%) placed some mark on the correct surgical site and 123 patients (62.1%) marked the site using "yes," per instructions. Sixty-three patients did not place any mark at all. No wrong-site surgery occurred during the study. Compliance was statistically significant when ages were compared. Patients with a mean age of 46.8 versus 51 years were more likely to comply. Compliance was also statistically significant from enrollment to time of surgery—10.4 days (more likely to comply) versus 23.1 days.	Not provided	Per Joint Commission on Accreditation of Healthcare Organizations recommendations, a physician personally explained the study to the patient, acquired written consent, and encouraged safety compliance. The patient also received written instructions with the same information the physician had provided. The approach provides a more effective outcome and increased compliance and does not rely on the patient to read and comply with written instructions. Only 68% of patients complied, so the protocol probably needs to be used in combination with another wrong-site prevention protocol.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Garnerin et al., 2008[8]	Verification protocol and periodic audits to measure compliance while also providing feedback	Verification protocol: (1) Anesthetist or nurse anesthetist in charge of patient performed checks on identity and site of surgery before administering the anesthetic. Patients who participated in the verification process were asked to provide their first and last names, date of birth, and, when applicable, the site of the surgery. (2) Following the checks, the identity data were compared with the information on the patient's wristband and with the data provided in the operating theater schedule and the patient's medical record. (3) The site of surgery had to be compared with the surgeon's check and with the information provided in the operating theater schedule and the patient's medical record. Audits were conducted throughout the 9-month period of the intervention. Audits consisted of direct observations of the first contact between a patient and the anesthetist or nurse anesthetist, during which checks on identity and site of surgery had to take place. Observational: compliance with the verification protocol was assessed over time as the percentage of	Intensive care unit	Of the 1,000 total interactions, in 985 interactions, patients participated in the verification process. Overall compliance with all audit criteria significantly improved over time ($p<0.001$), except for surgical site signed (77.5% CI, 80.6–83.5). During the followup period, over 90% compliance was reported for the two audit criteria: "patient wearing wristband" and "check of surgical site performed."	Not provided	Barriers to overcome: convincing providers to complete the protocol and improve collaboration with the surgical services. Verification protocol along with information technologies should be used. The verification protocol by itself is not sufficient.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
		observations that satisfied each audit criterion. The 95% confidence interval (CI) was computed assuming binomial distribution. During the intervention, 1,000 interactions between patients and anesthetists or nurse anesthetists were observed.					
Knight et al., 2010[7]	Anatomic marking form (AMF) to prevent wrong-site, wrong-procedure, and wrong-person surgery	Hospital staff submitted an AMF, which engaged the patient in confirming the surgical site, to the Joint Commission's Standard Interpretation Group. In addition to the AMF, an administrative policy was established to guide the appropriate use of the form as an alternative process for site-marking by the surgeon. Surgeon and nursing staff satisfaction with AMF was assessed through a qualitative electronic survey sent to 205 potential users (43 nurses responded and 23 surgeons responded).	Preoperative room/ operating room	The AMF has been used in more than 112,500 surgical procedures at the University of Illinois College of Medicine. Since the implementation of the AMF, there has only been one case of documented wrong-site surgery. Sixty-five percent of survey respondents indicated they used the AMF regularly for "most or all" procedures, and 23% indicated they regularly followed standard site-marking practices. Seventy-seven percent of respondents indicated they were very satisfied with the AMF, 16% were satisfied or neutral, and 7% were very dissatisfied and preferred traditional site-marking.	Not provided	Because of the rarity of wrong-site events, meaningful statistical comparisons are elusive. Authors mention they have not been able to find specific evidence that the Universal Protocol decreases incidence of wrong-site surgery. AMF, like the Universal Protocol, should be combined with participatory planning, checklists and redundant communication.	Low

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Masud et al., 2010[5]	Surgical site-marking	Prospective audit of 500 surgical markings for elective procedures carried out by surgeons between June 2008 and May 2009. Visibility pre and post draping was noted along with arrow markings and the use of an indelible pen. The location, laterality, and person marking were also noted. Total markings included: 204 inguinal hernias, 35 umbilical hernias, 48 varicose veins, 50 toenail removals, 123 excisions of skin lesions, 10 femoral artery procedures, and 40 breast procedures.	Preoperative room/ operating room	Three procedures (.6%) were not marked prior to theater; 497 procedures were all marked correctly for location and laterality and were marked by an operating surgeon present in the surgical procedures. An indelible marker pen was used for 88% of cases. An arrow was used for 64% of cases. Only 59% of markings remained visible after draping, and 31.4% of markings were placed where draping covered the markings.	Not provided	Incidents may be underestimated by at least a factor of 20 because they are self-reported.	Not provided
Moshtaghi et al. 2017[4]	Universal Protocol	Retrospective study of wrong-site surgery reports investigated by California's Department of Public Health between 2007 and 2014. A total of 142 cases were reviewed.	Operating room	The Joint Commission mandated the use of a timeout prior to each surgical procedure. Common causes of wrong-site surgery: lack of leadership (30.9%), human factors (23.4%), and miscommunication (10%).	Not provided	JC reporting is not mandatory; therefore, it is difficult to assess the true prevalence of wrong-site surgery. Although only 60% of patients correctly mark their surgery sites, it is still determined to be the most effective way of preventing wrong-site surgery. The analyzed data did not show any downward trend or reduction in wrong-site surgery since the implementation of the Universal Protocol	Not provided

Table B.56: Patient Identification Errors in the Operating Room–Systematic Reviews

Note: Full references are located in the Section 11.1 reference list.

Author, Year	Description of Patient Safety Practice	Setting	Summary of Systematic Review	Implementation Themes	Notes
Devine et al., 2010[1]	Joint Commission Checklist Universal Protocol for Preventing Wrong Site, Wrong Procedure, Wrong Person Surgery	Operating room	The estimated rate of wrong-site surgery varies, ranging from 0.09 to 4.5 per 10,000 surgeries performed. Many studies do not allow for the calculation of an event rate. Contributing factors to wrong-site surgery include incorrect patient positioning or preparation of operative site, patient or family providing incorrect information, incorrect or lack of patient consent, failure to use site-markings, surgeon fatigue, multiple surgeons, multiple procedures on same patient, unusual time pressures, emergent operations, unusual patient anatomy, and overall poor communication. No evidence exists to support the Joint Commission checklist, North American Spine Society checklist, or other preventive measures and their effectiveness in preventing a wrong-site surgery.	North American Spine Society and Joint Commission checklists are insufficient on their own to minimize wrong-site surgery.	Strength of evidence for the questions is very low (incidence/frequency of wrong-site surgery and what preoperative measures are effective in preventing wrong-site surgery) and low (what are the causes of wrong-site surgery?).
Hempel et al., 2015[3]	Joint Commission Universal Protocol	Operating room	Review examined the incidence, root cause of. and interventions to prevent wrong-site surgery, surgical fires, and retained objects since the implementation of the Universal Protocol. Authors reviewed 138 studies. and the most common cause for wrong-site surgery was miscommunication. Five studies examined the effect of the Universal Protocol intervention and, although there was a downward trend in wrong-site surgery, it was statistically insignificant.	Review identified 25 studies that evaluated operationalizing components of and alternatives to the Universal Protocol, but none of the studies reported a statistically significant effect on wrong-site surgery.	None
Kim et al., 2015[9]	Surgery safety practices	Operating room	Healthcare workers should use the following to reduce wrong-site surgeries: (1) When scheduling the procedure, schedulers should verify patient documentation and receive all surgery requests in writing. (2) During the preoperative visit, patient should provide informed consent, and should be involved in marking the procedure site. (3) Before the procedure, a safety checklist such as the World Health Organization (WHO) checklist should be fully implemented. (4) A discharge plan should be discussed before leaving the facility.	According to the author, patient safety guidelines in surgery are too general and need more standardization.	None

Author, Year	Description of Patient Safety Practice	Setting	Summary of Systematic Review	Implementation Themes	Notes
Ragusa et al., 2016[2]	Joint Commission Universal Protocol and WHO Safe Surgery Checklist	Orthopedic surgeons/ operating rooms	Surgical checklist compliance varies, and additional measures like audits or monitoring were necessary to maintain compliance. No reviewed study reported a 100% compliance rate. Literature shows that the use of the WHO surgical safety checklist in the operating room improves patient safety in the operating room by decreasing postoperative complications and mortality. This approach is also shown to improve processes such as the timely use of prophylactic antibiotics; and after the implementation of checklists, which help to improve team communication and decrease communication failures. Reporting of wrong-site surgery is voluntary and those that are reported represent only a portion of those that occur, so it is difficult to draw conclusions about the frequency of occurrence. Wrong-site surgeries are rare, and showing any statistically significant reduction in occurrences with the implementation of checklists would require a very large study.	Five implementation barriers: (1) unfamiliarity with checklist, (2) hierarchal style in operating room, (3) problems with timing of the time-out portion, (4) duplication or repetition of items on checklist, (5) inclusion of items on the checklist that were not relevant. Literature also showed that some key team members limited the successful implementation of checklists. Literature shows that some surgeons were not supportive, while anesthesiologists and nurses tended to be more supportive.	None

Table B.57: Infusion Pumps, Structured Process Change and Workflow Redesign—Single Studies

Note: Full references are available in the Section 12.1 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Biltoft and Finneman, 2018[10]	Hospital implemented smart pump- electronic medical record (EMR) interoperability to decrease opportunities for errors by reducing manual clinician keystrokes needed to program an infusion. Conducted workflow analyses prior to implementation. The team made necessary changes to streamline workflow, such as reconfiguring rooms so that infusion pumps and EMR computers could be accessed at the same time for the most accurate infusion documentation. In addition, implemented a double-check to ensure that all medication identifiers populated the correct drug library and corresponded to those in the EMR. This helps streamline nursing workflow, especially when there are patient transfers between units.	Case study	Hospital (286 beds) within a regional health system. United States	Pre-population of infusion parameters reduced manual keystrokes by 86%. Compliance with using interoperability technology averaged 70-80% in the first 7 months. Rate of appropriate entry of patient identification information by pump users increased from 35.5% to 81%. Mean monthly number of alert overrides decreased by 20%.	Not provided	Pharmacist-led implementation of smart pump-EMR interoperability led to measurable improvements in intravenous (IV) medication safety and improved accuracy, timeliness, and efficiency of IV infusion documentation.	High—case study

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Chaturvedi et al., 2019[9]	Hospital implemented intravenous clinical integration (IVCI), which links EMRs, computerized physician order entry (CPOE), smart pumps, and bar code medication administration systems in order to reduce human errors caused by manual documentation. During the planning process, hospital leaders discovered significant variation in nursing workflows for IV administration and engaged in multiple efforts to standardize workflows.	Qualitative description of hospital's IVCI implementation. Conducted semi-structured interviews with 33 informants: 4 pharmacists, 8 IT personnel, 10 frontline nurses, 4 nurse trainers, and 7 hospital leaders. Researchers observed nurse IVCI training and nurses on five units.	Large nonprofit academic medical center (886 beds), United States	Hospital leaders viewed standardization as extremely beneficial because it was perceived to reduce the frequency of nursing workarounds that could cause patient harm.	Nurses often forgot to validate infusion completion times, which led to large errors in recorded infusion volumes. Although the EMR automatically enters infused volumes into patients' charts, nurses are required to manually validate completion times. IVCI significantly reduced the amount of time required by nurses to program the pumps but did not decrease their workload overall. Many nurses reported that IVCI increased the number of computer steps required to administer medications. There were challenges gaining buy-in from nurses to adopt workflow changes, and frontline staff expressed concerns regarding safety of workflow changes. Since not all units had IVCI, moving patients required special procedures.	IVCI implementation is not just a technological intervention, but also requires workflow standardization in order to be successful.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
DeGraff, 2013[8]	In response to a shortage of IV pumps and staff members hoarding pumps, the team created a new procedure for cleaning and restocking pumps on floors. This allowed staff to easily see when the supply fell below a set minimum and pumps needed to be restocked.	Case study	Five hundred seventy-bed regional referral center and teaching hospital, United States	New process reduced pump handling steps from 26 to 8. Pumps were available when needed 94% of the time, compared to 28% before implementation.	Not provided	Hospital dramatically improved utilization of IV infusion pumps by streamlining their workflow.	High—case study
Iacovides et al., 2014[12]	Survey investigated the extent to which standardization of infusion devices has occurred.	Online survey sent to device managers and trainers within National Health Service (NHS) organizations. Forty-five respondents participated in study.	Staff were involved within 49 U.K. organizations representing 120 hospitals. United Kingdom.	A high level of standardization was reported. (Only 4% reported there was no standardization at all.)	Reasons for not using dose error reduction software included time required to implement and train staff, and not being able to standardize across the entire site.	To implement technology, organizations need to overcome challenges, including existing device contracts, infrastructure and resources available, required time and investment, and complications related to lack of standardization.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Lyons et al., 2018[7]	Observers compared medications being administered against the prescription and local policies/guidance. Recorded any deviations from a prescriber's written or electronic medication order, the hospital's intravenous policy and guidelines, or the manufacturer's instructions.	Point prevalence observational study. Data were collected on 1,326 patients who were administered 2008 infusions.	16 NHS trusts, England.	Most (90%) of the observed errors were considered unlikely to cause harm. One site responded to poor compliance with documentation of medication administration by purchasing handheld computers to allow staff to access electronic records in closer proximity to patients.	Nearly 48% (47.9%) of infusions had at least one procedural or documentation error. Non-compliance with hospital requirements for labeling infusion administration sets was most common. Discrepancy rates were higher in infusions delivered using smart pumps compared to those without safety features. Differences were linked with policy requirements. Error rates were similar.	Procedural deviations may not always represent poor practice, but rather poor fit between policy and everyday practice.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Pinkney et al., 2010[11]	Conducted 3 experiments to quantify the impact of infusion pump type, smart pump design, and training on nurses' ability to safety deliver IV medications.	Conducted 3 observational studies.	Usability lab that simulated an inpatient unit, Canada.	Smart infusion systems were found to statistically reduce the rate of medication errors. Users programmed almost all infusions within a drug library when the pump workflow either defaulted them into the drug library or prompted them to use the drug library.	Soft limit warnings had no impact on preventing errors since nurses simply overrode them.	Smart pumps that rely on users actively engaging the drug library are less preferable to those that encourage/require nurses to enter into the drug library. Supporting and constraining users to follow the preferred workflow is a design-oriented solution that can help ensure users employ the safety features of the smart pump. Smart pump implementation should be viewed as part of a larger safety initiative, not just technology replacement. Implementation should focus on design of workflows and environments.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Russell et al., 2015[4]	Study examined the impact of a bidirectional interface between CPOE and pharmacy systems on the frequency and types of discrepancies between orders for medication and intravenous fluid (IVF) infusions and pump settings. Pediatric intensive care unit (PICU) underwent expansion and relocation that caused changes in workflow.	Uncontrolled before and after study using a prospective, observational design. Compared proportion of discrepancies with results of a study conducted by the authors in 2007.	Children's hospital, PICU (72 beds), United States	Overall discrepancy rate did not change; however, type of discrepancy changed. Unauthorized medications decreased from 60% in 2007 to 4% in 2010. Bidirectional interface allowed pharmacist to immediately reconcile verbal orders. Change in workflow on rounds was likely responsible for decrease in discrepancies for parenteral nutrition subgroup medications. In the new environment, pharmacy and dietary presence on rounds increased, resulting in greater collaboration among pharmacists, dieticians, and the providers responsible for ordering, preventing the number of reorders that previously had occurred.	Fifty-four of 303 (18%) observations of medication infusions revealed order programming discrepancies, while 46 of the 152 (30%) observations of IVF revealed order-infusion pump discrepancies. There was significant increase in proportion of omitted medications and wrong dose. Change in workflow was suspected to be the reason for the increase.	Analysis suggests that the observed decreases in discrepancies were not solely attributable to the technology. Workflow and other factors had an impact on the observed changes.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Schnock et al. 2017[6]	Objective of the study was to investigate the frequency and types of IV medication errors associated with the use of smart pumps. Measured policy violations to assess the IV medication administration process.	Prospective point prevalence approach to capture errors associated with smart pump administered medications. Evaluated 478 patients receiving and/or prescribed IV medications.	Ten hospitals: seven academic medical centers and three community hospitals, United States		Violations of IV labeling and tubing change policies were the most frequent error types (60% and 35%, respectively). Infusion rate errors were the leading type of serious medication error.	High rate of errors was found in the administration of IV medications despite the use of smart pumps, but relatively few were harmful errors. In reviewing labeling policy, researchers found that some information needed prior to implementation of electronic records is no longer necessary. Team recognized the benefits of using standardized tubing labels to distinguish when nurse should change tubing. Results highlight the importance of reviewing existing practices and policies when implementing technologies such as smart pumps.	Moderate
Wiseman et al., 2018[5]	Implemented clinical pharmacist annotation on medication charts (i.e., completing missing information in infusion medication orders) and adopted smart pump technology. Smart pump adoption involved a 6-month development phase.	Semi-structured observational study conducted over four periods, pre and post intervention: July 2009, July 2011, April 2012, and June 2014. Over 5 years, 16,866 patients and 2,599 infusions were observed.	Four hundred fifty bed tertiary referral hospital, Australia.	After implementing pharmacist annotation, errors reduced from 16.6 to 8.1%. Implementation of smart pumps resulted in a reduction from 8.1 to 3.9%.	Not provided	Results suggest clinical pharmacists play a key role in reducing rate of errors.	Moderate

Table B.58: Infusion Pumps, Staff Education and Training—Single Studies

Note: Full references are available in the Section 12.2 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Carayon et al., 2010[14]	Nurses attended training sessions on smart intravenous (IV) pump use that occurred the week before pump implementation. Training consisted of hands-on skills training provided by nurse super-users and an optional computer-based training module.	Data were collected in three longitudinal surveys: pre-implementation of smart IV pumps and 6 weeks and 1 year post-implementation. Sample of nurses that responded to the surveys: pre-implementation survey (n=190, response rate: 32%), 6-week-post-implementation survey (n=322, response rate: 31%), and 1-year-post-implementation survey (n=399, response rate: 38%).	Academic hospital. United States	Overall, nurses' acceptance of the smart pump technology was positive and improved over time. Respondents rated the information they received about pump implementation as more useful before implementation than 6 weeks after. "Learning to operate the pump" became easier 1 year after implementation, compared to either before or 6 weeks after implementation.	Respondents reported that the training materials were more confusing in the 6-week and 1-year-post-implementation surveys.	Nurses reported more negative perceptions of the smart IV pump implementation process (e.g., usefulness of information received about pump implementation and clarity of training materials) 6 weeks after implementation, compared to what they perceived before implementation. This suggests more attention should have been devoted to the implementation process, especially regarding information and training materials.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Ferguson et al., 2010[4]	Hospital was following all the patient-controlled analgesia (PCA) guidelines recommended by USP except for annual retraining staff on the proper usage. Established mandatory training by nurse educators of registered nurses (RNs) who used PCA pumps. Participants were required to return within 1 hour of the review to demonstrate proper programming of a preprinted order set into the PCA pump without any assistance from the educator. All staff members were required to complete an online module and test.	Quality improvement (QI) project. Examined PCA errors in the pre-intervention and post-intervention periods to determine effectiveness of mandatory training. Pre-intervention data were collected from June to August 2006 and post-intervention from June to August 2007. The educational intervention occurred from January to April 2007.	Small Midwestern hospital with 22 patient care units. United States	Significant decrease from eight errors reported in the pre-intervention period to one in the post-intervention period.	Not provided	Results show that the educational intervention was effective in deceasing PCA pump errors. Adding additional mandated education programs must be carefully considered. Combining QI data with education initiatives can help provide objective measures that resources are well spent.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Gavriloff, 2012[8]	Staff education focusing on correct use of the safety software and the benefits of preventing medication errors. Super-user training for medical safety champions and education on the patient care units for nurses.	Performance improvement project using plan, do, study, act (PDSA) methodology.	359-bed pediatric hospital. United States	Within 2 months, 100% of RN staff were educated and the content was fully incorporated into nursing orientation. Adherence rate was 68% 1 month after staff education was completed, an increase from 28% at baseline. After the chief nursing officer sent a followup email encouraging nurses to use the medication safety software, adherence increased to 85%. In the following months, adherence continued to remain above 85%. Education on the smart pumps allowed for any safety concerns to be easily communicated and provided closed-loop communication with the nurses.	Not provided	The combined use of staff education, improving communication, programming strategies, medication safety champions, adherence monitoring, and technology acquisition increased nursing adherence to a rate consistently above 85%. Staff education that focuses not only on the “how” to use the smart pumps but also on the “why” it is used is important to increase medication safety software adherence.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Giuliano, 2015[6]	Study aimed to measure the impact of user training on programming times and use errors. User training consisted of a brief training, according to manufacturer's instructions, on the IV medication tasks being used in the study.	Pilot study using within-subjects design. Study measured differences in programming times and frequency of programming errors for three IV smart pumps. Fifteen critical care nurse participants completed five programming tasks in a simulation laboratory.	Study participants were recruited from Boston-area hospitals. Data collection took place in a simulation laboratory.	Programming time for all five tasks across the three pumps was shorter after the user training. Majority of the tasks had a statistically significant time difference. The percentage of use error decreased after user training for all three IV smart pumps: pump A, 30% to 7%; B, 17% to 3%; and C, 8% to 1%.	Not provided	Findings support the value of proper user training in helping clinicians learn to operate the IV smart pumps in a more time-efficient manner and make fewer use errors.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Herring et al., 2012[9]	Hospira Plum A+ smart pumps were implemented, and education about safety feature use was provided to bedside patient care nurses at program initiation through online computer modules designed by manufacturer. The researchers surveyed nurses and identified education and training as an obstacle to smart pump utilization. Over a 6-week period, a pharmacist provided education to target identified obstacles. Active learning, practical skills lab mandated for all institutional nurses. The skills lab included hands-on scenarios for programming, troubleshooting tactics, and hypothetical situations. Cardiovascular nurses were offered an optional educational presentation on use of safety features.	QI cross-sectional study. Rates of use of the delivery modes were captured through a wireless database. Nurses were surveyed to identify obstacles in the cardiovascular service clinical care areas; 35 of 60 nurses (58%) responded. Based on survey results, interventions were designed to target education and burden of use.	Academic center hospital (689 beds). United States	The majority of survey respondents agreed or strongly agreed that training and education were adequate, the drug library enhanced patient safety, and they knew how to use the drug library. Use of "with limits" mode (when all safety features are applied) increased from 5.5% to 30.5% after educational interventions.	Of the free-text survey comments, 44% requested additional training on the safety features.	Survey results indicate that education from the manufacturer alone may be insufficient. Supplemental hands-on training significantly increased safety feature use. Overall use was still low. One explanation may be related to the procedure for smart pump data entry.	Moderate
Lee, 2010[13]	Audit and response to findings, including standardized settings and controls to ensure consistent operation of pumps.	Conducted an audit and then developed coordinated approach in response	Two acute hospitals within a National Health System Trust, South Wales.	A series of training days and standardized practices were developed to ensure operators had a clear understanding of the limitations and correct procedures for setting up these devices.	Audit showed staff were being deployed to other wards and exposed to new devices they had not been trained to use.	Using a coordinated approach to replace infusion pump devices and setting short and long-term goals can be an effective way to manage risks.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Luctkar-Flude et al., 2012[11]	Online virtual IV pump educational module for undergraduate nursing students. Participants assigned to the experimental group were required to complete the virtual IV pump educational module.	Twenty-six nursing students in control group and 17 in the experimental group All participants completed an IV Pump Skills Self-Confidence Survey. Experimental group completed a Virtual IV Pump Educational Module Satisfaction Survey. Lab research assistant evaluated student performance of IV pump skills.	Academic hospital, Canada.	Majority of students felt the module enhanced their knowledge of programming the IV pump and felt the virtual IV pump module was convenient and easy to use. Overall, students in the experimental group had higher performance scores than those in the control group; however, they took longer to perform skills. Difference was not statistically significant. Experimental group participants scored significantly higher than control group participants in programming a continuous medication infusion.	Most students did not feel the module enhanced their ability to program a basic infusion, secondary medication bolus, or continuous medication infusion.	Findings suggest there is value in providing virtual online education module in the nursing skills lab.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Nemeth et al., 2014[10]	Research to understand the effect of introducing a smart pump through a naturalistic look into the experience of those who use it.	Mixed-methods field study combining 9 hours of observation, formal interviews, and Cognitive Task Analyses Sample: 9 nurses, 1 biomed engineer, 1 pharmacist.	Midwest tertiary care hospital. United States	The study found that, in the opinion of nurse study participants, the implementation of the smart pump has so far been a substantial success.	The research team found that there is a need for further investigation into system, performance, and organizational factors that affect nurses' understanding of how the smart pumps operate.	In training, nurses should hear information about the most relevant functions and potential challenges that they may encounter, and have opportunities to apply learning through case examples.	Moderate
Orto et al., 2015[7]	Study aims: (1) develop a nurse-led smart pump champion group and (2) revise existing protocol on IV therapy to integrate use of smart pumps. Two nurse directors trained the champion group to educate coworkers. Nurse champions in each unit conducted monthly education sessions. Over the 6 months of intervention, the champion group provided education to registered nurse (RN) staff individually and in groups to ensure that all RNs were using the smart pumps and associated drug libraries.	QI project: Single cohort pre/post design. 600 direct-care RNs.	Fourteen nursing units in a southeastern community hospital. United States	Overall hospital compliance rate post-implementation was significantly improved (increase from 83.5% to 92%). Costs avoided because severe harms were averted were $367,500 at the end of the intervention period compared with $612,500 6 months before the intervention. Severe harms averted dropped from 0.68 to 0.44 post-implementation.	Not provided	Development of a nurse-led champion program led to a significant improvement in compliance and decrease in number of severe harms. Nurse managers created a culture of safety and coached staff who were not compliant with smart pump drug library use.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Quattromani et al., 2018[12]	Study objective was to determine if the smart pump app is an effective and engaging educational tool for nursing students compared to existing traditional training methods. Traditional training consisted of small groups of students with one faculty member going over smart infusion pump training using a single smart infusion pump device per two students. The interventional group training consisted of small groups of students each using the mobile app smart pump training on a tablet. The smart pump app is an interactive self-contained learning encounter built on a mobile platform and designed for nurses. The app takes the students through each step of smart pump programming and allows for interactive trial and error,	Randomized controlled trial Students were randomized into either the traditional group or the intervention app group. Eighty-seven nursing students were assigned to the traditional group and 94 to the app group.	Large urban school of nursing simulation center in the Midwest. United States	Participant feedback on the app was overall positive, and 70.2% strongly agreed or agreed the app was easy to use.	There was no significant difference in outcomes of medical knowledge, simulation performance, and learner confidence. Students gave neutral ratings to whether they would like to use the tablet app teaching method more frequently and whether they will feel more comfortable at a patient's bedside as a result of using the app.	Study did not find significant differences in learner-centered outcomes or performance measures between the traditional teaching methods and app group.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Subramanyam et al., 2016[15]	Educated anesthesiologists and certified registered nurse anesthetists (CRNAs) who regularly provided anesthesia about the importance of safety checks to reduce medication errors. Educated stakeholders with a job aid (anesthesiologists, CRNAs, RNs) about the use of standardized pump programming, and RNs about anesthesia medications.	QI project using PDSA cycles.	Urban tertiary pediatric academic care center, anesthesia department. United States	Implementation of two- person verification resulted in >90% medication programming being double-checked prior to administration.	Cultural resistance to changing to two-person verification process. This challenge was discussed at departmental meetings.	A standardized team-based approach decreased the number of medication errors by early identification of programming errors.	Moderate
Van der Sluijs et al., 2019[5]	Implemented standard protocols on how to change syringes and a fixed, dedicated moment to perform double-checks. Used a Lean coach, a formally trained employee who supports Lean projects in hospitals, to support efforts.	Pre-post observational study; used Lean philosophy. Measured impact of interventions by performing unannounced sequential audits.	Tertiary care university hospital, 32-bed mixed medical surgical intensive care unit (ICU), Netherlands.	Over 18 months, the overall percentage of errors dropped from 17.7% to 2.3%.	Not provided	Results show a Lean approach is successful in reducing the number of errors with the administration of medication with syringe infusion pumps in the ICU.	Moderate

Table B.59: Alarm Fatigue, Safety Culture-Single Studies

Note: Full references are available in the Section 13.1 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
AMMI, 2013[18]	Implemented a systems approach, which involved a cycle of continuous improvement, including prioritizing improvement, designing and testing change, implementing change, and continuing to measure performance.	Case study	Dartmouth-Hitchcock Medical Center. Medical-surgical orthopedic unit (36 beds).	Rescue events decreased from 3.5 per 1,000 patient days before implementation to 1.2 afterward. Intensive care unit (ICU) transfers decreased from 5.6 per 1,000 patient days to 2.9. Documented high patient and clinical acceptance of the surveillance monitoring.	Not provided	Based on results, expanded surveillance monitoring to additional adult medical-surgical units and pediatric and adolescent unit. One of the researchers noted that "the key to success was that the technology was matched with a culture of caring."	High: case study and not peer reviewed	Pulled from Association for the Advancement of Medical Instrumentation (AAMI) Safety Innovations Series—manual search Included in PSP 2
Allen et al., 2013[14]	Adopting the lessons of the pilot, the team developed an evaluation tool to assess staff competency in identifying and responding to alarm systems management. Recognizing the lack of standardized protocols, the health system's leadership established its own protocol and adopted this tool as universal and standard across all departments in the system.	Case study	University of Pittsburgh Medical Center (UPMC), Presbyterian Hospital (737 beds).	Overall alarm signal time was reduced by approximately 80%. Since this protocol was put in place, there has been no increase in adverse patient events. Post-survey results of nurses showed a 13% decrease in number of nurses who rated themselves not confident in one or more aspects of monitor functionality.	Not provided	As nursing staff in the pilot units became more comfortable with the new process, interest among hospital leadership grew. Alarm management at UPMC is viewed as a team effort with bedside and clinical care nurses, clinical engineers, clinical directors, unit directors, and risk management personnel all having a stake in the success of initiatives that seek to improve patient safety.	High: case study and not peer reviewed	Pulled from AAMI Safety Innovations Series—manual search

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
						through alarm management.		
Alsaad et al., 2017[10]	Team of progressive care unit (PCU) nurse manager, nurse educator, and medical transcription manager participated in the creation and dissemination of clear guidelines and protocols for telemetry use. Protocols developed included: a flow diagram to assist providers in the determination of a patient's needs, a stepwise detailed process on how to check encounters to ensure the appropriateness of cardiac telemetry (CT) monitoring, and standard protocol for electrode placement.	Quality improvement (QI) study. Collected pre-post intervention data. Used different statistical methods to report the study results, including paired t-test, $\chi 2$, and Mann-Wilcoxon equation.	Mayo Clinic campus in Jacksonville, FL. PCU (27 beds).	Nurses reported 27% perceived decrease in alarm fatigue post-intervention and 10% reduction in CT assignment post-intervention. Significant cost reduction was achieved by implementing the protocols. No significant differences in mortality rate before and after intervention.	Not provided	Development of a clear and applicable protocol for the appropriate use of CT in non-cardiac-related hospitalized patients has led to fewer monitored patients and fewer telemetry alarms, which resulted in less alarm fatigue and reduced cost.	Moderate	Included in Patient Safety Practice (PSP) 2
Cameron and Little, 2018[12]	Hospital leadership directed the QI department to develop a plan to meet the Joint Commission National Patient Safety Goal (NPSG). Formed an alarm management committee that developed an alarm policy and planned	QI study using pre-/post-test design to evaluate the alarm management education program and nurses' perceptions and practices related to	Florida acute care hospital (257 beds).	Significant improvements reported in 8/12 of the questions related to alarm perceptions. Sixty-six percent of nurses who completed post-test reported they strongly agree or agree they have	Alarm perceptions were more negative post-test in 4 questions related to: alarms reducing attention to patients, feeling	The findings of this QI project indicate that nurses are receptive to education on alarms, and changed their perceptions and practices based on the education program and a new policy. Through strong leadership and a team approach, hospitals	Moderate	Included in PSP 2

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	an education program for nurses on alarm management.	clinical alarms. Likert questions were analyzed using Wilcoxon signed-rank test with a confidence interval of 95%. Participants: 417 nurses from all departments (215 completed post-test).		improved their alarm management practices. Nurse-initiated collaborative team-based alarm practices significantly improved, including consulting a provider for individualized monitor settings and judicious use of telemetry monitoring versus unnecessary use. Results also showed significant improvement in selecting appropriate intervention.	overwhelmed by alarms, alarms contributing to nurses' stress level, and some situations requiring alarm disabling.	have the opportunity to improve patient safety while improving the work environment, patient care, and overall staff morale. Leadership, equipment, policies, and staff education are the four cornerstones in developing and implementing effective alarm management evidence-based practices in a hospital setting. Hospitals should have policies and education in place to empower nurses to implement alarm management best practices and standards set forth by professional organizations.		
Dandoy et al., 2014[3]	Multidisciplinary alarm oversight task force created and implemented a standardized, team-centered, cardiac monitor care process (CMCP).	QI study using Model for Improvement to design, test, and implement changes. Tested hypotheses using PDSA (plan, do, study, act) measures.	Cincinnati Children's Hospital Medical Center. Bone marrow transplant unit (24 beds).	During implementation the median number of alarms per patient-day decreased from 180 to 40. Median number of false alarms on the floor fell from 95% to 50%. Compliance with the CMCP remained stable at a median of 38% through PDSA testing. Once roles	Not provided	Found significant decrease in the number of alarms per monitored patient with the implementation of a standardized process. Fewer false alarms allow staff to address alarms more promptly.	Moderate	Included in PSP 2

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
				and responsibilities were determined and the process was clearly defined, full implementation continued and the unit's overall compliance with the CMCP increased to a median of 95%.				
De Vaux et al., 2017[2]	Medical critical care leadership team organized an alarm management team. Leadership applied recommendations of Association of Critical-Care Nurses' clinical toolkit and distributed materials to staff to provide guidelines for alarm management.	QI study using direct observation methods once pre-intervention and at three points within 6 months post. Sample size of patients observed varied from 23 to 26 at data collection points.	Yale New Haven Hospital, York Street Campus. Two step down units (28 beds each).	Total alarms decreased from 251 in March 2014 to 12 in Feb 2015. False alarms decreased from 201 in March 2014 to 12 in Feb 2015. Alarm setting customization increased from 39% pre-intervention to 87.5% post. No adverse patient events were reported during the observational time period.	Not provided	Authors attributed increases in customization to cumulative effect of staff education and best practice interventions. Team shared findings with leadership, and as a result the St. Raphael campus of New Haven Hospital adopted default alarm changes.	Moderate	Included in PSP 2
Epstein et al., 2016[5]	Implemented a new lead hygiene policy and procedure, and educated staff on how to better manage telemetry station and patient-specific alarm settings.	Case study	NCH Healthcare System. Pilot telemetry unit.	Over 4 months, the pilot unit lowered its total number of alarm signals by 69% without a negative impact on patient safety.	Not provided	NCH discovered that a key factor in successful alarm management is continuing education for basic monitor and device management when setting device alarms. NCH has been successful in sustaining its alarm management process	High: case study and not peer reviewed	Pulled from AAMI Safety Innovations Series—manual search Included in PSP 2

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
						by constantly monitoring and responding to near real-time alarm data in the shift report. One researcher highlighted this by noting that "by driving our alarm management process with data, we know what we need to target and if we're making improvements."		
Graham and Cvach, 2010[6]	The Alarm Management Task Force tested interventions that informed the development of an interdisciplinary hospital-wide cardiac monitoring protocol. The medical PCU's (test unit) Comprehensive Unit-Based Safety Program (CUSP) team oversaw this project and led the small tests of change. The goals of a CUSP team are to (1) improve the culture of safety on the unit, (2) allow staff to focus safety efforts on unit-specific problems, and (3) collect and analyze data to improve patients' safety.	QI project. Collected baseline data and then implemented tests of change. Administered a pre- and post-intervention survey to nursing staff.	Northeastern Academic Medical Center. Medical PCU (15 beds, 30 nurses).	Forty-three percent reduction in critical physiological monitor alarms. Nurses perceived the unit's overall noise level as lower after the intervention.	Not provided	This QI initiative led to standardization of monitor education and implementation of a hospital-wide monitor protocol. Complete buy-in from staff was essential to achieving a true culture change in alarm management. Lessons learned include: (1) unit staff should analyze alarm parameters to determine if they are appropriate; (2) alarm parameters should be set to actionable levels; (3) nurses must be trained to individualize alarm parameters; (4) institutions should establish institution-wide standards for management.	Moderate	Included in PSP 2

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Jahrsdoerfer, 2016[17]	Hospital leadership team made the decision to move beyond its current alarm and event response model to maximize us of new technology. The leadership team collaborated with industry and implemented principles for an effective alarm system to guide its workflow.	Quasi-experimental study. Focus of evaluation was to determine value added of using secondary alarm notification with a unified alarm management technology platform, monitor technician and mobile device.	Large integrated delivery network on the East Coast. 4 units: ICU, progressive care, and two telemetry units (52 beds total).	Leveraging the monitor tech translated to a 68% reduction in alarms sent to the nurse. Overall 76% less alarms dispatched to nurses on their mobile devices.	Not provided	As a result of the reduction in the number of patient monitoring nonactionable alarms that reached nurses' mobile devices, clinical interruption fatigue was reduced. Using middleware alarm technology provided a safety net to ensure that red alarms were not missed by the monitor technician.	High: case study with quasi-experimental design	Pulled from AAMI BI&T journal—manual search
Ketko et al., 2015[11]	Multidisciplinary improvement task force determined patient care practices and systems/operational practices to be key drivers of alarm frequency. Processes to affect these key drivers were identified, and measures were selected and modified to align with those recommended by the Joint Commission.	QI study. Used control charts with many data points and conducted tests of significance.	C.S. Mott Children's Hospital at the University of Michigan. Neonatal ICU.	Modified SANS algorithm for high SpO2 delivery resulted in an immediate and sustained decrease in the escalation of high SpO2 alarms to nursing phones. Results of the survey regarding attitudes and perceptions in alarm frequency demonstrated that most respondents felt that alarm frequency had improved and alarm fatigue was being addressed.	Not provided	Recognition that alarm management must be a collaborative effort was an important first step—cultural change transitioning from alarm frequency being a nursing concern to everyone taking responsibility was key to successfully developing strategies.	Moderate	Pulled article from manual search of reference section of Jubic, K. 2017 *Strategies for Managing Alarm Fatigue in the PICU Setting* (included in PSP 2 literature pull) Included in PSP 2

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
McGrath et al., 2019[15]	Applied systems-level design and analysis methods to continuous monitoring technology workflow.	Difference in differences observational study.	Two surgical units (71 beds total).	Not a significant difference in the count of clinical alarms per monitored hour after implementation.	Significant increase when alarms per patient day were calculated. Greater than expected increase in non-clinical alarms.	Despite increase in non-clinical alarms, overall alarm rates were still below threshold where alarm fatigue would be a concern. Importance of adopting a system-level design and analysis, which provided a foundation for effective workflow redesign, change management, and measurement.	Moderate	Pulled article from PSP 2 literature search
Petersen and Costanzo, 2017[13]	Through this project a policy was developed by the alarm management team to ensure effective clinical alarm systems and the promotion of patient safety.	QI study with convenience sampling to understand nurses' perceptions of alarm fatigue and implement interventions that improve safety. Healthcare Technology Foundation's Clinical Alarms Committee Survey was sent to 31 nurses and 14 support staff (83.8% operational response rate).	Mary Lanning Healthcare (acute care facility). ICU and progressive care unit (29 beds total).	One nurse noted that patient safety is everyone's responsibility, and this change in philosophy and culture may be the next best step in improving the care patients receive via alarm management.	When surveyed about knowledge of Mary Lanning Healthcare's initiatives to improvement alarm fatigue, only 15% of nurses recognized that the alarm management team was implemented to assess current needs, edit policies, decrease overall alarm numbers, and change the culture of	Survey findings identified the need for alarm management assessment, policy creation, staff training, and continued improvement. Mary Lanning Healthcare implemented a variety of change initiatives based on assessment, current needs, nurse perception, and evidence-based practice.	Moderate	Included in PSP 2

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
					alarm management. Only 19% of nurses recognized that new technology had been implemented to improve clinical alarm safety.			
Rayo et al., 2016[4]	Secured leadership support and created an alarm management task force to develop and implement a new continuous cardiac monitoring policy. Aim of the policy was to change the default organizational culture with regard to monitoring. This initiative was identified as a high priority by the institutional leadership including the chief executive officer (CEO), chief financial officer (CFO), and chief operating officer.	Retrospectively collected data from an institutional data warehouse for the 12-week periods before and after the intervention was implemented. Percentages of true, false, and unnecessary alarms were collected by conducting six 2-hour observations across three different units.	Midwest tertiary care health system. Intervention was implemented in 5 hospitals, affecting 37 medical-surgical, cardiac, critical care, and hybrid units (over 1,000 beds total).	False alarm percentage decreased from 18.8% to 9.6% pre- to post-intervention. Percentage of unnecessary alarms remained consistent between the pre- (46.2%) and post-intervention (46.7%) periods. When comparing hospital-wide data before and after implementation, average cardiac monitoring rate decreased 53.2%, weekly monitoring rate decreased 15.5%, and emergency department boarding rate decreased 36.6%.	Not provided	Study indicates that when collaboration across a diverse team is coupled with strong leadership support, policies and procedures such as this one can improve clinical practice and patient care. Results suggest that the development and communication of this new policy safely reduced the length of time that patients spent on continuous cardiac monitoring. Factors of successful implementation include strong leadership support and widespread engagement of staff. Human factors engineers worked closely with clinicians and information technology	Moderate	Included in PSP 2

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
						(IT)professionals from the beginning, resulting in policy and technology solutions explicitly designed to optimize usability and mitigate the risk of increased workload and other unintended consequences sometimes associated with healthcare technology.		
Srinivasa et al., 2017[9]	Goal of this QI project was to facilitate an environment of care in which nurses are tuned into cardiac telemetry alarms that are clinically significant so more efficient patient care may be provided for truly actionable events.	QI study performed using two decision analysis models: fishbone analysis and Model for Improvement framework. Collected baseline and post-intervention alarm load and noise data.	Northeast healthcare facility, surgical telemetry unit (24 beds).	An 84% reduction in the premature ventricular contractions alarm rate and a 54% reduction in the total alarm rate. There was also an overall noise reduction on the surgical telemetry unit related to the cardiac telemetry alarms. Pre-intervention the average noise in decibels (dB) for the left wing and main hallway was 58.94 dB and 58.04 dB, respectively. Post-intervention it dropped to 57.84 dB and 54.43 dB, respectively.	Not provided	Factors that contributed to the success of reducing alarm load and alarm fatigue: (1) Change was integrated into the unit with very little interruption in the flow of the unit. (2) Stakeholder involvement and buy-in from beginning to end. (3) Joint Commission Sentinel alert and subsequent establishment of NPSG on Alarm Management enabled vigorous administrative support and resources required to successfully lead this project.	Moderate	Included in PSP 2
Vockley, 2012[7]	After two sentinel events, the hospital's	Case study	Beth Israel Deaconess	A 30% decrease in alarm signals.	Not provided	Resulted in a culture of taking action around	High: case study and	Pulled from AAMI Safety

