TABLE V.A.1 – Evidence table

Type of Evidence	Findings	Citations
Use of Trigger Tools to Identify Patient Harm		
Prospective Study	Investigators developed an automated computerized method to improve the detection and characterization of adverse drug events (ADEs) in hospitalized patients. Over 18 months, a total of 36,653 patients were monitored at LDS Hospital, Salt Lake City, Utah. The computerized ADE monitoring program consisted of two components: automated detection of potential ADEs and enhanced voluntary reporting at all computer terminals throughout the hospital. Verified ADEs were permanently stored in patients' medical records. Over the 18-month study period, 648 patients were found to have ADEs (731 total ADEs), resulting in an overall ADE rate of 1.67%. 90 of 731 ADEs were detected by enhanced voluntary reporting, while 641 were detected through automated methods. Analgesics and narcotics, antibiotics, cardiovascular agents, and anticoagulants accounted for 31%, 23.3%, 19.4%, and 9.3% of ADEs, respectively. Traditional voluntary reporting only identified 9 ADEs.	Classen DC, Pestotnik SL, Evans RS, Burke JP. Computerized surveillance of adverse drug events in hospital patients. *JAMA* 1991;266(20):2847-2851.[51]
Prospective Study	Investigators developed a computer-based monitoring system that identified "alerts" that possibly indicated an adverse drug event (ADE). The study population consisted of all patients admitted to nine medical and surgical units at Brigham and Women's Hospital from October 1994 to May 1995. Medical records flagged with an alert were reviewed to determine whether an ADE had occurred. This computer-based monitoring program was compared to more traditional	Jha AK, Kuperman GJ, Teich JM, Leape L, Shea B, Rittenberg E, Burdick E, Seger DL, Vander Vliet M, Bates DW. Identifying adverse drug events: development of a computer-based monitor and comparison with chart review and stimulated voluntary report. J Am Med Inform Assoc JAMIA.

	methods of monitoring ADEs: intensive chart review and voluntary reporting. The computer monitoring program identified 275 ADEs, chart review 398 ADEs, and voluntary report only 23 ADEs. There was an overlap of 76 ADEs identified by the computer monitor and chart review. Although chart review detected more ADEs overall, the computer monitor identified more ADEs in the "severe" category. Computer review required 20 percent as much time (11 person-hours/week) as chart review did (55 person-hours/week).	1998;5(3):305-314.[62]
Prospective Study	Investigators evaluated a semi-automated electronic surveillance system (ESS) with triggers to detect ventilator-associated pneumonia (VAP) and central line-associated blood stream infections (CLABSIs) in intensive care. 553 patients from October 2009 to October 2010 were screened, with patients with pneumonia at admission excluded. Whenever a trigger occurred, the data management system automatically sent an alert, leading reviewers to check the patient's chest X-rays and microbiology culture results. The semi-automated ESS was compared with traditional manual screening, which does not include trigger use. Therefore, reviewers had to screen chest X-rays and culture results for all hospitalization days for patients. For VAP, the trigger-based screening had a sensitivity of 92.3%, a specificity of 100%, and a negative predictive value of 99.8% compared to manual screening of all patients, and results for CLABSI were very similar. The trigger-based screening was only slightly less accurate and thus accurate enough to be used as a quality indicator over time. Based on an	Kaiser AM, de Jong E, Evelein-Brugman SF, Peppink JM, Vandenbroucke-Grauls CM, Girbes AR. Development of trigger-based semi-automated surveillance of ventilator-associated pneumonia and central line-associated bloodstream infections in a Dutch intensive care. *Ann Intensive Care*. 2014;4:40. doi:10.1186/s13613-014-0040-x.[61]

	approximate estimation of saved time, the trigger-based screening reduced workload by 90%.	
Prospective Study	Investigators developed an electronic trigger report system to detect patients at risk for nephrotoxic medication-associated acute kidney injury (NTMx-AKI) before the injury occurs. This system was developed using manual trigger screening protocols as a guide. After evaluating NTMx exposure trigger reports at Cincinnati Children's Hospital Medical Center from September 2011 to September 2013, sensitivity, specificity, positive and negative predictive values for NTMx exposure triggers were found to achieve ≥0.95. Although investigators encountered challenges with defining trigger logic and incorporating clinical work-flows, the electronic system was a technical, clinical, and quality improvement success. The automated trigger-based system proved much more efficient than manual screening since it reduced the time spent on manual data entry and transcription processes. The system also showed a higher ability to detect NTMx exposure.	Kirkendall ES, Spires WL, Mottes TA, Schaffzin JK, Barclay C, Goldstein SL. Development and Performance of Electronic Acute Kidney Injury Triggers to Identify Pediatric Patients at Risk for Nephrotoxic Medication-Associated Harm. Appl Clin Inform. 2014;5(2):313-333. doi:10.4338/ACI-2013-12-RA-0102.[64]
Cross-Sectional Study	Investigators developed and tested a pediatric intensive care unit- (PICU) specific trigger tool to identify adverse events, including adverse drug events (ADEs). The study population consisted of randomly selected patients from 15 hospitals across the U.S., who were in the PICU for a minimum of two days and were discharged, transferred out, or died between September 1 and December 31, 2005. 734 medical records were reviewed. Chart reviews identified a total of 1,488	Agarwal S, Classen D, Larsen G, Tofil NM, Hayes LW, Sullivan JE, Storgion SA, Coopes BJ, Craig V, Jaderlund C, Bisarya H, Parast L, Sharek P. Prevalence of adverse events in pediatric intensive care units in the United States. *Pediatr Crit Care Med J Soc Crit Care Med World Fed Pediatr Intensive Crit Care Soc*.