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	leadership and the physician, nursing, and clinical engineering staff focused comprehensively on alarmed medical devices and discovered inconsistent cardiac telemetry alarm system management. Implemented a centerwide cardiac alarm system management initiative including short-term fixes and long-term innovations.		Medical Center (631 beds).	Decrease in amount of time it takes to respond to an alarm.		auditing the standard of care and patient outcomes, and continuing to adjust alarm system parameters to meet clinical practice standards.	not peer reviewed	Innovations Series—manual search Included in PSP 2
Vockley and Kloewer, 2017[16]	Nurse-driven patient safety initiative: nursing leadership team evaluated different technology options and took the time to understand the rationale for more effective and comprehensive patient monitoring. After the nursing leadership selected continuous surveillance monitoring, they educated the hospital's CEO, CFO, and physician leaders and gained support for moving forward.	Case study	Methodist Specialty and Transplant Hospital, San Antonio, TX. Transplant unit (57 bed) and medical-surgical unit (47 bed).	Comparing time spent on traditional collection of vital signs vs. continuous surveillance determined a potential savings of 16.5 hours on surgical unit and 20 hours on transplant unit. Resulted in fewer and more meaningful alarm signals. The units where registered nurses led the charge (took ownership of the new system) had a	Not provided	After successful launch of continuous surveillance monitoring on its transplant and one medical surgical unit, the hospital began expanding to more medical surgical units. Decision around expansion was based on enhanced patient safety, strong support from clinicians, patient satisfaction, and improvements in clinical workflow efficiency.	High: case study and not peer reviewed	

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
				faster learning curve. For the units that deferred to patient-controlled analgesia pumps (PCAs), the leadership team added extra education and implemented a standard protocol for initial patient setup.				
Whalen et al., 2014[8]	Boston Medical Center senior leadership convened a multidisciplinary Telemetry Task Force (TTF) in 2008 to evaluate how cardiac telemetry monitoring equipment was being used in clinical areas, identify ways to improve management and utilization, and develop consensus for a common approach to cardiac monitoring. Reconvened the TTF in 2011 to explore the issue of alarm fatigue.	Two-phase study: (1) observation of nursing staff's response to monitor alarms and (2) QI project in pilot unit to respond to largest contributors to alarm fatigue identified in Phase 1.	Boston Medical Center, medical cardiology unit (24 beds).	An 89% reduction in total number of audible alarms per week on pilot unit. Decibel level narrowed from a range of 54–90 dB to 60–72 dB. Percentage of nurses who assessed the noise level as acceptable increased from 0% to 64%.	Not provided	Success of QI study was the result of a multidisciplinary approach with full engagement, support, and commitment of senior leadership, physician colleagues, IT, engineering, and, most importantly, nursing staff. Nurses became strong advocates of the pilot project, which resulted in sustained change and improvement. Engagement of nurses was critical to creating the culture change necessary to manage alarms and minimize alarm fatigue.	Moderate	Pulled article from PSP 2 literature search Included in PSP 2

Table B.60: Alarm Fatigue, Risk Assessment- Single Studies

Note: Full references are available in the Section 13.2 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
AMMI, 2013[4]	Multidisciplinary team (patient safety experts, researchers, physicians, nurses, biomedical and human factors engineers, and information technology [IT] experts) to identify and address the challenges with patient-controlled analgesia pump.	Case study	Dartmouth-Hitchcock Medical Center. Medical-surgical orthopedic unit (36 beds).	Rescue events decreased from 3.5 per 1,000 patient days before implementation to 1.2 afterward. Intensive care unit (ICU) transfers decreased from 5.6 per 1,000 patient days to 2.9. Documented high patient and clinical acceptance of the surveillance monitoring.	Not provided	Based on results, expanded surveillance monitoring to additional adult medical-surgical units and pediatric and adolescent unit. Team understood that implementing more advanced, IT-reliant medical equipment systems required a multidisciplinary perspective. Systems approach is a cycle of continuous improvement that includes prioritizing improvement, designing and testing change, implementing change, and continuing to measure performance.	High: case study and not peer reviewed	Pulled from Association for the Advancement of Medical Instrumentation (AAMI) Safety Innovations Series—manual search Included in patient safety practice (PSP) 1

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Alsaad et al., 2017[12]	Multidisciplinary team (MT) was involved in the study at varying levels. Ordering providers including attending physicians, residents, and advanced practice nurses, along with registered nurses and telemetry MT, were included in the educational sessions to familiarize them with the newly created protocols. The progressive care unit (PCU) nurse manager, nurse educator, and MT manager participated in the protocol creation and staff education.	Quality improvement (QI) study collected pre-post intervention data. Used different statistical methods to report the study results, including paired t-test, $\chi 2$, and Mann-Wilcoxon equation.	Mayo Clinic campus in Jacksonville, FL. PCU (27 beds).	Nurses reported 27% perceived decrease in alarm fatigue post-intervention. There was a 10% reduction in cardiac telemetry assignment post-intervention. Significant cost reduction was achieved by implementing the protocols. No significant differences in mortality rate before and after intervention.	Not provided	Study demonstrates that a significant reduction in alarm fatigue and cost can be accomplished through a multidisciplinary team focused on identifying process gaps and closing them.	Moderate	Article was pulled from PSP 1 literature search. Included in PSP 1

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Cameron and Little, 2018[5]	Multidisciplinary alarm management committee was formed with representation from administration, educators, QI, risk management, biomedical engineering, plant operations, and staff nurses. Committee developed alarm policy and planned educational program for nurses on alarm management.	QI study using pre-/post-test design to evaluate the alarm management education program, and nurses' perceptions and practices related to clinical alarms. Likert questions were analyzed using Wilcoxon signed-rank test with a confidence interval of 95%. Participants: 417 nurses from all departments (215 completed post-test).	Florida acute care hospital (257 beds).	Significant improvements reported in 8/12 of the questions related to alarm perceptions. Sixty-six percent of nurses who completed post-test reported they strongly agree or agree they have improved their alarm management practices. Nurse-initiated collaborative team-based alarm practices significantly improved, including consulting a provider for individualized monitor settings and judicious use of telemetry monitoring versus unnecessary use. Results also showed significant improvement in selecting appropriate intervention.	Alarm perceptions were more negative post-test in 4 questions related to: alarms reducing attention to patients, feeling overwhelmed by alarms, alarms contributing to nurses' stress level, and some situations requiring alarm disabling.	The findings of this QI project indicate that nurses are receptive to education on alarms, and changed their perceptions and practices based on the education program and a new policy. Through strong leadership and a team approach, hospitals have the opportunity to improve patient safety while improving the work environment, patient care, and overall staff morale.	Moderate	Article was pulled from PSP 1 literature search Included in PSP 1

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Dandoy et al., 2014[8]	Multidisciplinary alarm oversight task force consisting of key stakeholders, including physicians, nurse practitioners, nursing leadership, registered nurses, patient care assistants, clinical engineering, and patient family representatives. Team reviewed the current cardiac monitor care practice, published recommendations, identified gaps between practice and evidence, and identified areas of improvement.	QI study using Model for Improvement to design, test, and implement changes. Tested hypotheses using PDSA (plan, do, study, act) measures.	Cincinnati Children's Hospital Medical Center. Bone marrow transplant unit (24 beds).	During implementation, the median number of alarms per patient-day decreased from 180 to 40. Median number of false alarms on the floor fell from 95% to 50%.	Not provided	Found significant decrease in the number of alarms per monitored patient with the implementation of a standardized process. Fewer false alarms allow staff to address alarms more promptly.	Moderate	Included in PSP 1
De Vaux et al., 2017[6]	Alarm management team (clinical engineering, Yale School of Nursing, IT, nursing management, physician leadership, and bedside staff) with the goal of meeting the requirements of The Joint Commission (TJC) National Patient Safety Goal (NPSG). Alarm management team used gap analysis assessment tool provided by the American Association of Critical-Care Nurses.	QI study using direct observation methods once pre-intervention and at three points within 6 months post. Sample size of patients observed varied from 23 to 26 at data collection points.	Yale New Haven Hospital, York Street Campus. Two step-down units (28 beds each).	Total alarms decreased from 251 in March 2014 to 12 in February 2015. False alarms decreased from 201 in March 2014 to 12 in February 2015. Alarm-setting customization increased from 39% pre-intervention to 87.5% post. No adverse patient events were reported during the observational time period.	Not provided	The authors attributed increases in customization to cumulative effect of staff education and best practice interventions. Team shared findings with leadership and, as a result, St. Raphael campus of New Haven Hospital adopted default alarm changes.	Moderate	Article was pulled from PSP 1 literature search. Included in PSP 1

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Epstein et al., 2016[9]	In response to TJC NPSG, an alarm management committee began in Feb 2014 and included representation from nursing leadership, education, respiratory therapy, biomed, regulatory compliance, quality, vendor, and risk management. Goal of committee was to ensure that the data gathered from analysis of the alarm environment would find its way to frontline caregivers and managers.	Case study	NCH Healthcare System	Over 4 months, the pilot unit lowered its total number of alarm signals by 69% without a negative impact to patient safety.	Not provided	Findings highlighted the importance of having vendor representation on the committee to ensure that NCH is compliant with the alarm management goal, provide current best practice recommendations, and assist with analysis of operational reports from the device integration system.	High: case study and not peer reviewed	Pulled from AAMI Safety Innovations Series—manual search Included in PSP 1
Graham and Cvach, 2010[13]	Interdisciplinary alarm management task force was created and charged with (1) evaluating excessive equipment alarms that obscure and desensitize clinicians, (2) standardizing the hospital's approach to alarm management, (3) assessing the reliability of secondary or adjunct alarm notification devices, (4) determining the educational needs of clinicians regarding alarm management, and (5) assessing new technology and systems that may improve alarm management.	QI project. Collected baseline data and then implemented tests of change. Administered a pre- and post-intervention survey to nursing staff.	Northeastern academic medical center. Medical progressive care unit (15 beds, 30 nurses).	A 43% reduction in critical physiological monitor alarms. Nurses perceived the unit's overall noise level as lower after the intervention.	Not provided	Lessons learned include: (1) unit staff should analyze alarm parameters to determine if they are appropriate, (2) alarm parameters should be set to actionable levels, (3) nurses must be trained to individualize alarm parameters, and (4) institutions should establish institution-wide standards for management.	Moderate	Included in PSP 1

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Ketko et al., 2015[11]	Multidisciplinary improvement task force (physicians, nurses, respiratory therapists, biomed engineers, IT) developed an alarm management bundle applying strategies to decrease alarm frequency.	QI study. Used control charts with many data points and conducted tests of significance.	C.S. Mott Children's Hospital at the University of Michigan. neonatal ICU.	Modified SANS algorithm for high SpO2 delivery resulted in an immediate and sustained decrease in the escalation of high SpO2 alarms to nursing phones. Results of the survey regarding attitudes and perceptions in alarm frequency demonstrated that most respondents felt that alarm frequency had improved and alarm fatigue was being addressed.	Not provided	Recognition that alarm management must be a collaborative effort was an important first step—cultural change transitioning from alarm frequency being a nursing concern to everyone taking responsibility was key to successfully developing strategies.	Moderate	Pulled article from manual search of reference section of Jubic, K. 2017. *Strategies for Managing Alarm Fatigue in the PICU Setting* (included in PSP 2 literature pull) Included in PSP 1

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Petersen and Costanzo, 2017[14]	Multidisciplinary alarm management team, including nursing, clinical staff, critical care director, respiratory therapy, biomedical, and engineering staff. Team was established as part of a series of system changes to address alarm safety.	QI study with convenience sampling to understand nurses' perceptions of alarm fatigue and implement interventions that improve safety. Healthcare Technology Foundation's Clinical Alarms Committee Survey was sent to 31 nurses and 14 support staff (83.8% operational response rate).	Mary Lanning Healthcare (acute care facility). ICU and progressive care unit (29 beds total).		When surveyed about knowledge of Mary Lanning Healthcare's initiatives to improvement alarm fatigue, only 15% of nurses recognized that the alarm management team was implemented to assess current needs, edit policies, decrease overall alarm numbers, and change the culture of alarm management. Only 19% of nurses recognized that new technology had been implemented to improve clinical alarm safety.	Survey results illustrated a lack of knowledge and training in alarm management. Mary Lanning Healthcare implemented a variety of change initiatives based on assessment, current needs, nurse perception, and evidence-based practice.	Moderate	Included in PSP 1

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Rayo et al., 2016[10]	Alarms task force (physicians, nurses, subject matter experts in IT, human factors engineering, risk management, and data analysis) was formed in response to TJC NPSG. Task force was divided into subcommittees: executive steering, physiological monitoring oversight, platform, training and implementation, and monitoring and evaluation.	Retrospectively collected data from an institutional data warehouse for the 12-week periods before and after the intervention was implemented. Percentages of true, false, and unnecessary alarms were collected by conducting six 2-hour observations across three different units.	Midwest tertiary care health system. Intervention was implemented in 5 hospitals, affecting 37 medical-surgical, cardiac, critical care, and hybrid units (over 1,000 beds total).	False alarm percentage decreased from 18.8% to 9.6% pre- to post-intervention. Percentage of unnecessary alarms remained consistent between the pre- (46.2%) and post-intervention (46.7%) periods. When comparing hospital-wide data before and after implementation, average cardiac monitoring rate decreased 53.2%, weekly monitoring rate decreased 15.5%, and emergency department boarding rate decreased 36.6%.	Not provided	Results suggest that the development and communication of this new policy safely reduced the length of time that patients spent on continuous cardiac monitoring. Factors of successful implementation include strong leadership support and widespread engagement of staff. Human factors engineers worked closely with clinicians and IT professionals from the beginning, resulting in policy and technology solutions explicitly designed to optimize usability and mitigate the risk of increased workload and other unintended consequences sometimes associated with healthcare technology. Some subcommittees stayed intact after implementation to continue to monitor process/success of this and other alarm task force initiatives.	Moderate	Included in PSP 1

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Srinivasa et al. 2017[15]	Alarm Fatigue Group was formed to conduct a pilot study on the state of telemetry alarms on a surgical floor. The multidisciplinary team is made up of members representing nursing, biomedical engineers, patient safety, and providers.	QI study performed using two decision analysis models: fishbone analysis and Model for Improvement framework. Collected baseline and post-intervention alarm load and noise data.	Northeast healthcare facility, surgical telemetry unit (24 beds).	An 84% reduction in the premature ventricular contractions alarm rate, and a 54% reduction in the total alarm rate. There was also an overall noise reduction on the surgical telemetry unit related to the cardiac telemetry alarms. Pre-intervention the average noise in decibels (dB) for the left wing and main hallway was 58.94 dB and 58.04 dB, respectively. Post-intervention it dropped to 57.84 dB and 54.43 dB, respectively.	Not provided	Factors that contributed to the success of reducing alarm load and alarm fatigue: (1) Change was integrated into the unit with very little interruption in the flow of the unit. (2) Stakeholder involvement and buy-in from the start. (3) TJC Sentinel alert and subsequent establishment of NPSG on Alarm Management enabled vigorous administrative support and resources required to successfully lead this project.	Moderate	Included in PSP 1
Vockley, 2012[3]	Established telemetry task force that guides decisions around alarm system management. The multidisciplinary task force is made up of physicians, nurses, and clinical engineering, healthcare quality, facilities, and supply management staff.	Case study	Beth Israel Deaconess Medical Center (631 beds).	A 30% decrease in alarm signals. Decrease in amount of time it takes to respond to an alarm.	Not provided	Resulted in a culture of taking action around auditing the standard of care and patient outcomes, and continuing to adjust alarm system parameters to meet clinical practice standards.	High: case study and not peer reviewed	Pulled from AAMI Safety Innovations Series—manual search Included in PSP 1

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Whalen et al., 2014[7]	BMC senior leadership convened a multidisciplinary Telemetry Task Force (TTF) in 2008 to evaluate how cardiac telemetry monitoring equipment was being used in clinical areas, identify ways to improve management and utilization, and develop consensus for a common approach to cardiac monitoring. Reconvened the TTF in 2011 to explore the issue alarm fatigue.	Two-phase study: (1) observation of nursing staff's response to monitor alarms and (2) QI project in pilot unit to respond to largest contributors to alarm fatigue identified in Phase 1.	Boston Medical Center, medical cardiology unit (24 beds).	An 89% reduction in total number of audible alarms per week on pilot unit. Decibel level narrowed from a range of 54-90 dB to 60-72 dB. Percentage of nurses who assessed the noise level as acceptable increased from 0% to 64%.	Not provided	Success of QI study was the result of a multidisciplinary approach. Nurses became strong advocates of the pilot project, which resulted in sustained change and improvement.	Moderate	Included in PSP 1

Table B.61: Delirium, Screening and Assessment–Single Studies

Note: Full references are available in the Section 14.1 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Adamis et al., 2010[5]	Evaluation of evidence-based assessment tools	Literature review; sample size range 47–432; older adults	Acute care	The Confusion Assessment Method (CAM), Delirium Rating Scale (DRS), DRS-Revised-98 (DRS-R-98), Memorial Delirium Assessment Scale (MDAS), and Neelon and Champagne (NEECHAM) confusion scale are sufficiently validated.	Not provided	Not provided	Low
Adamis et al., 2015[10]	Comparison of four different tools to identify delirium	Prospective observational study; 200 patients; adults aged 70+	University teaching general hospital	Agreement between Diagnostic and Statistical Manual-5 (DSM-5), DSM-IV, DRS-R-98, and CAM were all significant. Highest agreement was between DSM and DRS-R-98, while lowest agreement was between DSM-IV and DSM-5.	Not provided	Not provided	Low
Adamis et al., 2016[11]	Comparison of clock drawing test as screening tool (with DRS)	Prospective, observational, longitudinal study; 200 patients; adults aged 70+	Acute medical wards of general hospital	There was a significant negative correlation between the Clock Drawing Test (CDT) and DRS-R-98 (Pearson correlation r=-0.62, p<0.0010), CDT and CAM (Spearman's rho=-0.40, p<0.001), CDT and Montreal Cognitive Assessment (MoCA) (Pearson's r=0.69, p<0.001), and CDT and MoCA (Pearson's r=0.77, p<0.001).	Not provided	Not provided	Moderate
Arendts et al., 2017[4]	Use of Emergency Department (ED) Delirium Screening Form	Prospective three-phase trial; 3,905 patients; adults age 65+ admitted to an inpatient hospital bed from the ED	EDs of two tertiary hospitals	An absolute increase in delirium diagnosis of 2% across study phases was statistically insignificant (Pearson chi-square=2.49, P=0.29).	Not provided	Not provided	Not provided

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Boettger et al., 2017[16]	Comparison of CAM and Intensive Care Delirium Screening Checklist (ICDSC) for delirium in intensive care unit (ICU) patients	Prospective, descriptive cohort study; 210 patients; adults under intensive care management for more than 18 hours	Twelve-bed ICU at level one trauma center	Agreement was moderate between the CAM-ICU and DSM-IV-TR (k=0.44, p<0.001), the ICDSC and DSM-IV-TR (k=0.60, p<0.001), and the CAM-ICU and ICDSC (k=0.56, p<0.001).	Not provided	Not provided	Low
Bull et al., 2017[22]	Evaluating telephone-based screening for delirium to be used by family members	Pre-post, quasi-experimental design; 34 family caregiver-older adult dyads; older adults aged 70+ who underwent joint surgery	Orthopedic clinic at a Veterans Affairs Medical Center	There was 94% agreement (32 out of 34) between the Family Confusion Assessment Method (FAM-CAM) and the researcher-led CAM 2 days after the patient's surgery. Cohen kappa for agreement was moderate (k=0.477; p=0.001). Two family caregivers reported positive FAM-CAM ratings during the 2 weeks after hospitalization, which led to the physician changing the prescribed pain medication.	Not provided	Not provided	Moderate
De et al., 2015[24]	Screening tools for culturally and linguistically different populations	Systematic review; hospitalized adult inpatients	Hospital, excluding ICU	CAM, DRS, Nursing Delirium Screening Scale (NuDESC), sleep quality rating, MDAS, 4 A's Test (4 AT)	Not provided	Not provided	Moderate
Van Eijk et al., 2009[17]	Comparison of screening tools (CAM-ICU vs. ICDSC)	One hundred twenty-six patients (mean age = 62.4 years)	Thirty-two-bed mixed medical and surgical ICU	The CAM-ICU showed superior sensitivity and negative predictive value (64% and 83%) compared with the ICDSC (43% and 75%). The ICDSC showed higher specificity and positive predictive value (95% and 82% vs. 88% and 72%). The sensitivity of the physician's view was only 29%.	Not provided	Not provided	Low

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Flanagan and Spencer, 2016[32]	Use of CAM in post-acute patients—informal caregivers	Community-dwelling older adults aged 65+ admitted to postacute care (rehabilitation or skilled nursing center) with the intention of returning to community living and their family member/informal caregivers. The participants had to be English-speaking and have a caregiver willing to participate in the study.	Post-acute care	The FAM-CAM highly correlates with the confusion assessment method and diagnostic and statistical manual of mental disorders text revision criteria for detecting delirium in older adults in the postacute care setting.	Not provided	This study was a convenience sample; subjects were not randomized. The sample size was small, which limits generalization of the findings. A replication of this study with a larger sample size, as well as additional sites, would be beneficial.	Moderate
Frisch et al, 2013[31]	Tools for assessing patients in transport by emergency medical services staff; compared CAM to Glasgow Coma Scale (GCS)	A convenience sample of matched dyads of emergency medical services providers and elderly patients (age ≥65 years)	Two academic, tertiary-care EDs	Prehospital providers' recognition of any delirium symptom resulted in a sensitivity of 0.63 (95% confidence interval [CI] 0.43–0.79) and a specificity of 0.74 (95% CI 0.73–0.84). Prehospital report of a GCS <15 has a sensitivity of 0.67 (95% CI 0.47–0.82) and a specificity of 0.85 (95% CI 0.80–0.89).	Not provided	Not provided	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Gelinas et al., 2018[13]	Evaluation of nursing assessment tools for delirium in ICU	Systematic review; two independent reviewers analyzed the psychometric properties of five delirium assessment tools by using a standardized scoring system (range, 0–20) to assess the development process, reliability, validity, feasibility, and implementation of each tool	Intensive care	Psychometric properties were very good for the CAM-ICU (19.6) and the ICDSC (19.2), moderate for the NuDSS (13.6), low for the Delirium Detection Score (DDS) (11.2), and very low for the Cognitive Test for Delirium (8.2).	Not provided	Not provided	Low
Khan et al., 2012[7]	Evaluation of Richmond Agitation-Sedation Scale (RASS) and Riker Sedation-Agitation Scale (SAS) in identifying patients eligible for delirium assessment	Quality improvement project; 975 patients; patients aged 18 and older admitted to the ICU	Four hundred fifty-seven-bed university-affiliated urban public hospital	The Spearman rank correlation between the RASS and SAS scores was estimated at 0.91; 70.1% of screens were eligible for CAM-ICU assessment using RASS ≥-3 compared with 72.1% using SAS ≥3. The agreement between RASS and SAS for assessing CAM-ICU eligibility as estimated by the k coefficient was 0.93.	Not provided	Not provided	Not provided
Kuczmarska et al., 2016[9]	Evaluated CAM-ICU and 3D-CAM for hospitalized general medical/surgical patients	Hospitalized general medicine patients aged ≥75 years	Two non-intensive care general medicine units at a single academic medical center	The sensitivity (95% CI) of delirium detection for the 3D-CAM was 95% (74%, 100%) and for the CAM-ICU was 53% (29%, 76%), while specificity was >90% for both instruments. Subgroup analyses showed that the CAM-ICU had sensitivity of 30% in patients with mild delirium vs. 100% for the 3D-CAM.	Not provided	Not provided	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Marcantonio et al., 2014[8]	Derivation and validation of 3D-CAM	Prospective validation study; 201 patients; adults aged 75+ admitted to general medicine or geriatric medicine services	Large urban teaching hospital	Compared with the reference standard delirium diagnosis, the 3D-CAM had a sensitivity of 95% (CI 90 to 97%), resulting in a positive likelihood ratio of 16.8 (95% CI 8.9 to 31.8) and a negative likelihood ratio of 0.05 (CI 0.01 to 0.20). In post-hoc analyses, sensitivity of the 3D-CAM improved to 96% and specificity to 98%.	Not provided	Not provided	Not provided
Mistarz at al., 2011[27]	Demonstrated importance of using a structured assessment tool rather than relying on nursing documentation	Bedside nurses assessed 35 patients for delirium during routine patient care throughout their shift; this assessment was then compared to an independent assessment using the CAM-ICU performed by a nurse trained in this delirium detection tool	A 12-bed general ICU	Not provided	There was a significant discrepancy between the ICU bedside nurses' assessment of delirium and the independent formal delirium assessment using the CAM-ICU. Routine bedside nursing patient interactions do not reliably detect delirium in a critically ill patient.	Not provided	High

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Moon et al., 2018[28]	Building delirium assessment tool into electronic health records; used CAM tool	Participants: a total of 3,284 patients for the development of Auto-DelRAS, 325 for external validation, 694 for validation after clinical applications	Medical and surgical ICUs in two university hospitals in Seoul, Korea.	The predictive validity, analyzed after the clinical application of Auto-DelRAS after 1 year, showed a sensitivity of 0.88, specificity of 0.72, positive predictive value of 0.53, negative predictive value of 0.94, and a Youden index of 0.59. A relatively high level of predictive validity was maintained with the Auto-DelRAS system, even 1 year after it was applied to clinical practice.	Not provided	Not provided	Moderate
Neufeld et al., 2011[18]	CAM-ICU and ICDSC in non-critically ill hospitalized patients	Not provided	Two medical oncology units at a large teaching hospital	Not provided	This study suggests that in non-critically ill hospitalized patients, the CAM-ICU and ICDSC intensive care delirium screening tools are not adequately sensitive for use in routine clinical practice.	Not provided	Low
Neufeld et al., 2013[14]	Comparison of CAM-ICU with NuDESC	Prospective study; 91 patients; adults aged 70+ receiving general anesthesia during surgery	One teaching hospital	CAM-ICU had sensitivity of 28% (95% CI 16 to 45) and specificity of 98% (95% CI 88 to 100). NuDESC (threshold ≥2) had similarly high specificity of 92% (95% CI 80 to 97) and low sensitivity of 32% (95% CI 19 to 48). The NuDESC (threshold ≥1) had improved sensitivity (80%; 95% CI 65 to 91) but reduced specificity (69%; 95% CI 54 to 80).	Not provided	Not provided	Not provided

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
O'Regan et al., 2014[25]	Spatial Span Forwards (SSF) and months of the year backwards (MOTYB) as bedside screening tests to detect delirium	Cross-sectional study; 265 patients; adult inpatients excluding patients in the ED, ICU, and hematology/burns isolation unit	Large tertiary referral hospital	MOTYB was most accurate of the three, with a sensitivity of 83.3% (95% CI 69.8 to 92.5) and specificity of 90.8% (95% CI 86.1 to 94.3). SSF5 had high sensitivity (91.7%, 95% CI 80 to 97.6) but low specificity (69.12%, 95% CI 62.5 to 75.2). SSF4 had the lowest sensitivity (77.1%, 95% CI 62.7 to 87.9)	Not provided	Not provided	Not provided
Radtke et al., 2008[15]	Use of CAM, NuDESC, and DDS	Observational study; 154 patients; adults aged 18+ admitted to recovery room after general anesthesia	Recovery room of hospital	The CAM had a sensitivity of 0.43 and specificity of 0.985; the DDS had sensitivity of 0.14 and specificity of 0.99; the Nu-DESC had sensitivity of 0.95 and specificity of 0.87. Sensitivity between the CAM and DDS did not differ significantly (p=0.07). The NuDESC was most sensitive compared to the DDS (p<0.001) and CAM (p=0.003). Specificity did not differ significantly between scores.	False positives were 1.5% for CAM, 12.8% for the Nu-DESC, and 0.8% for the DDS. False negative rates were 57% for the CAM, 85% for the DDS, and 5% for the Nu-DESC.	Not provided	Not provided
Rainsford et al., 2014[12]	Compare CAM, DRS-R-98, and chart review	Fifty-one patients; adults aged 18+ with a diagnosis of advanced cancer	Nineteen-bed acute inpatient specialist palliative care unit	The DRS-R-98 identified 21 patients positively for delirium (41.2%) and 30 negatively for delirium (58.8%). The CAM identified 21 patients positively for delirium (41.2%) and 36 negatively for delirium (70.6%). The clinical team identified only 15 patients positively for delirium (29.4%) and 30 negatively (58.8%). The data are unclear about agreement between the CAM and DRS-R-98.	Not provided	Not provided	Not provided

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Rice et al., 2011[26]	CAM performance in practice (nurse vs. researcher rating)	Prospective, descriptive design; 170 patients; adults aged 65+ at risk for delirium	Tertiary care teaching hospital (541 beds)	Sensitivity of nurses' rating of delirium using the CAM was low for all comparisons with researcher ratings (25% overall, 25% best case, 10% worst case). A significant difference was observed between nurses' recognition of delirium and that of the researcher, X^2 (1, n=170)= 40.21, p<0.001; Fisher exact p<0.001. Specificity was high (99.6% overall, 100% best case, 100% worst case). Agreement beyond chance in detecting delirium was poor for overall (k=0.34), best case (k=0.38) and worst case (k=0.14) comparisons.	Not provided	Not provided	Not provided
Ringdal et al., 2011[19]	Compare CAM with DSM-IV; evaluate Mini-Mental State Exam (MMSE) as screening tool	Mokken nonparametric latent trait model for unidimensional scaling; 365 patients; adults aged 65+ acutely admitted for hip fracture for at least 24 hours	Two hospitals in Oslo, Norway	The MMSE cutpoint of 24 had 84% agreement with the CAM for patients diagnosed with delirium. Using the total MMSE score had a sensitivity of 46% and specificity of 96%. Using step-wise logistic regression to locate a subset of MMSE items that may function as a screening tool resulted in a sensitivity of 51% and specificity of 95%.	Using the MMSE cutpoint of 24 had low agreement with the CAM for identifying negative cases (54% agreement), indicating a very high rate of false positives.	Not provided	Not provided

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Rippon et al., 2016[20]	Development and evaluation of Delirium Early Monitoring System (DEMS) (two versions)	Observational study; 501 and 474 participants; healthcare assistants and support workers	Acute ward for patients with moderate to severe dementia in North East of England	Seventy-nine percent of staff completed the DEMS-CAM and 68% completed the DEMS-DOSS (Delirium Observation Screening Scale). Completion rates relating to the number of occasions that completion of the DEMS-CAM/DEMS-DOSS led to appropriate clinical action was 46% of the time for DEMS-CAM and 54% of the time for DEMS-DOSS.	Not provided	An end of study questionnaire completed by 10 of the non-medically trained staff found the DEMS-CAM was easier to understand than the DEMS-DOSS.	Not provided
Ryan et al., 2009[30]	CAM in palliative care	One hundred six patients; patients admitted to specialist palliative care unit study	Thirty-bed specialist palliative care unit in Mid-West region of Ireland	The sensitivity of the CAM in the pilot phase was 0.5 (0.22 to 0.78) and specificity was 1.0 (0.81 to 1.0). In the main study, the sensitivity of the CAM was 0.88 (0.62 to 0.98) and the specificity was 1.0 (0.88 to 1.0).	In the pilot phase, the non-consultant hospital doctors (NCHDs) made six false negative diagnoses of delirium. In the main study, the NCHDs made two false negative diagnoses of delirium.	A significant difference in the sensitivity of the CAM in the pilot phase and the main study was found (X^2=5.15, $p<0.05$), demonstrating that the performance of the CAM was improved when the NHCDs received the “enhanced” training module.	Not provided

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Shulman et al., 2016[21]	Sour Seven questionnaire as screening tool for delirium	Pilot study; 80 patients; adults aged 65+ admitted to either the medical or surgical units of the study hospital and in the hospital for at least 1 day	Large academically affiliated community hospital in Canada.	Agreement between geriatric psychiatrist on Sour Seven questionnaire and untrained nurses ranged from 64.3 to 92.8%, between geriatric psychiatrist and caregivers ranged from 44 to 84%. For each of the seven questions, the Fisher exact test analysis had a p value greater than 0.05, suggesting there was no difference between the questionnaire posed to nurses versus informal caregivers. Out of a possible maximum total score of 18 on the Sour Seven Questionnaire, a score of 4 was selected as the screening cut-off and a score of 9 was selected as diagnostic of delirium because of its specificity of 100% and high Youden Index.	Not provided	Not provided	Not provided
Steis et al., 2012[23]	Convergent validation of FAM-CAM and CAM by family caregivers	Exploratory analysis of agreement between two primary studies: the eCare for Eldercare pilot study and the Hospital to Home: Cognitively Impaired Elders/Caregivers study; 52 paired assessments from patient-caregiver dyads; adults aged 65+ with preexisting cognitive impairment.	Communities across Pennsylvania	Overall agreement between the CAM and FAM-CAM was 96%. Compared with the original CAM algorithm, the FAM-CAM had a sensitivity of 88% (95% CI=47 to 99) and specificity of 98% (95% CI=86 to 100).	Not provided	Not provided	Not provided

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Vasilevskis et al., 2011[29]	Evaluate performance of CAM-ICU (nurse vs. researcher)	Prospective cohort study; 510 patients; critically ill patients admitted to the ICU	Nine hundred-bed teaching hospital	Substantial agreement between bedside and research nurses on measures done within 2 hours of each other (CAM-ICU weighted kappa=0.67, 95% CI=0.66 to 0.70; RASS weighted kappa=0.66, 95% CI=0.64 to 0.68). Of 3,856 paired assessments for delirium within 2 hours, bedside nurses identified delirium with a sensitivity of 0.81 (95% CI=0.78 to 0.83) and specificity of 0.81 (95% CI=0.78 to 0.85) compared with research nurse reference standard.	Agreement between research and bedside nurses was slightly lower for mechanically ventilated patients and in nurses assessing delirium in patients aged 65+ compared to in assessments in patients younger than 65.	Not provided	Not provided

Table B.62: Delirium, Staff Education and Training–Single Studies

Note: Full references are available in the Section 14.2 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Babine et al., 2018[1]	Education and training to reduce falls and length of stay via delirium recognition	Retrospective study looking at delirium and falls. Two chart reviews were performed on patient falls as identified in the hospital safety reporting system in 2009–2010 (98 fallers) and 2012 (108 fallers).	Hospital; 637-bed urban tertiary teaching organization	After the education, documentation of the "diagnosis of delirium" and "no evidence of delirium" increased from 14.3% to 29.5% and from 27.6% to 44.4%. The Confusion Assessment Method (CAM) identified the diagnosis of delirium at 76% accuracy. The length of stay decreased by 7.3 days. The fall rates in 2011 and 2012 were 3.01 and 2.82 falls per 1,000 patient days and in 2013 decreased to 2.16.	The results indicate that improving delirium recognition and treatment through interprofessional education can reduce falls and length of stay.	Moderate
Baird and Spiller, 2017[11]	Use of 4 A's Test (4AT) and CAM tools to assess cognition upon admission for hospice patients	A quality improvement (QI) approach (PDSA: Plan, Do, Study, Act) was used to improve screening for delirium on admission to a hospice unit. A baseline measure was taken of the rate of performance of cognitive assessment on admission. Five PDSA cycles were then undertaken which involved implementing change and then evaluating results through auditing case notes and interviewing staff.	Hospice	The 4AT is a usable tool in the hospice inpatient setting to assess patients' cognitive state on admission and can easily be incorporated into the admission process.	Not provided	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Belanger and Ducharme, 2015[14]	Educational intervention in one hospital designed to improve management of delirium	This study was undertaken to field test and qualitatively evaluate a narrative-based educational intervention for nurses in hospital units with a high incidence of delirium.	Acute care; cardiac and orthopedic surgery units at a short-stay hospital	The educational nursing intervention under study affords promising possibilities for improving the care provided older adults at risk for delirium and their families. It is also potentially transferable to populations of nurses who attend to other patient groups with complex health needs, particularly in geriatric care, oncology, and palliative care.	Not provided	Moderate
Booth et al., 2019[27]	"Virtual ACE Intervention" on two medical/surgical units in an academic medical setting	The "Virtual ACE Intervention" standardizes care processes for cognition and function without daily geriatrician oversight on two non-ACE units. The Virtual ACE Intervention includes staff training on geriatric assessments for cognition and function and on nurse-driven care algorithms.	Acute care; 1,152-bed tertiary care academic hospital with 52 acute care units, including one ACE Unit; the target units were two medical-surgical units serving hospitalist and orthopedic patients, selected based on having a high percentage of older adults and engaged physician leaders	Postintervention, the completion of the assessments for current functional status and delirium improved (62.5% vs. 88.5%, P <.001 and 4.2% vs. 96.5%, P <.001, respectively). In a subsample analysis in the postintervention period, more patients were "up to the chair" (i.e., had improved mobility) in the past day (36.4% vs. 63.5%, P .04) and the prevalence of an abnormal delirium screening score was lower (13.6% vs. 4.8%, P .16).	The Virtual ACE Intervention is a feasible model for disseminating ACE Unit principles to non-ACE Units and may lead to increased adherence to recommended care processes and improved clinical outcomes.	Low
Brooke et al., 2018[19]	Better understanding of "lived experience" of nurses caring for patients with delirium to improve care	Semi-structured interviews	Acute care (England)	These researchers concluded that there is a need for education about delirium across specialties.	Not provided	High
Coyle et al., 2017[20]	New educational initiatives for nurses	Semi-structured interviews	Hospital	Thematic analysis revealed that nurses described delirium assessment and identification variously as "it's not my job," "it is my job," and "it's complex." New educational initiatives are needed.	Not provided	High

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Detroyer et al., 2018[13]	E-learning tool that will be easier and more cost-effective for educating nurses on delirium screening and management	A before-after study in a sample of patients enrolled pre-intervention (non-intervention cohort; n = 81) and post-intervention (intervention cohort; n = 79), and nurses (n = 17)	Hospital; geriatric ward of a university hospital	No significant difference was found between the intervention cohort and the non-intervention cohort for in-hospital prevalence and duration of delirium.	This study, the first in its area to investigate effects of delirium e-learning on patient outcomes, demonstrated no benefits for either geriatric patients or nurses.	Moderate
Devlin et al., 2008[6]	Didactic and clinical-reasoning based educational approach to improve nurses' ability to identify delirium using a standardized tool correctly	Fifty intensive care unit (ICU) nurses evaluated an ICU patient for pain, level of sedation, and presence of delirium before and after an educational intervention	Intensive care; two different hospitals (university medical and community teaching)	After education, the number of nurses able to evaluate delirium using any scale (12% vs. 82%, P < 0.0005) and use it correctly (8% vs. 62%, P < 0.0005) increased significantly.	A simple composite educational intervention incorporating script concordance theory improves the capacity of ICU nurses to screen for delirium nearly as well as experts.	Moderate
DiLibero et al., 2016[7]	Improve use of CAM; included a feedback loop, real time auditing, and just- in-time learning	QI study (pre-test-post-test design) was used to evaluate the effectiveness of a program to improve the accuracy of delirium screenings among patients admitted to a medical ICU or coronary care unit	Acute care; medical ICU and cardiac care unit at an urban tertiary academic medical center and level I trauma center in the northeast region with more than 600 licensed beds, including 77 adult ICU beds.	Compliance with performing at least one delirium assessment every shift was 85% at baseline and improved to 99% during the postintervention period. Baseline assessment accuracy was 70.31% among all patients and 53.49% among sedated and agitated patients. Postintervention assessment accuracy improved to 95.51% for all patients and 89.23% among sedated and agitated patients.	The results from this project suggest the effectiveness of the program in improving assessment accuracy among difficult-to-assess patients. Further research is needed to demonstrate the effectiveness of this model across other critical care units, patient populations, and organizations.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
DiLibero et al., 2018[15]	Multifaceted nurse-led education program on delirium assessment among neuroscience patients	QI project; a multifaceted nurse-led intervention was implemented, and a retrospective analysis of preintervention and postintervention data on assessment accuracy was completed; results were stratified by population, level of sedation, and level of care; differences were analyzed using Fisher exact test	Acute care; urban tertiary academic medical and level I trauma center in the northeast region with more than 600 licensed beds, including 77 ICU beds	Data from 1,052 delirium assessments were analyzed and demonstrated improvement in assessment accuracy from 56.82% to 95.07% among all patients and from 29.79% to 92.98% among sedated or agitated patients.	Results from this project demonstrate the effectiveness of the nurse-led intervention among neuroscience patients. Future research is needed to explore its effectiveness across other institutions and to describe the effectiveness of new interventions to improve outcomes at the patient and organizational levels.	Moderate
Forsgren and Eriksson, 2010[24]	Education and implementation of validated screening tools to improve care	National survey (Sweden)	Intensive care	Awareness of delirium in ICUs is low, with a lack of implementation of validated screening tools for its diagnosis. Education is needed to improve quality of care.		Low

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Gesin et al., 2012[8]	Multifaceted education program on delirium using Intensive Care Delirium Screening Checklist (ICDSC) in surgical trauma ICU (STICU)	The knowledge and perceptions of subject nurses about delirium, and agreement between the independent assessments of delirium by the subject nurse and by a validated judge (who always used the ICDSC), were compared across three phases: Phase 1: No delirium screening tool and no education, Phase 2: ICDSC and minimal education (i.e., ICDSC validation study only), Phase 3: ICDSC and multifaceted education (i.e., pharmacist-led didactic lecture, Web-based module, and nurse-led bedside training)	Intensive care; ICU units at Carolinas Medical Center, an 813-bed community teaching hospital with 140 adult ICU beds located in Charlotte, NC	Agreement between nurses and the validated judge in the assessment of delirium increased from Phase 1 (k = 0.40) to Phase 2 (k = 0.62) to Phase 3 (k = 0.74). Nurses perceived use of the ICDSC as improving their ability to recognize delirium.	Use of a multifaceted education program improves both nurses' knowledge about delirium and their perceptions about its recognition. Implementation of the ICDSC improves the ability of STICU nurses to evaluate delirium correctly.	Low

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Godfrey et al., 2013[21]	Integrated delirium prevention system of care	Participatory action research (England); data collection included facilitated workshops, relevant documents/records, qualitative one-to-one interviews, and focus groups with multiple stakeholders and observation of ward practices; grounded theory strategies were used in analyzing and synthesizing data	Acute care	"Awareness of delirium was variable among staff, with no attention on delirium prevention at any level; delirium prevention was typically neither understood nor perceived as meaningful. The busy, chaotic, and challenging ward life rhythm focused primarily on diagnostics, clinical observations, and treatment. Ward practices pertinent to delirium prevention were undertaken inconsistently. Staff welcomed the possibility of volunteers being engaged in delirium prevention work, but existing systems for volunteer support were viewed as a barrier. [The] evolving conception of an integrated model of delirium prevention presented major implementation challenges flowing from minimal understanding of delirium prevention and securing engagement of volunteers alongside practice change. The resulting Prevention of Delirium Programme combines a multicomponent delirium prevention and implementation process, incorporating systems and mechanisms to introduce and embed delirium prevention into routine ward practices."	Not provided	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Gordon et al., 2013[3]	Use of evidence-based screening tools to detect delirium in patients with neuroscience diagnoses	Pre-post design; 47 registered nurses	Hospital; 31-bed neuroscience intermediate care unit at a large academic medical center in Boston, MA	Findings reveal that the neuroscience nurses recognize the absence of delirium 94.4% of the time and the presence of delirium 100% of the time after a didactic session and coaching.	Expert coaching at the bedside may be a reliable method for teaching nurses to use evidence-based screening tools to detect delirium in patients with neuroscience diagnoses.	Moderate
Horvath et al., 2011[12]	Use of pocket cards with a variety of assessment tools for delirium in a primary care setting	Project target: practitioners in primary care settings, in particular physicians, nurse practitioners, and physician assistants	Primary care (Veterans Health Administration)	A low-tech, easy-to-use pocket card and assessment guide to evaluate delirium, dementia, and depression received favorable reception from an interdisciplinary group of clinical providers.	Not provided	Moderate
Johnson et al., 2016[18]	Education program to emphasize importance of delirium screening in trauma unit to reduce harm	Evaluate change in practice and beliefs regarding delirium among nurses, pharmacists, respiratory therapists, and physicians after an educational intervention	Acute care (trauma ICU); the hospital consists of 266 beds, with a 22-bed TICU. The hospital is one of eight trauma facilities in Arizona designated as level I by the State, annually caring for more than 3,000 of the region's most critically injured patients.	Changes in staff responses to the statement, ''Delirium is largely preventable'' were statistically significant ($p = 0.035$). The questionnaire revealed that the healthcare team believes that delirium is largely preventable. Early identification of delirium and risk factors associated with delirium can initiate the first step in preventing, identifying, and correctly treating delirium in the TICU.	An educational intervention emphasizing the importance of screening for delirium, risk factors for delirium, and approaches to decrease the incidence of delirium can improve identifying and correctly treating delirium in a critical care setting.	Moderate
Kennelly et al., 2013[22]	Understanding provider knowledge, skills, and attitudes toward assessing cognition to improve care	Self-administered questionnaire	Emergency Department (Ireland); older patients	One-third of respondents felt they lacked the relevant expertise to perform cognitive screening, with those with training in geriatrics being less likely to cite lack of experience as a factor.	Not provided	Moderate-High

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Kubota et al., 2016[25]	Program to increase oncology nurses' confidence and knowledge regarding care of patients, focused on four "psychological issues": normal reactions, clinically significant distress, suicidal thoughts, and delirium	A stratified, open, parallel-group, randomized trial; oncology nurses were assigned randomly to either the intervention group (n= 50) or the waiting list control group (n= 46)	Oncology hospitals and clinics (Japan)	In the intervention group, confidence and knowledge (but not attitudes) were significantly improved relative to the control group. No significant intervention effects were found for job-related stress and burnout. A high percentage (98%) of participants considered the program useful in clinical practice.	This psycho-oncology training program improved oncology nurses' confidence and knowledge regarding care for patients with psychological problems.	Moderate
LaFever et al., 2015[16]	Delirium education program to increase oncology registered nurses' (RNs') confidence and knowledge in a community hospital	A repeated-measures research design using general linear modeling was used for this study; an evidence-based delirium protocol and an educational session were developed for the nursing staff; the nurses attended a delirium educational session to learn about risk factors, prevention, assignment, and management of delirium	Inpatient medical-surgical oncology unit	The nursing educational program on the topic of delirium increased the nursing staff's knowledge from 69% to 86%, and overall confidence in managing patients with delirium increased from 47% to 66%.	This study confirms the benefits of delirium education in the inpatient medical-surgical oncology setting.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Marino et al., 2015[9]	Use of ICDSC to increase awareness and knowledge among ICU nurses regarding how best to care for patients with delirium	QI project; a didactic training program for bedside critical-care nurses was developed and implemented; upon completion of the educational sessions, a daily bedside delirium screening and care bundle protocol were implemented for all patients in ICUs throughout the facility; bedside critical-care nurses were invited to participate in the formal teaching sessions	Intensive care; 446-bed local teaching facility	All five nursing attitude and perceived confidence statements measured before and after the educational sessions showed a significant increase in positive perceptions overall (P.0001).	This quality improvement project demonstrates that a formal didactic training program for ICU nurses can result in increased awareness and knowledge of ICU delirium, and adequately prepare them for how to properly screen and treat patients.	Moderate
Meako and Thompson, 2011[17]	Educational program for orthopedic nurses; curriculum based on Hartford Foundation for Geriatric Nursing in a Nurses Improving Care to Healthsystem Elders (NICHE) unit	A pre-test–post-test quasi-experimental design was used to test the effectiveness of an educational intervention and to describe orthopedic nurses' knowledge about delirium and delirium risk in hospitalized orthopedic patients	Hospital; convenience sample of RNs working on a 39-bed orthopedic unit was used in this study	Regardless of education, years of experience, or shift worked, orthopedic RNs had difficulty with questions related to recognition of delirium, predisposing, and precipitating risk factors, and medications that can contribute to delirium. The educational intervention was effective, and scores significantly improved from baseline following the intervention.	Baseline knowledge assessment confirmed orthopedic nurses' lack of understanding of delirium. The 1-hour educational intervention, based on nationally recommended standards, improved the nurses' knowledge and could be useful in orthopedic nursing continuing education.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Nelson, 2009[10]	Teaching the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) to staff nurses, using RDSS and Richmond Agitation Assessment Scale	The CAM-ICU is a tool for screening for delirium in ventilated patients that with proper training can be administered quickly by staff nurses in the ICU. This article explains six preparatory decisions required in training staff to use the CAM-ICU	Hospital (ventilated patients)	The CAM-ICU tool is designed to allow nurses in the ICU to screen ventilated patients for delirium. The features of the tool can be easily taught and the tool, once understood, requires very little time for administration.	The challenge of teaching nurses is to assist them to embrace the tool as part of their routine assessment, rather than as something to be added on to existing procedures.	Moderate
Nydahl et al., 2018[23]	Evaluate delirium management in nurses and physicians in critical care to improve education and training to improve care	Open online survey	Intensive care (Germany)	More nurses than physicians reported screening for delirium. A majority reported screening when delirium was suspected, and more than 50% used validated instruments. Half of the clinicians surveyed had structures in place, such as a delirium-related process of care. Authors concluded that both nurses and physicians need more knowledge and training on when and how to use validated assessment instruments for identifying and managing delirium.	Not provided	Moderate
Sockalingam et al., 2014[2]	Interprofessional education (IPE) to improve delirium care	Systematic review	N/A	Review of the limited evidence suggests that IPE programs may influence team and patient outcomes in delirium care. More systematic studies of the effectiveness of interprofessional delirium education interventions are needed.	Not provided	Low

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Sockalingam et al., 2016[2]	Flipped classroom (FC) approach to improving the quality of delirium care using an interprofessional train-the-trainer (TTT) program	Implementation of novel education methods and post-implementation evaluation of test scores; delirium care self-efficacy and knowledge test scores were measured before, after, and 6 months after the training session; clinician delirium assessment rates were measured by chart audits before and 3 months after implementation of delirium training sessions	Hospital	Delirium knowledge test scores (7.8 ± 1.6 versus 9.7 ± 1.2, P <.001) and delirium care self-efficacy were significantly higher immediately after the TTT session compared with those of pre-session, and these differences remained significant at 6 months after the TTT session. Trainer sessions significantly improved clinician delirium assessment rates, from 53% for pretraining to 66% for post-training. Data suggest that a TTT FC delirium training approach can improve participants' perceived delirium care skills, confidence, and knowledge up to 6 months after the session. This approach provides a model for implementing hospital-wide delirium education that can change delirium assessment behavior while minimizing time and personnel requirements.	Not provided	Moderate
Young et al., 2012[5]	Understanding barriers to systematic inpatient delirium screening to improve staff education and improve quality of patient care	Survey	Hospital	Eighty-two percent of respondents had never used or heard of the CAM; only three respondents felt proficient with the use of CAM.	Not provided	Moderate
Wong et al., 2018[4]	Understanding barriers to inpatient delirium screening to improve staff education and improve quality of patient care	Qualitative focus group survey of nurses	Hospital (orthopedic unit; Canada)	While those surveyed had mixed feelings about the CAM, only 35% of participants recalled receiving training on the tool in the past.	Not provided	Moderate

Table B.63: Delirium, Nonpharmacological Interventions To Prevent Intensive Care Unit Delirium–Single Studies

Note: Full references are available in the Section 14.3 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Alvarez et al., 2017[1]	Cognitive and sensorial stimulation, physical therapy, and family involvement in care	Design: Randomized controlled trial (RCT) Sample Size: n=65 Patient Population: Older adults	Intensive care	Multicomponent nonpharmacological intervention effective in prevention of delirium among critically ill patients	No adverse events reported.	Not provided	Moderate
Black, et al., 2011[2]	Family participation in care: nurses provided verbal and written advice to patients and families about communication and delirium	Design: Cohort study with control group Sample size: n=170 (83 control, 87 intervention) Patient population: Adult patients and families	Intensive care	Incidence of delirium (measured at days 1–7 and 14) did not differ significantly between intervention and control groups.	No adverse events reported.	Intervention is not described in sufficient detail for replication.	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Foster and Kelly, 2013[3]	Promotion of sleep-wake cycles; sensory stimulation; mobility; preferred music listening	Design: Quality improvement pre-post design Sample Size: n=32 for intervention Patient Population: Adult hemodynamically stable; hearing able	Intensive care	Delirium assessment improved post-intervention compared to baseline (likely the reason for slightly increased prevalence of delirium reported).	No adverse events reported.	Barriers to feasibility of the pilot study: protocol adherence for sleep promotion (due to care activity interruptions) and mobility (due to nurse reported time constraints and lack of assistance); Director of Physical Therapy declined to participate in mobility activity due to lack of personnel; physicians did not write orders for the mobility protocol; lack of support from other disciplines; patient/family consent process; documentation deficiencies (some study items not available for documentation in electronic medical record and required additional hard copy documentation, leading to missing data).	High

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Guo and Fan, 2016[4]	Preoperative orientation visit to intensive care unit (ICU), flexible visiting hours; social, emotional, informational support; improving sleep quality: use of single room, reduction of multiple sensory experiences; cluster care to avoid night hours; provision of back massages; playing relaxation music; provision of warm milk before sleeping	Study Design: Controlled trial, no randomization Sample Size: n=59 (intervention), and n=63 (control) Patient Population: Adult abdominal or cardiac surgery patients	Intensive care	Delirium measured at 2, 4, 8, and 16 hours after awakening from anesthesia postoperatively. Significantly fewer intervention than control group patients experienced delirium at each time point measured. Multicomponent nonpharmacological intervention effective for reduction of delirium incidence.	No adverse events reported.	Not provided	Low
Guo et al., 2016[5]	Preoperative orientation visits to the surgical ICU (SICU); reorientation measures; noise reduction; day and night light; cluster care; eyeshades and acoustic earplugs allocated; minimized restraints; patient selected preferred music; optimized nutrition	Study Design RCT with random assignment Sample Size: n=160 (81 intervention and 79 control group) Patient Population Post-surgical older adult oral cancer patients, with postoperative SICU stay of 3 days or more	Intensive care	Postoperative delirium occurred significantly less frequently among intervention than control patients (10 vs. 25; 15%–31.25%, p=0.006). Duration of postoperative delirium was significantly less among intervention than control group patients (28.1 vs. 60.2 hours, p<0.001). Multicomponent nonpharmacological interventions reduced incidence and duration of postoperative delirium.	No adverse events reported.	The impact of each component was not assessed; reproduction of the intervention must include all components.	Low

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Ono et al., 2011[6]	Efficacy of bright light therapy	Design: RCT Sample Size: 26 Patient Population: Patients with esophageal cancer	Intensive care	Reduction in risk of developing delirium in patients receiving bright light therapy, but not statistically significant.	No adverse events reported.	Not provided	High
Rivosecchi et al., 2016[7]	Music; light adjustment; reorientation, cognitive stimulation; assure use of glasses, hearing aids	Design: Pre-post quality improvement project Sample Size: n=230 in pre-phase and 253 in post-phase Patient Population: Adult critically ill patients	Intensive care	Reduction of 50.6% (16.1% vs. 9.6%, p<.001) in delirium days. Incidence of delirium was reduced (15.7% vs. 9.4%, p=.04). The intervention reduced the odds of developing delirium by 57% (odds ratio 0.43, p=.005) after adjusting for age, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, mechanical ventilation, and dementia. Multicomponent nonpharmacological intervention effective in prevention of delirium, reduction of delirium duration.	No adverse events reported.	Not provided	High
Schweickert et al., 2009[8]	Effect of early physical and occupational therapy on delirium, functional outcomes	Design: RCT, with random assignment Sample Size: n=104 Patient Population: Critically ill adult patients	Intensive care	Shorter duration of delirium (median 2.0 days, interquartile range (IQR) 0.0–6.0 vs. 4.0 days, 2.0–8.0 days; p=0.02). Early physical and occupational therapy effective in reduction of delirium duration.	One serious adverse event in 498 therapy sessions (desaturation less than 80).	Not provided	Low

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Flannery et al., 2016[9]	Nonpharmacological interventions for sleep in the ICU; impact on ICU delirium	Studies Included: 10 studies with 1,639 patients	Intensive care	Six studies reported statistically significant reductions in rate of ICU delirium. Two reported nonsignificant reductions. Four studies reported duration of delirium, of which three demonstrated reduction in delirium duration. Five studies reported ICU length of stay (LOS), and two demonstrated reduction. Evidence is mixed about whether interventions to promote sleep prevent ICU delirium; reduce duration of delirium, or reduce ICU LOS.	Not provided	Not provided	Low

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Ghaeli et al., 2018[10]	Any non-pharmacological intervention to prevent or manage delirium Interventions: HELP; mobility; environmental noise reduction; sleep promotion and sleep-wake cycle protection; music; orientation; addressing risk factors and sensory impairment (vision, hearing)	Narrative review Adults, older adults	Intensive care	Based on review and classification of level of evidence*, the authors made the following recommendations: • Mobility/rehabilitation therapy at the first possible opportunity (1B) • Reduce noise to improve sleep (1B) • Soft, soothing music to reduce anxiety and confusion (1B) • Pleasant fragrance/scents to make the environment more soothing (5) • Orientation with visible clock, calendar; promote day light and night light cycles (1B) • Ensure patients who use glasses and hearing aids have access to these devices to improve interaction and reduce confusion (IB) *1A - SR of RCTs; 1B - RCT; 2A - SR of cohort studies; 2B - cohort studies; 3A - SR of case control studies; 3B - case control studies; 4A - SR of case series; 4B - Case series, or cross-sectional studies; 5 - Other studies	Not provided	Not provided	Moderate-High

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Hu et al. 2015[11]	Nonpharmacological interventions for sleep promotion	Systematic review Samples: Total 1,569 participants Population: Critically ill adults (aged 18 years and older) Studies Included: 30 RCT and quasi-RCT	Intensive care	Outcome: risk of delirium (sleep outcomes also reported) Three trials of earplugs or eye masks or both were suitable for meta-analysis. Findings demonstrated a lower incidence of delirium during the ICU stay (risk ratio 0.55, 95% CI 0.38 to 0.80, p=0.002) for these interventions; the reviewers rated the quality of this evidence as low. Clinical heterogeneity of the studies limited quantitative synthesis; only a small number of studies available for most interventions; quality of the evidence generally low or very low. Use of earplugs or eye masks or both for ICU patients may help prevent delirium.	Not provided	Not provided	Low

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Luther and McLeod, 2018[12]	Chronotherapy—"modifying circadian rhythms with therapeutic intent": dynamic light application (DLA) versus usual lighting (control); bright light therapy (BLT) versus usual lighting (control) (n=2 studies); reduction of lighting and noise (no control); use of ear plugs, eye shades, reduction in noise and lighting versus usual care (control)	Studies included: Six included in review: five RCTs and one cohort study	Intensive care	Statistically significant reductions in incidence of delirium among intervention versus control or post- vs. pre-intervention participants was demonstrated in three studies. One study identified a slight increase (not statistically significant) in occurrence of delirium among participants receiving DLA versus control group. The two final studies reported decreased occurrence of delirium in the intervention groups, but these were non-significant results, due to small sample sizes. Two studies identified statistically significant reductions in duration of delirium among multicomponent intervention recipients vs. controls (where interventions comprised reduction of light and noise, and reduction of light and noise plus use of ear plugs and eye shades). One study reported nonsignificant (due to small sample size) reduction in duration of delirium symptoms among the intervention group. Use of multicomponent interventions reduced prevalence of delirium; to enable use, education of the multidisciplinary team is a key factor. Insufficient evidence to recommend BLT or DLA; however, all studies agreed natural bright lighting is preferable in critical care. Need for large, multicenter RCTs that measure all relevant outcomes reliably.	All studies reviewed had limitations regarding design, control of confounding variables, and lack of validated measurement of important outcomes such as sleep.	Not provided	Moderate

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcome: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Zaal and Slooter, 2012[13]	Interventions: Reduction of environmental precipitating factors (noise, light); use of earplugs; early mobilization protocol (physical and occupational therapy); use of bright day-light	Studies Included: Five included in the review: one published prior to 2008, excluded from this review; two RCTs; one before and after; one design not reported.	Intensive care	One RCT of ICU patients compared 69 patients sleeping with earplugs during the night to 67 without; use of earplugs did not prevent delirium, as measured by the Neelon and Champagne (NEECHAM) confusion scale. One study found the number of days patients spent delirious was on average 0.4 days shorter in single-room ICU rather than in ICU with wards, although occurrence rate of delirium did not differ. An early exercise and mobilization protocol in the ICU showed lower incidence and shorter duration of ICU delirium in one before-after study, and one RCT. The RCT showed, as a secondary endpoint, a reduction of delirium days from 4 days in the control group to 2 days in the intervention group. Heterogeneity of design, aim, intervention, measures and outcomes prevents summarizing results. Evidence of included studies was rated low to moderate.	Not provided	Not provided	Moderate

Table B.64: Care Transitions, Use of Multi-Element Models To Improve Care Transitions–Single Studies

Note: Full references are available in the Section 15.2 reference list (except where noted).

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Coleman et al., 2004[3]	Implementing the Care Transitions Intervention (CTI), developed by Eric A. Coleman	Quasi-experimental; intervention subjects (n= 158), control subjects (1,235); patients aged 65 or older living in community	Nonprofit group managed care delivery system located in Colorado that cares for more than 56,000 patients aged 65 or older	Lower odds of rehospitalization; patients had high levels of confidence in obtaining essential information for managing their condition, communication with members of the healthcare team, and their medication regimen.	Not provided	Hospitalized subjects who received CTI were half as likely to return to the hospital as subjects who did not receive CTI. Intervention patients reported high levels of confidence in obtaining essential information for managing their condition, communicating with members of the healthcare team and understanding their medication regimen.	Not provided
Coleman et al., 2006[2]	Implementing CTI	Randomized controlled trial; n=750, community dwelling adults age 65 or older with 1 of 11 diagnoses, including stroke, congestive heart failure, coronary artery disease, cardiac arrhythmias, chronic obstructive pulmonary disease, diabetes mellitus, spinal stenosis, hip fracture, peripheral vascular disease, deep venous thrombosis and pulmonary embolism	Large not-for-profit capitated delivery system that cares for more than 60,000 patients 65 years or older in Colorado	Encouraging patients and their caregivers to assert a more active role in their care transitions lowers readmission rates and lowers costs.	Not provided	Intervention patients had lower rehospitalization rates at 30 days and at 90 days than control subjects. The mean hospital costs were lower for intervention patients ($2,508) vs. controls ($2,546) at 180 days. Transition coach and personal health record enabled patients/caregivers to ensure greater proportions of their needs were met.	Not provided

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Coleman et al., 2015[8]	Implementing CTI	Prospective cohort study; n=83, patient/care giver partnerships; patients were Medicare recipients aged 65 years and older admitted to hospital between May 1, 2012, and March 31, 2013	Nonprofit acute care hospital (253 beds) serving a geographically isolated community	Increased caregiver activation of care.	Generalizability of study is unknown.	Family caregivers experienced a mean improvement in activation of 6 points on a 0-10 scale. Transition coaches identified 71% of patients as having medication discrepancies or errors after hospital discharge and coached family caregivers on how to respond. The enhanced family caregiver CTI significantly improved activation, quality, goal achievement, satisfaction, and medication safety.	Not provided
Gardner et al., 2014[9]	Implementing CTI	Quasi-experimental cohort study, intervention group (n=321), internal control group (n=919); fee-for-service Medicare beneficiaries hospitalized from January 1, 2009, to May 31, 2011	Six Rhode Island acute care hospitals	Lower healthcare utilization after discharge; lower total healthcare costs.	Not provided	Compared to control group, the intervention group had significantly lower utilization in 6 months after discharge and lower mean healthcare costs. The cost avoided per patient receiving CTI was $3,752, driven by lower 6-month rates of hospital admissions, and lower emergency department visits and observation stays.	Not provided

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Hansen et al., 2013[10]	Implementing BOOST (Better Outcomes for Older Adults through Safe Transitions), which was created by the Society of Hospital Medicine	Semi controlled pre-post study, (n=11); hospitals serving medical or mixed medical-surgical patient populations	Sample of 11 hospitals varying in geography, size, and academic affiliation, including community teaching hospitals, community non-teaching hospitals, academic medical centers; range of 300-600 beds	Decrease in readmission rates post-intervention.	Not provided	Participation in Project BOOST seemed to be associated with a decrease in readmission rates but no significant change in length of stay among hospitals implementing BOOST tools.	Not provided
Hirschman et al., 2015[11]	Implementing the Transitional Care Model (TCM)	Evidence summary	Not provided	A cumulative per-member savings of $2,170 at 1 year post-enrollment ($p<.05$) was observed in the TCM intervention relative to comparison group.	Not provided	Not provided	Not provided
Lee et al., 2016[12]	Implementing BOOST, which was created by the Society of Hospital Medicine	Retrospective design; case notes review; sample: n=324 (mean age 75); patients age 65 and older readmitted to acute medical unit	Large hospital in South London; acute medical unit with 58 beds	Use of BOOST Tool correctly predicted readmissions in U.K. and assisted in identifying high-risk patients.	BOOST Tool precision in the U.K. has yet to be determined.	Three hundred twenty-four patients were admitted for readmissions with a median of 7 days between discharge and readmission. The BOOST Tool correctly predicted 90% of readmissions using two or more risk factors and 99.1% of readmissions if one risk factor was included.	Not provided

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Parrish et al., 2009[7]	Implementing CTI	Implementation study; n=791; 18 years and older; average CTI patients: white women aged 76–85	Ten sites: five hospital led, 5 community led	Increased patient self-management of conditions.	Not provided	Presence of leadership support was determined to be critical factor in support of CTI. Sites identified engaging hospital and community-based leaders, providing additional transition coach training, and the assigning of consistent and dedicated transition coaches as available lessons. Future CTI should focus on medication management, patients with cardiovascular disease conditions or diabetes, patients older than 85 years, and African-American and Latino patients.	Not provided
Parry et al., 2009[4]	Implementing CTI	Randomized controlled trial; intervention group (n=44), control group (n=42); fee-for-service Medicare patients	Two community based hospitals in Colorado with the same parent company	Reduced hospital readmissions,	Not provided	Intervention patients were less likely to be readmitted to a hospital in general and for the same condition at 30, 90, and 180 days in comparison to control patients.	Not provided

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Naylor et al., 2012[1] (full reference available in Section 15.3 reference list)	Implementation of TCM	Prospective, quasi-experimental study; 172 patients; community-based older adults coping with common chronic illnesses (i.e., all primary diagnoses except neurological disorders or cancer, end-stage renal disease, and untreated psychiatric disorders) in Aetna's Medicare Advantage program in the mid-Atlantic region	Community/outpatient	There was a significant reduction in hospital re-admissions at 3 months post-enrollment among TCM enrollees compared to the control group (45 readmissions in intervention group, 60 in controls, p<0.041). There also was a 28% reduction in total hospital days (252 vs. 351, p, 0.032). Mean score for satisfaction level with the model was 9.6 out of maximum of 10 for overall patient satisfaction.	Each advanced practice nurse (APN) managed a caseload of 18-–20 members. APNs completed a mean of 8.2 (standard deviation [SD] 3.5, range 1-25) home or physician office visits with each enrollee. Each visit lasted approximately 50 minutes. A mean of 8.4 (SD 7.21, range 151) phone contacts were completed. Total cost of TCM for the 155 Aetna enrollees included was $217,000. In comparison to the matched control group and taking into consideration cost of intervention, TCM was associated with a significant short-term decrease in total healthcare costs at 3 months of $439 per member per month (P, 0.026) and cumulative per-member savings of $2,170 over the 52-week post-enrollment period (P<0.037).	Not provided	The matched control group was obtained from a geographic area which had a 20% lower acute care utilization rate at baseline compared to the mid-Atlantic region where TCM was implemented. The higher rate in the intervention group region may suggest greater opportunity for improvement. Also, the matched control group did not have data on health status, quality of life, and satisfaction data.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Naylor et al., 2014[2] (full reference available in Section 15.3 reference list)	Augmented Standard Care (ASC) versus Resource Nurse Care (RNC) versus TCM	Prospective comparative effectiveness study; 202 patients with caregiver; community-dwelling adults age 65 years and older who were hospitalized with plan to return home, lived within 30 miles of admitting hospital, spoke English, and had a family caregiver willing to enroll in the study	Three hospitals within an academic health system	Twenty-five percent of the TCM group were rehospitalized or died by day 83, compared to day 58 for the RNC group and day 33 for the ASC group. The TCM group had lower mean readmission rates per patient at 30 days compared with the RNC (P<0.001) and ASC groups (p=0.06). At 90 days post-index hospitalization, the TCM group had significant lower mean readmission rates per patient compared to the ASC group (p=0.02) only. No significant group differences in functional status were observed.	Not provided	Not provided	Not provided

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Roper et al., 2017[5] (full reference available in Section 15.3 reference list)	Implementing the TCM	Systematic review; 23,354 patients total sorted into 3 patient groups; 1. Medicaid Recipients intervention group (n=13,476), control group (n=7,899); 2. Medicare Recipients intervention group (n=254), control group (n=764) 3. Adult Patients intervention group (n=685), control group (n=276)	120 general hospitals across 14 regional networks (NC); metropolitan (Southern CA), 13 system-affiliated medical centers; metropolitan (Portland), 4 university-based practice groups and 12 community county health centers	The three identified studies each reported reduced all-cause hospital readmissions within the first month following discharge. Effects varied from modest (1.8% reduction) to substantial (approximately 20% reduction).	Not provided	Not provided	Two of the studies were institutional improvement designs, none were randomized controlled trials.
Solomon et al., 2014[4] (full reference available in Section 15.3 reference list)	Implementing TCM with psychiatric patients	Randomized pilot study; 20 patients in intervention group; adults with psychiatric diagnosis discharged from hospital for acute physical illness	Two psychiatric units of an acute care hospital	Not provided	Not provided	Participants with an active need for medical services were most receptive to the program. Provider challenges included poor communication and coordination with other services. Additionally, the research team decided from the pilot to add a social worker and peer specialist to the care team.	The pilot study had reflections and lessons learned, but no concrete outcomes.
Voss et al., 2011[5]	Implementing CTI	Not provided	Not provided	Reduced hospital readmissions.	Limited generalizability.	Thirty-day readmissions were fewer for participants who received CTI.	Not provided

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)
Williams et al., 2014[2] (full reference available in Section 15.1 reference list)	Implementing BOOST	Qualitative evaluation; n=6 pilot site hospitals and 27 later sites; patient population not available (focus is on hospitals)	Cohort of hospitals including community non-teaching and community teaching, ranging from 100 to 800 beds	Unique mentorship element of Project BOOST proved valuable in helping sites overcome unique challenges and identify factors for success.	Barriers led to less complete implementation of Project BOOST in some hospitals.	Facilitators of Project BOOST implementation included mentor, a small beginning teamwork, and proactive engagement. Common barriers included inadequate understanding of current discharge process, insufficient administrative support, lack of protected time or dedicated resources, lack of front staff buy-in.	Not provided

Table B.65: Venous Thromboembolism Prophylaxis—Systematic Reviews and Meta-Analyses

Note: Full references are available in the Section 16.1 reference list.

Author, Year	Description of Patient Safety Practice	Settings and Population	Summary of Findings	Implementation Themes/Findings
Brown, 2009[5]	Use of pharmacologic agents for venous thromboembolism (VTE) prophylaxis after total hip arthroplasty (THA), total knee arthroplasty (TKA), or hip fracture.	Patients undergoing THA, TKA, hip fracture surgery (HFS).	The VTE rates with aspirin were not significantly different than the rates for vitamin K antagonists, low molecular weight herarin (LMWH), and pentasaccharides. The operative site bleeding relative risks of vitamin K antagonists, LMWH, and pentasaccharides versus aspirin, are 4.9, 6.4, and 4.2, respectively. A pooled analysis of randomized controlled trial (RCTs) supports the use of aspirin for VTE prophylaxis after major orthopedic surgery.	This quantitative systematic review found no significant difference in clinically relevant VTE outcomes, except that vitamin K antagonists have a higher rate of symptomatic deep vein thrombosis (DVTs) compared with aspirin.
Drescher et al., 2014[7]	Treatment with anticoagulation or antiplatelet agents following major lower extremity orthopedic surgery.	Patients undergoing major lower extremity orthopedic surgery.	Eight clinical trials were included in analysis. Overall rates of DVT did not differ statistically between aspirin and anticoagulants (relative risk [RR]: 1.15 [95% confidence interval (CI), 0.68 to 1.96]). However, by type of surgery, there was a nonsignificant trend favoring anticoagulation following hip fracture repair but not knee or hip arthroplasty (hip fracture RR: 1.60 [95% CI,: 0.80 to 3.20], 2 trials; arthroplasty relative risk (RR): 1.00 [95% CI, 0.49 to 2.05], 5 trials). The risk of bleeding was lower with aspirin than anticoagulants following hip fracture repair (RR: 0.32 [95% CI, 0.13 to 0.77], 2 trials), with a nonsignificant trend favoring aspirin after arthroplasty (RR: 0.63 [95% CI, 0.33 to 1.21], 5 trials). Rates of pulmonary embolism were too low to provide reliable estimates.	Aspirin may be associated with a higher risk of DVT in hip fracture repair, but not lower extremity arthroplasty. Across procedures, aspirin may be associated with a lower risk of bleeding.

Author, Year	Description of Patient Safety Practice	Settings and Population	Summary of Findings	Implementation Themes/Findings
Mistry et al., 2017[6]	Aspirin for VTE prophylaxis after lower limb arthroplasty.	Patients undergoing lower limb arthroplasty surgery.	Eight articles were found. Five articles concluded that aspirin was an effective prophylactic. The collation of results on the DVT rate involved 43,012 patients who were prescribed aspirin, of whom 283 (0.66%) suffered from symptomatic DVTs. Aspirin was noted for its good side effect profile and cost effectiveness. It was noted that anticoagulants had a higher rate of complications, including bleeding and wound-oozing.	Aspirin is an effective and safe prophylactic against DVT following major elective lower limb arthroplasty surgery.
Stewart et al., 2013[9]	Aspirin administered solely or in combination with mechanical compression devices in patients undergoing THA, TKA, or HFS.	Patients undergoing high-risk orthopedic surgery.	Trials evaluating aspirin have not consistently shown benefit in the reduction of VTE after TKA, THA, and HFS. Nor have they definitively demonstrated a decreased risk of bleeding for aspirin compared with other anticoagulants. Suggests that LMWH and warfarin have consistently demonstrated benefit with limited bleeding risk.	RCTs, meta-analyses, and retrospective reviews do not consistently conclude that aspirin is safe and effective for preventing VTE.
Wang et al., 2017[4]	Treatment with anticoagulation or antiplatelet agents following THA or TKA.	Primarily patients with knee or hip replacement or arthroplasty, but 13 trials included patients with major joint surgery.	Factor XI antisense oligonucleotide (FXI-ASO), ardeparin, aspirin, and apixaban were ideal for preventing all-cause VTE and reducing all bleeding events, while betrixaban, dalteparin, warfarin, and eribaxaban were ideal for preventing major VTE and reducing major/clinically relevant nonmajor bleeding events.	While the meta-analysis is supportive of the use of aspirin, apixaban was found to have the most favorable outcomes.
Wilson et al., 2016[8]	Treatment with anticoagulation or antiplatelet agents following THA or TKA.	Patients undergoing THA or TKA.	Thirteen studies were included in analysis. There was limited evidence (one RCT study) that there was no difference between aspirin and LMWH following TKA. In all other instances there was insufficient evidence to draw conclusion regarding whether aspirin is more or less effective than anticoagulation agents. However, there appears to be better safety outcomes in the use of aspirin.	Aspirin may be suitable for VTE prophylaxis, but evidence is limited with potential for bias.

Table B.66: Venous Thromboembolism Prophylaxis—Single Studies

Note: Full references are available in the Section 16.1 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Agaba et al., 2017[11]	Use of pharmacologic prophylactic agents following total hip arthroplasty (THA), including aspirin, enoxaparin, warfarin, and factor Xa inhibitors	Retrospective review of data collected from January 2007 to April 2016 within a nationwide private and Medicare insurance healthcare database. A total of 25,966 patients who underwent THA and received a single medication for venous thromboembolism (VTE) prophylaxis during the early postoperative period, including 551 receiving aspirin alone, 6,791 receiving enoxaparin alone, 12,008 receiving warfarin alone, 337 receiving apixaban alone, 876 receiving fondaparinux alone, and 5403 receiving rivaroxaban alone.	Nationwide	Warfarin was associated with a higher risk for deep vein thrombosis (DVT) and had the highest risk for 30-day and 90-day complications. Despite 3 times increased 30-day risk for bleeding, apixaban was effective in preventing VTE during the high-risk 3-month period. Enoxaparin had the lowest risk for pulmonary embolism (PE) and DVT, while rivaroxaban had the lowest risk for prosthetic joint infection hematoma, incision and discharge hemorrhage, and transfusion.	Aspirin had the highest risk for incision and drainage (I&D).	Aspirin has a relatively low bleeding and thromboembolic complication profile and is an inexpensive, easy-to-administer option for VTE prophylaxis following total joint arthroplasty (TJA).	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Anderson et al., 2013[14]	After an initial 10-day course of low molecular weight heparin (LMWH) following elective THA, patients were randomly assigned to an additional 28 days of LMWH or aspirin.	Multicenter randomized controlled trial included 778 patients receiving elective unilateral THA between 2007 and 2010; 400 received LMWH and 386 received aspirin.	12 tertiary care orthopedic referral centers in Canada	Five of 398 patients (1.3%) randomly assigned to LMWH and 1 of 380 (0.3%) randomly assigned to aspirin had VTE. Aspirin was noninferior (p<0.001) but not superior (p=0.22) to LMWH. The absolute between-group difference in a composite of all VTE and clinically significant bleeding events was 1.7 percentage points (confidence interval [CI], 0.3 to 3.8 percentage points; p=0.091) in favor of aspirin.	Clinically significant bleeding occurred in five patients (1.3%) receiving LMWH and two (0.5%) receiving aspirin.	Given its low cost and convenience to access and administer, aspirin may be considered a reasonable alternative for extended thromboprophylaxis after THA.	Included in Wang et al., 2017[4]
Anderson et al., 2018[15]	All patients received once-daily oral rivaroxaban (10 mg) until postoperative day 5 and then were randomly assigned to continue rivaroxaban or switch to aspirin (81 mg daily) for an additional 9 days after total knee arthroplasty (TKA) or for 30 days after THA.	Double-blind randomized controlled trial; 3,427 patients undergoing elective unilateral primary or revision hip or knee arthroplasty underwent randomization; 1,707 received aspirin and 1,717 received rivaroxaban.	15 university-affiliated health centers in Canada	In the comparison with rivaroxaban, aspirin was found to be noninferior (p<0.001) but not superior (p=0.84) for the prevention of postoperative proximal DVT or PE.	A combination of major bleeding and clinically relevant nonmajor bleeding occurred in 22 patients (1.29%) in the aspirin group and in 17 (0.99%) in the rivaroxaban group (95% CI, −1.07 to 0.47; p=0.43).	Aspirin is not significantly different than rivaroxaban in the prevention of VTE following THA or TKA.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Azboy et al., 2017[29]	Treatment with VTE prophylaxis following hip preservation surgery (HPS). Patients received warfarin, aspirin 325 mg twice daily, or aspirin 81 mg twice daily for 4 weeks postoperatively, beginning on the day of surgery along with compression mechanical prophylaxis for the length of the hospital stay.	Retrospective study of prospective data 2003 to 2016; 683 patients undergoing HPS, 448 receiving aspirin 325 mg, 238 receiving aspirin 81 mg, 44 receiving warfarin.	Single site, performed by single surgeon	There was no difference between aspirin 325 mg and aspirin 81 mg in regard to the VTE rate after HPS (p=0.653). Also, there was no difference between aspirin 325 mg and warfarin in regard to VTE rate after HPS (0.911). No difference in VTE rate was observed between aspirin 325 mg and aspirin 81 mg after femoroacetabular osteoplasty (p=0.667). Furthermore, no difference in VTE rate was observed between aspirin 325 mg and aspirin 81 mg after periacetablular osteotomy (p=0.516).	Not provided	No significant difference in symptomatic VTE rates following HPS in patients receiving warfarin, aspirin 325 mg, or aspirin 81 mg.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Bala et al., 2017[12]	Use of one of four thromboprophylactic agents (aspirin, warfarin, enoxaparin, factor Xa inhibitors) during primary TKA.	Retrospective study of prospective data from 2007 to 2016; 1,016 patients undergoing primary TKA who received aspirin age- and sex-matched with 6,096 patients taking enoxaparin, 6.096 patients taking warfarin, and 5,080 patients taking factor Xa inhibitors.	Nationwide	There was a difference in the incidence of DVT at 90 days ($p<0.01$). Factor Xa inhibitors (2.9%) had the lowest incidence of DVT, followed by aspirin (3.0%), enoxaparin (3.5%), and warfarin (4.8%). There was a difference in the incidence of PE at 90 days ($p<0.01$). Factor Xa inhibitors (0.9%) had the lowest incidence of PE, followed by enoxaparin (1.1%), aspirin (1.2%), and warfarin (1.6%).	There were no differences in bleeding-related complications ($p=0.81$) between the groups.	Aspirin provided comparable VTE prophylaxis compared with factor Xa inhibitors and improved VTE prophylaxis compared with enoxaparin and warfarin, with the lowest risk of bleeding.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Bayley et al., 2016[30]	Use of one of three thromboprophylactic agents for patients undergoing THA: warfarin, LMWH, or aspirin in combination with calf compression, foot pumps, anti-embolism stockings, and early mobilization.	Retrospective study of prospective data from 2000 to 2012; 7,983 patients undergoing THAs. Warfarin used in 1,571 patients, LMWH used in 1,838 patients, and aspirin used in 4,574 patients.	Single hospital, UK	A total of six (0.08%) deaths were attributable to PE, three occurring within 42 days of surgery and three within 90 days. All three of the early PEs were in the LMWH group. Of those occurring later, two were in the LMWH group and one in the warfarin group.	The 90-day mortality for the three groups was six patients, 0.38% (95% CI, 0.18 to 0.83); 20 patients, 1.09% (95% CI, 0.71 to 1.67); and 20 patients, 0.43% (95% CI, 0.28 to 0.67), respectively. The difference between LMWH and aspirin reaches statistical significance ($p<0.05$, 95% CIs do not overlap).	PE is rare after elective primary THA. No such events occurred in those treated with aspirin.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Bozic et al., 2010[31]	Use of either aspirin or another guideline-approved prophylactic agent following TKA. Other agents may include warfarin, LMWH, or synthetic pentasaccharides. Aspirin may be the sole prophylaxis method or in combination with mechanical prophylaxis.	Retrospective analysis of data collected in Perspective, a Premier proprietary database of patients undergoing TKA between October 2003 and September 2005; 51,923 patients received warfarin, 37,198 received injectable agents, and 4,719 received aspirin.	307 hospitals	Unadjusted odds ratios (ORs) for DVT or PE were significantly higher in the warfarin group (1.69 times higher odds, 95% CI, 1.39 to 2.05), and the LMWH/ fondaparinux group (1.34 times higher odds, 95% CI, 1.10 to 1.63) when compared with aspirin. The adjusted analysis indicated that the magnitude of the differences in risk of VTE between the aspirin and warfarin groups decreased, and for the LMWH group was no longer significant.	No differences were observed between the groups with regard to bleeding risk.	Aspirin may be effective for VTE prophylaxis in certain TKA patients.	Reference article
Chu et al., 2017[32]	Patients undergoing TKA or THA received either (1) aspirin only; (2) anticoagulants only; or (3) aspirin and anticoagulants. Anticoagulants included warfarin, injectable heparin sodium, LMWH heparin, fondaparinux, or direct oral anticoagulation.	Retrospective cohort analysis of data collected in Perspective, a Premier proprietary database of patients undergoing TKA or THA from 2009 to 2012; 231,780 underwent TKA and 110,621 underwent THA.	Hospitals participating in Premier consortium	Compared with anticoagulants, aspirin was not associated with a higher risk for postoperative VTE either after TKA (adjusted OR and 95% CI 0.34 [0.24–0.48]) or THA (OR 0.82 [0.45–1.51]). For both TKA and THA, the lowest bleeding risk was found in patients who received aspirin only.	Not provided	Aspirin resulted in similar rates of postoperative VTE as anticoagulants.	Reference article

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Daniel et al., 2008[19]	All patients received an oral antiplatelet agent, starting on the day of operation and continuing for 30 days after discharge. Half also received mechanical devices (cohort B).	Retrospective study of THA and hip resurfacing surgeries occurring in 2006; 487 procedures—258 procedures with no mechanical compression and 229 with mechanical compression.	UK	No symptomatic calf or above-knee DVT or PE occurred. In 25 patients in cohort A (10.2%) and in 10 patients in cohort B (4.6%) asymptomatic calf DVTs were detected ultrasonographically. This difference was statistically significant (p=0.03).	Not provided	Aspirin followed by mechanical compression supports a low incidence of VTE without subjecting patients to the higher risk of bleeding associated with anticoagulant use.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Deirmengian et al., 2015[17]	In all patients, aspirin or warfarin treatment was initiated on the day of surgery for patients undergoing TJA and continued for 6 weeks postoperatively. In addition to chemoprophylaxis, intermittent pneumatic compression devices were applied immediately after the surgery and used throughout the hospital stay. In addition, patients were mobilized with physical therapy beginning the day of surgery.	Retrospective review of institutional arthroplasty database of patients undergoing TJA between 2005 and 2013 and treated with intermittent pneumatic compression devices; 534 patients received aspirin, 2,463 patients received warfarin.	Medical institution in Philadelphia, PA	The differences between the groups with regard to DVT or PE alone were not statistically significant (p=0.15; p=0.06, respectively). Fisher's exact test showed a significantly higher risk for any symptomatic VTE in patients receiving warfarin (43 events, 1.75%) compared with patients receiving aspirin (3 events, 0.56%; OR: 3.2; 95% CI, 1.03 to 16.3; p=0.03). Twenty-nine patients (1.0%) were reoperated on for evacuation of hematoma: 2 patients (0.4%) in the aspirin group and 27 patients (1.1%) in the warfarin group. Ten patients (0.3%) had bleeding events: five with upper gastrointestinal (GI) bleeding, two with lower GI bleeding, and three with genitourinary bleeding. All bleeding events were in the warfarin group.	Not provided	Aspirin associated with lower rate of complications and may be more effective than warfarin.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Faour et al., 2018[33]	Patients received aspirin twice daily for 4 to 6 weeks after THA surgery and were grouped into two cohorts: a low-dose (81 mg) aspirin group and a standard-dose (325 mg) aspirin group. All patients also received pneumatic compression stockings.	Retrospective analysis of existing database of patients who underwent THA between September 2012 and December 2016; 1,033 patients received low-dose aspirin, 2,903 patients received standard-dose aspirin.	Not provided	The 90-day incidence of symptomatic VTE was 1.0% in the 325 mg group and 0.6% in the 81 mg group (p=0.35). Symptomatic DVT incidence was 0.8% in the 325 mg group and 0.5% in the 81 mg group (p=0.49), and the incidence of symptomatic PE was 0.3% in the 325 mg group and 0.2% in the 81 mg group (p=0.45). After accounting for confounders, regression analyses showed no difference between aspirin doses and the 90-day incidence of symptomatic VTE (OR, 0.90; 95% CI, 0.29 to 2.85; p=0.85) or symptomatic DVT (OR, 0.96; 95% CI, 0.26 to 3.59; p=0.95).	Bleeding was observed in 0.8% of the 325 mg group and 0.5% of the 81 mg group (p=0.75), and 90-day mortality was not different (0.1%) between the groups (p=0.75).	Low-dose aspirin appears to be a reasonable option for VTE prophylaxis in otherwise healthy patients undergoing elective THA.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Faour et al., 2018[23]	All included TKA patients received either 81 mg aspirin twice daily or 325 mg aspirin twice daily on the evening of or the next day after the procedure for 4 to 6 weeks depending on the surgeons' preference. In addition, all patients received pneumatic compression stockings after the procedure as standard of care. Physical therapy was initiated either on the day of surgery or on postoperative day 1 and continued daily throughout the hospital stay.	Retrospective cohort study of patients undergoing elective primary TKA between 2012 and 2016; 4,339 patients receiving 325 mg aspirin and 1,327 receiving 81 mg aspirin.	Not provided	There was a significant difference (p=0.02) in the incidence of VTE between groups: 0.7% in the 81 mg aspirin group compared to 1.5% in the 325 mg aspirin group. The incidence of symptomatic DVT in the 325 mg aspirin group was 1.4% compared with 0.3% in the 81 mg aspirin group (p<0.001). As for PE, the overall incidence in the study population was 0.2% (12/ 5,666 patients). The incidence of PE in the 325-mg aspirin group was 0.2% compared with 0.4% in the 81-mg aspirin group (p=0.13). Regression model showed no correlation between aspirin dose and VTE incidence (OR=1.03; 95% CI, 0.45 to 2.36; p=0.94) or DVT (OR = 0.50; 95% CI, 0.16 to 1.55; p=0.20).	Not provided	Low-dose aspirin was not inferior to high-dose aspirin for the prevention of VTE after TKA. Low-dose aspirin can be considered a safe and effective agent in the prevention of VTE after TKA.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Feldstein et al., 2017[24]	Patients undergoing TJA received standard-dose aspirin (325 mg) or low-dose aspirin (81 mg) twice daily.	One-year prospective cohort study for patients undergoing primary unilateral TJA; 643 patients were included, 282 received 325 mg and 361 received 81 mg.	All surgeries were performed by a single surgeon	Only one patient in the acetylsalicylic acid (ASA) 81 mg group (0.3%) developed a DVT.	The overall rate of GI side effects (GI upset and nausea) was 1.9%, but ASA 325 mg had a higher rate 9/282 (3.2%) than ASA 81 mg 3/361 (0.8%), p=0.04. Overall GI bleeding was 0.9%, with 2/282 (0.7%) in the ASA 325 mg group vs. 4/361 (1.1%) in the ASA 81 mg group, p=0.70.	There is a higher rate of GI distress and nausea among patients taking standard-dose aspirin compared with low dose.	Reference article

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Gesell et al., 2013[34]	Patients undergoing TKA received multimodal thromboprophylaxis. Aspirin was used in 67% of patients and Coumadin in 33% (high-risk patients, or those who were on Coumadin before surgery). This study group was compared with 1,001 consecutive patients who received multimodal thromboprophylaxis and routine Coumadin chemoprophylaxis. Patients also received pneumatic compression devices, flexion and extension exercises of the ankles, and early mobilization.	A retrospective study comparing two patient cohorts undergoing primary TKA procedures; 1,016 patients undergoing 1,118 procedures.	All surgeries in study group performed by same two surgeons; all surgeries in control group performed by one surgeon.	There was no difference in the rate of symptomatic PE or VTE between the groups. In the study group, 25 patients developed VTE. In the control group, 22 patients developed VTE. There were no major bleeding complications due to thromboprophylaxis in the study group. In the control group, one patient required re-admission for hemarthrosis and two patients required readmission for upper GI bleed while on Coumadin (p=0.12). There was a higher incidence of wound complications in the control group (p=0.03).	There was one death in each group (0.1%).	Multimodal thromboprophylaxis with a preference for the use of aspirin in low-risk patients is safe and efficacious in elective TKA surgery. However, risk stratification is necessary to identify patients at increased risk of VTE and to diminish the exposure of patients to anticoagulation, thus reducing the risk of bleeding and wound-related complications.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Goel et al., 2018[10]	Patients undergoing TKA were divided into four groups based on VTE prophylaxis, as determined by institutional electronic databases, and whether they had undergone simultaneous bilateral total knee arthroplasty (SBTKA) or unilateral total knee arthroplasty (UTKA): (1) unilateral aspirin, (2) bilateral aspirin, (3) unilateral warfarin, (4) bilateral warfarin.	A retrospective, multi-institutional study of patients undergoing SBTKA or UTKA between 2000 and 2017; 18,951 patients, 3,685 who underwent SBTKA and 15,266 who underwent UTKA.	Two large academic institutions	The adjusted incidence of PE following SBTKA was 1.0% (95% CI, 0.86 to 1.2) with aspirin and 2.2% (95% CI, 2.0 to 2.4) with warfarin. Similarly, the adjusted incidence of VTE following SBTKA was 1.6% (95% CI, 1.1 to 2.3) with aspirin and 2.5% (95% CI, 1.9 to 3.3) with warfarin. The risks of PE and VTE were reduced by 66% (OR 0.44, 95% CI, 0.25 to 0.78) and 38% (OR 0.62, 95% CI, 0.38 to 1.0), respectively, using aspirin.	Not provided	Aspirin is more effective than warfarin for the prevention of VTE following SBTKA, and serves as the more appropriate agent for VTE prophylaxis for patients in all risk categories.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Griffiths et al., 2012[20]	Between 2003 and 2006 (inclusive), patients undergoing foot and ankle surgery were given aspirin 75 mg once daily starting on the first postoperative day. In patients undergoing surgery to the forefoot, this was continued for 2 weeks; in those undergoing midfoot or hindfoot surgery, it was continued for 6 weeks or until they were out of plaster. Between 2007 and 2010, no form of chemical thromboprophylaxis was used. All patients had pneumatic compression foot pumps placed on the non-operated limb in theater and antiembolism compression stockings on the ward.	Retrospective analysis of patients undergoing foot and ankle surgery; of 2.654 patients, 1,078 received aspirin postoperatively and 1,576 received no form of chemical thromboprophylaxis.	UK	There was no statistical difference in the rate of thromboembolic events between the two groups (p=0.985). However, the overall rate of thromboembolic events was very small; the incidence of a DVT and PE was 0.27% and 0.15% respectively. There was no statistical difference in the rate of PE or DVT between those who received aspirin and those who did not (p=0.9 and p=0.615).	Not provided	The reported risks of routine chemical thromboprophylaxis appear to outweigh any potential benefits, and the use of aspirin does not appear to confer significant protection against symptomatic VTE. An alternative form of thromboprophylaxis should be considered in high-risk patients such as those who are obese, continue with the combined oral contraceptive pill, or have a previous history of VTE or a pro-coagulant condition.	None

Hamilton et al., 2012[16]	Mechanical calf compression devices were used in all patients. Physical therapy was begun the day of surgery or on postoperative day 1 for afternoon operations. Enoxaparin was begun on postoperative day 1 and renally dosed. For a creatinine of less than 1.5, enoxaparin dosing was 30 mg twice daily for knee arthroplasty and 40 mg once daily for hip arthroplasty. For a creatinine of greater than 1.5, enoxaparin dosing was 30 mg daily for both hip and knee arthroplasty. Upon discharge from the hospital, patients were prescribed enteric-coated aspirin 325 mg twice daily for 28 days. A control group of 500 hip and knee cases received enoxaparin for a total of 2 weeks postoperatively and then aspirin 325 mg twice daily for an additional 2 weeks. Anesthesia, therapy, enoxaparin therapy guidelines, and general	A retrospective review; 500 primary hip and knee arthroplasties between January 2009 and February 2019 in 472 patients.	Single site where all hip and knee arthroplasty surgeries were performed by two surgeons.	There was a trend for a lower rate of DVT in the study group compared with the control group, but this difference did not reach statistical significance using a Fisher exact test (p=0.07). There was a significant difference in the average number of packed RBCs transfused between the study (0.39 units/patient) and control (0.57 units/patient) groups, but there was no significant difference between the number of patients receiving 3 or more units. There was no significant difference between the two groups in the number of patients with the following outcomes: pulmonary embolus, deep infection, superficial infection, readmission, or death.	Not provided	A protocol of inpatient enoxaparin and outpatient aspirin proved safe and effective in standard-risk patients after hip and knee arthroplasty. When combined with mechanical compression devices and early mobilization, a low rate of symptomatic thromboembolic disease was noted. There were significant cost savings with a low complication rate and no deaths.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
	postoperative protocol were otherwise similar between the two groups.						
Huang et al., 2016[27]	Following TJA, patients either received aspirin of warfarin in combination with mechanical prophylaxis.	Retrospective analysis of an institutional database of patients undergoing TJA; 30,270 patients were included.	Medical institution in Philadelphia, PA	The incidences of VTE and mortality were higher in patients receiving warfarin compared with aspirin. In multivariate analysis, warfarin was an independent risk factor for VTE and mortality in the higher risk VTE patients ($p<0.001$).	There was no significant difference in GI complications between groups.	Aspirin may be safer than and as effective as warfarin for VTE prophylaxis, even among higher risk patients.	Reference article
Jameson et al, 2011[35]	Following THA, patient received either LMWH or aspirin in combination with mechanical prophylaxis.	Retrospective review of the National Registry combined with Hospital Episode Statistics data for patients undergoing THA; 22,942 included patients received aspirin and 85,642 received LMWH.	UK	Without adjustment, there were no significant differences between the two treatments. The rate of PE was 0.68% in both groups, and 90-day mortality was 0.65% with aspirin and 0.61% with LMWH (OR 0.93; 95% CI, 0.77 to 1.11).	Risk adjustment increased the difference in mortality (OR 0.84; 95% CI, 0.69 to 1.01) and was increased further still with propensity score matching to 0.65% with aspirin and 0.51% with LMWH (OR 0.77; 95% CI, 0.61 to 0.98).	Aspirin is not inferior to LMWH. However, there may be a slightly increased risk of mortality.	Reference article

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Ji et al., 2011[22]	Compared the incidence of symptomatic VTE in hip fracture surgery patients taking low-dose aspirin or other antiplatelet to prevent thrombosis with non-users. Patients received thigh-length antiembolic stockings, and use of the ankle pump was encouraged in bed during the inpatient stay.	Retrospective review of medical records of patients undergoing hip fracture surgery for femoral neck and interochanteric fractures from May 2003 to April 2010; 245 antiplatelet users compared with 579 non-users.	Single institution, Korea	The incidence of symptomatic VTE was 4.8% (12/ 250) in antiplatelet users and 4.3% (26/608) in non-users (p=0.718). Symptomatic VTE after hip fracture surgery (HFS) was not reduced in Korean patients who received antiplatelet agent including aspirin in this study.	Not provided	Results indicate that thromboprophylaxis after HFS is not necessary in Korean patients.	None
Jiang et al., 2014[25]	Patients undergoing TKA were randomly allocated to either receive aspirin or receive LMWH. Both groups also received mechanical prophylaxis.	Prospective randomized study conducted between January 2012 and May 2013; 120 patients underwent randomization.	Single site	DVT was detected in 10 of 60 patients receiving aspirin (16.7%, 95% CI, 7.3% to 26.1%) compared with 11 of 60 receiving LMWH (18.3%, 95% CI, 8.5% to 27.8%). The difference was not significant (p=0.500). Patients receiving aspirin had a lower blood loss index compared to those patients receiving LMWH. This finding was significant.	Not provided	Aspirin combined with mechanical prophylaxis is not inferior to LMWH combined with mechanical prophylaxis in preventing VTE following TKA.	Reference article

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Kaye et al., 2015[21]	Arthroscopic knee surgery patients were randomly allocated to the aspirin or no aspirin group by using sealed envelopes; the operating surgeon sequentially opened the envelope after each surgical procedure. Patients allocated to the aspirin group took 325 mg aspirin tablet daily for 14 days starting on the first postoperative day. Patients allocated to the nonpharmacologic group (control group) did not take any nonsteroidal anti-inflammatory drugs for the first 14 days postoperatively. All patients participating in the study had bilateral, whole leg, compression venous duplex ultrasonography 10 to 14 days postoperatively.	Prospective randomized, single-blind controlled study of patients undergoing arthroscopic knee surgery between June 2011 and June 2013; 170 patients.	East Asian institute	No DVTs or PEs were identified in either group.	29 patients (17%) experienced a complication. While no significant complications were found, minor complications existed, including pain and swelling, residual join line tenderness, incidental finding of a Baker's cyst, arthrofibrosis, instability after a fall, and a limp. Following a logistic regression, aspirin was not statistically significant for a decreased risk of complication following arthroscopic knee surgery.	As no cases of VTE were identified in the patient population, the use of aspirin in a low-risk population undergoing arthroscopic knee surgery is not warranted.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Mendez et al., 2017[3]	Compared patients undergoing surgery for a primary malignant soft-tissue or bone tumor, or metastatic carcinoma who received 325 mg of aspirin twice daily following the operation with patients receiving nonaspirin prophylaxis.	Retrospective review of medical records of patients who had been surgically treated for a primary malignant soft-tissue or bone tumor, or metastatic carcinoma, from 2012 to 2015; 130 patients with 142 surgical procedures. Aspirin given after 103 procedures, non-aspirin prophylaxis after the remaining surgeries.	Surgeries performed by one of two orthopedic oncologists at a single institution	There were six DVTs and one PE after 7 (4.9%) of the 142 surgical procedures. A VTE developed in 3 (2.9%) of the 103 cases with aspirin prophylaxis and 4 (10.3%) of the 39 cases in the non-aspirin group. In the non-aspirin cohort, a DVT developed in 1 (7.1%) of the 14 cases treated with only an intermittent pneumatic compression device, 1 (8.3%) of the 12 treated with LMWH, and 1 (16.7%) of the 6 treated with unfractionated heparin. A PE developed in 1 (20.0%) of the 5 cases in which warfarin had been used.	Not provided	Aspirin for VTE prophylaxis in patients undergoing orthopedic oncologic surgery was positive, especially for patients with soft-tissue sarcoma, who had no documented VTEs.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Parvizi et al., 2017[28]	Six adult-reconstruction surgeons agreed to enroll TJA patients into the study. Three surgeons prescribed 325 mg aspirin twice a day to their patients for a defined period of time (the 325 -mg aspirin group) and then switched to 81 mg aspirin twice a day (the 81 mg aspirin group) for the remainder of the study. The other three surgeons would do the same but in a reverse order. Treatment was in combination with compression devices and early mobilization.	Prospective crossover study from July 1, 2013, through June 30, 2015, of patients receiving joint arthroplasty; 4,651 patients.	Medical institution in Philadelphia, PA	The incidence of venous thromboembolism of 0.1% (95% CI, 0% to 0.3%) in the 81 mg aspirin group was not significantly different (p=0.345) from 0.3% (95% CI, 0.1% to 0.6%) in the 325 mg aspirin group.	The incidence of GI bleeding or ulceration of 0.3% (95% CI, 0% to 0.5%) in the 81 mg aspirin group was slightly, but not significantly (p=0.66), lower than the 0.4% (95% CI, 0.2% to 0.6%) in the 325 mg aspirin group.	Low-dose aspirin is not inferior to high-dose aspirin for VTE prophylaxis following TJA.	None
Raphael et al., 2014[18]	Patients undergoing TJA received either aspirin (325 mg twice daily) or warfarin prophylaxis. All patients received treatment in combination with compression devices.	Retrospective analysis of a prospective database of patients undergoing TJA between January 2000 and June 2012; 28,923 patients, 2,800 receiving aspirin and 26,123 receiving warfarin.	Medical institution in Philadelphia, PA	The overall symptomatic PE rate was lower (p<0.001) in patients receiving aspirin (0.14%) than in patients receiving warfarin (1.07%). The incidence of symptomatic DVT was significantly lower in the aspirin group (0.29%) than in the warfarin group (0.99%) (OR=3.50; 95% CI, 1.75 to 8.19; p<0.001).	Not provided	Aspirin offers effective prophylaxis and is appropriate for use.	Included in Mistry, 2017

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
				The risk of symptomatic DVT remained lower in the aspirin group than in the warfarin group even after propensity score matching was performed. With 3:1 matching, the symptomatic DVT rate was lower in the aspirin group (0.11%) than in the warfarin group (0.91%) (OR=8.57; 95% CI, 2.25 to 72.58; p<0.001). In the unmatched patients, the incidences of wound-related complications and 90-day mortality were significantly higher in the warfarin group than in the aspirin group. However, after propensity score matching, the incidences were not significantly different between groups, except for wound drainage, which was lower in the aspirin group than in the warfarin group after 5:1 matching (p=0.016). Unmatched and matched analyses			

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				both showed the mean length of hospital stay to be significantly shorter for patients receiving aspirin.			
Jiang et al., 2014[36]	Postoperative administration of aspirin (group A) versus postoperative administration of LMWH and rivaroxaban sequentially (group B) in patients undergoing TKA. All patients also received mechanical prophylaxis.	Prospective randomized comparative study of patients undergoing primary unilateral TKA for degenerative arthritis from January 2012 to May 2013; 120 patients—60 in Group A and 60 in Group B.	Beijing Jishuitan Hospital	DVT was detected in 10 of 60 patients in the aspirin group (16.7%, 95% CI, 7.3% to 26.1%) compared with 11 of 60 in the LMWH and rivaroxaban group (18.3%, 95% CI, 8.5% to 27.8%; p=0.500). Patients in the aspirin group had the lower blood loss index as compared with patients in the LMWH and rivaroxaban group (p=0.000).	Not provided	The results of this study suggest that aspirin is not inferior in preventing VTE following TKA when compared with sequential LMWH and rivaroxaban.	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Comments
Zou et al., 2014[26]	Three groups of TKA patients each received a different postoperative anticoagulant/ antiplatelet treatment. Group A was given rivaroxaban, Group B was given LMWH sodium, and Group C was given aspirin.	Prospective randomized controlled trial of patients with osteoarthritis undergoing primary unilateral TKA from July 2011 to July 2013; 324 patients randomized into three groups: Group A=102 patients, Group B=112 patients, Group C=110 patients.	China	The incidence of DVT was lower in Group A compared with the other two groups (3 [2.94%] vs. 14 [12.50%], p=0.029; 3 [2.94%] vs. 18 [16.36], p=0.017). Hidden blood loss (1.71 [1.19–2.97] vs. 1.18 [0.77–2.31], p=0.009; 1.71 [1.19–2.97] vs. 1.30 [0.61–2.43], p=0.004) and wound complications (5 [4.90] vs. 3 [2.67], p=0.027; 5 [4.90] vs. 2 [1.82], p=0.014) were more common in Group A than in the other groups. There were no significant differences between Group B and Group C in the incidence of DVT (14 [12.50%] vs. 18 [16.36%], p=0.831), hidden blood loss (1.18 [0.77–2.31] vs. 1.30 [0.61–2.43], p=0.327), or wound complications (3 [2.67] vs. 2 [1.82], p=0.209).	Not provided	No significant difference in post-TKA DVT prophylaxis was found between aspirin and LMWH.	None

Table B.67: Cross-Cutting Factors Patient Safety Topics/Practices, Patient and Family Engagement—Single Study

Note: Full references are available in the Section 17.1 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits
Eden et al., 2017[5]	Condition Help (CH), a patient and family-initiated rapid response system	Observational study. The number of CH calls was recorded from January 2012 through June 2015. A patient care liaison and the unit charge nurse responded to CH calls. Each call reason was sorted into 1 of 10 categories. After a CH call, the patient's chart was reviewed to examine if it was related to a patient safety issue. Patient outcomes after the CH call were documented.	Two adult tertiary care referral hospitals	During collection period, 367 CH calls were made by 240 patients. Of the 240 patients, 43 (18%) activated the CH team with multiple calls, which comprised 46.3% of all calls (170/367). The majority of calls were made by patients, not family members (76.8%). Most of the CH calls were related to inadequate pain control (48.2%), followed by dissatisfaction with staff (12.5%). The majority of calls involved non-safety issues (83.4%) and safety issues (11.4%). In 152 calls (41.4%) of the 367 total calls, a change in care was made. The other 53 calls (34.9%) involved additional patient counseling or nonmedical changes. The traditional rapid response team (RRT) was activated within 24 hours of the CH for 19 cases (5.2%). Of the 19 cases, 6 were transferred to the intensive care unit. Overall, RRT was seldom activated, level of care was seldom escalated, and mortality was rare.

Table B.68: Cross-Cutting Patient Safety Topics/Practices, Patient and Family Engagement—Systematic Reviews

Note: Full references are available in the Section 17.1 reference list.

Author, Year	Description of Patient Safety Practice	Setting; Population	Summary of Systematic Review Findings
Park et al., 2019[1]	Patient and family engagement	Hospitals, nursing homes, private clinics, and academic medical centers; 42 studies reviewed	Both study participants and healthcare providers expressed positive attitudes toward patient and family engagement. Successful implementation of patient and family engagement is hampered by lack of patient safety knowledge among patients and lack of clear implementation guidelines for healthcare providers. The impact of patient and family engagement is hard to determine because there are few studies that evaluate such interventions.
Berger et al., 2014[3]	Patient and Family Engagement	Hospitals; 12 studies reviewed	Overall, there is a lack of high-quality evidence to inform successful implementation of patient and family engagement. More studies are needed to evaluate the effectiveness of such interventions.

Table B.69: Cross-Cutting Patient Safety Topics/Practices, Safety Culture—Single Studies

Note: Full references are available in the Section 17.2 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Sexton et al., 2018[18]	Leadership WalkRounds with feedback: Conducting Leadership WalkRounds and providing feedback about the risks that were reduced as a result of conducting them.	Cross-sectional survey administered to a convenience sample of 31 hospitals through the Michigan Health and Hospital Association (MHA) Keystone Center; 28,853 surveys were sent out and 16,797 were returned (response rate=70.4%); 53.9% of respondents reported at least 10 years in their specialty, and nurse was the most frequently selected role (27.1%).	Thirty-one Michigan hospitals were invited to participate. Seventeen (55%) had 99 or fewer beds, five (16%) had between 100 and 199 beds, six (19%) had 200 to 299 beds, and two (6%) had more than 400 beds.	Significant differences were found between the first and fourth WalkRounds, with feedback quartiles on all safety culture SCORE subscales measured: teamwork climate, safety climate, improvement readiness, local leadership, personal burnout, and burnout climate. Respondents who reported higher levels of WalkRounds with feedback also had higher scores on the safety culture subscales (including more positive safety climate, lower personal burnout, and lower burnout climate), two out of the three resilience subscales, and four out of the five engagement subscales.	Not provided	The authors note that one of the most cited methods for reducing burnout is Krasner's physician mindfulness training. This training usually spans 27 hours over an 8-week period and has demonstrated an effect size of 0.62 (based on Cohen's *d*) for burnout reduction. The current study calculated an effect size of 0.43 between the first and fourth quartiles of WalkRounds with feedback, suggesting the usefulness of this relatively brief intervention on burnout reduction.	High	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Sexton et al., 2014[17]	Leadership WalkRounds	Cross-sectional survey administered to a convenience sample of 44 NICUs; 3,294 surveys were sent out and 2,073 were completed (response rate=62.9%); 706 units (adult clinical areas) in 49 hospitals were used as a comparison group.	Forty-four NICUs in California: 10 were from regional hospitals, 28 were from community hospitals, and 6 were from intermediate hospitals.	The first and fourth WalkRounds feedback quartiles differed significantly on the two SAQ dimensions measured ("safety climate" and "teamwork climate") and on two of the four HSOPS dimensions measured ("overall perceptions of safety" and "feedback and communication"). The first WalkRounds feedback quartile reported less burnout than the fourth quartile, but was not statistically significant.	Not provided	Participation in Leadership WalkRounds and WalkRounds feedback was lower in NICUs compared with adult clinical areas. There were no significant differences in safety climate between the NICU and adult clinical areas. The authors note that it may be more difficult for some staff to participate in Leadership WalkRounds (e.g., nightshift, non-nursing providers).	High	None
Schwendimann et al., 2013[16]	Leadership WalkRounds	Retrospective, cross-sectional survey; 19,053 surveys were received for a response rate of 80.2%. (The total number of surveys sent out was not specified.)	Forty-nine hospitals within a nonprofit healthcare system. A total of 706 clinical and nonclinical units participated.	A significantly higher safety climate was found in the units where there was greater exposure to WalkRounds. The units where 60% or more of respondents indicated that they had at least one WalkRound exposure also reported significantly higher patient safety risk reduction and higher feedback about WalkRound actions that had been taken.	Not provided	Anecdotal evidence suggested that the WalkRounds provided the forum for team members to speak up about errors and safety risks, as well as adopt new practices and share lessons learned.	High to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Frankel et al., 2008[15]	Leadership WalkRounds. Senior leaders, quality and safety personnel, and clinical managers/ directors attended a half-day WalkRounds training session. Coaching sessions were conducted via the telephone every 2 months for 2 years.	Pre-post design. The SAQ safety climate subscale (7 items) was administered prior to the WalkRounds project (n=790) and approximately 18 months later (n=702).	Two hospitals in Massachusetts implemented weekly WalkRounds, including an academic teaching institution and a community teaching hospital.	The baseline SAQ data indicated that 10 out of 21 clinical care areas had safety climate scores below 60%, whereas only 3 clinical areas had scores below 60% post-WalkRounds. The academic teaching institution's safety climate score significantly improved, from 62% on the pre-SAQ to 77% on the post-SAQ. The safety climate score for the community hospital significantly improved following the WalkRounds project, from 46% to 56%. Safety climate scores increased from pre to post for all caregiver types except nurse managers/charge nurses, whose scores decreased over time. Paired sample t-tests showed significant improvement on items related to: discussing and learning from errors, feeling encouraged by colleagues to report concerns, and knowing how to report concerns.	Not provided	The types of problems discussed during Leadership WalkRounds varied by caregiver type, with nurses focusing on operational problems and physicians focusing on issues related to clinical decision making. Some issues could be resolved locally, some required collaboration across departments, and some required significant resources/budget allocations. Many of the concerns that were shared during the Leadership WalkRounds were addressed and resolved. The authors note that WalkRounds is an inexpensive intervention relative to other quality improvement efforts, but it does require a strong commitment from leadership, a project champion trained in quality or safety, and time and resources to manage the data and feedback gathered.	High to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Hefner et al., 2017[21]	Crew Resource Management, including facilitated training, day-long retreats to develop/tailor CRM safety tools, and role-playing.	One-group pre-post design; 784 staff completed the pre-HSOPS survey; 667 staff completed the post-HSOPS survey.	The Ohio State University Wexner Medical Center. Eight departments from the main and satellite hospital, the comprehensive cancer hospital, and the heart hospital participated.	Overall, significant improvements were observed on 10 of the 12 HSOPS dimensions. The two dimensions for which no significant improvement was observed were "supervisor promotes patient safety" and "staffing." Staff consistently responded less positively on the pre- and post-assessments than did practitioners. While most departments saw pre to post improvements on a minimum of seven dimensions, the radiation oncology department scores significantly improved on only two dimensions from pre to post and the interventional radiology department's scores significantly improved on five dimensions after training.	Not provided	To examine the decreasing scores for radiation oncology, the open-ended comments provided by survey respondents were reviewed. They suggested that this most likely was a result of staff changes and turnover that occurred in that department during the study period, as the comments were related to understaffing, workflow problems, communication failures, and lack of buy-in. The authors proposed that strong, stable leadership and human resources may mediate the relationship between CRM and patient safety culture. The authors also noted that the project was a significant undertaking and required staff allocation and buy-in at all levels.	High	The article did not provide details regarding the length of the CRM training (e.g., 1 day, 4 hours).

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Schwartz et al., 2018[24]	Clinical Team Training (based on Crew Resource Management Training) and implementing a patient safety project.	Cross-sectional study design. Thirty-three VA facilities participated in the initial training, and 17 facilities participated in the 12-month recurrent training. Participants represented a variety of clinical areas.	VA medical facilities in the United States.	Scores on all 27 TSCQ items improved over time. Significant improvement was found on 8 of 27 items at the 6-month assessment (5 items related to teamwork, 3 items related to safety climate), and significant improvements were found on 11 of the 27 items at the 12-month follow-up (6 items related to teamwork, 4 items related to safety climate, and 1 item related to perceptions of management).	Not provided	The most pronounced improvements identified through the TSCQ data were: (1) briefings at the start of a shift/case had become a standard method of communication in many clinical areas, (2) respondents believed that the organization was doing more for patient safety than it had a year ago, (3) respondents were more likely to know the first and last names of those with whom they had worked on their last shift, (4) personnel felt encouraged to report any safety concerns, (5) respondents were aware of the proper channels in which to direct their patient safety questions, (6) nurses' input was well received, and (7) physicians and nurses worked as a coordinated team.	High	The article did not provide details regarding the length of the training (e.g., 1 day, 4 hours). No specific information was presented on the facilities (e.g., number of beds).
Budin et al., 2014[20]	Four-hour Crew Resource Management Training with a 2-hour refresher class 1 year following implementation. Training was led	One-group pre-post design with external benchmarking comparisons. Seventy nurses and 88 physicians completed the	Perinatal units at a large urban academic medical center in the northeastern United States. The center has three triage	Prior to the intervention, physicians' perceptions on the Teamwork Climate subscale were significantly more positive than nurses'. Both nurses' and	Not provided	The authors stressed the positive results achieved by this low-tech intervention. However, other changes were also implemented, such as creation of a medical safety officer role. Four officers	High	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	by five nurse-physician teams who were trained in CRM first and then trained others.	Teamwork and Safety Climate subscales of the SAQ prior to the initial training. Fifty-eight nurses and 46 physicians completed the same subscales after they had completed a refresher course conducted 1 year following implementation.	beds, 10 L&D rooms, three ORs, a three-bed post-anesthesia care unit, and four antepartum beds.	physicians' perceptions of teamwork climate significantly improved at the 1-year follow-up, although physicians remained more positive than nurses. No differences were found between nurses and physicians on the safety climate subscale prior to the CRM intervention, but significant improvements in safety climate were reported for both groups on the follow-up assessment. Post-intervention data were also compared with available benchmark data. Post-intervention means on the Teamwork subscale and the Safety Climate subscale were significantly more positive than the mean for two benchmark groups: nurses and physicians working in various inpatient settings and as U.S. intensive care unit caregivers.		rotated to provide constant coverage. Team meetings were held with all disciplines twice a day to improve communication and outcomes. Huddles were conducted with the primary team, safety officer, charge nurse, and/or leadership throughout the day if there were patient concerns. Four large flat screens were purchased to support huddles, handoffs, situational awareness, and cross-monitoring.		

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Jones et al., 2013[25]	TeamSTEPPS® Team Training program developed by AHRQ.	Quasi-experimental design: Static group (n=1,328) and pre-post comparison for intervention group (n=2,137). Safety culture was measured using the Hospital Survey on Patient Safety Culture (HSOPS).	Thirty-seven critical access hospitals in the central United States with fewer than 25 beds): 24 hospitals participated in the intervention, and 13 served as a static comparison group. Participants represented a variety of work areas, with the majority reporting that they had direct patient contact (control= 77.2%, intervention= 80.1%, p=0.009).	The intervention group had significantly more positive scores on three HSOPS dimensions: Organizational learning/continuous improvement, teamwork within departments, and teamwork across hospital departments. Early adopters of TeamSTEPPS® had significantly higher scores on three HSOPS dimensions when compared with early/late majority and laggard hospitals (frequency of events reported, staffing, and hospital management support for patient safety). No statistically significant differences were found between the intervention and static groups in terms of the adoption of team behaviors (transfer). The proportion of respondents who reported transfer were 26% for early adopters, 18% for early/late majority, and 7% for laggard hospitals.	Not provided	Participating in the TeamSTEPPS® training had a minimal impact on perceptions of safety culture, learning the TeamSTEPPS® tools had a moderate impact, and transfer of team behaviors had the greatest impact. Although laggard hospitals may have been most in need of team training, they were slower to adopt the TeamSTEPPS® training due lack of management support.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Berkowitz et al., 2012[27]	Team Improvement for Patient and Safety (TIPS) conferences. These conferences were 30 minutes long and used to discuss potentially avoidable acute care hospital transfers or adverse events that may have ended in an acute care hospital transfer. The TIPS conferences were held every 2 weeks over the course of the 1-year study period.	Pre-post design. Ten participants completed the baseline Nursing Home Survey on Patient Safety Culture, 41 completed the 6-month post-assessment, and 40 completed the 12-month post-assessment of this measure.	Subacute rehabilitation unit with 50 beds that admits approximately 1,000 patients per year. This unit resides within a 600-unit long-term care, religious-affiliated, not-for-profit organization located in Boston, Massachusetts.	Mean scores on the Nursing Home Survey on Patient Safety Culture significantly improved over time. When looking at overall survey results, the percentage of respondents that agreed or strongly agreed with all survey items increased by almost 20 percentage points.	Not provided	The unit was able to conduct 22 of the 26 intended TIP meetings (84.6%) during the course of the study. The TIP conferences functioned as a structured debrief. Individuals submitted problematic cases for discussion. Effort was made to discuss each submitted case within 1–2 weeks of its occurrence. Actionable steps were recorded and "tips from TIPS" emails were sent to all staff. The times for the TIP conferences were varied to allow staff from all shifts to participate. The small sample size for the baseline administration of safety culture survey was explained as fear of submitting data. The increase in sample size on the post-intervention measures is attributed to the changes in culture that were occurring.	High	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Carney et al., 2011[23]	VA Medical Team Training Program.	One-group pre-post design; 3,419 OR staff from high- and medium-complexity facilities completed the "Safety Climate" subscale of the Safety Attitudes Questionnaire (SAQ) prior to the training; 1,454 OR staff from high- and medium-complexity facilities completed the "Safety Climate" subscale of the SAQ after training.	One hundred and one Veterans Health Administration hospitals.	Significant pre-post differences were reported for respondents working at both high and medium complexity facilities on all seven items on the SAQ safety climate dimension.	Not provided	The Medical Team Training Program involved 2 months of preparation and planning, development of an action plan to identify problem areas, an agreement to use perioperative briefings and debriefings, and a 1-year implementation commitment. Monthly meetings were also held so that the interdisciplinary team could receive coaching on project implementation.	High	No information about the length of the training program (e.g., 1 day, 4 hours).

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Blegen et al., 2010[26]	Four-hour interdisciplinary team training with follow-on unit-based support team; 454 healthcare staff received the training.	One-group pre-post design (surveys were anonymous and not matched); 434 trainees completed the HSOPSC pre-intervention survey and 368 completed the HSOPSC post-intervention survey 1 year following the training.	Inpatient medical units of three hospitals in California: academic university medical center, non-teaching community hospital, and an integrated healthcare system hospital.	No pre-post improvement was observed for one of the participating hospitals. The remaining two hospitals reported significant improvements on 10 of the 12 HSOPC dimensions.	Not provided	The program had a positive impact on safety culture in two of the participating hospitals. The differential impact of the team training program and the unit-based support team was not examined. It is unclear whether one may have had a stronger effect than the other, although the authors felt that both were necessary to achieving the overall results.	High	This was a pilot test, but reads like a true empirical study.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Gore et al., 2010[22]	An 8-hour seminar based on Crew Resource Management was delivered to all OR personnel. Perioperative briefings were implemented following the seminar to improve communication and teamwork.	One-group pre-post design; 207 pre-intervention surveys were returned (34.5% response rate) and 156 post-intervention surveys were returned (27.6% response rate). The survey contained three subscales related to teamwork, safety climate, and reporting of errors.	OR department within one hospital.	Significant improvements were reported for 2 of 13 items related to error reporting and 2 of 11 items related to safety climate. There were no significant improvements reported related to teamwork. A look at the data by respondent demographics revealed that nurses were most impacted by the training. The scores of nurses significantly improved on 3 of the 4 items related to teamwork, 1 of the 13 items related to error reporting, and 3 of the 11 items related to safety climate.	Not provided	The post-intervention surveys were sent only 8 months following the initial training seminar (and 6 months after the implementation of perioperative briefings), which may not have been a sufficient amount of time to observe pre-post change.	High	The specific name of the survey administered was not included, only that it was made available by AHRQ. The CRM seminar was taught by aviation pilots who presented information, facilitated roleplays, and facilitated OR personnel in conducting perioperative briefing. Perhaps this initiative would have had a greater impact if it had been tailored more to the participants and their environment.
Lin et al., 2018[33]	Statewide Comprehensive Unit-based Safety Program (CUSP) and individualized bundles.	Pre-post cohort design. Pre-post design.	Fifteen hospitals in the State of Hawaii ranging from a 25-bed critical access hospital to a 533-bed	Significant pre-to-post improvement was reported for 10 of the 12 HSOPS subscales, with the most notable improvement on: "organizational	Over the course of the study period, the rate of SSI decreased significantly	The authors noted that they felt that the learning platform used in this project was very beneficial, as it allowed communication and networking among	Moderate	There are no details as to how many respondents completed the pre-and post-

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
	Hospitals were encouraged to implement as many interventions as they liked, but were required to select a minimum of three.		academic medical center.	learning/continuous improvement" (59% vs. 70%), "frequency of events reported" (51% vs. 60%), "feedback and communication about error" (52% vs. 59%), "teamwork within units" (58% vs. 75%), "supervisor/managers expectations and action promoting safety" (53% vs. 60%). No statistically significant improvement was found on the "staffing" or "handoffs and transitions" subscales. Over the course of the study period, the rate of SSI decreased significantly (from 12.08% to 4.63%). The superficial SSI rate decreased significantly, from 8.08% to 2.78%, with little change in deep SSI rate (1.70% to 0%), nor organ/space SSI rate (2.56% to 1.85%). Correlations between safety culture subscales and SSI rates were negligible or weak.	(from 12.08% to 4.63%). The superficial SSI rate decreased significantly from 8.08% to 2.78% with little change in the deep SSI rate (1.70% to 0%), nor organ/space SSI rate (2.56% to 1.85%). Correlations between safety culture subscales and SSI rates were negligible or weak.	participants and created a sense of community. They further highlighted the importance of operating room debriefs. While participating hospitals were urged to incorporate briefings as part of their bundled interventions, analyses regarding the use of debriefs were not reported.		measures of safety culture.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Hsu and Marsteller, 2016[29]	Comprehensive Unit-based Safety Program (CUSP) and five evidence-based practices for reducing CLASBI rates.	Fifty-four ICUs used CUSP and 17 ICUs not using CUSP served as a comparison group.	All hospitals in Michigan that have an adult ICU were invited to participate. The majority of the ICUs that participated in the study were from teaching hospitals.	No statistically significant improvement was found for the non-CUSP group from the pre-to-post SAQ administration (n=19 at baseline and n=14 at time 2). For the CUSP group, pre-SAQ data were available for 47 ICUs and 38 completed post-SAQ. The ICUs in the CUSP group statistically improved their post-SAQ scores on four of the six subscales measured. No statistically significant change was found for either "stress recognition" or "perceptions of management" over the study period.	There were no statistically significant differences found in CLASBI rates between the CUSP and non-CUSP groups.	Not provided	High to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Saladino et al., 2013[19]	Comprehensive Unit-based Safety Program (CUSP), which included: educate staff on the "science of safety," identify safety concerns, implement executive WalkRounds, implement improvements, and document/share results.	Single-group repeated measures design. The sample included 81 unit-based staff members (51% were nurses).	Twenty-two-bed surgical critical care unit within a 369-bed Magnet-designated community hospital.	The 36-item critical care version of the Safety Attitudes Questionnaire (SAQ) was administered to evaluate changes in safety culture. Sixty participants (74%) completed the pre-SAQ and 55 (69%) completed the post-SAQ. No statistically significant pre-to-post changes were reported for any of the SAQ subscales. Safety concerns were gathered during monthly WalkRounds that occurred over a 6-month period. A total of 77 safety issues were identified over this period, with 44 being resolved (57.1%).	Not provided	Some scores on the SAQ actually declined over the study period. The authors believe this may have occurred because they posted the safety issues identified during the monthly WalkRounds, and this heightened awareness of how frequently safety issues were arising and may have made the staff feel that there was a lack of safety within the unit. The authors note that the 6-month study period was likely too short to result in significant changes and that the literature suggests there should be approximately 12 to 18 months between pre- and post-safety culture assessments.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Simpson et al., 2011[30]	Comprehensive Unit-based Safety Program (CUSP).	Pre-post design.	Fifteen Michigan hospitals with perinatal service.	This study reported improvements on several dimensions of the Safety Attitudes Questionnaire. They also reported significant improvement on all six process measures collected. There were no significant differences in the outcomes measured, although the data were trending in the right direction.	Not provided	The implementation of CUSP included: assessing and promoting a culture of safety, interdisciplinary team building, case review, coaching, administrative support of the safety infrastructure, and ongoing evaluation of care processes and outcomes.	Moderate	None
Vigorito et al., 2011[31]	Comprehensive Unit-based Safety Program (CUSP). Based on results from the Safety Attitudes Questionnaire (SAQ), units were encouraged to develop an action plan for how they would improve their scores.	Pre-post design; 841 of 1,024 participants completed the pre-intervention SAQ (82%) and 918 of 1,080 completed the post-intervention SAQ (85%). Pre-to-post change was examined for units that had submitted a SAQ action plan and those that had not. CLASBI and VAP infection data were also collected as outcome measures.	Twenty-three ICUs from 11 hospitals enrolled in the Rhode Island ICU Collaborative.	Nine units completed and submitted action plans following the pre-intervention SAQ. Units that had a SAQ action plan demonstrated greater improvement on five of the six SAQ subscales than the units that did not have a SAQ action plan (although not statistically significant). Perceptions of "teamwork climate" and "stress recognition" decreased from pre to post for units without an action plan (-6.4% and -6.6%, respectively), whereas	CLASBI rates decreased by 10.2% for units that had a SAQ action plan over the course of the study period as compared with a 2.2% decrease for the units without an action plan. VAP rates decreased by 15.2% for units with a SAQ action plan and	The only SAQ subscale for which no improvement was seen was "working conditions." The authors noted a high turnover rate for nurse clinical manager and ICU directors (61% during the study period) which likely accounted for lower scores in this area. This quality improvement effort has continued and the authors report that the ICUs continue to make improvements in their SAQ scores every year.	Moderate	Participation was voluntary and anonymous.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
				they improved for units that had a SAQ action plan (18.4% and 4.5%, respectively). Pronounced improvement in “job satisfaction” was observed for the units with an action plan (25.9%) versus those without an action plan (7.3%). Decreases in perceptions of “working conditions” were found for both groups.	increased by 4.8% for those without an action plan. Differences in CLASBI and VAP rates for the two groups were not statistically significant.			

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Paine et al., 2010[32]	Comprehensive Unit-based Safety Program (CUSP) was introduced to over 30 units.	Pre-post design; 144 units completed all seven subscales of the SAQ in 2006 (pre-assessment) as well as in 2007 and 2008.	Academic teaching hospital (i.e., Johns Hopkins Hospital) in Baltimore, Maryland.	Scores on the SAQ improved over time, with statistically significant improvements observed on all of the SAQ except "stress recognition" from 2006 to 2008. Scores on "stress recognition" remained at 45.36% and 45.84% across the years. Scores increased from 61.01% to 69.37% on the "safety climate" subscale and from 64.74% to 70.64% on the "teamwork climate" subscale.	Not provided	Units were given a goal to either maintain their "safety climate" and "teamwork climate" scores on the pre-SAQ (if it was 60% or higher) or to improve their score on the subscales by 10 points.	High	The article says that units initially volunteered to implement CUSP, and later units were encouraged to adopt CUSP if their safety culture scores were low. The authors further noted that the units varied in the degree that they fully implemented CUSP. Data are presented for 144 units, but the units that actually implemented CUSP are not identified. During the study period, approximately a dozen other quality improvement interventions were happening across the hospital. Not

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
								able to establish the amount of time between pre-SAQ, intervention, and post-SAQ.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Edwards et al., 2008[34]	Multiple interventions, including: safety rounds, self-reporting system enhancements, and the SBAR (Situation, Background, Assessment, and Recommen-dation) communication strategy.	Pre-post design. Clinical staff, including nurses, respiratory therapists, and other staff, were participants. Physicians did not participate. Participants were surveyed (using the 9 subscales from the HSOPS and 2 overall patient safety outcomes) prior to the interventions and again approximately 1 year later. Pre-intervention data were available for 394 staff and post-intervention data were available for 428 staff.	Two inpatient facilities of Children's Healthcare of Atlanta: one academic hospital (235 beds) and one community-based hospital (195 beds).	Statistically significant improvements were found on the following HSOPS subscales: "Non-punitive response to error" (3.09 vs. 3.24), "frequency of event reporting" (3.47 vs. 3.62), "feedback and communication regarding error" (3.42 vs. 3.59), "organizational learning" (3.77 vs. 3.88), "supervisor/manager expectations and actions" (3.60 vs. 3.85), and "teamwork within units" (3.98 vs. 4.14). Scores declined on one HSOPS subscale ("teamwork across units") and significantly declined on the other ("hospital handoffs and transitions") over time, although followup analyses indicated that results were pulled down by stagnant or declining scores from respondents from the academic hospital.	Not provided	The changes observed in HSOPS scores seem to align with the safety initiatives that were chosen. Together, these initiatives relayed the importance of (and commitment to) patient safety. Staff discussions revealed that the decline in "handoffs and transitions" may have been related to workflow changes related to the self-reporting system enhancements (e.g., workarounds that didn't work anymore), which made communication at shift changes and transfers more difficult. This also affected some of the teamwork between units at the academic hospital that participated in the study.	High	None

Table B.70: Cross-Cutting Patient Safety Topics/Practices, Safety Culture—Systematic Reviews and Meta-Analyses

Note: Full references are available in the Section 17.2 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Sacks et al., 2015[13]	Briefings/ debriefings, team-building exercises, educational campaigns, checklists, and bundled interventions.	Surgical settings, including labor and delivery and other surgical subspecialties.	Ten studies were evaluated as moderate quality and reported improvement in at least one dimension of safety culture measured, such as communication and job satisfaction. Thirty studies reported no improvement in one or more measures. Longer term positive effects on culture were reported in four studies (median followup was 9 months). Increased efficiency following safety culture interventions was reported by two moderate-quality studies. Finally, two moderate-quality studies measured patient outcomes, with both reporting a reduction in post-operative complications. Ten low-quality studies also provided evidence that safety culture initiatives were associated with better patient outcomes.	Studies varied widely in how interventions were implemented and measured. Multiple interventions were often bundled together (e.g., team building program such as MTT or TeamSTEPPS® combined with briefings or a checklist). The two primary obstacles to safety culture initiatives were participant resistance and regression toward baseline performance.	None
Weaver et al., 2013[12]	Team training, Executive WalkRounds, CUSP.	Hospital settings.	Sixteen of the 20 team training studies reported significant improvement in safety culture, five reported improvements in care processes, and seven reported improved patient safety outcomes. All eight studies of WalkRounds reported improvement in perceptions of safety culture, while three of the eight provided evidence of improved care processes or patient outcomes. Six of the eight CUSP studies showed improvement in perceptions of safety culture and two found improvement in care processes.	The best strategy for improving safety culture may be to include bundled interventions in which team training is accompanied by other tools that support communication and engagement, such as WalkRounds or briefings.	None

Table B.71: Cross-Cutting Patient Safety Topics/Practices, Clinical Decision Support—Single Studies

Note: Full references are available in the Section 17.3 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Abdel-Kader, et al. 2011[38]	CDSS and education intervention vs. education intervention alone to enhance referrals and quantitative proteinuria assessments in chronic kidney disease (CKD) patients. CDSS intervention consisted of two separate alerts within the ambulatory electronic medical record (EMR), EpicCare.	Small cluster RCT. Study duration: 10 months. Patient population: 58 in the control group, 60 in the intervention group. Fifteen GIM faculty were randomized into the CDSS intervention group. Primary outcome was the presence of an EMR order for a nephrology consultation or presence of nephrology encounter in EMR. Secondary outcomes were measures of quality of CKD care.	Large university-based outpatient general internal medicine practice	CKD was documented in the EMR in 37% of patients in intervention group and 21% in control. For this, ~39% of patients in the intervention arm had a proteinuria assessment vs. 30.1% in the control. Among patients without a proteinuria assessment at baseline, 16.3% in the control group had one at follow-up vs. 27.7% in the intervention group.	Ten percent of patients in the alert group were referred to a nephrologist vs. 17% in the control group.	The intervention did not increase renal referrals, but it may have improved proteinuria assessments in patients who lacked one at baseline.	Low/ moderate—small patient population	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Abramson, et al. 2013[10]	E-prescribing application within the EHR included CDS to aid with prescribing.	Retrospective study of 20 ambulatory care providers. Reviewed prescription data from 3 months and 1 year post EHR implementation.	Eight sites, parts of an FQHC	Rates of prescribing errors were low at 3 months and 1 year. Rates of errors between the two time periods were not significantly different.	Rule violations were high but not statistically different between 3 months and 1 year.	Low rates of errors after intervention suggest that e-prescribing in the ambulatory setting can improve prescribing safety.	Moderate—retrospective, small population	None
Ahuja et al., 2018[11]	Implemented CCDS tools to enhance medication and patient safety related to the direct oral anticoagulants (DOACs). Assessed the effectiveness of the CCDS by measuring adherence to the dosing strategy recommendation for each DOAC.	Retrospective study; 121 patients—30 patients received dabigatran, 61 apixaban, and 30 rivaroxaban.	Tertiary academic center, 725 beds	Achieved 80% adherence to dabigatran CCDS dosing recommendations, 75% for apixaban, and 87% for rivaroxaban.	There was minor bleeding in 11 patients and major bleeding in 4 patients. Bleeding events did not correlate with nonadherence to CDSS. Thirty-five orders were non-adherent—of these 49% were lower doses than recommended in CCDS.	Study demonstrates that implementing CCDS may ensure safe prescribing of high-risk medications. Difficult to ascertain the reason for nonadherence due to retrospective nature. Lower dose may have been selected to potentially mitigate a higher risk of individual bleeding.	Moderate—retrospective, small population	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Awdishu et al., 2016[12]	CDS tool contained in EHR to improve the appropriate prescribing of medications for patients with renal insufficiency. Intervention arm received CDS while control did not.	Prospective cluster RCT.	University health system. Study population: all physicians who cared for patients with impaired kidney function in outpatient or inpatient. Utilized Best Practice Alert functionality within EHR to design custom alerts for medications—prospective drug ordering and look-back alerts. Medication alerts in the control were not displayed to the physician.	Drug discontinuation or dosage adjustment occurred in 17% of the intervention vs. 5.7% in control. Drug dose adjustment alerts were acted on more frequently than alerts for contraindicated drugs. Prospective alerts were associated with higher proportion of appropriate medication adjustment than look-back alerts.	Appropriate medication adjustment occurred in <20% of cases in intervention group.	Found that alerts significantly increased appropriate modifications to prescriptions. Impact of alerts was greater for dose adjustment rather than discontinuation.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Bode et al., 2017[28]	Purpose was to improve the quality of care of at-risk patients through the addition of connected blood glucose (BG) meters and CDSS to improve workflow and thus provide more efficient titration of patient's insulin regimens remotely. Glytec CDSS is an FDA-cleared cloud-based clinical decision support tool utilized by a health care provider to assist with insulin dose titration.	Retrospective paired before and after design without a control group. Intervention was a system involving the addition of a cellular enabled BG meter and insulin dose titration guided by Glytec CDSS. Population: 46 patients with type 1 or type 2 diabetes.	Not provided	During treatment with CDSS, A1C decreased from a baseline average of 10.2% to 7.8% at 3 months, 7.8% at 6 months, 7.8% at 9 months, and 7.2% at 12 months.	Not provided	Use of CDSS was shown to effectively get patients to their glucose targets while also improving the efficiency and workflow of the care team to allow for remote insulin titration between office visits.	Moderate—no control	None
Boustani et al., 2012[34]	Interdisciplinary team used available guidelines and two recently published systematic evidence reviews to develop the content and the format of the electronically delivered CDSS.	RCT evaluating the efficacy of a screening program coupled with a CCDS in enhancing hospital care for elders with cognitive impairment (CI). Primary outcome: orders of Acute Care for Elders (ACE) consultation.	University-affiliated, public hospital, 340 beds; population: 998 patients. >65 years, hospitalized on medical ward, have CI	Physicians receiving CDSS issued more discontinuation orders of definite anticholinergics but was not statistically significant.	CDSS did not increase physicians' orders for ACE consults, physicians' discontinuation of Foley catheterization, or discontinuation of physical restraints. CDSS had no statistically significant impact on health outcomes (hospital stay, mortality, home discharge, etc.)	Findings show the CDSS did not significantly change physician prescribing behavior.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Burgess et al., 2016[27]	Evaluated the impact of using online care process model (CPM) clinical decision support tool vs. not during care of patients hospitalized for management of lower extremity cellulitis (LEC). AskMayoExpert (AME) is an online clinical support tool that contains clinical decision algorithms termed "care process models" (CPMs).	Pre/post-intervention study; 37 patients pre-intervention and 48 post-intervention. Primary aim was to compare the initial antibiotic regimen prescribed for patients in the pre-intervention phase vs. the post-intervention phase, and to perform a sensitivity analysis of all LEC admissions, comparing when the CPM was used vs. not.	Mayo Clinic Hospital, St. Mary's Campus	During pre-intervention phase, CPM was used in 14% of LEC admissions. In post phase CPM utilization increased to 50%. During the 14 months, a total of 85 LEC admissions were analyzed, and the CPM was utilized during 29 of them. The appropriate antibiotic was prescribed by Hospital Day 2 in 62% of admissions when the CPM was utilized as compared to 21% when it was not used.	Significant difference in need for broadening coverage of antibiotics between CPM users and non-users. Antibiotics were broadened in 14% of the CPM group vs. 2% of the non-CPM group.	Results showed that when CPM was utilized it was associated with increased prescribing of the recommended antibiotic regimen.	Low/ moderate—small population	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Chaparro et al., 2017[14]	Pediatric Leapfrog CPOE evaluation tool uses simulated patients with associated test orders to evaluate a CPOE's ability to alert providers to potentially harmful medication errors. Tool evaluates CDS and provides a onetime cross-sectional assessment of whether appropriate decision support is being provided.	Evaluated 41 institutions over 2 years. Longitudinal analysis of test performance was carried out.	Hospitals—majority were free-standing pediatric institutions	CPOE systems that underwent testing performed significantly better in the basic decision support grouping than in the advanced grouping. Linear regression between basic and advanced decision support scores showed a moderate positive relationship. Found that pediatric CPOE systems intercepted ~2/3 of medication errors using the Leapfrog evaluation tool.	Not provided	Found that pediatric CPOE systems showed significant improvement in test scores of 4%/year with repeated testing using the Leapfrog tool, suggesting that repeated evaluations of CPOE/CDS systems may lead to improved ability to intercept potential medication errors.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Felcher et al., 2017[40]	Implemented three CDS tools in the EHR of a large health plan: (1) a new vitamin D screening guideline, (2) an alert that requires clinician acknowledgment of current guidelines to continue ordering the test, and (3) a modification of laboratory ordering preference lists that eliminates shortcuts.	Retrospective, descriptive analysis of an internal QI initiative. Compared the rate of vitamin D screening among adult health plan members in the 6 months prior to implementation of CDS tools to the rate 6 months following this intervention using a repeated cross-sectional design.	Large integrated group model health care delivery system	Vitamin D screening rates decreased from 74.0 tests per 1,000 members in the pre-implementation period to 24.2 tests per 1,000 members in the post-implementation period. Rates of appropriate vitamin D screening increased significantly. Cost of unnecessary testing significantly decreased (estimated annual cost saving for the system of $1.4M).	Not provided	Implementation of CDS tool was associated with significantly reduced overall rates of vitamin D screening and a significant increase in the proportion of ordered vitamin D screening tests that were clinically appropriate.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Field et al., 2009[13]	CDSS providing specific dose recommendations for long-term care residents with renal insufficiency. CDSS built on commercially purchased CPOE system. Developed four types of alerts.	RCT. The 22 long-stay units were randomly assigned for prescribing physicians to either receive or not receive the alerts.	Academically affiliated long-term care facility in Canada; resident care unit	Rates of alerts were nearly equal in intervention and control units. Proportions of final drug orders for which doses were appropriate were similar between the intervention and control units. Across all categories of alerts, drug orders in the intervention units were appropriate significantly more often than in control units.	Not provided	CDS system did not improve rate at which physicians order appropriate doses but did produce a substantial improvement in prescribing.	Low	International—Canada
Fitzgerald et al., 2011[41]	Real-time, computer-prompted, evidence-based decision and action algorithms (computer-assisted decision support).	Randomized controlled interventional study: 1,171 patients (3 groups); severely injured adults.	Level 1 adult trauma center	Error-free resuscitations were increased with the intervention. Morbidity from shock management, blood use, and aspiration pneumonia were decreased. Protocol compliance was improved. and errors and morbidity were reduced.	Not provided	Not provided	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Flanders et al., 2009[29]	CDS tool (CDT) for intravenous insulin dosing: the CDT allows for automated and standardized calculation of IV insulin drip rates.	Comparison of performance of the glucose control initiative as either a paper protocol or a computer based tool. Prospective cohort study. Piloted CDT in 1 ICU and then implemented across all.	ICUs at Methodist Hospital and Indiana University Hospital from 2004-2007	Percentage of blood glucose measures under the GCI upper limit increased from 68.33% at baseline to 79.53% in 2005 and 83.09% in 2007, indicating a reduction in hyperglycemia.	Initially, incidence of hypoglycemia increased slightly. Conducted a QI program root cause analysis to determine causes and made adjustments.	Following the successful pilot of the CDT, little resistance was encountered when it was expanded to other units.	Low	None
Genco et al., 2016[30]	Secondary objective of study was to determine whether CDSS alerts are successful at preventing opioid-related ADEs.	Retrospective chart review; 4,581 eligible ED visits were studied.	Urban academic medical center ED	None of the adverse drug events experienced by patients in this study were considered preventable by clinical decision support.	Providers sorted through 4,692 alerts to avert 38 potential adverse drug events—high sensitivity=low specificity.	None of the ADEs experienced by patients in this study were preventable by the CDSS. However, 46 alerts were accepted for 38 patients that averted a potential ADE.	Moderate—retrospective	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Gill et al., 2011[17]	her-based CDS coupled with clinician education about national guidelines for GI risk reduction for patients on NSAIDs. Two-part form automatically activated when EHR office note was started for these patients: (1) alert indicating patient was on NSAID and was high risk, and (2) tools to prescribe a gastro-protective medication, discontinue NSAID, or change it to one with less GI risk.	RCT. Intervention group received: full intervention packet, including the EHR-based CDS form, training regarding this form, the educational module, and the newsletter. Control did not receive any intervention. Study population: intervention 2,222 patients, control 3,012 patients.	National network of primary care offices (27 offices/ 14 States)	For at-risk patients, 25.4% in the intervention and 22.4% in the control were provided guideline-concordant care during the study year.	After the study, only 42% of intervention clinicians said they would provide care according to American College of Gastroenterology guidelines for patients on low-dose aspirin and 58% for elderly patients with no other risk factors. Only 23% said they were likely to continue using the form after the study. A reported 44% found the form disruptive on office work flow.	Findings showed her-based CDS with clinician education had a small but statistically significant positive impact on guideline-concordant care. Small but statistically significant impact on the individual component of prescribing a new gastro-protective medication, but not the component of discontinuing the traditional NSAID.	Low	None
Harinstein et al., 2012[32]	Goal was to determine performance of active medication monitoring system for drug-induced thrombocytopenia using a commercially available CDSS. Drug-laboratory result alert contained CDSS.	Population: 64 adult patients.	MICU and CICU at a university affiliated medical center	Not provided	CDSS did not interface with electronic medication administration record contained within the her, which caused an increase in the number of false positive alerts.	Found the alert to have more favorable performance characteristics when compared with other prior alerts.	Moderate—no control	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Kharbanda et al., 2016[42]	Developed, implemented. and evaluated the safety and effectiveness of an EHR-linked CDS tool for patients with suspected appendicitis. Goal was to reduce computed tomography (CT) use. CDS tool included a (1) standardized abdominal pain order-set, (2) web-based risk stratification tool, and (3) "time of ordering alert."	Quasi-experimental study. Population: children 3-18 years; intervention cohort=2,803.	Large pediatric hospital system, pediatric EDs	During the implementation period, CT use declined each month by 2.5%, resulting in a 54% relative decrease in CT use from the pre-implementation period to the end of the study. No significant change in ultrasound trend from pre- to post-implementation. Found no significant differences in the rates of negative appendectomies or missed appendicitis.	Not provided	Findings indicate that key elements for successful implementation include: (1) creating a collaborative guideline committee to ensure widespread acceptance; (2) obtaining support of leadership, especially in IT; and (3) integrating the CPG into the clinical workflow.	Low/ moderate—quasi-experimental	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Lavin and Ranta, 2014[43]	Transient ischemic attack (TIA)/Stroke Electronic Decision Support tool designed to improve diagnostic accuracy of GPs, limit ED referrals to high-risk patients, and prompt GPs to initiate secondary prevention immediately if specialist review is anticipated to be delayed by more than 24 hours.	Safety Audit: monitoring for major morbidity and mortality potentially attributable to TIA/Stroke EDS use after its launch.	Not provided	Seventy-nine patients managed with the aid of EDS, resulting in eight appropriate immediate hospital admissions because of patients being at high risk of stroke. Three patients had delayed admission, but care was fully guideline based, and patients had no adverse outcomes.	Two deaths occurred but not as a result from inappropriate EDS advice.	Study aimed to assess the safety of EDS tool in clinical practice and found no evidence to indicate any serious associated risk. No evidence to indicate serious preventable harm due to misdiagnosis, inappropriate triage, or over/under medication prompted by the EDS.	Moderate—safety audit	International—New Zealand

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Lilih et al., 2017[31]	Implemented a CDSS for gastrointestinal prophylaxis based on the Dutch guideline for gastrointestinal prophylaxis.	Pre/post intervention study. Objective was to determine whether CDSS resulted in improved compliance with the Dutch guideline for gastrointestinal prophylaxis.	Dutch hospital, inpatient and outpatient	Before implementation, 84.0% of prescriptions for gastrointestinal prophylaxis were co-prescribed during or within 1 hour after the order. After implementation this increased to 94.5%. Before implementation, 11.2% of drug safety alerts were correct according to guidelines; after implementation, 100% were correct. Before implementation, 4.4% of the correct drug safety alerts resulted in the addition of gastrointestinal prophylaxis within one hour after ordering the medication, while in the post-implementation period, 44.7% of the clinical rule pop-ups resulted in the addition of gastrointestinal prophylaxis.	Not provided	Results show that the CDSS is capable of improving patient safety.	Low	International—Netherlands

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Milani et al., 2011[36]	Evaluate whether CPOE with enabled decision support (CPOE-DS) is feasible in the acute coronary syndrome setting. On admission the admitting physician had the choice of using pre-printed paper orders with check boxes that followed the AHA/ACC guideline recommendations or CPOE-DS software that generated a paper order set.	Recorded clinical characteristics, hospital length of stay, and 30-day, 90-day, and 1-year mortality in 1,321 ACS patients. Used logistic regression analysis.	Ochsner Foundation Hospital cardiac service	Attainment of "perfect" care (every quality measure successfully completed) occurred in 89% of CPOE-DS patients vs. 61% of patients admitted with standard order sets.	Not provided	Findings show that use of CPOE with decision support is feasible in the ACS process of care and increases the likelihood of achieving perfect care.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Mishuris et al., 2014[45]	Categorized practices into three groups: all CDS tools active, without one or more CDS functions, and any disabled CDS.	Retrospective, cross-sectional analysis that used logistic regression to determine whether CDS is associated with improved quality indicators. Used data from the National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS) outpatient department records.	Ambulatory clinic visits	Rates of visits for new problems and follow-up of chronic problems were less common at clinics without at least one of the CDS functions vs. clinics with all the CDS functions. Visits for preventive care were more common at clinics without at least one of the CDS functions.	Not provided	Found significant associations between the use of CDS and some (but not all) clinical quality measures before the enactment of meaningful use.	Low/ moderate	None
Olsho et al., 2014[46]	On-Time Quality Improvement for Long-Term Care: CDS intervention for pressure ulcers that uses risk reports embedded in HIT systems to identify recent changes in risks and guided facilitation to support integration of these reports into practices.	Interrupted time series design. Intervention group: 12 nursing homes; analyzed data from 13 nursing homes that did not implement On-Time.	Nursing homes	Found large and statistically significant reductions in pressure ulcer incidence associated with implementation of core On-Time components. Results imply approximately 2.6 pressure ulcers avoided per 100 residents per month.	Use of the optional behavioral report was associated with a large and statistically significant increase in pressure ulcer incidence.	Results imply a cost savings of $250,000 per year.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Prewitt et al., 2013[15]	Examination of whether there is a difference in ADE rates after simultaneous implementation of clinical decision support via CPOE and smart pump patient controlled analgesia (PCA).	Retrospective review of ADEs found by VRS and ADEs pre- and post-implementation.	Large tertiary and quaternary care hospital	Identified decrease in the risk of PCA events but was not statistically significant. Difference in pre- and post-implementation causality of five or greater for ADEs, indicating the event correlates with the drug; however, there was no difference in severity of three or greater, indicating no change in patient harm. VRS data showed obesity and weight were statistically significant with fewer events post.	Not provided	Results support the recommendation of CDS via CPOE and PCA smart pump technology.	Moderate—retrospective	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Ranta et al., 2014[44]	Transient ischemic attack (TIA)/Stroke Electronic Decision Support tool is designed to improve diagnostic accuracy of GPs, limit ED referrals to high-risk patients, and prompt GPs to initiate secondary prevention. Aim of this study was to assess if the implementation of a TIA/Stroke EDS (following safety audit) would be associated with a reduction of avoidable TIA management delays without incurring additional patient risk.	Prospectively identified all patients referred with a diagnosis of TIA. Compared data prior to EDS launch (2009) with 2 years after (2011).	Outpatient TIA clinic or inpatient stroke service	Best medical therapy was achieved by 43% of patients in 2009 and 57% in 2011. Behavioral counseling was provided to 40% of patients in 2009 and 66% in 2011. Time from first point of contact to stroke specialist review was significantly shorter in 2011. No instances of medication-related adverse events or treatment delays due to EDS misdiagnosis or inappropriate triage advice.	Not provided	Results suggest that tool was associated with significant improvement in the rate of initiating the best medical TIA therapy.	Moderate—non-randomized observational	Same intervention tool as Lavin and Ranta article; International—New Zealand
Schnipper et al., 2010[39]	Smart Forms for coronary artery disease (CAD) and diabetes mellitus (DM) enable writing a multi-problem visit note while capturing coded information and providing decision support.	Controlled trial randomized by physician.	Ten adult primary care clinics associated with Partners HealthCare	Patients of PCPs assigned to the intervention arm were more likely to have deficiencies in care addressed in the month following the index visit.	Overall use of Smart Forms was low. PCPs assigned to intervention arm used Smart Form for 5.6% of eligible patients. Use was higher for patients with DM (7.4%) than for patients with CAD (3.5%).	Documentation-based CDS led to a statistically significant, but clinically small, improvement in the care of patients with CAD/DM in primary care. Low use is likely related to usability, since Smart Forms require PCPs to actively change the way they document visits.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Stevens et al., 2017[16]	EQUiPPED: multicomponent QI initiative combining education, electronic CDS, and individual provider feedback to influence prescribing and improve medication safety for older adults. Evaluating the effectiveness of EQUiPPED to reduce use of potentially inappropriate medications (PIMs).	Pre/post-intervention evaluation. Sites employed a PDSA cycle to test change as components were implemented. Based on site-specific findings, EQUiPPED elements were adapted for site-specific needs.	Four VA medical center EDs	Rate of PIMs prescribing at baseline varied from 7.4% to 11.9%. After implementation, sites achieved a monthly PIM of between 4.5% and 6.1%. Adaptation occurred based on results of the PDSA cycle. The most prominent adaptation included site-specific strategies for releasing the EHR-based clinical decision support.	Not provided	EQUiPPED intervention positively influenced provider prescribing behavior and resulted in sustained safer prescribing for older adults discharged from the ED across multiple VA sites.	Low	Bundle not designed to assess impact of individual components.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Umscheid et al., 2012[23]	Examined effect of integrating a CDS intervention that does not involve pop-ups on VTE prophylaxis and event rates.	Retrospective study; population: 223,062 inpatients.	Quaternary care academic health system (3 hospitals)	In the unadjusted analyses, "recommended" prophylaxis significantly increased across the three study periods across all hospitals and services. Adjusted estimates suggest the intervention increased the use of "recommended" and "any" prophylaxis at all three hospitals when comparing the baseline time period 1 with time period 2.	Adjusted estimates suggest that the CDS intervention did not significantly increase the use of "pharmacologic" prophylaxis. VTE event rates increased across the study population; however, sub-analysis using only admissions with appropriate POA documentation suggested no change in VTE rates.	Analysis demonstrated significant increases in VTE prophylaxis that were associated with a CDS intervention.	Low/ moderate	None

Table B.72: Cross-Cutting Patient Safety Topics/Practices, Cultural Competency—Single Studies

Note: Full references are available in the Section 17.4 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Bailey et al., 2012[19]	Rx bottles with ConcordantRx (language concordant) instructions.	Randomized, experimental evaluation; 202 LEP adults who spoke five non-English languages (Chinese, Korean, Russian, Spanish, Vietnamese), recruited from nine clinics and community organizations.	Nine clinics and community organizations in San Francisco and Chicago.	Subjects receiving the ConcordantRx instructions demonstrated significantly greater Rx understanding, regimen dosing, and regimen consolidation compared with those receiving standard instructions (incidence rate ratio [IRR]: 1.25; 95% confidence interval [CI], 1.06 to 1.48; p=0.007 for Rx understanding, IRR: 1.19; 95% CI, 1.03 to 1.39; p=0.02 for regimen dosing, and IRR: 0.76; 95% CI, 0.64 to 0.90; p=0.001 for regimen consolidation). In most cases, instruction type was the sole independent predictor of outcomes in multivariate models controlling for relevant covariates.	At time of article, California was the first and only State to mandate that pharmacies use a standardized, patient-centered prescription label, through a bill passed in October 2007. The California Patient Medication Safety Act enlisted the California Board of Pharmacy to create a set of requirements for the design and content of Rx labels. The purpose of this bill, implemented in 2011, was to improve comprehension of Rx instructions by ensuring that the information provided is grounded in evidence from health literacy research. Language concordance was not included as a requirement. Regardless, the ConcordantRx instructions comply with the recommendations set forth in this bill in terms of patient-centered labeling and can be used to fulfill California's labeling requirements for the LEP community.	Moderate; convenience sample; qualitative	Process measure

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Cardarelli et al., 2018[53]	Use of lay health workers for post-discharge follow-up calls for high-need patients. Discharge plans were developed from patients' self-identified needs. The care plan and LHW's contact information was provided to the patient upon discharge. The LHW conducted a follow-up call 24–48 h after discharge to review any issues during the interim post-discharge period, assess patient follow-through in engaging with identified community resources and review plans for appropriate follow-up visits.	Pre-post study design. Baseline period of 4 months in which high-need patients did not receive the LHW follow-up calls, compared to 6-month intervention period. Hospitalized patients (males and females over 18 years old of any racial/ethnic group and admitting diagnosis) at high risk of a 30-day readmission to the hospital participated in study. There were 46 patients in the baseline phase and 61 in the intervention phase. Almost all participants were Caucasian, reflecting the predominant population found in Appalachia Kentucky; also, most participants had only a high school education or less (70%) and over 55% had either Medicare or Medicaid as their primary insurance.	A hospital in in Morehead, KY, in Northeast Appalachia Kentucky	Thirty-day readmission rates decreased from 28.3 to 14.8% (p = 0.09) between the baseline and intervention phases. When adjusted for education, transportation cost, and a positive anxiety screen, the odds of being readmitted within 30 days further decreased to 77% (OR 0.33; 90% CI 0.14–0.81; p =0.04) among those exposed to the LHW program. In addition, those with transportation cost barriers were over three times more likely to be readmitted within 30-days.	The authors assert that LHWs help transition patients from the hospital to their home by assuring that patients sustain healthy behaviors and access needed services. Because they serve the community in which they live, they often share a similar socioeconomic status and are able to relate to the psychosocial and economic stressors met by their clients. Communicating with the hospitalized patient about social needs and ways to address these needs not only gives patients the tools to improve their situation; it may also instill a sense of empowerment. When considering implementing LHWs in care transition programs, it is important to consider patient population to target (i.e. risk stratification) and the effort level at which a LHW should be employed. The studied model may be an cost-effective alternative for resource-limited rural and community hospitals.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Flores et al., 2012[56]	Professional interpreters for translation accuracy (compared with ad hoc or no interpreter).	A cross-sectional error analysis of audiotaped emergency department (ED) visits over 30 months; 57 encounters included 20 with professional interpreters, 27 with ad hoc interpreters, and 10 with no interpreters.	Two of the largest pediatric EDs in MA	The analysis found 1,884 interpreter errors, of which 18% had potential clinical consequences. The proportion of errors of potential consequence was significantly lower for professional (12%) versus ad hoc (22%) versus no interpreters (20%) ($p<0.01$). The median errors by professional interpreters with 100 or more hours of training were significantly lower, at 12, versus 33 for those with fewer than 100 hours of training.	Focus on meaning rather than word-for-word translation. Errors of potential clinical consequence were significantly more common with ad hoc interpreters and no interpreters than with professional hospital interpreters. Hours of training, not experience, were associated with greater accuracy for professional interpreters. One hundred or more hours of training might have major impact on reducing errors.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Karliner et al., 2017[51]	Increasing access to professional interpreters by providing a dual-handset telephone with a direct connection to interpreter services at each hospital bedside that would facilitate use by all clinical providers. These 66 telephones had a programmed button that allowed 24-hour access to a professional (trained and tested) medical interpreter for more than 100 languages.	Observational, natural experiment. Of 8,077 discharges, 1,963 were for limited English proficient (LEP) and 6,114 for English-proficient (EP) patients. Discharges occurred over 3 years. This time-frame begins 18 months prior to the intervention, includes the 8-month intervention period, and continues for 10 months after the intervention.	A medicine floor of an academic medical center consisting of two separate nursing units; one a step-down unit for higher acuity patients and the other for patients with less intensive nursing needs.	There was a significant decrease in observed 30-day readmission rates for the LEP group during the 8-month intervention period compared with 18 months pre-intervention (17.8% vs. 13.4%). At the same time, EP readmission rates increased (16.7% vs. 19.7%). Readmission results remained significant in adjusted analyses (pre-intervention OR=1.07; 95% CI, 0.85 to 1.35; intervention CI, 0.64; 95% CI, 0.43 to 0.95). There was no significant intervention impact on length of stay (LOS) in either unadjusted or adjusted analyses. After accounting for interpreter services costs, the estimated 119 readmissions averted during the intervention period were associated with estimated monthly hospital expenditure savings of $161,404.	Prior to the intervention, usual-care communication included in-person staff interpreters who could be scheduled during usual business hours, and a slowly increasing number of dual-handset interpreter telephones (ranging from 0 to 5 during the pre-intervention period). It took additional time to locate interpreters and bring them to the patient's room, and often they were in use elsewhere. Having a telephone in every patient room, immediately available to clinicians at any time, was a key component to the success of the intervention.	Low	Twenty-five million people in the United States have limited English proficiency (LEP); this growing and aging population experiences worse outcomes when hospitalized. Federal requirements that hospitals provide language access services are very challenging to implement in the fast-paced, 24-hour hospital environment.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Lee et al., 2017[55]	Bedside interpreter phone system at every bedside, enabling 24-hour immediate access to professional interpreters.	Prospective, pre-post intervention implementation study using propensity analysis. Hospitalized patients undergoing invasive procedures on three hospital floors. Chinese- and Spanish-speaking patients with LEP (84 pre and 68 post implementation) and 86 English speakers.	Cardio-vascular, general surgery or orthopedic surgery floors of a hospital.	Post-implementation (vs. pre-implementation) patients with LEP were more likely to meet criteria for adequate informed consent (54% vs. 29%, p=0.001) and, after propensity score adjustment, had significantly higher odds of adequate informed consent (AOR 2.56; 95% CI, 1.15 to 5.72) as well as of each consent element individually. However, compared with post-implementation English speakers, post-implementation patients with LEP had significantly lower adjusted odds of adequately informed consent (AOR, 0.38; 95% CI, 0.16 to 0.91).	Prior to implementation, Interpreter Services staff met with all hospital nurse managers to plan the implementation and communication with nursing staff. Nurse managers educated nurses. Additionally, the physician champion contacted all clinical Chiefs of Service about the phones, who in turn communicated by email with their attending and resident physicians. An article describing the phones was posted in the internal Graduate Medical Education online newsletter. No other system interventions occurred. Despite the observed improvements after interpreter phone implementation, post-implementation patients with LEP still had lower odds of informed consent than English-speakers, even when adjusting for health literacy.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Lindholm, et al., 2012[50]	Professional interpretation at patient admission or discharge.	This study is a retrospective analysis of length of stay and 30-day readmission rates among patients who were admitted to a tertiary care, university hospital. The study population includes 3,071 admissions with an LOS between 1 and 85 days. Multivariable regression models explored differences among patients who had received interpretation at admission, discharge, or both, controlling for patient characteristics, including age, illness severity, language, and gender.	A tertiary care, university hospital; size not provided.	Of the 3,071 patients included in the study, 39% received language interpretation on both admission and discharge date. Patients who did not receive professional interpretation at admission or both admission and discharge had an increase in their LOS of between 0.75 and 1.47 days, compared with patients who had had an interpreter on both day of admission and discharge ($p<0.02$). Patients receiving interpretation at admission and/or discharge were less likely than patients receiving no interpretation to be readmitted within 30 days.	In this study, the length of a hospital stay for LEP patients was significantly longer when professional interpreters were not used at admission or both admission and discharge. As a measure of severity of illness, the researchers used the hospital's diagnoses cost weight that accounts for differences in patients' illness burden. The researchers felt that interpretation at admission was especially important, as it has the greatest impact on LOS. This intuitively makes sense, since a patient's history accounts for approximately 70% of the necessary information to formulate a correct diagnosis.	Moderate—no comparison group, some patient characteristics not included, single site	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Sudore et al., 2018[54]	To mitigate literacy, cultural, and language barriers to advance care planning, easy-to-read advance directives and a patient-directed, online advance care planning program called PREPARE For Your Care (PREPARE) were created in English and Spanish.	A comparative efficacy randomized clinical trial was conducted from February 1, 2014, to November 30, 2017, among 986 English-speaking or Spanish-speaking primary care patients 55 years or older with two or more chronic or serious illnesses.	Four San Francisco, safety-net, primary-care clinics.	No participant characteristics differed between the two comparison groups, and retention was 85.9% (832 of 969) among survivors. Compared with the advance directive alone, PREPARE resulted in a higher rate of advance care planning documentation (unadjusted, 43.0% [207 of 481] vs. 33.1% [167 of 505]; p<0.001; adjusted, 43.0% vs. 32.0%; p<0.001) and higher self-reported advance care planning engagement scores (98.1% vs. 89.5%; p<0.001). Results remained significant among English speakers and Spanish speakers.	The patient-facing PREPARE program was easy-to-read and did not require clinician/system-level interventions to assist the patient. Materials were written at a fifth-grade reading level. Advance care planning (ACP) improves value-aligned care, yet, it remains suboptimal among diverse patient populations. Was successful among both English- and Spanish-speaking older adults.	Low to moderate	Among the 986 participants (603 women and 383 men), the mean (SD) age was 63.3 (6.4) years; 387 of 975 (39.7%) had limited health literacy, and 445 (45.1%) were Spanish speaking.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Woerner et al., 2009[52]	Delivery of home nursing care using a culturally congruent approach. Hired Hispanic nurses and teachers, added a Spanish language phone line. Allowed nurses to give personal phone numbers to patients; surveyed the patient population about their educational needs and the most appropriate methods for providing healthcare information. Creation of a patient education series in telenovela format. Education on healthy food using culturally appropriate food. Identified non-Hispanic learner needs.	A retrospective analysis of pre-intervention (March 2006 to March 2007)/post-intervention (April 2007 to April 2008) data was done to determine whether or not care delivery outcomes improved for Hispanic patients following introduction of the ¡EXITO! model. Outcome and Assessment Information Set (OASIS) data from 125 unduplicated home care patients were tracked. Nursing care delivery was analyzed using ethnographic research techniques.	Home nursing care for 125 patients.	Acute hospitalization for Hispanic patients/all patients pre-intervention was 43%/30%; post-intervention, it was 24%/17%. Emergency department rate pre-intervention was 23%/24%; post-intervention, it was 21%/26%. Oral medication adherence pre-intervention was 22%/42%; post-intervention, it was 28%/42%. Response rates for satisfaction surveys were low, ranging from 2% to 32% per quarter. For all but one quarter, satisfaction rates were above the targeted 96% rate. Followup analysis found numerous discrepancies between which meds the patient was taking and what the physician and pharmacy thought the patient was taking.	Theory-based intervention for culturally congruent care: theory of transcultural nursing, as explicated in Leininger's Sunrise Enabler model. Prior to implementation, a survey was conducted to identify the learning needs of non-Hispanic nurses. Language is critical but not sufficient to reduce Hispanic population healthcare disparities to the levels of the general population. For project ¡EXITO!, language and access concerns were not the key barriers to the achievement of targeted home care delivery outcomes. Both translators and Spanish-speaking providers were used during the delivery of services, and all patients had some form of third-party payment, most commonly Medicare and Medicaid. Attention to cultural concerns and designing programs that incorporate strategies responsive to culturally based preferences and beliefs can have a positive impact on home care patients.	Low to moderate; p-values not provided.	None

Table B.73: Cross-Cutting Patient Safety Topics/Practices, Cultural Competency—Systematic Reviews

Note: Full references are available in the Section 17.4 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Forsetlund et al., 2011[48]	Interventions to improve healthcare services for ethnic minorities.	Healthcare for ethnic minority populations.	Eight studies examined the effect of educational interventions in improving outcomes within cross-cultural communication, smoking cessation, asthma care, cancer screening, and mental healthcare. Most patients were African-Americans and Latin Americans, and all ages were represented. The review concluded that different forms of education, either alone or as part of a more complex intervention, may have a small to moderate but context-dependent effect on improvement of health personnel practices, as well as a smaller effect on patient outcomes across patient populations. Five of the six studies that examined computerized reminders, either alone or as part of a complex intervention, showed statistically significant positive effects for the selected outcomes. Unable to decide whether follow-up and support in terms of personnel resources may affect patient outcomes. Two randomized controlled trials examined the effect of using simultaneous translation via remote consecutive medical interpreting. Two randomized controlled trials examined the effect of matching clients and therapist.	Educational interventions and electronic reminders to physicians may in some contexts improve healthcare and health outcomes for minority patients. The quality of the evidence varied from low to very low. The quality of available evidence for the other interventions was too low to draw reliable conclusions. Researchers found no studies that included only young patients, suggesting that interventions targeting health personnel or health organizations may be applicable regardless of the age of the patient population. This review reveals that the evidence for interventions to improve healthcare for minorities is sparse and generally of low quality.	None

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Horvat et al., 2014[49]	Cultural competency education for health professionals.	Patients from minority culturally and linguistically diverse (CALD) backgrounds.	Searched multiple databases up to 2014. To assess efficacy, the researchers developed a four-dimensional conceptual framework comprising educational content, pedagogical approach, structure of the intervention, and participant characteristics to provide consistency in describing and assessing interventions. Included five RCTs involving 337 healthcare professionals and 8,400 patients; at least 3,463 (41%) were from CALD backgrounds. Health behavior (client concordance with attendance) improved significantly among intervention participants compared with controls (relative risk [RR] 1.53, 95% CI, 1.03 to 2.27, 1 study, United States, ESS 28 women, low quality). Involvement in care by "non-Western" patients (described as "mainly Turkish, Moroccan, Cape Verdean and Surinamese patients") with largely "Western" doctors improved in terms of mutual understanding (SMD 0.21, 95% CI, 0.00 to 0.42, 1 study, the Netherlands, 109 patients, low quality). Evaluations of care were mixed (3 studies). Further research is required to establish greater methodological rigor and uniformity on core components of education interventions, including how they are described and evaluated.	There was positive, low-quality evidence showing improvements in the involvement of CALD patients. Findings either showed support for the educational interventions or no evidence of effect. No studies assessed adverse outcomes. The quality of evidence is insufficient to draw generalizable conclusions, largely due to heterogeneity of the interventions in content, scope, design, duration, implementation, and outcomes selected.	None

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Lie et al., 2011[16]	Cultural competency training for healthcare professionals.	Healthcare, general.	Search of databases for articles in English published between January 1990 and March 2010. Seven studies met inclusion criteria. Three involved physicians, two involved mental health professionals, and two involved multiple health professionals and students. Two were quasi-randomized, two were cluster randomized, and three were pre/post field studies. Study quality was low to moderate, with none of high quality; most studies did not adequately control for potentially confounding variables. Effect size ranged from no effect to moderately beneficial (unable to assess in 2 studies). Clinical endpoints were at least one of the outcomes of interest in three studies. Three studies reported positive (beneficial) effects; none demonstrated a negative (harmful) effect. The studies, albeit of limited quality, reveal a trend in the direction of a positive impact on patient outcomes. However, overall, the current evidence appears to be neither robust nor consistent enough to derive clear guidelines for CC training to generate the greatest patient impact.	Some research shows a positive relationship between cultural competency training and improved patient outcomes, but there remains a paucity of high-quality research. Future work should address challenges limiting quality. The authors propose an algorithm to guide educators in designing and evaluating curriculums to rigorously demonstrate the impact on patient outcomes and health disparities. It is possible that cultural competency training as a standalone strategy is inadequate to improve patient outcomes, and that concurrent systemic and systems changes, such as those directed at reducing errors or improving practice efficiency, and the inclusion of interpreters and community health promoters as part of the healthcare team, are needed to optimize its impact.	None

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings	Notes
Truong et al., 2014[2]	Cultural competency in healthcare.	Healthcare settings, general.	As cultural competency did not achieve popularity until the late 1990s, and government policies mandating cultural competency did not appear until the early 2000s, a search timeframe of 2000 to 2012 was chosen. Nineteen published reviews were identified. Reviews addressed between 5 and 38 studies, and included a variety of healthcare settings/contexts and a range of study types. There were three main categories of study outcomes: patient-related outcomes, provider-related outcomes, and health service access and utilization outcomes. The majority of reviews found moderate evidence of improvement in provider outcomes and healthcare access and utilization outcomes, but weaker evidence for improvements in patient/client outcomes. Overall, positive effects were reported by most reviews, particularly in relation to provider outcomes. Reviews that compared different types of interventions found that the use of culturally trained health workers was the most effective. However, rather than being comparable, many of the primary studies in these reviews were a mixture of study designs focused on various interventions. Four of five reviews that included studies related to health service outcomes found some evidence of improvement. Seven of the nine reviews that examined patient/client-related outcomes generally found evidence of some improvement in health outcomes. A variety of patient/client outcomes were reported, including physiological outcomes such as blood glucose, weight, and blood pressure, as well as outcomes such as patient satisfaction and trust, knowledge of cancer screening, and knowledge of health conditions. Behavioral outcomes such as dietary and exercise behaviors were examined in three reviews.	There is some evidence that interventions to improve cultural competency can improve patient/client health outcomes. However, a lack of methodological rigor is common among the studies included in reviews, and many of the studies rely on self-report, which is subject to a range of biases, while objective evidence of intervention effectiveness was rare. Future research should measure both healthcare provider and patient/client health outcomes, consider organizational factors, and use more rigorous study designs. Cross-cultural interactions are likely structured and shaped by the worldviews and past experiences of not only the staff and clients but also the culture of the organization, which is embedded in and produced by policy frameworks, organizational arrangements, and physical settings of the organization. Interventions to improve cultural competency need to consider the individual and organizational contexts and the interplay between them.	This article is a review of systematic reviews.

Table B.74: Cross-Cutting Patient Safety Topics/Practices, Monitoring, Audit, and Feedback—Single Studies

Note: Full references are located in the Section 17.5 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Boet et al., 2018[4]	Audit and feedback	Prospective, randomized controlled trial (RCT). Baseline: control: n=1,384; benchmarked n=1,466; ranked n=1,222. Intervention: control n=1,225; benchmarked n=1,428; ranked n=1,121. Patients undergoing surgery >60 minutes and not on cardiac bypass.	Large health science center serving 26,000 patients annually in Ottawa, Canada	Using benchmarked or ranked feedback was no more effective than no feedback in influencing anesthesiologists' performance related to patient temperature outcome in the clinical setting.	Not provided	Not provided	Low	None
Byrnes et al., 2010[21]	Monitoring and feedback	Quality improvement pre-post intervention design; average annual number of patients n=1,206; patients referred to American College of Surgeons (ACS)-verified level I trauma center	Nine hospitals; average licensed bed count was 45, average number of staffed beds was 39	Among patients with an Injury Severity Score (ISS) of <15, the incidence of a good outcome or mild disability was 93% after the intervention compared with 84% before the intervention (p=0.07). Among patients with an ISS ≥15, the incidence of outcomes was nearly identical between the groups.	Not provided	Not provided	High	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Coleman et al., 2013[8]	Multicomponent intervention including clinical dashboard	Retrospective time series analysis; n=1,200; prescription data extracted from PICS	NHS Foundation Trust	Omission rates were reduced from 10.3 to 4.4% for antibiotics (57% reduction) and from 16.4 to 8.2% for non-antibiotics (50%). The reporting of overdue doses on clinical dashboards resulted in a step-change reduction in missed antibiotic doses of 0.60 (95% CI, 0.26 to 0.95) percentage points (p=0.001).	Not provided	Not provided	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Colquhoun et al., 2017[1]	Audit and feedback	Systematic review; n=140 studies; RCTs	Various	Feedback identified the specific behavior to be changed 86% of the time.	Not provided	Feedback was given on patient outcomes in 14% of the studies, and process of care in 79% of studies. Feedback content included other content 32% of the time, including patient-level data and cost data. Feedback presented aggregated patient data 81% of the time and feedback about individual patients' care 25% of the time. Comparison data were to peers' performance or "others'" previous performance 49% of the time and to a standardized guideline as a comparator 15% of the time.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Dawson, 2015[16]	Auditing and feedback	Qualitative study; n=30; nurses, healthcare support staff, Infection Prevention and Control Team, and people with managerial/ administrative roles	2 NHS hospitals in the UK	Not provided	Not provided	The perception of participants across all Audit Process Involvement (API) groups was that data generated by the current measurement process were "meaningless." Participants had concerns about how data generated by the audit process were used to engender change and found it hard to perceive any change stemming from the audit process.	High	None
Diamantourous et al., 2017[9]	Audit and feedback	Cluster randomized trial; n=720; patients with various risks for VTE	Seven community hospitals and one academic medical center in Toronto, Canada	The rates of appropriate thromboprophylaxis increased in both control and intervention groups. Greater improvement in the intervention group was statistically significant for the major general surgery patient subgroup (p=0.048).	Not provided	Not provided	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Dinescu et al., 2011[13]	Audit and feedback	Pre-post intervention study; n=5; geriatric fellows	Department of Geriatrics and Palliative Medicine at Mount Sinai Medical Center	After intervention, fellows were more likely to complete all required discharge summary data compared with pre-intervention (91% vs. 71%, p<0.001). Discharge summary completeness improved for all composite outcomes examining the four domains of care: admission (93% vs. 70%, p<0.001), hospital course (93% vs. 78%, p<0.001), discharge planning (93% vs. 77%, p<0.02), and post-discharge care (83% vs. 57%, p<0.001).	Not provided	Not provided	High	None
Doers et al., 2015[22]	Audit and feedback	Prospective Quality Improvement Project	4 general internal wards at Milwaukee Veterans Affairs (VA) Medical Center	The total scores significantly improved from 7.0 to 8.2 out of a possible 11 (p<0.0001). Documentation of many essential elements improved significantly during this intervention, such as mental status (p<0.0001), decisionality (p<0.0001), lab or test results (p<0.0001), degree of acuity (p<0.0001), anticipatory guidance (p<0.0001), and future plans (p<0.0005). The use of vague language declined (p<0.0001).	Not provided	Not provided	High	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Fraser et al., 2017[23]	Audit and feedback	Interrupted time series design; n=548; home health clients	Seven offices within Alberta, Canada	There were no significant trends from baseline to the post-intervention period in number of clients reporting pain, falls, delirium, hospital visits, or pressure ulcers.	Not provided	Not provided	High	None
Gilkes et al., 2017[12]	Audit and feedback	Non-randomized, before-after interventional study; 3,076 patients; ages 15–69 years	Primary care in Australia	Statistically and clinically significant increase in recording patients' alcohol consumption (24% to 36%; OR 1.19; 95% CI, 1.10 to 1.29). There was a significant increase in proportion of patients who had detailed family history of type 2 diabetes (23% to 32%), early ischemic heart disease (24% to 33%), breast cancer (21% to 32%), and colorectal cancer (20% to 30%).	There was a significant reduction in the recording of mammograms from 46% to 36%.	Not provided	High	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Hubner et al., 2017[3]	Audit and feedback	Prospective; n=2,209; patients who had an out-of-hospital cardiac arrest	Emergency medical technicians (EMTs) and emergency physicians before hospital in Vienna, Austria	No differences in the rates of sustained return of spontaneous circulation (sROSC) (p=0.95) or the fraction of patients pronounced dead in the field (p=0.47). No impact on 30-day survival (p=0.95). Found a strong linear increase of good neurological outcome among survivors during the observation period (p=0.02), showing an increase of 16.2% comparing the first with the last observation interval.	Not provided	Not provided	High	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Ivers et al., 2014[24]	Audit and feedback	Qualitative study; n=54; family physicians	Not provided	Not provided	Not provided	None of the participants reported that they found the feedback particularly useful. Participants commonly reported that they intended to improve performance by being more mindful of the relevant targets during patient encounters. However, no participants reported using the feedback to set specific goals for improvement or action plans for reaching these goals.	High	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Ivers et al., 2012[6]	Audit and feedback	Systematic review and meta-analysis of RCTs	80 trials based in North America, 21 in the UK or Ireland, 10 in Australia or New Zealand, and 29 elsewhere	Eighty-two comparisons from 49 studies measured improved compliance with desired practice. Median 4.3% absolute increase in desired practice (IQR 0.5% to 16%). Twenty-six studies measured compliance with desired practice (continuous outcomes): median 1.3% improvement in desired practice (IQR 1.3% to 28.9%).	Not provided	Not provided	Low	None
Ivers et al., 2013[17]	Audit and feedback	RCT; n=4,617 at baseline; 2,157 in feedback plus worksheet arm, and 2,460 in usual feedback arm; adult patients 18 and over with diabetes and/or ischemic heart disease	Primary care clinic in Ontario	No clinically or statistically significant differences were observed across groups in the primary outcomes in either the adjusted or unadjusted models.	Not provided	Not provided	Not provided	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Jeffs et al., 2014[19]	Audit and feedback	Qualitative; n=56; nurses	Five hundred-bed teaching hospital in Toronto, Ontario, Canada	Not provided	Not provided	Participants saw value of seeing the data, as the data provided a visualization of how they were doing. Participants reported the Care Utilising Evidence (CUE) dashboard acknowledged and highlighted the work that nurses do to provide high-quality care and maintain standards of practice. Twenty-seven participants said the data displayed on the dashboard were useful to guide improvement efforts.	High	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Johri et al., 2017[14]	Audit and feedback	RCT; n=105,351; women giving birth	Thirty-two public hospitals in Quebec Canada	Analyses including all patients showed a small non-significant reduction in caesareans in the intervention group compared with controls and an important reduction in costs, yielding adjusted estimates per-patient of a reduction of 0.005 caesarean sections (95% CI, -0.015 to 0.004, p=0.09) and $180 saved (95% CI, −$277 to −$83, p<0.001).	Not provided	Not provided	Low	None
Kreitmeyer et al., 2017[26]	Audit and feedback	Prospective: n=273 pre-intervention; n=263 post-intervention; pediatric patients	Academic tertiary care hospital with 61 beds in Munich, Germany	Percentage of hospitalized children receiving at least one antibiotic did not change significantly. Antibiotic treatment days decreased by 10.5% (p<0.001), from 483.6 (pre-intervention) to 432.9 (post-intervention) days of therapy per 1,000 patient-days, with a significant effect regarding cephalosporin consumption (-35.5%, p<0.001).	Not provided	Not provided	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Laskshminarayan et al., 2010[25]	Audit and feedback	Cluster-RCT; pre-intervention control n=622, experimental n=589; post-intervention control n=648, experimental n=446; patients age 30–84 with acute ischemic stroke and admitted through the emergency room	Twenty-four acute care hospitals in Minnesota	There was no significant intervention effect for acute, in-hospital, or discharge cases.	Not provided	Not provided	Moderate	None
Langston, 2011[10]	Audit and feedback	Pre/post-intervention study=263 pre-intervention and 253 post-intervention; registered nurses (RNs), nursing assistants (NAs), medical doctors (MDs), and ancillary staff	SICU, neurosurgery ICU, and surgical intermediate care unit at University of North Carolina Hospitals	There was a significant increase overall for hand hygiene compliance after no patient contact (p=0.006). There was a significant increase (16.9%) in hand hygiene compliance for RNs after nonpatient contact (p=0.03). There were no significant differences in hand hygiene compliance after patient contact overall or for any particular type of provider.	Not provided	Not provided	High	Small sample sizes; same people analyzed

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Le Grand Rogers et al., 2015[15]	Audit and feedback	Systematic review; n=24 studies	Various EDs	Of the 24 studies, 23 resulted in improvement in the measured outcomes. There was substantial heterogeneity in the included studies, with an I2 index of 83%. The included studies had an average Downs and Black score of 15.6 of 30 (range, 6–22).	Not provided	In the 24 studies, feedback was given as one-on-one, as a group, or in both manners. Only 2 studies used one-on-one feedback alone. Seven of the 24 studies used the group method to provide feedback. Fifteen of the 24 studies used both the one-on-one and group methods to provide feedback. In seven studies, feedback was provided by a supervisor, whereas in five studies, feedback was provided by a peer or colleague.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Mahant et al., 2008[2]	Audit and feedback	Prospective observational study; n=1,705 pre-intervention, n=1,489 in intervention; 60 beds; pediatric patients	Pediatric inpatient unit at a tertiary care pediatric academic medical center in Toronto, Canada	The intervention was associated with a significant reduction in the proportion of nonqualified hospital days, from 47% to 33% of hospital days (RR: 0.71 [95% CI 0.74 to 0.68] p<0.0001). There was no significant difference in the hospital readmission rate.	Not provided	Not provided	High	None
Redwood et al., 2013[18]	Feedback	Mixed methods; n=88; junior doctors	Teaching hospital with 1,200 inpatient beds	No evidence that the introduction of the dashboard had a significant effect on either the prescribing behavior or the response to laboratory alarms of the junior doctors in the trial.	Not provided	Junior doctors found the dashboard helpful in stimulating reflection on their clinical behaviors and responsibilities. However, they expressed reservations about the sort of performance data that were collected and given as feedback via the clinical dashboard.	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Roberts et al., 2015[27]	Audit and feedback	Before and after design; n=2,609 prescriptions; patients on acute medical unit receiving antimicrobial prescriptions	Acute medical unit in UK	The change from baseline was statistically significant ($p<0.01$) in all follow-up periods for two indicators: "antimicrobials should have a documented indication in the medical notes" (6.0% at the 5th follow-up) and "antimicrobials should adhere to guideline choice or have a justification for deviation" (8.7% at the 5th follow-up).	Not provided	Not provided	Moderate	None
Sales et al., 2014[28]	Monitoring and feedback	Interrupted time series; n=500; long-term care residents	Nine long-term care units in four facilities in Alberta, Canada	Not provided	Study found no immediate change in the level or number of falls at the outset of the intervention and a modest but significant increase in the rate of falls over the intervention period.	Not provided	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Scales et al., 2011[20]	Multicomponent intervention including audit and feedback, and educational outreach	RCT; n= 9.29 ICU admissions; patients admitted to ICU	Fifteen community hospital ICUs in Ontario, Canada	Improvements to adherence rates in intervention ICUs were similar to control ICUs (ratio of ORs, 3.12; 95% CI, 0.79 to 12.41; p=0.11). There was no change in the proportion of eligible patients receiving deep vein thrombosis prophylaxis among intervention ICUs (OR, 1.28; 95% CI, 0.67 to 2.45; p=0.46) or among control ICUs (OR, 0.52; 95% CI, 0.20 to 1.30; p=0.16).	Not provided	Not provided	Moderate	None
Tuti et al., 2017[7]	Audit and feedback	Systematic review of RCTs; n=81,700 patients	Various settings	Meta-analysis was highly heterogeneous. Three studies found a positive effect of the e-audit and feedback intervention on quality of care. None of the other studies found an effect of the intervention on all the outcome measures evaluated. Dichotomous process measures, clinical process measures, dichotomous clinical outcomes, continuous clinical outcomes	Not provided	Not provided	Low	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Van der Veer et al., 2013[5]	Audit and feedback	RCT; 15 ICUs in intervention, 13,539 total admissions; 15 ICUs in control arm, 12,013 total admissions. All patients admitted except patients following coronary artery bypass graft surgery and organ donation.	Thirty ICUs in the Netherlands	Study did not find significant difference in ICU length of stay or time to ICU death between intervention and control arms.	Not provided	Not provided	Low	None
Weston et al., 2017[29]	Audit and feedback	Retrospective; n=175 patient encounters; adult patients with cardiac arrest who received cardiopulmonary resuscitation (CPR) in the out-of-hospital setting from basic life support and/or advanced life support (ALS) providers present from the Milwaukee Fire Department	EMS system covering 600,000 individuals in Milwaukee, WI	There was a significant improvement in compression depth >5cm ($p<0.001$) in benchmark achievement. The difference between groups for pre-shock pause times was not significant and the means in both groups were above the benchmark goal.	Not provided	Not provided	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Zoutman et al., 2012[11]	Feedback	Randomized study; n=5,032 patient encounters; patients' age newborn–102	Primary care practices in southeastern Ontario	Feedback did not influence the rate of prescribing of physicians in the monthly feedback condition when compared with baseline prescribing and the delayed feedback group (f=0.01, p=0.9); however, monthly feedback increased first-line antibiotic choices when compared with baseline prescribing and the delayed feedback group (F=8.1, p=0.005).	Not provided	Not provided	Moderate	None

Table B.75: Cross-Cutting Patient Safety Topics/Practices, Teamwork and Team Training—Single Studies

Note: Full references are available in the Section 17.6 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Bliss et al., 2012[43]	Surgical Checklist (implemented after team training)	Prospective cohort design with historical controls. One cohort represented where team training had been introduced and one cohort represented where the checklist had been implemented. The historical control group was based on all ACS NSQIP cases that had occurred before the team training intervention had been introduced and that met the study inclusion criteria.	Surgical unit of 600-bed tertiary care facility and teaching hospital located in the Northeast	Overall compliance using the checklist was reported as 97.26%, although individual checklists were not always fully completed, especially the items that appeared redundant/ unnecessary (e.g., introducing team members when individuals were already familiar with one another).	A significant decrease in adverse event rates was noted from the historical control (23.6%) and from the team training-only cases (15.9%) to the cases where the checklist was used (8.2%). Completion of three checklist items was shown to significantly decrease morbidity rates. The occurrence of deep surgical site infections significantly increased when "confirmation of identity, procedure, procedure site, and consent(s) filled out" and "procedure and procedure site filled out" were not completed on the checklist (p=0.014 and p=0.041, respectively). Major morbidity	Team training followed up with an accountability measure such as a checklist is relatively inexpensive and leads to improvements. The length of the checklist may reduce compliance over time, so revising the checklist to include only the most essential items is desirable.	Moderate	The surgical services staff had participated in a team training program prior to the introduction of the perioperative briefing and postoperative debriefing checklist. Training participants were oriented to the Association of Perioperative Registered Nurses Comprehensive Surgical Checklist on the last day of the training.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
					and infectious events were significantly higher when the checklist item related to team introductions was left incomplete (p=0.004 and 0=0.015, respectively).			
Fargen et al., 2013[41]	Pre/peri-procedural checklist	Seventy-one procedures were included in the baseline period and 60 procedures were included after the implement-tation of the checklist. One hundred twenty-one post-procedural surveys were collected in the baseline period and 132 post-procedural surveys were collected in the post-intervention period.	Neuro-interventional suite	Communications significantly improved from the baseline to the post-intervention period (baseline=38.8% were rated as excellent, 43% were rated as good; post=68.2% were rated as excellent, 28.8% were rated as good, p<0.001). Twenty-one individuals provided opinions about the effectiveness of the checklist. Ninety-five percent believed that the use of the checklist should continue.	The overall number of adverse events decreased after the implementation of the checklist as compared with at the baseline (6 with the checklist vs. 25 in the baseline, p=0.001). Eight of the nine specific adverse events/near misses decreased after the checklist was implemented (non-significant), and one adverse event/near miss remained the same.	The checklist had a positive impact on team communication, and adverse events/near misses decreased.	Moderate to high	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Halverson et al., 2009[19]	Team Training curriculum based on Crew Resource Management	1,150 trainees participated in the training, including attending physicians, house staff, and nurses working in the operating room. Additional preoperative and postoperative personnel were also included in the mandatory training.	University-affiliated hospital	Post-intervention perceptions of teamwork significantly improved on 14 of the 19 items ($p < .05$). Briefings were not observed in the pre-training period, whereas preoperative briefings were observed 66% of the time at the 6-month follow-up ($p < .001$). Survey data indicated that respondents held positive perceptions regarding the utility of the briefings, with nurses and anesthesia providers providing higher utility ratings than surgeons. Pre- to post-compliance related to time-outs increased (47% to 86%).	The percentage of on-time first case starts increased over the study period from 69% (pre-intervention) to 76% (post-intervention). No significant changes were reported in the timely administration of prophylactic antibiotic or in turnover times.	Thirty-seven percent of respondents reported that they had communicated information during the preoperative debrief that could have increased the risk to the patient or delayed the case if they had not shared the information ahead of time.	Moderate	The 4-hour team training program was mandatory. Two weeks after the training, instructors coached teams in conducting preoperative briefings and debriefings.
Halverson et al., 2011[14]	Team Training curriculum based on Crew Resource Management	Pre-post observational study; 76 hours of operating room observations were made in the pre-Team Training condition, and 74 hours of observations were made in the post-Team	Operating rooms of Northwestern Memorial Hospital	Prior to the team training intervention, communication errors occurred at a rate of 0.737 per hour; they significantly decreased to 0.270 per hour following the intervention ($p < .001$). In the pre-intervention period, communication errors were most frequently related to progress reports (32%)	Not provided	Not provided	High	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
		Training condition. Post-training observations were made approximately 6 to 9 months after the training.		and equipment (23%), whereas the majority of communication errors in the post-intervention period (70%) were related to equipment. Communication errors in the pre-intervention period were classified as resulting in inefficiencies (24%), delays (20%), and tension (12%). The highest proportion of communication errors in the post-intervention period resulted in delays (33%), tension (17%), and inefficiencies (13%). Some communication errors were categorized as having no effect these occurred more frequently following the training (pre=12%, post=25%).				

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Kleiner et al., 2014[36]	Coaching on conducting effective pre-briefs/debriefs	Pre-intervention/ post-intervention evaluation design	Surgical department with 17 inpatient and 8 outpatient ORs in an academic hospital	There was a significant increase in the briefing score from the pre-intervention to post-intervention (mean= 3.478 to 3.644, p=.044). For the debriefings, quality items included using a standardized checklist, discussing what went well, discussing what did not go well, and thanking the team. A significant increase was also reported for the debriefing score from the pre- to post-intervention (mean=2.377 to 2.991, p <.0001).	Not provided	Sustaining change following team training can be a challenge. This study used a coach who was familiar to and respected by faculty and staff members at this hospital to aid surgical teams in making continual improvement.	Moderate to high	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Krimminger et al., 2018[39]	Handovers	Pre-post observational study	Twenty-one-bed cardiothoracic intensive care unit (CTICU) in a large university-affiliated medical center that performs over 19,400 surgical procedures a year	There was a significant decrease in the mean number of handover process errors from the pre- to post-intervention periods (pre=6.1, post=2.8, p<.001). An average of 5.2 information-sharing errors occurred per handoff in the pre-intervention period; this decreased significantly to 2.3 following the intervention (p<.001). All items on a survey that measured satisfaction with the handover showed improvement from pre to post, and 8 out of 12 improvements were statistically significant. The item that measured overall satisfaction with the OR to ICU handover failed to reach statistical significance (mean rank=147 at T1 to 165 at T2, p=0.065).	Not provided	The new handover process was associated with improvements in the post-intervention period, including fewer process and information sharing errors per handover. The time per handover slightly increased in the post-intervention period, but this increase was not significant. Based on survey data collected, reaction to the new handover process was generally positive.	Moderate to high	Participation in the observed handovers was voluntary. Ten of the 143 staff members declined to participate (7%); they were all nurses. Trained observers were used who did not work at the facility. Satisfaction surveys were anonymous.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Levy et al., 2014[15]	Crew Resource Management Training (5 hours)	Retrospective study with some pre-post measures. A total of 352 participants attended the training.	Three hospitals: (1) Moses Cone Hospital in Greensboro, NC, is a community-based, urban Level 2 trauma center. (2) Detroit Receiving Hospital in Detroit, MI, is an academic teaching hospital and Level I trauma center. (3) Harper University Hospital is an academic teaching hospital and tertiary care facility.	Pre and post-data across the three hospitals demonstrated significant improvement on all three confidence items (p<.001), which was maintained at the 30-day follow-up assessment. Participants significantly improved their knowledge from the pre- to post-assessments (61% of items correct on pre-test, 73% of items correct on post-test, p<.001). At the 30-day post intervention assessment, knowledge had decreased some since the training but was still significantly higher than at the baseline (61% at baseline vs. 66 at 30-day post-assessment, p=.026).	There was an increase in the proportion of patients at Moses Cone Hospital who received reperfusion in less than 90 minutes after the training (80% vs. 92%, ns). A significant increase was observed for guideline-compliant anticoagulant use at Harper University Hospital (29% vs. 63%, p<. 001). There was a significant increase in documented risk score at Detroit Receiving Hospital (0% vs. 7%, p=.007).	One of the aims of the study was to improve patient care, although the outcome measures collected showed mixed results across the three hospitals. The authors note that the CRM training was not mandatory and the effort lacked a strong champion. As a result, the use of CRM principles was not reinforced and not consistently implemented. Staffing changes and lack of resources were also cited as barriers in this study.	Moderate to high	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Lisbon et al., 2016[23]	TeamSTEPPS® Training (4-hour didactic session)	Pre-post design; 113 participants attended the TeamSTEPPS® training; 113 respondents completed the measures before the training, 60 completed the measures again on day 45, and 59 completed the measures at day 90.	Emergency department in an academic medical center	Scores on the TeamSTEPPS® Knowledge Test had significantly improved at a 45-day check-in on 15 of the 21 questions (as compared with the baseline). Sustained improvement was reported on 13 out of 21 on a 90-day assessment. Responses on all items of the Communication dimension of AHRQ's Hospital Survey on Patient Safety significantly improved from the baseline to the 45-day assessment and remained at that level at the 90-day assessment. Following the training, huddles (implemented as a strategy during the TeamSTEPPS® training) were observed 64% of the time. CUS, which was another strategy that was implemented as a result of the TeamSTEPPS® training, had been used by almost half (47%) of the respondents at least once.	Not provided	The authors felt that the use of the huddle and CUS strategies were critical to sustaining teamwork-related improvements over the 90-day period following the TeamSTEPPS® training.	High	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Lutgendorf et al., 2017[28]	Multi-disciplinary simulation/ structured debriefs following TeamSTEPPS® principles	Pre-post design; 113 participants completed 16 simulations/ debriefings over a 2-day period.	Military tertiary care medical center	Participants felt significantly more comfortable managing hypertensive emergencies, responding to shoulder dystocia, and handling postpartum hemorrhage following the simulation exercises than they had prior to the exercises.	Time to prepare emergency release blood products decreased from 6 minutes on the first day to 4 minutes on the second day of the simulation intervention. Decreases in the number of postpartum hemorrhage cases were observed following the 2-day simulation exercises as compared with the rates 6 months leading up to the intervention.	Hands-on experience gained through the simulation exercises helped build participants' confidence in managing obstetric emergencies. Observations also indicated that teams were more efficient when dealing with emergency cases after the second day of exercises than on the first. Further, this intervention allowed a new massive transfusion system to be tested and for improvements to be made regarding supplies that were not available within the L&D unit, processes for requesting/ obtaining blood products during emergencies, and the location of the blood bank.	Moderate to high	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Mahoney et al., 2012[24]	TeamSTEPPS® Training	Pre-post design; 284 participants were trained in TeamSTEPPS; 108 respondents completed the pre-training Team Assessment Questionnaire (invited=296, response rate=36%), and 108 respondents completed the post-assessment of this measure (303 invited, response rate=47%).	The Menniger Clinic, which is a private, not-for-profit, 120-bed psychiatric hospital located in Houston, Texas	A comparison of means indicated significant differences on the pre-and-post scores on team foundation (pre=3.76, post=4.10, p=.001), team functioning (pre=3.88, post=4.16, p=.003), team performance (pre=3.78, post=4.10, p=.001), team skills (pre=3.76, post=4.08, p=.001), and climate and atmosphere (pre=3.68, post=3.97, p=.004).	Not provided	The teamwork skills covered in the TeamSTEPPS® training were integrated into daily practice. New hires are trained in TeamSTEPPS® as part of their onboarding and orientation process.	High	None
Mancuso et al., 2016[18]	Crew Resource Management (CRM) Training	Prospective study, pre-post design	Obstetrics unit at the University of Colorado Hospital	Observations of the quantity and quality of communication were made during six phases of cesarean births. There was a significant increase in quantity of communication (i.e., count of communication checklist items covered during procedure) for the obstetrics team at three of the four key points and for the	Not provided	The quantity of pre-briefs and debriefs that participants engaged in was sustained for 3 months following the CRM intervention. The authors suspect that the obstetrics team, who felt more resistant to pre-briefing following the intervention may	Moderate to high	The CRM training was tailored to focus on the communication and teamwork required of obstetrics teams and neonatal resuscitation teams.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
				neonatal team at two of the four key points following the CRM training intervention. Significant changes in the quality of communication (i.e., number of team members that communicated with each other) were reported for the obstetrics team and for the neonatal teams. A greater number of team members gave their full attention during the pre-brief following the training, but this was significant in the obstetrics team only (obstetrics team baseline=2.13, post=4.46, p<.001; neonatal team baseline=2.78, post=3.18, p=.178). The obstetrics team was significantly more resistant to pre-briefing following the training (baseline=1.00, post=1.25, p <.01), although the neonatal team showed a significant decrease in resistance to pre-briefing after the training intervention		have been more focused on the case than on pre-briefing.		

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
				(baseline=1.18, post=0.92, p <.01).				
Mayer et al., 2011[25]	TeamSTEPPS® Training—Customized 2.5 hour version.	Pre-post design. A comparison group was used for some of the process measures.	Twenty-bed pediatric intensive care unit and a 16-bed surgical intensive care unit	Scores on all six teamwork dimensions measured had significantly improved (as compared with at the baseline) 1 month after the training. Scores on five of the six teamwork dimensions were significant at 12-month assessment (except situation monitoring). Pre to post scores on the Hospital Survey on Patient Safety Culture indicated significant increases in "overall perceptions of safety" and "communication openness" for participants in both units. Significant increases in perceptions were also reported for SICU participants on "teamwork within unit." Participants in the PICU significantly improved their ratings of how well their unit worked together following the training.	The average time to place patients on ECMO was significantly lower after training. No significant difference was reported for the length of RRT events. Decreases in the frequency of nosocomial infections were observed in both units following the training; this frequency was below the upper control limit for seven out of eight months in both units.	The shortened TeamSTEPPS® training still had positive effects on the training participants.	Moderate	Regarding the finding of no significant difference in the length of RRT events after the TeamSTEPPS® training, follow-up interviews indicated that it was difficult to use the TeamSTEPPS® skills they had learned with primary staff at the bedside who had not been trained in TeamSTEPPS®

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Mukhopadhyay et al., 2018[40]	Handoff	Pre-post observation design	Twenty-two-bed surgical and trauma intensive care unit of a 635-bed non-profit tertiary academic medical center	The presence of a surgical team member at handoff had increased from 32% of the time in the baseline period to 84% post-intervention (p <0.001).The presence of a physician team member had also increased significantly, from 52% of the time to 94% (p <0.001). All elements of the surgical report were communicated significantly more frequently in the post-intervention period (84%) as compared with the pre-intervention period (29%, p <.05). The completeness of the anesthesia report also significantly improved, from 15% to 40% following the intervention (p <.05). There was some increased efficiency observed in the average time for patients to be placed on the ventilator and time to complete transfer to ICU monitors, but these decreases were not statistically significant.	Not provided	The implementation of the handoff protocol resulted in greater improvement from all members of the care team. It also reduced the amount of missing information during handoffs.	Moderate to high	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Murphy et al., 2015[37]	Roundtable debriefs	Retrospective analysis pre-post design; 28 pre-intervention cases were compared with 36 post-intervention cases.	Emergency department in an urban academic hospital with 751 beds	Not provided	No statistical differences were found between the pre- and post-intervention data on the frequency of assisted falls (p=0.17), unassisted falls (p=0.28), and the rate of falls per 1,000 patient encounters (p=0.28).	Falls had been on an increase prior to the roundtable debriefing intervention, and this trend was somewhat disrupted following the intervention.	High to moderate	None
Paull et al., 2013[29]	Simulation-Based Crew Resource Management Training	Pre-post design. Participants received CRM training with 2-hour simulation session. Sample size of 334 participants.	Surgical care floors at 12 facilities within the Veterans Health Administration	Confidence in using CRM techniques significantly improved on all eight communication and teamwork items over baseline scores following the intervention. Significant improvements were reported on 14 of 15 of the teamwork behaviors observed. Scores increased by 15 to 23%. No difference was found on the teams' skills related to "resource allocation."	Not provided	The authors felt that including simulated exercises was an important part of their team training effort, as it gave participants the chance to put their teamwork skills to work. The didactic training, simulated scenario, and feedback gained during the debriefings helped participants build confidence and improve their skills.	Moderate to high	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Peckler et al., 2012[30]	Team training with high-fidelity simulation	Pre-post design; 41 first-year interns who work in the trauma room. Two groups participated in the training on two separate days.	Southeastern American Level I Trauma Center and university-affiliated teaching hospital	Scores on a situational judgment test increased following the training for Group 1 (pre mean=15.63, post mean=17.29, p<0.10) but did not reach statistical significance. A statistically significant increase was observed in Group 2's scores for the pre to post assessment (pre mean=13.77, post mean=16.55, p<0.01).	Not provided	This study emphasizes the importance of practicing teamwork concepts and receiving feedback, especially for less experienced providers such as residents.	High	None
Petrovic et al., 2015[38]	Handoff protocol	Prospective, unblinded cross-sectional study; 53 handoffs observed in pre-intervention and 50 handoffs observed in the post-intervention period.	Peri-anesthesia care unit in a tertiary care facility serving 55,000 patients annually	The duration of the handoff increased from the pre- to post-intervention period (from an average of 9 minutes to 11 minutes, p=.01). The handoff also started more quickly when the patient arrived in the post-intervention cases (pre-mean=4.4, post-mean=2.9 minutes, p<.01). The total number of defects per handoff significantly decreased, from 9.92 prior to the intervention to a post-intervention average of 3.68 (p<.01). The number of missed items on the anesthesia report and on the surgery report both significantly	Not provided	A 77% reduction in communication errors between the OR to PACU was achieved using the new handoff protocol. Nurses were the most satisfied with the new handoff protocol. Some resistance to participating was seen among the surgical team, but a combination of leadership support, education, and peer pressure successfully got them on board.	No control group	Participation in this study was voluntary and anonymous.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
				decreased (from 2.02 to 0.94, p<.01 and from 7.57 to 2.64, p<.01, respectively). Significantly fewer technical defects (i.e., equipment problems) occurred per handoff in the post-intervention period (0.34 vs. 0.1, p=.04). There was a pre to post increase on all items for PACU nurses, five of which increases were significant (p<.05). Anesthesia providers completed only four items on the satisfaction assessment that were relevant to their role. Satisfaction scores declined for anesthesia providers following the intervention, but not significantly. Finally, surgery providers did not complete the pre-satisfaction survey, since there was low participation for this group at bedside handoffs prior to the intervention. Post-intervention data indicated high levels of satisfaction from surgery providers (percentage favorable				

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
				across 4 of 7 items=94%)				
Porter et al., 2014[42]	Pre-procedural pause with checklist	Pre-post design. Data were gathered on 31 cases in the baseline period, 36 cases in the immediate post-intervention, and 34 cases in the 18-month post-intervention.	Virginia Mason Hospital, a 335-bed community teaching hospital with 24 ORs and three surgical groups located in Seattle, Washington	Compliance with the pre-procedural pause increased significantly from the baseline to the post-intervention period (from 78% to 96% cases, p<.0001). At an 18-month audit, compliance remained at 96%. Team members introduced themselves significantly more in the post-intervention period (94% from an average of 44%, p<.0001), and this practice had continued to increase at the 18-month audit (97%, p<.0001). All checklist items were completed for 54% of cases in the baseline, whereas all items were completed in 97% of cases in the immediate post-intervention period. There was no change in the frequency of the surgeon's soliciting input from the rest of the team from the baseline to immediately after the intervention (56%), but this had increased to 94% at the 18-month audit.	Not provided	Providing each team member a specific role in the PPP checklist increased participation and the exchange of information, and resulted in more thoroughly completed checklists. Early involvement of all team members in the development of the PPP checklist protocol was critical to its success. Since this study was conducted, the PPP checklist has been extended to use in other areas of the hospital, including interventional radiology, gastroenterology, and electrophysiology.	Moderate to high	Audits were performed by a trained anesthesia technician or junior member of the surgical teams, as introducing an external observer had caused enhanced performance in previous audits.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Riggall and Smith, 2015[33]	Inter-professional simulation training	Convenience sample with pre-post measures; 84 staff participated in 17 simulations; 53 participants completed both the pre- and post-TeamSTEPPS® Teamwork Perceptions Questionnaire (T-TPQ).	40-bed medical unit in a northeastern tertiary-care teaching hospital	Pre-post T-TPQ data indicated that only perceptions of "leadership" significantly improved following the simulation training (pre-test mean=2.167 vs. post-test mean=2.566, p=.003). Scores on "team structure" and "communication" remained stable, and scores on "mutual support" slightly decreased on the post-simulation survey.	None of the resuscitation events requiring defibrillation met the guidelines provided by the AHA in the pre-intervention period. However, resuscitation events that required defibrillation in the post-intervention period all received it within the AHA guidelines of 2 minutes.	The authors point out that the participants who took part in the simulations had not received TeamSTEPPS® training. Thus, they may have been unfamiliar with the terms used in the measure as well as when specific components of teamwork were needed/ demonstrated in the simulations.	Moderate to high	None
Riley et al., 2011[31]	TeamSTEPPS® training workshop with in situ training exercises	Pre-post design with three groups: control, condensed TeamSTEPPS® workshop delivered, and condensed TeamSTEPPS® training with in situ training exercises (i.e., full intervention).	Perinatal units in three small community hospitals (50 to 66 beds) in the Midwest	There were no changes in safety culture reported either for groups that received interventions (condensed TeamSTEPPS® workshop or condensed TeamSTEPPS® training with in situ training exercises) or for the control group.	Only the hospital that received the full intervention (i.e., TeamSTEPPS® with in situ simulation) significantly decreased their Weighted Adverse Outcome Score, from 1.15 to 0.72 (p <.05).	This study provides evidence that an interdisciplinary team training program coupled with ongoing simulation practice sessions and debriefings can contribute to a decrease in neonatal outcomes.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Sawyer et al., 2013[22]	TeamSTEPPS® Training	Prospective pre-post design. Forty-two physicians, nurses, and respiratory therapists.	Twenty-bed, Level IIIB NICU at Tripler Army Medical Center in Honolulu, Hawaii	Significant improvement in attitudes toward teamwork (using the T-TAQ) from a pre-test average of 4.4 to a post-test average of 4.7 ($p < .001$). Teamwork knowledge on the TeamSTEPPS® Learning Benchmarks also improved from a pre-test average of 86.8% to an average of 92.6% on the post-test ($p<.001$). Significant improvements on all five teamwork skills were observed during simulated neonatal resuscitations ($p<.001$).	Not provided	Not provided	Moderate to high	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Sax et al., 2009[17]	Crew Resource Management	Prospective pre-post design. A total of 857 participants were trained at the two hospitals.	A 722-bed university hospital and a 247-bed affiliated community hospital	Immediately after the training, significant improvement was reported on all 10 items measuring empowerment ($p<.05$). At a minimum of 2 months, these improvements were maintained, with further improvement related to leadership (pre-training mean rating=3.0; immediate post-training mean=3.4; and 2 months post-training mean=3.6; $p<.05$). Consistent use of a checklist increased from 75% of the time to 100% during the study period. There was an increase in willingness to report unsafe conditions or near misses over the course of the study period (15.9% in 2002 and 2003 vs. 20.3% in 2004 through 2008; $p<.01$).	Not provided	The authors believe that the CRM training helped participants use a checklist, feel more empowered to speak up, and report unsafe conditions.	Moderate to high	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Sonesh et al., 2015[20]	Adapted TeamSTEPPS® Training	Pre-post design with a control group. Forty-three clinical obstetric staff members.	2,338-bed southeastern U.S. teaching hospital	Training participants shared positive reactions to the training. Some improvements were found in knowledge of situation awareness and teamwork following the training. Self-reported perceptions of teamwork improved following training, but were not significant. Observational data on decisions indicated that decision accuracy significantly improved following the training ($p < 0.05$).	Length of stay for infants decreased, from 3.85 days to 2.83 days ($p <= .07$). There were no differences in pre-post comparisons of mother length of stay, transfer to NICU, morbidity of infant.	Not provided	High	This study trained only three teams.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Tapson et al., 2011[16]	Crew Resource (5 hours). The intervention combined traditional clinical education regarding VTE prophylaxis (1 hour) in the surgical setting with a comprehensive program on CRM principles and techniques (3.5 hours).	Pre-post design	The study was conducted at Citrus Memorial Health System, a 198-bed community hospital located in Florida.	A statistically significant increase was reported for all three confidence questions (i.e., ability to identify process-related factors that may lead to medical errors in a surgical setting, use of CRM techniques to enhance patient care, ability to identify which of their surgical patients would be appropriate candidates for VTE prophylaxis). A much smaller sample of 29 participants who completed the 30-day survey showed a significant longer term gain in confidence for two of the three confidence questions. Reviews of patient charts demonstrated performance improvement in the post-training period in meeting guideline recommendations for timing, inpatient duration, and use of VTE prophylaxis beyond discharge.	Not provided	The CRM intervention resulted in some improvements related to teamwork processes as well as clinical processes.	Moderate to high	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Thomas et al., 2010[32]	Simulation-Based Team Training	Randomized trial with two experimental groups (high-fidelity and low-fidelity skills stations) with control group. Interns for pediatrics, pediatrics and internal medicine combined, family medicine, emergency medicine, and obstetrics and gynecology received the simulation-based team training. Post-intervention data were collected on 43 participants.	Surgical and Clinical Skills Center at the University of Texas Medical School	Teams that completed high-fidelity and low-fidelity skills stations exhibited a greater number of teamwork behaviors, managed workload more effectively, and completed the resuscitation more quickly than the control participants. At the 6-month follow-up assessment, teams in both training groups (high fidelity and low fidelity) exhibited a greater number of teamwork skills than control teams.	Not provided	The simulation-based training curriculum had been introduced to reduce errors. However, this objective was not met. The only long-term effect of the intervention was an increase in teamwork behaviors.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Weaver et al., 2010[21]	TeamSTEPPS® Training	Mixed-model design with one between-groups factor (Team-STEPPS® training vs. no training) and two within-groups factors (time period, team). The trained and control groups were located at separate campuses to minimize treatment diffusion.	The trained campus, which included 112 beds, 11 surgical suites, and more than 52,400 emergency department (ED) visits	Eighty-one participants felt more confident about their ability to work as an effective team member after training. No significant improvements in knowledge were found following the training. Trained teams engaged in significantly more pre-briefings after attending training ($p < .001$), and a greater number of team members spoke up during the briefings ($p<.001$). Trained teams significantly improved over control teams on two teamwork behaviors: communication ($p<.05$) and mutual support ($p<.01$). Scores on all four safety culture dimensions of the HSOPS improved following the TeamSTEPPS® training.	Not provided	There were positive results on all levels of evaluation. Pre-briefings significantly increased for the trained teams, and significantly more team members shared information during the briefings. Trained teams engaged in significantly more behaviors related to communication and mutual support. Improvements were reported on all dimensions of patient safety culture for those who participated in the TeamSTEPPS® training.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Wolf et al., 2010[26]	Veterans Health Administration Medical Team Training (MTT)	The OR teams consist of an attending surgeon, one to two residents, an attending anesthesiaol-ogist, an anesthesia resident or CRNA, scrub nurse/ tech, and a circulating nurse.	San Francisco VA Medical Center, an academic-affiliated hospital and regional referral center with eight ORs. More than 3,500 surgeries are performed per year.	Safety attitudes had improved 1 year after MTT on all dimensions, with significant improvement noted on "perceptions of management" and "working conditions." Case delays significantly decreased (23% to 10%, p<0.0001), mean case score increased (4.07–4.87, p<0.0005), and both changes were sustained at 24 months. One-year and 24-month follow-up data demonstrated decreased frequency of preoperative delays (16%–7%, p<0.004), handoff issues (5.4%–0.3%, p<0.0001), equipment issues/delays (24%–7%, p<0.0001), cases with low (<3) case scores (23%–3%, p<0.0005). Adherence to timing guidelines for prophylactic antibiotic administration improved (85%– 97%, p<0.0001).	Not provided	MTT training was delivered and debriefs were implemented. Sustained improvements were observed in teamwork, clinical processes, and patient safety culture.	Low to moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Wolfe et al., 2014[35]	Briefing/ debriefing	Prospective study with historical controls	ICU within an academic, tertiary pediatric facility with 516 inpatient beds	The quality of chest compression was better during the debriefing intervention period. The percentage of epochs that met designated quality targets significantly improved for all comparisons. Rate improved from 71 to 90, depth from 81 to 91, CPR fraction from 64 to 82, and excellent CPR from 20 to 61 (p <0.01).	Two survival outcomes were measured. First, survival to hospital discharge improved in the cases that were debriefed, but was not statistically significant (33% in pre-intervention cases, 52% in the debrief intervention cases, p=0,054). Second, survival with favorable neurological outcomes significantly increased in the debriefing intervention cases (29% in pre-intervention cases, 50% in the debriefing intervention cases).	The cardiac arrest debriefing program significantly improved CPR quality.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/ Findings	Risk of Bias (High, Moderate, Low)	Comments
Young-Xu et al., 2011[27]	Veterans Health Administration Medical Team Training (MTT). Checklists and briefing/ debriefing tools were implemented at the participating facilities and adapted to their needs.	Retrospective cohort study with a contemp-oraneous control group	Seventy-four VA facilities that had participated in MTT training and had 3 years of annual surgical morbidity rate data	Not provided	Facilities in the MTT program (n=42) had a significant decrease of 17% in observed annual surgical morbidity rate (rate ratio, 0.83; 95% CI, 0.79 to 0.88; p=.01). After adjusting for surgical risk, a decrease of 15% in morbidity rate was reported for facilities in the MTT program and a decrease of 10% for those who had not yet participated in the program. The risk-adjusted annual surgical morbidity rate declined in both groups, and the decline was 20% steeper in the MTT program group (p=.001) after propensity-score matching.	A 2-month preparation and planning period was required leading up to the MTT training. This period allows each facility to gain an understanding of their underlying problems. The use of a checklist can improve communication prior to surgery, but the use of briefings was believed to facilitate continued communication throughout surgeries, when unforeseen complications can occur.	Low to moderate	None

Table B.76: Cross-Cutting Patient Safety Topics/Practices, Teamwork and Team Training—Systematic Reviews and Meta-Analyses

Note: Full references are located in the Section 17.6 reference list.

Author, Year	Description of PSP	Setting/s, Population/s	Summary of SR Findings	Implementation Themes/Findings	Notes
Boet et al., 2014[11]	Simulation-based team training	Hospital settings	Four studies in the review assessed transfer of KSAs back to the job setting. Three studies demonstrated that the simulation intervention was significantly more effective than didactic training. Five studies measured the impact of simulation on patient outcomes, with one study reporting a significant reduction in patient mortality.	The small number of studies and lack of significant evidence make it difficult to conclude that simulation training improves patient outcomes.	None
Dietz et al., 2014[12]	Standardized protocols, daily rounds, and training	Intensive care unit	One study investigated the use of a standardized protocol (i.e., daily goal sheet), and reported that it significantly increased the care team's understanding of patient care objectives and reduced length of stay among ICU patients. Studies that incorporated/improved the rounding process reported shorter hospitals stays, reduced postoperative complications, and improved clinical outcomes (e.g., infections, ventilator-associated pneumonia). Five studies incorporated simulation team training; they reported that the training resulted in an increase of teamwork skills and that participants were more confident in their abilities following the training.	Across studies, communication was considered the most important teamwork skill to measure and improve.	None

Author, Year	Description of PSP	Setting/s, Population/s	Summary of SR Findings	Implementation Themes/Findings	Notes
Hughes et al., 2016[13]	Team training	Not specified	Team training significantly improved participant reactions. Team training had a significant positive impact on participant learning. A significantly increased number of team KSAs were applied on the job following team training delivery. Team training improved results such as length of stay and patient mortality. Participant learning positively impacted transfer of training to the job environment. Transfer of training positively impacted results/outcomes achieved. No differences in effectiveness were reported between trainings that included high physical fidelity versus those that used low physical fidelity. Team training was equally beneficial for healthcare students and clinicians.	Team training was beneficial regardless of stage of career, as students and experienced clinicians benefited from the intervention. The results of team training for patient and clinical outcomes were based on a limited number of studies, so those results should be interpreted with caution.	None
Weaver et al., 2014[2]	Team training	Hospital settings	Reactions to team training programs have generally been positive. Studies have demonstrated that team training has a positive impact on participant learning (i.e., knowledge, confidence, attitudes). Team training has also been associated with an increased use of teamwork skills. Half of the studies in this review attempted to measure clinical processes or patient outcomes, with 10 studies reporting some significant improvements.	The authors note that studies of team training have increased, but that many of the studies have been of low to medium quality. Additionally, identifying how long effects can be maintained and identifying appropriate intervals for refresher training require more attention.	None

Table B.77: Cross-Cutting Patient Safety Topics/Practices, Education and Training Through Simulation—Single Studies

Note: Full references are available in the Section 17.7 reference list.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Bae et al., 2017[10]	2.5-hour simulation-based curriculum where third-year residents were asked to perform a simulated reduction of a distal radial fracture, apply a well-molded short arm cast application, and later remove the cast using a standard cast oscillating saw.	Retrospective, comparison cohort design. A total of 627 patients were included in the study; 188 patients were treated in the pre-simulation group and 439 were treated in the post-simulation group.	Tertiary-care pediatric teaching hospital.	There were eight cast saw injuries in the pre-simulation period and three in the post-simulation period. The rate of cast saw burns was significantly lower following the simulation curriculum ($p = 0.002$).	Not provided	The authors also estimated the return on investment associated with the simulation curriculum introduced in this study. The total cost calculated for the simulation curriculum was $2,465.31 for seven residents. The authors estimated that the cast saw burns in the pre-simulation period were associated with $32,320 in costs, whereas the cast saw burns in the post-simulation period were associated with $5,188 in costs. All rotating orthopedic residents at this facility now receive the simulation curriculum tested in this study.	Moderate	None
Barsuk et al., 2009[12]	High-fidelity simulation.	Observational cohort study with historical controls. A total	Tertiary-care urban teaching hospital.	Residents who received the simulation intervention	Not provided	As a result of the study, the hospital began to require that all residents	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
		of 103 internal medicine and emergency medicine second- and third-year residents served as participants; 76 received the simulation intervention, 27 residents received traditional training.		significantly improved their performance on clinical skills pre- to post-intervention for internal jugular central venous catheter (CVC) insertion (pre = 50.6%, post = 93.9%, $p < 0.005$) and subclavian CVC (pre= 48.4%, post = 91.5%, $p < 0.005$). Residents in the simulation group also significantly improved their scores on a written exam (pre = 70.1%, post = 85.3%, $p < 0.005$). A number of quality indicators were collected to assess the effect of simulation on quality indicators related to CVC insertion. Residents who received the simulation intervention reported significantly fewer needle passes (total, $p < 0.005$; internal jugular, $p < .0.005$); arterial punctures (total, $p < 0.005$; internal jugular, $p < .0.005$); and CVC		demonstrate mastery of CVC skills in a simulated environment before performing them independently in the ICU.		

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
				adjustments (total, p = 0.002; internal jugular, p = 0.001); and higher successful CVC insertion rates (total, p = 0.005; internal jugular, p = 0.018). No differences were found between the group that received the simulation intervention and the traditional training when examining pneumothorax rates or assessing the quality of subclavian CVCs.				
Gerolemou et al., 2014[13]	Simulation-based training of critical care nurses in sterile techniques during central vein catheterization. Training took place in a simulation laboratory.	Prospective controlled study with a simulation-based educational intervention. Forty-six critical care nurses received the simulation intervention.	University-affiliated, 450-bed urban teaching hospital with 23 medical, surgical and neurological CCU beds.	Performance of sterilization techniques was scored before and after the simulation intervention. The median score in the pre-simulation period was 7 out of 24. The median score in the post-simulation period was 23 out of 24. These data reflect a significant improvement following the intervention (p < 0.01). The rate of catheter-related bloodstream infection was examined as an	Not provided	Studies have emphasized training physicians in central venous catheterization. The current study demonstrates that nurses had a low level of knowledge of proper sterilization techniques and benefited from the simulation intervention.	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
				outcome in this study. Prior to the simulation intervention, there were 2.61 infections per 1,000 catheter-days (6 catheter infections in 2,297 catheter-days) in the CCU. The average rate of CRBSIs in the CCU was 0.4 per 1000 catheter-days (1 catheter infection in 2,514 catheter-days). Over the course of the next 12 months, an 85% reduction in the average rate of CRBSI was observed.				
Harting et al., 2008	Computer-based simulation involving 2–3 cancer-related pain management cases.	Quasi-experimental, pre-post design. 20 patients admitted with cancer-related pain were in the pre-intervention group and 20 patients admitted with cancer-related pain were in the post-intervention group.	Academic medical center.	Residents in the post-intervention period administered a higher proportion of long-acting oral medications as compared to residents in the pre-intervention period (pre-intervention = 35%, post-intervention = 90%, P < 0.001).	Pain control improved for patients in the post-simulation period. The slope of pain scores was found to have been increasing in the pre-intervention period and decreased significantly in the post-intervention period (P < .01)	The authors note that they had not seen any pain management improvements when they had only provided didactic training with grand rounds.	Moderate to high	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Hebbar et al., 2018[14]	Two-hour simulation workshop where two to three simulations targeting medication administration were conducted in a simulation laboratory. Each simulated scenario was debriefed.	Pre-post design. A total of 1,434 nurses participated in the simulation training over a 7-month period. These included general care nurses, critical care nurses, and emergency department nurses.	Egleston Children's Hospital: 278 beds, 36-bed pediatric ICU, a 25-bed cardiac PICU, with 1,234 nurses. Scottish Rite Children's Hospital: 273 beds, a 34-bed PICU, and 1,206 nurses. Hughes Spalding Children's Hospital: 130 non-critical care beds and 89 nurses.	Following the simulation intervention, average compliance to the medication bundle significantly increased from 51% (month 1) to 84% (month 18, $P < 0.001$). The rate of medication administration events significantly decreased over the course of the simulation study. During the 12-month pre-intervention period, the rate of medication administration events was recorded at 2.5 per month. The rate significantly decreased to 1.4 events per month during the simulation intervention ($P = 0.029$), and further decreased to 0.86 events per month in the 7-month post-intervention period ($P = 0.014$).	Not provided	Overall, there was a 63% reduction in medication administration events from the pre-intervention period to the 18-month post-intervention period. The authors pointed out that although they had trained only 56% of the inpatient and emergency department staff at two of the participating hospitals, rates of medication administration errors have been sustained for 3 years. They suggest this is due to cross-pollination (i.e., those who were trained went on to train others).	Moderate to high	The authors estimated the financial savings of the simulation intervention to be approximately $165,000 to $225,000 (charge savings) with a cost impact of $90,000 to $130,000 per year.

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Mosier et al., 2015[8]	Simulation lab with some didactic training.	Pre- and post-intervention analysis of the airway management program.	Academic referral center with a 201 bed medical ICU staffed by two teaching teams.	The success rate of first-attempt intubations significantly improved in the post-simulation period. Successful first attempts increased from 73.5% in the pre-intervention period to 81.6% in the post-intervention period (P = 0.006). The incidence of desaturation decreased following the simulation-based training curriculum from 25.9% to 16.8%.	Not provided	Not provided	Moderate	None

Author, Year	Description of Patient Safety Practice	Study Design; Sample Size; Patient Population	Setting	Outcomes: Benefits	Outcomes: Harms	Implementation Themes/Findings	Risk of Bias (High, Moderate, Low)	Comments
Wayne et al., 2008[9]	Simulation laboratory.	Retrospective case-control study. Thirty-eight second-year internal medicine residents received simulation-based education curriculum and were compared to 40 third-year residents who received the traditional training curriculum.	Northwestern Memorial Hospital, a tertiary health-care facility.	Second-year residents who received simulation training demonstrated significantly higher compliance with the American Heart Association standards when leading with real advanced cardiac life support events as compared to third-year residents who had received traditional training (simulation group = 68%, traditional group = 44%, $p \leq 0.001$).	No differences were found in patient survival of the ACLS event between the simulation-trained and traditionally trained residents (simulation group = 45%, traditional group = 46.4%). However, there was an increase in the average survival time to death or hospital discharge for patients treated by residents in the simulation-trained group compared to the patients who received care from traditionally trained residents (simulation trained residents = 194.7, traditionally trained residents = 107.1, $p = 0.11$).	The short simulation intervention (1-hour baseline assessment, four 2-hour teaching sessions, 1-hour post-assessment) improved procedural skills and quality of patient care.	Moderate	None

Table B.78: Cross-Cutting Patient Safety Topics/Practices, Education and Training Through Simulation—Systematic Reviews and Meta-Analyses

Note: Full references are available in the Section 17.7 reference list.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings
Griswold-Thoeodorson et al., 2015[4]	Simulation-based mastery learning.	Twelve out of 14 studies were conducted with postgraduate trainees, one study was conducted with medical students, and one introduced simulation to staff physicians.	Eight studies demonstrated a positive impact on procedural performance. Three studies provided evidence of improved success rate, while four studies reported that simulation training resulted in decreased time to complete the procedures. Two studies demonstrated a reduction in patient discomfort. Four studies reported a decrease in complication rates and four provided evidence of cost savings.	Taking a simulation-based mastery approach may take more time than traditional classroom learning. However, the amount of time can be justified if trainees gain greater competence without risk to patients.
Madenci et al., 2014[7]	Simulation training to improve central venous catheter manipulation.	Medical trainees.	Based on the analyses of five studies, the proportion of overall successful CVC insertion was significantly higher for those who received simulation training ($P < 0.01$). Participants who received simulation also required significantly fewer attempts ($P < 0.01$). There were no differences in adverse events between the participants who received simulation training (3.8%) compared to those who received traditional instruction (4.9%, $P = 0.15$).	This meta-analysis assessed the impact of simulation on real patient outcomes. Although there were fewer adverse events for the simulation group, it did not reach statistical significance.
McGaghie et al., 2011[6]	Simulation-based medical education.	Medical residents	Studies of central venous catheter insertion reported positive benefits of simulation-based medical education programs, including: significantly fewer needle passes, catheter adjustments, arterial punctures; higher success rates; and fewer catheter-related bloodstream infections as compared to traditionally trained residents. Research conducted in ophthalmology demonstrated that residents enrolled in the simulation-based curriculum developed better surgical skills and a significant reduction in sentinel complication rates.	Not discussed.

Author, Year	Description of Patient Safety Practice	Setting/s, Population/s	Summary of Systematic Review Findings	Implementation Themes/Findings
Schmidt et al., 2013[5]	Simulation to improve diagnostic procedures, surgical procedures, central venous catheterization.	Hospital setting, tertiary care facilities, trauma centers, and multispecialty medical groups. Participants were largely residents and fellows.	The studies that provided simulation to improve diagnostic procedures reported mixed results on patient discomfort, and some evidence that procedure time decreased and success rates were higher following simulation training. Studies of surgical procedures demonstrated improvements following simulation training, including: increased accuracy, fewer errors, lower rate of sentinel complications, and faster procedures. Studies of central venous catheterization reported that participants who received simulation required fewer needle passes and reduced pneumothoraxes, and fewer catheter-related bloodstream infections, but mixed results were reported on other major complications and patient safety events.	The development of realistic exercises (high in cognitive fidelity) and debriefing are believed to be critical to simulation training. The costs associated with simulation training vary widely depending on the type of exercise, as well as the equipment and personnel needed.

Appendix C. Search Terms

Table C.1: Diagnostic Error Search Terms

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Clinical Decision Support	(((MH "Diagnostic Errors" OR "Delayed Diagnosis") OR (AB "Diagnostic Errors" OR "Error(s), Diagnostic" OR Misdiagnosis OR Misdiagnoses OR "Delayed Diagnosis" OR "Missed Diagnosis")) AND ((MH "Decision Support Systems, Clinical" OR ("Medical Informatics Applications" AND "Information Systems") OR "Reminder Systems" OR "Decision Making, Computer-Assisted" OR "Decision Support Techniques" OR "Diagnosis, Computer-Assisted" OR "Diagnosis, Differential" OR "Artificial Intelligence" AND "Machine Learning" OR "Decision Making, Organizational") OR AB (“Clinical Decision Support” OR (“Medical Informatics Applications” AND “Information Systems”) OR "Decision Support Systems, Clinical" OR "Reminder Systems" OR “Decision Making, Computer-Assisted” OR "Diagnosis, Computer-Assisted" OR “Decision Support Techniques" OR “Artificial Intelligence” OR “IBM Watson” OR “Machine Learning” OR “Decision Support Techniques” OR “Decision Making, Organizational” OR “Differential Diagnosis Generation” OR "Diagnostic Algorithms" OR "Clinical Algorithms" OR "Test Selection Support")))	(((MH "Diagnostic Errors" OR "Delayed Diagnosis") OR (AB "Diagnostic Errors" OR "Error(s), Diagnostic" OR Misdiagnosis OR Misdiagnoses OR "Delayed Diagnosis" OR "Missed Diagnosis")) AND ((MH "Decision Support Systems, Clinical" OR ("Medical Informatics Applications" AND "Information Systems") OR "Reminder Systems" OR "Decision Making, Computer-Assisted" OR "Decision Support Techniques" OR "Diagnosis, Computer-Assisted" OR "Diagnosis, Differential" OR "Artificial Intelligence" AND "Machine Learning" OR "Decision Making, Organizational") OR (AB “Clinical Decision Support” OR (“Medical Informatics Applications” AND “Information Systems”) OR "Decision Support Systems, Clinical" OR "Reminder Systems" OR “Decision Making, Computer-Assisted” OR "Diagnosis, Computer-Assisted" OR “Decision Support Techniques" OR “Artificial Intelligence” OR “IBM Watson” OR “Machine Learning” OR “Decision Support Techniques” OR “Decision Making, Organizational” OR “Differential Diagnosis Generation” OR "Diagnostic Algorithms" OR "Clinical Algorithms" OR "Test Selection Support")))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Performance Review and Feedback	(((MH "Diagnostic Errors/PC" OR "Delayed Diagnosis/PC") OR (AB "Diagnostic Error*" OR "Error*, Diagnostic" OR Misdiagnosis OR Misdiagnoses OR "Delayed Diagnosis" OR "Missed Diagnosis" OR "Diagnostic Error* Prevention" OR "Diagnostic Error* Control")) AND ((MH "Peer Review" OR "Peer Review, Health Care/ST" OR "Quality Assurance, Health Care/ST" OR "Feedback") OR (AB "Performance Review" OR "Performance Feedback" OR "Clinical Correlation" OR "Peer Review" OR "Feedback" OR "Quality Assurance" OR "Standards" OR "Human Performance")))	(((MH "Diagnostic Errors/PC" OR "Delayed Diagnosis/PC") OR (AB "Diagnostic Error*" OR "Error*, Diagnostic" OR Misdiagnosis OR Misdiagnoses OR "Delayed Diagnosis" OR "Missed Diagnosis" OR "Diagnostic Error* Prevention" OR "Diagnostic Error* Control")) AND ((MH "Peer Review" OR "Peer Review, Health Care/ST" OR "Quality Assurance, Health Care/ST" OR "Feedback") OR (AB "Performance Review" OR "Performance Feedback" OR "Clinical Correlation" OR "Peer Review" OR "Feedback" OR "Quality Assurance" OR "Standards" OR "Human Performance")))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Result Notification System	(((MH "Diagnostic Errors" OR "Delayed Diagnosis") OR (AB "Delayed Diagnosis" OR "Diagnoses, Delayed" OR "Diagnosis, Delayed" OR “Errors, Diagnostic” OR “Error, Diagnostic” OR “Missed Diagnosis” OR Misdiagnosis OR Missed Diagnoses OR Misdiagnoses)) AND (((MH Communication OR "Reminder System" OR "Hospital Communication Systems") OR (AB "Reminder System" OR "System, Reminder" OR "Systems, Reminder" OR "Systems, Communication Hospital" OR "Communication Hospital System" OR "Communication Hospital Systems" OR "Hospital System, Communication" OR "Hospital Systems, Communication" OR "System, Communication Hospital" OR "Hospital Communication System" OR "System, Hospital Communication" OR "Communication System, Hospital" OR "Systems, Hospital Communication" OR "Systems, Hospital Communication" OR "Patient Notification" OR "Automated System" OR "Alert Notification" OR "Critical Test Result" OR "Provider Communication"))	(((MH "Diagnostic Errors" OR "Delayed Diagnosis") OR (AB "Delayed Diagnosis" OR "Diagnoses, Delayed" OR "Diagnosis, Delayed" OR “Errors, Diagnostic” OR “Error, Diagnostic” OR “Missed Diagnosis” OR Misdiagnosis OR Missed Diagnoses OR Misdiagnoses)) AND ((MH Communication OR "Reminder System" OR "Hospital Communication Systems") OR (AB "Reminder System" OR "System, Reminder" OR "Systems, Reminder" OR "Systems, Communication Hospital" OR "Communication Hospital System" OR "Communication Hospital Systems" OR "Hospital System, Communication" OR "Hospital Systems, Communication" OR "System, Communication Hospital" OR "Hospital Communication System" OR "System, Hospital Communication" OR "Communication System, Hospital" OR "Systems, Hospital Communication" OR "Systems, Hospital Communication" OR "Patient Notification" OR "Automated System" OR "Alert Notification" OR "Critical Test Result" OR "Provider Communication")))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Staff Training and Education	(((MH "Diagnostic Errors" OR "Delayed Diagnosis") OR (AB "Diagnostic Errors" OR "Error(s), Diagnostic" OR Misdiagnosis OR Misdiagnoses OR "Delayed Diagnosis" OR "Missed Diagnosis")) AND ((MH "Education, Professional" OR "Simulation Training" OR "Patient Simulation") OR AB (“Education, Professional” OR Training OR “Structured Practice” OR Simulation Training” OR “Patient Simulation”)) AND ((MH Physicians OR "Students, Medical" OR Nursing) OR (AB Physicians OR "Resident Physicians" OR "Medical Students" OR Nursing OR "Healthcare Staff")))	(((MH "Diagnostic Errors" OR "Delayed Diagnosis") OR (AB "Diagnostic Errors" OR "Error(s), Diagnostic" OR Misdiagnosis OR Misdiagnoses OR "Delayed Diagnosis" OR "Missed Diagnosis")) AND (((MH "Education, Professional" OR "Simulation Training" OR "Patient Simulation") OR (AB “Education, Professional” OR Training OR “Structured Practice” OR Simulation Training” OR “Patient Simulation”)) AND ((MH Physicians OR "Students, Medical" OR Nursing) OR (AB Physicians" OR "Resident Physicians" OR "Medical Students" OR Nursing OR "Healthcare Staff")))

Table C.2: Failure To Rescue Search Terms

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Rapid Response Systems	(((MH "Failure to Rescue, Health Care") OR (AB "Failure-to-Rescue" OR "Failure to Rescue" OR "Patient Deterioration" OR "Patient Decompensation" OR "Death After a Treatable Complication")) AND ((MH "Hospital Rapid Response Team") OR (AB "Rapid Response System" OR "Rapid Response Team" OR "Rapid Response" OR "Hospital Medical Emergency Team" OR "Medical Emergency Team, Hospital")))	(((MH "Failure to Rescue, Health Care") OR (AB "Failure-to-Rescue" OR "Failure to Rescue" OR "Patient Deterioration" OR "Patient Decompensation" OR "Death After a Treatable Complication")) AND ((MH "Hospital Rapid Response Team") OR (AB "Rapid Response System" OR "Rapid Response Team" OR "Rapid Response" OR "Hospital Medical Emergency Team" OR "Medical Emergency Team, Hospital")))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Patient Response Systems	(((MH "Failure to Rescue, Health Care") OR (AB "Failure-to-Rescue" OR "Failure to Rescue" OR "Patient Deterioration" OR "Patient Decompensation" OR "Death After a Treatable Complication")) AND ((MH "Monitoring, Physiologic" OR "Hemodynamic Monitoring" OR "Monitoring, Ambulatory" OR ("Telemetry" AND "Remote Sensing Technology")) OR (AB "Monitoring, Physiologic" OR "Hemodynamic Monitoring" OR "Monitoring, Ambulatory" OR "Intraoperative Monitoring" OR (Telemetry AND "Remote Sensing Technology") OR "Physiologic Monitoring" OR "Patient Monitoring")))	(((MH "Failure to Rescue, Health Care") OR (AB "Failure-to-Rescue" OR "Failure to Rescue" OR "Patient Deterioration" OR "Patient Decompensation" OR "Death After a Treatable Complication")) AND ((MH "Monitoring, Physiologic" OR "Hemodynamic Monitoring" OR "Monitoring, Ambulatory" OR (Telemetry AND "Remote Sensing Technology")) OR (AB "Monitoring, Physiologic" OR "Hemodynamic Monitoring" OR "Monitoring, Ambulatory" OR "Intraoperative Monitoring" OR (Telemetry AND "Remote Sensing Technology") OR "Physiologic Monitoring" OR "Patient Monitoring")))

Table C.3: Sepsis Recognition Search Terms

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Screening Tools	(((MH Sepsis/DI/PC) OR (AB "Blood Poisoning" OR "Poisoning, Blood" OR "Pyaemia" OR "Pyemia" OR "Pyohemia" OR "Septicemia" OR "Severe Sepsis" OR "Septic Shock" OR ("Systemic Inflammatory Response Syndrome" AND Infection)) AND ((MH "Mass Screening") OR (AB "Mass Screening" OR "Decision Support Techniques" OR "Screening" OR "Screening tool" OR "Screening algorithm" OR "Algorithm" OR "Triage Tool" OR "Early Warning Score" OR "Early Detection" OR "Early Alert" OR "Pre-Hospital Screening" OR "Risk Assessment")))	(((MH Sepsis/DI/PC OR "Shock, Septic" OR "Systemic Inflammatory Response Syndrome") OR (AB "Blood Poisoning" OR "Poisoning, Blood" OR "Pyaemia" OR "Pyemia" OR "Pyohemia" OR "Septicemia" OR "Severe Sepsis" OR "Septic Shock" OR ("Systemic Inflammatory Response Syndrome" AND Infection)) AND ((MH "Mass Screening" OR "Decision Support Techniques") OR (AB "Mass Screening" OR "Decision Support Techniques" OR "Screening" OR "Screening tool" OR "Screening algorithm" OR "Algorithm" OR "Triage Tool" OR "Early Warning Score" OR "Early Detection" OR "Early Alert" OR "Pre-Hospital Screening" OR "Risk Assessment")))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Surveillance	(((MH (Sepsis/DI/PC) OR (AB "Blood Poisoning" OR "Poisoning, Blood" OR "Pyaemia" OR "Pyemia" OR "Pyohemia" OR "Septicemia" OR "Severe Sepsis" OR "Septic Shock" OR ("Systemic Inflammatory Response Syndrome" AND Infection))) AND (AB "Surveillance" OR "Monitoring and Surveillance" OR "Epidemiologic Surveillance" OR "Infectious Diseases Surveillance" OR "Ongoing Surveillance" OR Monitoring" OR "Routine Screening" OR "Regular Screening"))	(((MH (Sepsis/DI/PC) OR (AB "Blood Poisoning" OR "Poisoning, Blood" OR "Pyaemia" OR "Pyemia" OR "Pyohemia" OR "Septicemia" OR "Severe Sepsis" OR "Septic Shock" OR ("Systemic Inflammatory Response Syndrome" AND Infection))) AND (AB "Surveillance" OR "Monitoring and Surveillance" OR "Epidemiologic Surveillance" OR "Infectious Diseases Surveillance" OR "Ongoing Surveillance" OR Monitoring" OR "Routine Screening" OR "Regular Screening"))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Performance Review	(((MH Sepsis/DI/PC) OR (AB "Blood Poisoning" OR "Poisoning, Blood" OR "Pyaemia" OR "Pyemia" OR "Pyohemia" OR "Septicemia" OR "Severe Sepsis" OR "Septic Shock" OR ("Systemic Inflammatory Response Syndrome" AND Infection))) AND (AB "Performance Review" OR "Performance Feedback" OR "Root Cause Analysis" OR "Peer Review" OR "Audit" OR "Audit and Feedback"))	(((MH Sepsis/DI/PC) OR (AB "Blood Poisoning" OR "Poisoning, Blood" OR "Pyaemia" OR "Pyemia" OR "Pyohemia" OR "Septicemia" OR "Severe Sepsis" OR "Septic Shock" OR ("Systemic Inflammatory Response Syndrome" AND Infection))) AND (AB "Performance Review" OR "Performance Feedback" OR "Root Cause Analysis" OR "Peer Review" OR "Audit" OR "Audit and Feedback"))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Antibiotics	(((MH Sepsis/DI/PC) OR (AB "Blood Poisoning" OR "Poisoning, Blood" OR "Pyaemia" OR "Pyemia" OR "Pyohemia" OR "Septicemia" OR "Severe Sepsis" OR "Septic Shock" OR ("Systemic Inflammatory Response Syndrome" AND Infection))) AND (AB "Readily Available Antibiotics" OR "Accessible Antibiotic" OR "Antibiotic Access" OR "Available Antibiotic" OR "Antibiotic Availability"))	(((MH Sepsis/DI/PC) OR (AB "Blood Poisoning" OR "Poisoning, Blood" OR "Pyaemia" OR "Pyemia" OR "Pyohemia" OR "Septicemia" OR "Severe Sepsis" OR "Septic Shock" OR ("Systemic Inflammatory Response Syndrome" AND Infection))) AND AB ("Readily Available Antibiotics" OR "Accessible Antibiotic" OR "Antibiotic Access" OR "Available Antibiotic" OR "Antibiotic Availability"))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Performance Improvement	(((MH Sepsis/DI/PC) OR (AB "Blood Poisoning" OR "Poisoning, Blood" OR "Pyaemia" OR "Pyemia" OR "Pyohemia" OR "Septicemia" OR "Severe Sepsis" OR "Septic Shock" OR ("Systemic Inflammatory Response Syndrome" AND Infection))) AND (AB "Performance Improvement Programs" OR "Performance Improvement" OR "Performance Enhancement" OR "Quality Improvement" OR "Compliance" OR "Compliance Improvement" OR "Guideline Compliance"))	(((MH Sepsis/DI/PC) OR (AB "Blood Poisoning" OR "Poisoning, Blood" OR "Pyaemia" OR "Pyemia" OR "Pyohemia" OR "Septicemia" OR "Severe Sepsis" OR "Septic Shock" OR ("Systemic Inflammatory Response Syndrome" AND Infection))) AND (AB "Performance Improvement Programs" OR "Performance Improvement" OR "Performance Enhancement" OR "Quality Improvement" OR "Compliance" OR "Compliance Improvement" OR "Guideline Compliance"))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search Limiters: 2008-Present Language: English Only Limit to Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies	Clinical Decision	(((MH Sepsis/DI/PC) OR (AB "Blood Poisoning" OR "Poisoning, Blood" OR "Pyaemia" OR "Pyemia" OR "Pyohemia" OR "Septicemia" OR "Severe Sepsis" OR "Septic Shock" OR ("Systemic Inflammatory Response Syndrome" AND Infection))) AND ((MH "Decision Support Systems, Clinical" OR "Clinical Decision Making") OR (AB "Clinical Decision Support" OR "Medical Decision Making" OR "Decision Support Techniques" OR "Medical Order Entry Systems" OR "Computerized Physician Order Entry" OR "Alert Systems, Medication" OR "CPOE" OR "Computerized Physician Order Entry" OR "Computerized Physician Order Entry System" OR "Computerized Provider Order Entry" OR "Computerized Provider Order Entry System" OR "Medication Alert Systems" OR "Order Entry Systems, Medical")))	(((MH Sepsis/DI/PC) OR (AB "Blood Poisoning" OR "Poisoning, Blood" OR "Pyaemia" OR "Pyemia" OR "Pyohemia" OR "Septicemia" OR "Severe Sepsis" OR "Septic Shock" OR ("Systemic Inflammatory Response Syndrome" AND Infection))) AND ((MH "Decision Support Systems, Clinical" OR "Clinical Decision Making") OR (AB "Clinical Decision Support" OR "Medical Decision Making" OR "Decision Support Techniques" OR "Medical Order Entry Systems" OR "Computerized Physician Order Entry" OR "Alert Systems, Medication" OR "CPOE" OR "Computerized Physician Order Entry" OR "Computerized Physician Order Entry System" OR "Computerized Provider Order Entry" OR "Computerized Provider Order Entry System" OR "Medication Alert Systems" OR "Order Entry Systems, Medical")))

Table C.4: *Clostridioides difficile* Search Terms

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Antimicrobial Stewardship	(((MH "Clostridium Difficile" OR "Clostridium Infections" OR "Enterocolitis, Pseudomembranous" OR "Clostridium Infections/PC") OR AB ("Clostridium Difficile Infection" OR "Infections, Clostridium" OR "Antibiotic-Associated Colitis" OR "Clostridium Enterocolitis" OR "Colitis, Pseudomembranous" OR "Pseudomembranous Colitis" OR "Pseudomembranous Enteritis" OR "Pseudomembranous Enterocolitis" OR ("Clostridium Difficile" AND Colonization)) AND ((MH "Antimicrobial Stewardship" OR MH "Antibiotic Stewardship") OR (AB "Antibiotic Prescribing Practices")) AND ((MH Hospitals OR Inpatients OR Outpatients OR “Ambulatory Care Facilities OR "Practitioner's Office” OR “Long Term Care” OR “Palliative Care” OR “Subacute Care” OR “Rehabilitation Centers” OR “Residential Facilities” OR “Transitional Care” OR “Primary Health Care” OR “Home Health Care” OR “Nursing Homes” OR “Surgicenters”) OR AB ("Hospital" OR "Inpatient" OR "Ambulatory Care" OR "Ambulatory Care Facilities" OR "Physicians' Offices" OR "Long-Term Care" OR "Long-Term Care Facilities" OR "Palliative Care" OR "Subacute Care" OR "Rehabilitation Centers" OR "Residential Facilities" OR "Transitional Care" OR "Ambulatory Surgery Center" OR "Primary Care" OR "Specialty Care" OR "Home Health")))	(((MH "Clostridium Difficile" OR "Clostridium Infections" OR "Enterocolitis, Pseudomembranous" OR "Clostridium Infections/PC") OR (AB "Clostridium Difficile Infection" OR "Infections, Clostridium" OR "Antibiotic-Associated Colitis" OR "Clostridium Enterocolitis" OR "Colitis, Pseudomembranous" OR "Pseudomembranous Colitis" OR "Pseudomembranous Enteritis" OR "Pseudomembranous Enterocolitis" OR ("Clostridium Difficile" AND Colonization)) AND ((MH "Antimicrobial Stewardship" OR MH "Antibiotic Stewardship") OR (AB "Antibiotic Prescribing Practices")) AND ((MH Hospitals OR Inpatients OR Outpatients OR “Ambulatory Care Facilities OR "Practitioner's Office” OR “Long Term Care” OR “Palliative Care” OR “Subacute Care” OR “Rehabilitation Centers” OR “Residential Facilities” OR “Transitional Care” OR “Primary Health Care” OR “Home Health Care” OR “Nursing Homes” OR “Surgicenters”) OR AB ("Hospital" OR "Inpatient" OR "Ambulatory Care" OR "Ambulatory Care Facilities" OR "Physicians' Offices" OR "Long-Term Care" OR "Long-Term Care Facilities" OR "Palliative Care" OR "Subacute Care" OR "Rehabilitation Centers" OR "Residential Facilities" OR "Transitional Care" OR "Ambulatory Surgery Center" OR "Primary Care" OR "Specialty Care" OR "Home Health")))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Testing	(((MH "Clostridium Difficile" OR "Clostridium Infections" OR "Enterocolitis, Pseudomembranous") OR (AB "Clostridium Difficile Infection" OR "Infections, Clostridium" OR "Antibiotic-Associated Colitis" OR "Clostridium Enterocolitis" OR "Colitis, Pseudomembranous" OR "Pseudomembranous Colitis" OR "Pseudomembranous Enteritis" OR "Pseudomembranous Enterocolitis" OR ("Clostridium Difficile" AND Colonization)) AND (AB "Diagnostic Test" OR "Testing Algorithms" OR Diagnosis OR "Stool Sampling" OR Technique OR Detection OR "Clinical Laboratory Tests" OR "Laboratory Diagnosis" OR "Clinical Laboratory Techniques" OR "Screening" OR "Diagnostic Testing" OR "Identification" OR "Recognition" OR "Rapid Identification" OR "Rapid Diagnostics"))	(((MH "Clostridium Difficile" OR "Clostridium Infections" OR "Enterocolitis, Pseudomembranous") OR (AB "Clostridium Difficile Infection" OR "Infections, Clostridium" OR "Antibiotic-Associated Colitis" OR "Clostridium Enterocolitis" OR "Colitis, Pseudomembranous" OR "Pseudomembranous Colitis" OR "Pseudomembranous Enteritis" OR "Pseudomembranous Enterocolitis" OR ("Clostridium Difficile" AND Colonization)) AND (AB "Diagnostic Test" OR "Testing Algorithms" OR Diagnosis OR "Stool Sampling" OR Technique OR Detection OR "Clinical Laboratory Tests" OR "Laboratory Diagnosis" OR "Clinical Laboratory Techniques" OR "Screening" OR "Diagnostic Testing" OR "Identification" OR "Recognition" OR "Rapid Identification" OR "Rapid Diagnostics"))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Surveillance	(((MH "Clostridium Difficile" OR "Clostridium Infections" OR "Enterocolitis, Pseudomembranous") OR (AB "Clostridium Difficile Infection" OR "Infections, Clostridium" OR "Antibiotic-Associated Colitis" OR "Clostridium Enterocolitis" OR "Colitis, Pseudomembranous" OR "Pseudomembranous Colitis" OR "Pseudomembranous Enteritis" OR "Pseudomembranous Enterocolitis" OR ("Clostridium Difficile" AND Colonization)) AND ((MH "Mass Screening") OR (AB Surveillance OR "Monitoring and Surveillance" OR "Epidemiologic Surveillance" OR "Infectious Diseases Surveillance" OR Screening OR "Diagnostic Tests, Routine")))	(((MH "Clostridium Difficile" OR "Clostridium Infections" OR "Enterocolitis, Pseudomembranous") OR (AB "Clostridium Difficile Infection" OR "Infections, Clostridium" OR "Antibiotic-Associated Colitis" OR "Clostridium Enterocolitis" OR "Colitis, Pseudomembranous" OR "Pseudomembranous Colitis" OR "Pseudomembranous Enteritis" OR "Pseudomembranous Enterocolitis" OR ("Clostridium Difficile" AND Colonization)) AND ((MH "Mass Screening") OR (AB Surveillance OR "Monitoring and Surveillance" OR "Epidemiologic Surveillance" OR "Infectious Diseases Surveillance" OR Screening OR "Diagnostic Tests, Routine")))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Hand Hygiene	(((MH "Clostridium Difficile" OR "Clostridium Infections" OR "Enterocolitis, Pseudomembranous") AND (AB "Clostridium Difficile Infection" OR "Infections, Clostridium" OR "Antibiotic-Associated Colitis" OR "Clostridium Enterocolitis" OR "Colitis, Pseudomembranous" OR "Pseudomembranous Colitis" OR "Pseudomembranous Enteritis" OR "Pseudomembranous Enterocolitis" OR ("Clostridium Difficile" AND Colonization)) AND ((MH “Hand Hygiene” OR MH “Hand Disinfection”) OR (AB Handwashing OR “Hand Washing” OR “Hand Sanitization” OR “Hand Hygiene” OR “Hand Disinfection”)))	(((MH "Clostridium Difficile" OR "Clostridium Infections" OR "Enterocolitis, Pseudomembranous") OR (AB "Clostridium Difficile Infection" OR "Infections, Clostridium" OR "Antibiotic-Associated Colitis" OR "Clostridium Enterocolitis" OR "Colitis, Pseudomembranous" OR "Pseudomembranous Colitis" OR "Pseudomembranous Enteritis" OR "Pseudomembranous Enterocolitis" OR ("Clostridium Difficile" AND Colonization)) AND ((MH “Hand Hygiene” OR MH “Hand Disinfection”) OR (AB Handwashing OR “Hand Washing” OR “Hand Sanitization” OR “Hand Hygiene” OR “Hand Disinfection”)))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Environmental Cleaning and Decontamination	(((MH "Clostridium Difficile" OR "Clostridium Infections" OR "Enterocolitis, Pseudomembranous" OR "Clostridium Infections/PC") OR (AB "Clostridium Difficile Infection" OR "Infections, Clostridium" OR "Antibiotic-Associated Colitis" OR "Clostridium Enterocolitis" OR "Colitis, Pseudomembranous" OR "Pseudomembranous Colitis" OR "Pseudomembranous Enteritis" OR "Pseudomembranous Enterocolitis" OR ("Clostridium Difficile" AND Colonization)) AND ((MH "Disinfection/I/M/OA/S/U" OR "Decontamination/I/M/S") OR (AB "ATP Bioluminescence" OR "Pulsed UV Treatment" OR "Ultraviolet light" OR "UV Light" OR "No-Touch Decontamination")))	(((MH "Clostridium Difficile" OR "Clostridium Infections" OR "Enterocolitis, Pseudomembranous" OR "Clostridium Infections/PC") OR (AB "Clostridium Difficile Infection" OR "Infections, Clostridium" OR "Antibiotic-Associated Colitis" OR "Clostridium Enterocolitis" OR "Colitis, Pseudomembranous" OR "Pseudomembranous Colitis" OR "Pseudomembranous Enteritis" OR "Pseudomembranous Enterocolitis" OR ("Clostridium Difficile" AND Colonization)) AND ((MH "Disinfection/I/M/OA/S/U" OR "Decontamination/I/M/S") OR (AB "ATP Bioluminescence" OR "Pulsed UV Treatment" OR "Ultraviolet Light" OR "UV Light" OR "No-Touch Decontamination")))

Table C.5: Multidrug-Resistant Organisms Search Terms

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Hand Hygiene	(((MH “Drug Resistance, Microbial” OR MH “Drug Resistance, Multiple”) OR (AB “Microbial Drug Resistance” OR “Bacterial Drug Resistance”)) AND ((MH Handwashing) OR (AB Handwashing OR “Hand Washing” OR “Hand Sanitization” OR “Hand Hygiene” OR “Hand Disinfection”)))	(((MH “Drug Resistance, Microbial” OR MH “Drug Resistance, Multiple, Bacterial”) OR (AB “Microbial Drug Resistance” OR “Bacterial Drug Resistance”)) AND ((MH “Hand Hygiene” OR MH “Hand Disinfection”) OR (AB Handwashing OR “Hand Washing” OR “Hand Sanitization” OR “Hand Hygiene” OR “Hand Disinfection”)))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Surveillance	(((MH “Infection Control”) OR (AB “Infection Control” OR “Infection Prevention”)) AND ((MH “Drug Resistance, Microbial” OR MH “Drug Resistance, Multiple”) OR (AB “Microbial Drug Resistance” OR “Bacterial Drug Resistance”)) AND (AB “Monitoring” OR “Surveillance” OR "Monitoring and Surveillance")	((MH “Infection Control”) OR (AB “Infection Control” OR “Infection Prevention”)) AND ((MH “Drug Resistance, Microbial” OR “Drug Resistance, Multiple, Bacterial”) OR (AB “Microbial Drug Resistance” OR “Bacterial Drug Resistance”)) AND (AB Monitoring OR Surveillance OR "Monitoring and Surveillance")))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Minimize Use of Devices	(((MH “Infection Control”) OR (AB “Infection Control” OR “Infection Prevention”)) AND ((MH “Drug Resistance, Microbial” OR MH “Drug Resistance, Multiple”) OR (AB “Microbial Drug Resistance” OR “Bacterial Drug Resistance”)) AND ((MH Catheters or MH “Catheter-Related Infections”) OR (AB Catheter* OR “Catheter Related Infection*” OR “Catheter-Related Infection*” OR “Endotracheal Tubes” OR “Cannula*”)))	(((MH “Infection Control”) OR (AB “Infection Control” OR “Infection Prevention”)) AND ((MH “Drug Resistance, Microbial” OR MH “Drug Resistance, Multiple”) OR (AB “Microbial Drug Resistance” OR “Bacterial Drug Resistance”)) AND ((MH Catheters or MH “Catheter-Related Infections”) OR (AB Catheter* OR “Catheter Related Infection*” OR “Catheter-Related Infection*” OR “Endotracheal Tubes” OR Cannula*)))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Chlorhexidine Bathing	((MH “Drug Resistance, Microbial” OR MH “Drug Resistance, Multiple”) OR (AB “Microbial Drug Resistance” OR “Bacterial Drug Resistance”)) AND ((MH Chlorhexidine) OR AB (Chlorhexidine AND Bathing OR Bath*)))	(((MH “Drug Resistance, Microbial” OR MH “Drug Resistance, Multiple”) OR (AB “Microbial Drug Resistance” OR “Bacterial Drug Resistance”)) AND ((MH Chlorhexidine) OR (AB Chlorhexidine AND Bathing OR Bath*)))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Communication of MDRO Status	(((MH “Drug Resistance, Microbial” OR MH “Drug Resistance, Multiple”) OR (AB “Microbial Drug Resistance” OR “Bacterial Drug Resistance”)) AND ((MH “Communication”) OR (AB “Information Sharing” “Information Dissemination” OR “Communication”)))	(((MH “Drug Resistance, Microbial” OR MH “Drug Resistance, Multiple, Bacterial”) OR (AB “Microbial Drug Resistance” OR “Bacterial Drug Resistance”)) AND ((MH “Information Dissemination" OR MH “Communication”) OR (AB “Information Sharing” “Information Dissemination” OR “Communication”)))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Environmental Cleaning and Disinfection	(((MH “Drug Resistance, Microbial" OR MH “Drug Resistance, Multiple, Bacterial”) OR (AB “Microbial Drug Resistance” OR “Bacterial Drug Resistance”)) AND ((MH “Disinfection/Methods” OR MH “Environmental Monitoring”) OR (AB “Environmental Cleaning” OR “Environmental Monitoring” OR “Environmental Disinfection”)))	(((MH “Drug Resistance, Microbial" OR MH “Drug Resistance, Multiple, Bacterial”) OR (AB “Microbial Drug Resistance” OR “Bacterial Drug Resistance”)) AND ((MH “Disinfection/Methods” OR MH “Environmental Monitoring”) OR (AB “Environmental Cleaning” OR “Environmental Monitoring” OR “Environmental Disinfection”)))

Table C.6: Carbapenem-Resistant *Enterobacteriaceae* Search Terms

Methods	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	CRE: Transmission-based Precautions: Contact Precautions, Patient Isolation, Dedicated Staff	((MH "Patient Isolation") OR (AB "Contact Precautions" OR "Contact Precaution" OR "Patient Isolation" OR "Transmission-Based Precaution*" OR "Transmission Based Precaution*" OR "Dedicated Staff")) AND ((MH "Carbapenem-Resistant Enterobacteriaceae") OR (AB "Carbapenem-Resistant Enterobacteriaceae")))	(((MH "Patient Isolation") OR (AB "Contact Precautions" OR "Contact Precaution" OR "Patient Isolation" OR "Transmission-Based Precaution*" OR "Transmission Based Precaution*" OR "Dedicated Staff")) AND ((MH "Carbapenem-Resistant Enterobacteriaceae") OR (AB "Carbapenem-Resistant Enterobacteriaceae")))

Table C.7: Harms Due to Anticoagulants Search Terms

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Single Provider	(((MH "Anticoagulants") OR (AB Anticoagulant*)) AND ((MH Nurses OR Pharmacists OR "Physician Assistants" OR "Nurse Practitioners") OR (AB Nurse OR Pharmacist OR "Physician Assistant*" OR "Nurse Practitioner*")) AND (AB “Warfarin Clinic” or “Anticoagulation Clinic” or “Coumadin Clinic") AND ((MH Hemorrhage) OR (AB Bleeding OR Hemorrhage OR Haemorrhage)) AND ((MH "Patient Safety") OR (AB "Patient Safety" OR "Safety Management")))	(((MH "Anticoagulants") OR (AB Anticoagulant*)) AND ((MH Nurses OR Pharmacists OR "Physician Assistants" OR "Nurse Practitioners") OR (AB Nurse OR Pharmacist OR "Physician Assistant*" OR "Nurse Practitioner*")) AND (AB “Warfarin Clinic” or “Anticoagulation Clinic” or "Coumadin Clinic”) AND ((MH Hemorrhage) OR (AB Bleeding OR Hemorrhage OR Haemorrhage)) AND ((MH "Patient Safety" OR "Safety Management") OR (AB "Patient Safety" OR "Safety Management")))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Nomograms	(((MH "Dabigatran Etexilate" OR Bivalirudin OR "Argatroban") OR (AB "Thrombin Inhibitors" OR Dabigatran OR Bivalirudin OR Argatroban)) AND ((MH Rivaroxaban OR "Fondaparinux Sodium") OR (AB "Factor Xa Inhibitors" OR Rivaroxaban OR Apixaban OR Edoxaban OR Fondaparinux)) AND (AB "New Oral Anticoagulants") AND ((MH "Medical Orders" OR Protocols OR Algorithms) OR (AB Protocol* OR "Medication Orders" OR "Order Sets" OR Algorithm* OR "Dosing Nomograms" OR Nomograms)) AND ((MH Hemorrhage) OR (AB Bleeding OR Hemorrhage OR Haemorrhage)) AND ((MH "Patient Safety") OR (AB "Patient Safety" OR "Safety Management")))	(((MH Dabigatran) OR (AB "Thrombin Inhibitors" OR Dabigatran OR Bivalirudin OR Argatroban)) AND ((MH "Factor Xa Inhibitors" OR Rivaroxaban OR Fondaparinux) OR (AB "Factor Xa Inhibitors" OR Rivaroxaban OR Apixaban OR Edoxaban OR Fondaparinux)) AND (AB "New Oral Anticoagulants") AND ((MH "Medication Order Entry Systems" OR Algorithms OR Nomograms) OR (AB Protocols OR "Medication Orders" OR "Order Sets" OR Algorithm* OR "Dosing Nomograms" OR Nomograms)) AND ((MH Hemorrhage) OR (AB Bleeding OR Hemorrhage OR Haemorrhage)) AND ((MH "Patient Safety" OR MH "Safety Management") OR (AB "Patient Safety" OR "Safety Management")))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Medication Reconciliation and Handoff	(((MH Anticoagulants) OR (AB Anticoagulant*)) AND ((MH "Medication Reconciliation") OR (AB "Medication Reconciliation")) AND ((MH "Patient Discharge" OR "Patient Handoff") OR (AB “Discharge Planning” OR "Patient Discharge" OR "Patient Transfer" OR "Patient Handoff" OR "Hospital Discharge")) AND ((MH Hemorrhage) OR (AB Bleeding OR Hemorrhage OR Haemorrhage)) AND ((MH "Patient Safety") OR (AB "Patient Safety" OR "Safety Management")))	(((MH Anticoagulants) OR (AB Anticoagulant*)) AND ((MH "Medication Reconciliation") OR (AB "Medication Reconciliation")) AND ((MH "Patient Discharge" OR "Patient Handoff") OR (AB “Discharge Planning” OR "Patient Discharge" OR "Patient Transfer" OR "Patient Handoff" OR "Hospital Discharge")) AND ((MH Hemorrhage) OR (AB Bleeding OR Hemorrhage OR Haemorrhage)) AND ((MH "Patient Safety" OR MH "Safety Management") OR (AB "Patient Safety" OR "Safety Management")))

Table C.8: Harms Due to Diabetic Agents Search Terms

Method	Search	Search String for: CINAHL	Search String for MEDLINE	Search String for: PubMed
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Standard Insulin Protocol	((MH "Insulin/AD" OR "Insulin, Long-Acting/AD" OR "Insulin, Short-Acting/AD") AND (MH "Drug Therapy, Computer-Assisted" OR "Insulin Infusion Systems") OR (AB "Standardized Orders" OR "Standardized Order" OR "Clinical Algorithm" OR "Clinical Algorithms" OR "Standard Order Set" OR "Standard Order Sets" OR "Insulin Protocol" OR "Insulin Protocols" OR "Standard Insulin Protocol" OR "Standard Insulin Protocols" OR "Standing Order" OR "Standing Orders" OR "Standardized Insulin Protocol" OR "Standardized Insulin Infusion Protocol " OR "Treatment Protocol" OR "Order Set")) AND (MH Hypoglycemia) AND ((MH "Hospitals" OR "Inpatients" OR "Intensive Care Units" OR "Hospitalization") OR (AB Inpatient OR Hospital* OR "Acute Care" OR "Critical Care" OR "Intensive Care" OR "Emergency Department" OR "Emergency Room")) NOT ((MH "Hyperglycemia" OR "Fatty Liver" OR "Fatty Liver, Alcoholic" OR "Non-alcoholic Fatty Liver Disease" OR "Heart Transplantation") OR (AB Hyperglycemia OR Hyperglycemic OR Neonatal OR "Fatty Liver" OR Heart OR Transplant OR "Heart Transplantation")))	(((MH "Insulin/AD" OR "Insulin, Long-Acting/AD" OR "Insulin, Short-Acting/AD") AND ((MH "Standing Orders" OR "Clinical Protocols" OR "Drug Therapy, Computer-Assisted" OR "Insulin Infusion Systems") OR (AB "Standardized Orders" OR "Standardized Order" OR "Clinical Algorithm" OR "Clinical Algorithms" OR "Standard Order Set" OR "Standard Order Sets" OR "Insulin Protocol" OR "Insulin Protocols" OR "Standard Insulin Protocol" OR "Standard Insulin Protocols" OR "Standing Order" OR "Standing Orders" OR "Standardized Insulin Protocol" OR "Standardized Insulin Infusion Protocol " OR "Treatment Protocol" OR "Order Set")) AND (MH Hypoglycemia) AND ((MH Hospitals OR Inpatients OR "Intensive Care Units" OR "Hospitalization) OR (AB Inpatient OR Hospital* OR "Acute Care" OR "Critical Care" OR "Intensive Care" OR "Emergency Department" OR "Emergency Room"))) NOT ((MH "Hyperglycemia" OR "Fatty Liver" OR "Fatty Liver, Alcoholic" OR "Non-alcoholic Fatty Liver Disease" OR "Heart Transplantation") OR (AB Hyperglycemia OR Hyperglycemic OR Neonatal OR "Fatty Liver" OR Heart OR Transplant OR "Heart Transplantation")))	((("Insulin/Administration and Dosage"[MeSH] OR "Insulin, Long-Acting/Administration and Dosage"[MeSH] OR "Insulin, Short-Acting/Administration and Dosage"[MeSH]) AND ("Standing Orders"[MeSH] OR "Clinical Protocols"[MeSH] OR "Drug Therapy, Computer-Assisted"[MeSH] OR "Insulin Infusion Systems"[MeSH] OR "Standardized Orders"[tiab] OR "Standardized Order"[tiab] OR "Clinical Algorithm" [tiab] OR "Clinical Algorithms"[tiab] OR "Standard Order Set" [tiab] OR "Standard Order Sets"[tiab] OR "Insulin Protocol" [tiab] OR "Insulin Protocols"[tiab] OR "Standard Insulin Protocol"[tiab] OR "Standard Insulin Protocols"[tiab] OR "Standing Order" [tiab] OR "Standing Orders"[tiab] OR "Standardized Insulin Protocol"[tiab] OR "Standardized Insulin Infusion Protocol "[tiab] OR "Treatment Protocol"[tiab] OR "Order Set"[tiab]) (("Hypoglycemia"[MeSH]) AND ("Hospitals"[MeSH] OR "Inpatients"[MeSH] OR "Intensive Care Units"[MeSH] OR "Hospitalization"[MeSH] AND Inpatient[tiab] OR Hospital*[tiab] OR "Acute Care"[tiab] OR "Critical Care"[tiab] OR "Intensive Care"[tiab] OR "Emergency Department"[tiab] OR "Emergency Room"[tiab])) NOT

Method	Search	Search String for: CINAHL	Search String for MEDLINE	Search String for: PubMed
				("Hyperglycemia"[MeSH] OR "Fatty Liver"[MeSH] OR "Fatty Liver, Alcoholic"[MeSH] OR "Non-alcoholic Fatty Liver Disease"[MeSH] OR "Heart Transplantation"[MeSH] OR Hyperglycemia[tiab] OR Hyperglycemic[tiab] OR Neonatal[tiab] OR "Fatty Liver"[tiab] OR Heart[tiab] OR Transplant[tiab] OR "Heart Transplantation"[tiab]))

Method	Search	Search String for: CINAHL	Search String for MEDLINE	Search String for: PubMed
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Teach-Back	((MH “Diabetes Mellitus” OR AB “Diabetes”) AND (AB “Teach-Back” OR “Teach Back” OR Teachback))	((MH “Diabetes Mellitus” OR AB “Diabetes”) AND (MH “Teach-Back Communication” OR AB “Teach-Back” OR “Teach Back” OR Teachback))	((“Diabetes Mellitus”[MeSH] OR “Diabetes”[tiab]) AND (“Teach-Back Communication”[MeSH] OR “Teach-Back”[tiab] OR “Teach Back”[tiab] OR Teachback[tiab]))

Table C.9: Reducing Adverse Drug Events in Older Adults Search Terms

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Deprescribing	(((MH "Inappropriate Prescribing/PC") OR (MH "Adverse Drug Event/PC") OR (AB “Deprescription*” OR “Deprescribing” OR “Cessation” OR “Discontinuation” OR “Withdrawal”)) AND ((MH "Polypharmacy" OR AB (Polymedication OR Polypharmacy)) AND ((MH Aged OR AB ("Older Adult*" OR Elder* OR Aged OR "Elder Adult" OR Senior)))	(((MH "Deprescriptions") OR (MH "Drug-Related Side Effects and Adverse Reactions/PC") OR (MH "Inappropriate Prescribing/PC") OR AB (“Deprescription*” OR “Deprescribing” OR “Cessation” OR “Discontinuation” OR “Withdrawal”)) AND ((MH "Polypharmacy" OR AB (polymedication OR Polypharmacy)) AND ((MH Aged OR AB ("Older Adult*" OR Elder* OR Aged OR "Elder Adult" OR Senior)))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Use of STOPP Criteria	((AB "Potentially Inappropriate Medication List") AND ((MH Aged OR AB ("Older Adult*" OR Elder* OR Aged OR "Elder Adult" OR Senior)))	(((MH "Potentially Inappropriate Medication List") OR (AB "Potentially Inappropriate Medication List")) AND ((MH Aged OR AB ("Older Adult*" OR Elder* OR Aged OR "Elder Adult" OR Senior)))

Table C.10: Harms Due to Opioids Search Terms

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Opioid Stewardship	((MH "Overdose" OR "Analgesics, Opioid") OR (AB "Drug Overdose*" OR "Opioid Abuse*" OR "Opioid Misuse" OR "Opioid Addiction" OR "Opioid*" OR "Prescription Drug Misuse" OR "Prescription Drug Overuse")) AND ((MH "Hospitals" OR "Inpatients" OR "Ambulatory Care Facilities" OR "Practitioner's Office" OR "Long-Term Care" OR "Palliative Care" OR "Subacute Care" OR "Rehabilitation Centers" OR "Residential Facilities" OR "Substance Use Rehabilitation Programs" OR MH "Transitional Care" OR "Primary Health Care" OR "Home Health Care" OR "Nursing Homes" OR "Emergency Service" OR "Dentists" OR "Ambulatory Care") OR (AB "Ambulatory Care" OR "Specialty Care" OR "Hospital*" OR "Long Term Care" OR "Long-Term Care" OR "Palliative Care" OR "Physicians' Office*" OR "Subacute Care" OR "Residential Facilit*" OR "Primary Care" OR "Transitional Care" OR "Rehabilitation Center*" OR "Primary Health Care" OR "Dentist" OR "Emergency Room" OR "Nursing Home" OR "Emergency Department")) AND ((MH "Decision Support Systems, Clinical" OR "Electronic Data Interchange" OR "Health Information Systems" OR "Prescription Drug Monitoring Programs" OR "Drug Monitoring") OR (AB "Stewardship" OR "Prescription Drug Monitoring Program" OR "Treatment Agreement" OR "Patient Contract" OR "Clinical Decision Support" OR "Health Information Technology" OR "Prescribing" OR "Monitoring" OR "Patient Registry" OR "Dashboard" OR "Feedback Approach")))	((MH "Drug Overdose" OR "Opioid-Related Disorders" OR "Prescription Drug Overuse" OR "Prescription Drug Misuse" OR "Analgesics, Opioid") OR (AB "Drug Overdose*" OR "Opioid Abuse*" OR "Opioid Misuse" OR "Opioid Addiction" OR "Opioid*" OR "Prescription Drug Misuse" OR "Prescription Drug Overuse")) AND ((MH "Hospitals" OR "Inpatients" OR "Ambulatory Care Facilities" OR "Physicians' Offices" OR "Rehabilitation Centers" OR "Residential Facilities" OR "Substance Abuse Treatment Centers" OR "Transitional Care" OR "Primary Health Care" OR "Emergency Service, Hospital" OR "Ambulatory Care" OR "Patient Discharge") OR (AB "Ambulatory Care" OR "Specialty Care" OR "Hospital*" OR "Physicians' Office*" OR "Residential Facilit*" OR "Primary Care" OR "Transitional Care" OR "Rehabilitation Center*" OR "Primary Health Care" OR "Emergency Room" OR "Patient Discharge" OR "Emergency Department")) AND ((MH "Decision Support Systems, Clinical" OR "Health Information Exchange" OR "Health Information Systems" OR "Prescription Drug Monitoring Programs" OR "Drug Monitoring") OR (AB "Stewardship" OR "Prescription Drug Monitoring Program" OR "Treatment Agreement" OR "Patient Contract" OR "Clinical Decision Support" OR "Health Information Technology" OR "Prescribing" OR "Monitoring" OR "Patient Registry" OR "Dashboard" OR "Feedback Approach")))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Medication-Assisted Treatment	(((MH “Overdose”) OR (AB “Opioid Abuse*" OR "Opioid Misuse" OR "Opioid Addiction" OR "Prescription Drug Misuse" OR "Prescription Drug Overuse" OR "Opioid Use Disorder" OR "OUD" OR "Opioid-Use Disorder")) AND ((MH “Hospitals” OR “Inpatients” OR “Ambulatory Care Facilities” OR “Practitioner's Office” OR “Rehabilitation Centers” OR “Residential Facilities” OR "Substance Abuse Rehabilitation Programs" OR “Transitional Care” OR “Primary Health Care” OR "Emergency Service" OR "Ambulatory Care" OR "Patient Discharge") OR (AB “Ambulatory Care” OR “Specialty Care” OR “Hospital*” OR "Physicians' Office*" OR "Residential Facilit*" OR “Primary Care” OR "Transitional Care" OR "Rehabilitation Center*" OR "Primary Health Care" OR "Emergency Room" OR "Patient Discharge" OR "Emergency Department")) AND ((MH "Opiate Substitution Treatment") OR (AB "MAT" OR "Medication Assisted Treatment" OR "Medication-Assisted Treatment" OR "Medication-Assisted-Treatment" OR "Opiate Substitution Treatment" OR "Medication Assisted Treatment of Opioid" OR "Opiate Medication-Assisted Treatment" OR "Opiate Replacement Therapy" OR "Opioid Medication Assisted Treatment" OR "Opioid Replacement Therapy" OR "Opioid Substitution Therapy" OR "Opioid Substitution Treatment")))	(((MH “Opioid-Related Disorders” OR "Prescription Drug Overuse" OR "Prescription Drug Misuse") OR (AB “Opioid Abuse*" OR "Opioid Misuse" OR "Opioid Addiction" OR "Prescription Drug Misuse" OR "Prescription Drug Overuse" OR "Opioid Use Disorder" OR "OUD" OR "Opioid-Use Disorder")) AND ((MH “Hospitals” OR “Inpatients” OR “Ambulatory Care Facilities” OR “Practitioner's Office” OR “Rehabilitation Centers” OR “Residential Facilities” OR "Substance Abuse Rehabilitation Programs" OR “Transitional Care” OR “Primary Health Care” OR "Emergency Service" OR "Ambulatory Care" OR "Patient Discharge") OR (AB “Ambulatory Care” OR “Specialty Care” OR “Hospital*” OR "Physicians' Office*" OR "Residential Facilit*" OR “Primary Care” OR "Transitional Care" OR "Rehabilitation Center*" OR "Primary Health Care" OR "Emergency Room" OR "Patient Discharge" OR "Emergency Department")) AND ((MH "Opiate Substitution Treatment") OR (AB "MAT" OR "Medication Assisted Treatment" OR "Medication-Assisted Treatment" OR "Medication-Assisted-Treatment" OR "Opiate Substitution Treatment" OR "Medication Assisted Treatment of Opioid" OR "Opiate Medication-Assisted Treatment" OR "Opiate Replacement Therapy" OR "Opioid Medication Assisted Treatment" OR "Opioid Replacement Therapy" OR "Opioid Substitution Therapy" OR "Opioid Substitution Treatment")))

Table C.11: Patient Identification Error in the Operating Room Search Terms

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Operating Room/Surgery Specific Practices	(((MH "Patient Identification" OR "Operating Room Information Systems" OR "Patient Record Systems") OR (AB "Patient Identification System*" OR "Patient Identification Card" OR "Patient ID System" OR "Patient ID Card" OR "Operating Room Information System*" OR "Debriefing" OR "Identification Process" OR "Safeguard" OR "Patient Wristband" OR "Universal Protocol for Preventing Wrong Site, Wrong Procedure, Wrong Person Surgery" OR "Structured Communication" OR "Bar Coding" OR "Consent Form" OR "Patient Safety Checklist" OR "Electronic Health Record" OR "CPOE" OR "Computerized Physician Order Entry" OR "Bar Code Scanner" OR "Identification Method" OR "ID Method" OR "Identification Alert*" OR "ID Alert*" OR "SAFER Checklist" OR "Structured Communication Tool*" OR "Radiofrequency Device")) AND ((MH "Treatment Errors") OR (AB "Surgical Error*" OR "Wrong Patient Surger*" OR "Wrong-Patient Surger*" OR "Wrong Procedure Error*" OR "Wrong-Procedure Error*" OR "Wrong Site Surger*" OR "Wrong-Site Surger*" OR "Surger*, Wrong-Site" OR "Surger*, Wrong Site" OR "Medical Mistake*" OR "Disclosure of Error*" OR "Mental Error*" OR "Action Error*")))	(((MH "Patient Identification Systems" OR "Operating Room Information Systems") OR (AB "Patient Identification System*" OR "Patient Identification Card" OR "Patient ID System" OR "Patient ID Card" OR "Operating Room Information System*" OR "Debriefing" OR "Identification Process" OR "Safeguard" OR "Patient Wristband" OR "Universal Protocol for Preventing Wrong Site, Wrong Procedure, Wrong Person Surgery" OR "Structured Communication" OR "Bar Coding" OR "Consent Form" OR "Patient Safety Checklist" OR "Electronic Health Record" OR "CPOE" OR "Computerized Physician Order Entry" OR "Bar Code Scanner" OR "Identification Method" OR "ID Method" OR "Identification Alert*" OR "ID Alert*" OR "SAFER Checklist" OR "Structured Communication tool*" OR "Radiofrequency Device")) AND (AB "Surgical Error*" OR "Wrong Patient Surger*" OR "Wrong-Patient Surger*" OR "Wrong Procedure Error*" OR "Wrong-Procedure Error*" OR "Wrong Site Surger*" OR "Wrong-Site Surger*" OR "Surger*, Wrong-Site" OR "Surger*, Wrong Site" OR "Medical Mistake*" OR "Disclosure of Error*" OR "Mental Error*" OR "Action Error*") AND ((MH "Operating Rooms") OR (AB "Operating Room*" OR "Surger*")))

Table C.12: Infusion Pumps Search Terms

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Structured Process Changes/Workflow Redesign	(((MH "Infusion Pumps") OR AB ("Infusion Pump*" OR "Smart Pump*")) AND ((MH "Medication Errors" OR "Product Recalls and Withdrawals" OR "Workflow") OR (AB "Medication Error*" OR "Workflow" OR "Workflow Redesign" OR "Product Recall*" OR "Product Withdrawal*")))	(((MH "Infusion Pumps") OR (AB "Infusion Pump*" OR "Smart Pump*")) AND ((MH "Medication Errors" OR "Product Recalls and Withdrawals" OR "Workflow") OR (AB "Medication Error*" OR "Workflow" OR "Workflow Redesign" OR "Product Recall*" OR "Product Withdrawal*")))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Staff Education and Training	(((MH "Infusion Pumps") OR (AB "Infusion Pump*" OR "Smart Pump*" OR "Dose Error Reduction System" OR DERS OR "Intravenous Clinical Integration" OR IVCI OR "Barcode Medication Administration System" OR BMA)) AND ((MH "Medication Errors") OR (AB "Medication Error*" OR "Adverse Event")) AND ((MH "Education") OR AB (Inservice or "In-Service" OR "Staff Education" OR "Staff Training" OR Training OR Education OR Clinician OR Employee OR Staff OR Physician* OR Doctor* OR Nurse* OR "Nurse Practitioner*" OR "Physical Therapist*" OR "Social Worker*" OR "Physician Assistant*" OR "Occupational Therapist*")))	(((MH "Infusion Pumps") OR (AB "Infusion Pump*" OR "Smart Pump*" OR "Dose Error Reduction System" OR DERS OR "Intravenous Clinical Integration" OR IVCI OR "Barcode Medication Administration System" OR BMAS)) AND ((MH "Medication Errors") OR (AB "Medication Error*" OR "Adverse Event")) AND ((MH "Education") OR (AB Inservice or "In-Service" OR "Staff Education" OR "Staff Training" OR Training OR Education OR Clinician OR Employee OR Staff OR Physician* OR Doctor* OR Nurse* OR "Nurse Practitioner*" OR "Physical Therapist*" OR "Social Worker*" OR "Physician Assistant*" OR "Occupational Therapist*")))

Table C.13: Alarm Fatigue Search Terms

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Safety Culture	(((MH "Organizational Efficiency" OR "Organizational Culture" OR "Health Care Errors") OR (AB "Safety Performance" OR "Safety Program" OR "Safety Culture" OR "Comprehensive Safety Program" OR "Safety Climate" OR "Leadership Walk Rounds" OR "Guideline" OR "Clinical Protocol" OR "Team Training")) AND (AB "Alarm Desensitization" OR (Alarm AND Desensitization) OR ("Clinical Alarm" AND Desensitization)))	(((MH "Efficiency, Organizational" OR "Organizational Culture" OR "Safety Management/OG" OR "Medical Errors" OR "Quality Improvement") OR (AB "Safety Performance" OR "Safety Program" OR "Safety Culture" OR "Comprehensive Safety Program" OR "Safety Climate" OR "Leadership Walk Rounds" OR "Guideline" OR "Clinical Protocol" OR "Team Training")) AND (AB "Alarm Desensitization" OR (Alarm AND Desensitization) OR ("Clinical Alarm" AND Desensitization)))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Alarm Risk Assessment	(((MH "Risk Assessment" OR "Multidisciplinary Care Team") OR (AB "Risk Assessment" OR "Assessment" OR "Monitor" OR "Comprehensive Unit-Based Safety Program" OR "Interdisciplinary" OR "Management Committee")) AND (AB "Alarm Desensitization" OR (Alarm AND Desensitization) OR ("Clinical Alarm" AND Desensitization))	(((MH "Risk Assessment" OR "Patient Care Team") OR (AB "Risk Assessment" OR "Assessment" OR "Monitor" OR "Comprehensive Unit-Based Safety Program" OR "Interdisciplinary" OR "Management Committee")) AND (AB "Alarm Desensitization" OR (Alarm AND Desensitization) OR ("Clinical Alarm" AND Desensitization))

Table C.14: Delirium Search Terms

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Screening and Assessment	(((MH “Delirium/Prevention AND Control” OR “Delirium/Diagnosis”) OR (AB Delirium)) AND ((MH “Diagnostic Techniques and Procedures”) OR (AB “Screening*” OR “Assessment*” OR “Structured Approach*” OR “Confusion Assessment Model” OR “CAM”)) NOT ((MH "Alcohol Withdrawal Delirium”) OR (AB "Alcohol Withdrawal Delirium” OR "Delirium, Alcohol Withdrawal" OR “Ped*” OR “Child*”)))	(((MH “Delirium/Prevention AND Control” OR MH “Delirium/Diagnosis”) OR (AB Delirium)) AND ((MH “Diagnostic Techniques and Procedures”) OR (AB “Screening*” OR “Assessment*” OR “Structured Approach*” OR “Confusion Assessment Model” OR “CAM”)) NOT ((MH "Alcohol Withdrawal Delirium”) OR (AB "Alcohol Withdrawal Delirium” OR "Delirium, Alcohol Withdrawal" OR “Ped*” OR “Child*”)))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Staff Education and Training	((((MH Delirium) OR (AB Delirium)) AND ((MH Education) OR (AB Inservice OR “In-Service” OR “Staff Education“ OR “Staff Training” OR Training OR Education)) AND (AB Clinician* OR Employee* OR Staff OR Physician* OR Doctor* OR Nurse* OR “Nurse Practitioner*” OR “Physical Therapist*” OR “Social Worker*” OR “Physician Assistant*” OR “Occupational Therapist*”)) NOT ((MH "Alcohol Withdrawal Delirium”) OR (AB "Alcohol Withdrawal Delirium” OR "Delirium, Alcohol Withdrawal" OR “Ped*” OR “Child*”)))	((((MH Delirium) OR (AB Delirium)) AND ((MH Education) OR (AB Inservice OR “In-Service” OR “Staff Education“ OR “Staff Training” OR Training OR Education)) AND (AB “Clinician*” OR “Employee*” OR “Staff” OR “Physician*” OR “Doctor*” OR “Nurse*” OR “Nurse Practitioner*” OR “Physical Therapist*” OR “Social Worker*” OR “Physician Assistant*” OR “Occupational Therapist*”)) NOT ((MH "Alcohol Withdrawal Delirium”) OR (AB "Alcohol Withdrawal Delirium” OR "Delirium, Alcohol Withdrawal" OR “Ped*” OR “Child*”)))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Non-Pharmacologic Intervention Programs	((((MH Delirium) OR (AB Delirium)) AND ((MH “Quality Improvement”) OR (AB “Non-Pharmacologic*” OR “Nonpharmacologic*” OR “Intervention Program*” OR “Quality Improvement”))) NOT ((MH "Alcohol Withdrawal Delirium") OR (AB "Alcohol Withdrawal Delirium” OR "Delirium, Alcohol Withdrawal" OR “Ped*” OR “Child*”)))	((((MH Delirium) OR (AB Delirium)) AND ((MH “Quality Improvement”) OR (AB “Non-Pharmacologic*” OR “Nonpharmacologic*” OR “Intervention Program*” OR “Quality Improvement”))) NOT ((MH "Alcohol Withdrawal Delirium") OR (AB "Alcohol Withdrawal Delirium” OR "Delirium, Alcohol Withdrawal" OR “Ped*” OR “Child*”)))

Table C.15: Care Transitions Search Terms

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	BOOST Model	((AB “BOOST” OR “Better Outcomes by Optimizing Safe Transitions”) AND ((MH “Patient Discharge” OR "Transfer, Discharge" OR “Hand Off (Patient Safety)" OR "Discharge Planning") OR (AB “Discharge Planning” OR "Patient Discharge" OR "Patient Transfer" OR "Patient Handoff")))	((AB “BOOST” OR “Better Outcomes by Optimizing Safe Transitions”) AND ((MH “Patient Discharge” OR “Patient Transfer” OR "Patient Handoff") OR (AB “Discharge Planning” OR "Patient Discharge" OR "Patient Transfer" OR "Patient Handoff")))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Care Transitions Intervention (CTI) Model	((AB "Care Transitions Intervention" OR “CTI”) AND ((MH “Patient Discharge” OR "Transfer, Discharge" OR “Hand Off (Patient Safety)" OR "Discharge Planning") OR (AB “Discharge Planning” OR "Patient Discharge" OR "Patient Transfer" OR "Patient Handoff"))) AND ((MH “Patient Safety”) OR (AB "Patient Safety")))	((AB “Care Transitions Intervention” OR “CTI”) AND ((MH “Patient Discharge” OR “Patient Transfer” OR "Patient Handoff") OR (AB “Discharge Planning” OR "Patient Discharge" OR "Patient Transfer" OR "Patient Handoff")) AND ((MH “Patient Safety”) OR (AB "Patient Safety")))
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study	Teach-Back Model	(((MH “Teaching") OR (AB "Teach-Back Communication" OR “Teach-Back” OR “Teachback”)) AND ((MH “Patient Discharge” OR "Transfer, Discharge" OR “Hand Off (Patient Safety)" OR "Discharge Planning") OR (AB “Discharge Planning” OR "Patient	(((MH “Teaching") OR (AB "Teach-Back Communication" OR “Teach-Back” OR “Teachback”)) AND ((MH “Patient Discharge” OR “Patient Transfer” OR "Patient Handoff") OR (AB “Discharge Planning” OR "Patient

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
• Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study		Discharge" OR "Patient Transfer" OR "Patient Handoff")))	Discharge" OR "Patient Transfer" OR "Patient Handoff")))

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
• Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review			

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Transitional Care Model (TCM)	((AB “Transitional Care Model” OR “TCM”) AND ((MH “Patient Discharge” OR "Transfer, Discharge" OR “Hand Off (Patient Safety)" OR "Discharge Planning") OR (AB “Discharge Planning” OR "Patient Discharge" OR "Patient Transfer" OR "Patient Handoff")))	((AB “Transitional Care Model” OR “TCM”) AND ((MH “Patient Discharge” OR “Patient Transfer” OR "Patient Handoff") OR (AB “Discharge Planning” OR "Patient Discharge" OR "Patient Transfer" OR "Patient Handoff")))

Table C.16: Venous Thromboembolism Search Terms

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
Search 2008-Present, English Only MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research Review • Systematic Review	Post-Surgical VTE Prophylaxis using Aspirin	((((MH "Aspirin/Therapeutic Use*") OR (AB Aspirin)) AND ((MH "Venous Thrombosis/Prevention & Control" OR "Pulmonary Embolism/Prevention & Control*") OR (AB "Deep Vein Thrombosis" OR "Pulmonary Embolism" OR PE OR DVT)) AND ((MH "Operative, Surgery" OR "Perioperative Care/Methods*" OR "Postoperative Complications/Prevention & Control*") OR (AB Surgery OR "Surgical Procedure*" OR "Postoperative Complication*" OR "Perioperative Care Methods" OR Operation))) NOT ((MH "Cardiovascular Diseases" OR Heart) OR (AB "Cardiovascular Disease*" OR Heart OR Cardiac)))	((((MH "Aspirin/Therapeutic use*") OR (AB Aspirin)) AND ((MH "Venous Thrombosis/Prevention & Control" OR "Pulmonary Embolism/Prevention & Control*") OR (AB "Deep Vein Thrombosis" OR "Pulmonary Embolism" OR PE OR DVT)) AND ((MH "Surgical Procedures, Operative" OR "Perioperative Care/Methods*" OR "Postoperative Complications/Prevention & Control*") OR (AB Surgery OR "Surgical Procedure*" OR "Postoperative Complication*" OR "Perioperative Care Methods" OR Operation))) NOT ((MH "Cardiovascular Diseases" OR Heart) OR (AB "Cardiovascular Disease*" OR Heart OR Cardiac)))

Table C.17: Cross-Cutting Patient Safety Topics/Practices Search Terms

Method	Search	Search String for: CINAHL	Search String for: MEDLINE
MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research • Review • Systematic Review	Patient and Family Engagement	(((MH “Patient Participation” OR "Professional-Patient Relations" OR "Physician-Patient Relations" OR "Professional-Family Relations") OR (AB "Patient Participation" OR "Patient Engagement" OR "Patient Involvement" OR "Family Engagement" OR "Family Involvement" OR "Patient and Family Engagement" OR "Patient and Family Involvement" OR "Patient Empowerment" OR "Patient/Family Engagement")) AND ((MH "Patient Safety") OR (AB "Patient Safety" OR "Safety Management")))	MH “Patient Participation” OR "Professional-Patient Relations" OR "Physician-Patient Relations" OR "Professional-Family Relations") OR (AB "Patient Participation" OR "Patient Engagement" OR "Patient Involvement" OR "Family Engagement" OR "Family Involvement" OR "Patient and Family Engagement" OR "Patient and Family Involvement" OR "Patient Empowerment" OR "Patient/Family Engagement")) AND ((MH "Patient Safety" OR "Safety Management") OR (AB "Patient Safety" OR "Safety Management")))

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MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research • Review • Systematic Review	Safety Culture	(((MH "Patient Safety" OR "Risk Management" OR "Treatment Errors" OR "Quality of Health Care" OR "Outcome Assessment" OR "Program Evaluation") OR (AB “Medical Error*” OR “Safety, Patient” OR “Patient Safety” or “Health Care Quality” OR “Healthcare Quality” OR “Quality of Health Care” OR “Quality of Healthcare” OR “Quality of Care” OR "Risk Management" OR "Safety Management" OR "Patient Harm" OR "Program Evaluation" OR ("Outcome Assessment*" AND "Healthcare") OR ("Outcome Assessment*" AND "Health Care")) AND ((MH "Organizational Culture") OR (AB "Organizational Culture" OR “Patient Safety Culture” OR "Patient Safety Climate")) AND ((MH "Quality Improvement") OR (AB “Leadership Walk Rounds” OR “Comprehensive Unit-Based Safety Program” OR “Performance Improvement” OR "Quality Improvement" OR “Team Training” OR “Training Workshop”)))	(((MH “Patient Harm” OR “Patient Safety” OR “Safety Management” OR “Risk Management” OR “Medical Errors” OR “Quality of Health Care” OR “Outcome Assessment (Health Care)" OR “Program Evaluation”) OR (AB “Medical Error*” OR “Safety, Patient” OR “Patient Safety” or “Health Care Quality” OR “Healthcare Quality” OR “Quality of Health Care” OR “Quality of Healthcare” OR “Quality of Care” OR "Risk Management" OR "Safety Management" OR "Patient Harm" OR "Program Evaluation" OR ("Outcome Assessment*" AND "Healthcare") OR ("Outcome Assessment*" AND "Health Care")) AND ((MH “Organizational Culture”) OR (AB "Organizational Culture" OR “Patient Safety Culture” OR "Patient Safety Climate")) AND ((MH "Quality Improvement") OR (AB “Leadership Walk Rounds” OR “Comprehensive unit-Based Safety Program” OR “Performance Improvement” OR "Quality Improvement" OR “Team Training” OR “Training Workshop”)))

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MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research • Review • Systematic Review	Clinical Decision Support	(((MH "Decision Support Systems, Clinical" OR "Decision Making, Computer-Assisted" OR ("Medical Informatics" AND "Reminder Systems") OR ("Medical Informatics" AND "Decision Support Techniques") OR ("Medical Informatics" AND "Clinical Decision-Making")) OR (AB "Clinical Decision Support")) AND ((MH "Patient Safety" OR "Treatment Errors" OR "Quality of Health Care" OR "Quality Assurance") OR (AB "Medical Error*" OR "Patient Harm" OR "Patient Safety" OR "Quality of Health Care" OR "Quality of Care")))	(((MH "Decision Support Systems, Clinical" OR "Decision Making, Computer-Assisted" OR ("Medical Informatics Applications" AND "Reminder Systems") OR ("Medical Informatics Applications" AND "Decision Support Techniques") OR ("Medical Informatics Applications" AND "Clinical Decision-Making")) OR (AB "Clinical Decision Support")) AND ((MH "Patient Harm" OR "Patient Safety" OR "Medical Errors" OR "Quality of Health Care" OR "Quality Assurance, Health Care") OR (AB "Medical Error*" OR "Patient Harm" OR "Patient Safety" OR "Quality of Health Care" OR "Quality of Care")))

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MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study	Monitoring Auditing and Feedback	((MH "Patient Safety" OR "Risk Management" OR "Treatment Errors" OR "Quality of Health Care" OR "Outcome Assessment" OR "Program Evaluation") OR (AB "Patient Harm" OR "Patient Safety" OR "Safety Management" OR "Risk Management" OR "Medical Error*" OR "Quality of Health Care" OR "Quality of Healthcare" OR ("Outcome Assessment*" AND Healthcare) OR	((MH "Patient Harm" OR "Patient Safety" OR "Safety Management" OR "Risk Management" OR "Medical Errors" OR "Quality of Health Care" OR "Outcome Assessment (Health Care)" OR "Program Evaluation" OR "Quality Assurance, Health Care") OR (AB "Patient Harm" OR "Patient Safety" OR "Safety Management" OR "Risk Management" OR

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MedLine Publication Types: • Clinical Trial • Clinical Trial, Phase I • Clinical Trial, Phase II • Clinical Trial, Phase III • Clinical Trial, Phase IV • Comparative Study • Controlled Clinical Trial • Corrected and Republished Article • Evaluation Studies • Guideline • Journal Article • Meta-Analysis • Multicenter Study • Practice Guideline • Published Erratum • Randomized Controlled Trial • Review • Scientific Integrity Review • Technical Report • Twin Study • Validation Studies CINAHL Publication Types: • Clinical Trial • Corrected Article • Journal Article • Meta-Analysis • Meta Synthesis • Practice Guidelines • Randomized Controlled Trial • Research • Review • Systematic Review	Staff Education and Training (Simulation)-Without Settings	((MH “Treatment Errors” OR “Quality of Health Care” OR "Quality Assurance") OR (AB “Medical Error*” OR "Patient Harm" OR "Patient Safety" OR "Quality of Health Care")) AND ((MH “Patient Simulation” OR “Computer Simulation” OR “Virtual Reality”) OR (AB "Simulation Training" OR "Patient Simulation" OR "Computer Simulation" OR "Virtual Reality" OR "Serious Games" OR "Serious Gaming")))	((MH “Patient Harm” OR “Patient Safety” OR “Medical Errors” OR "Quality of Health Care” OR "Quality Assurance, Health Care") OR (AB “Medical Error*” OR "Patient Harm" OR "Patient Safety" OR "Quality of Health Care")) AND ((MH “Simulation Training” OR “Patient Simulation” OR “Computer Simulation” OR “Virtual Reality”) OR (AB "Simulation Training" OR "Patient Simulation" OR "Computer Simulation" OR "Virtual Reality" OR "Serious Games" OR "Serious Gaming")))

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