	adverse events, including 256 ADEs. The trigger tool was responsible for the identification of 2,816 triggers and 1,250 (84%) of the total adverse events. The positive predictive value of the overall tool was 0.44, with a range of 0.2 to 1.25 for individual triggers. Use of the trigger tool resulted in a mean chart review time of 24.7 minutes per reviewer. Only 4% of the identified adverse events were also identified via incident reports.	2010;11(5):568-578. doi:10.1097/PCC.0b013e3181d8e405.[12]
Cross-Sectional Study	Investigators estimated the incidence of adverse events (AEs) in acute care hospital patients. The study population consisted of a random sample of adult (≥18 years) admissions to hospitals in five Canadian provinces. Chart reviews were conducted in a 2-stage process. In stage 1, nurses or health records professionals screened each chart for the presence of 1 or more of 18 criteria deemed to be associated with AEs. In stage 2, physicians reviewed charts in which at least one criteria was identified. Inter-rater reliability was assessed on a 10% random sample of charts during the chart review training process. Nurses and health records professionals had moderate agreement for the 10% sample of charts (Kappa = 0.70; 95% confidence interval [CI] 0.63 to 0.76) and physicians had moderate agreement for various aspects of AE assessment, such as whether an AE occurred (Kappa = 0.47; 95% CI 0.35 to 0.58) and the preventability of the event (Kappa = 0.69; 95% CI 0.55 to 0.83). A total of 289 AEs were found in 858 charts.	Baker GR, Norton PG, Flintoft V, Blais R, Brown A, Cox J, Etchells E, Ghali WA, Hébert P, Majumdar SR, O'Beirne M, Palacios-Derflingher L, Reid RJ, Sheps S, Tamblyn R. The Canadian Adverse Events Study: the incidence of adverse events among hospital patients in Canada. *Can Med Assoc J* 2004;170(11):1678-1686.[29]
Cross-Sectional Study	Investigators examined the utility of a trigger tool to detect adverse drug events (ADEs) in pediatric oncology and	Call RJ, Burlison JD, Robertson JJ, Scott JR, Baker DK, Rossi MG,

	hematology patients. The study population consisted of patients from Saint Jude Children's Research Hospital, which participates in the Automated Adverse Event Detection Collaborative (AAEDC). An electronic trigger tool package was used to analyze electronic health records from February 2009 to February 2013. Chart review determined whether the trigger had an associated ADE. A total of 706 trigger occurrences were detected in 390 patients by 6 triggers. 33 ADEs were identified. Chart reviewers took an average of three minutes per event to determine if a trigger was associated with an ADE. The positive predictive value (PPV) of individual triggers ranged from 0 to 60%, while the overall tool had a PPV of 16%. The most successful trigger was hyaluronidase (PPV 60%). Of the 21 ADEs detected via trigger tool that were deemed preventable, 3 were identified through voluntary reports.	Howard SC, Hoffman JM. Adverse Drug Event Detection in Pediatric Oncology and Hematology Patients: Using Medication Triggers to Identify Patient Harm in a Specialized Pediatric Patient Population. *J Pediatr*. 2014. doi:10.1016/j.jpeds.2014.03.033.[52]
Cross-Sectional Study	Investigators evaluated the adverse event (AE) detection ability of three different detection methods: the Institute for Healthcare Improvement's (IHI) Global Trigger Tool (GTT), each hospital's voluntary reporting system, and the Agency for Healthcare Research and Quality's (AHRQ) Patient Safety Indicators (PSIs). The study population consisted of randomly selected adult (≥18 years) inpatients who were admitted to three U.S. tertiary care centers during the period of October 1-31, 2004. A total of 795 randomly selected medical records were reviewed from the three hospitals. To evaluate sensitivity, specificity, and positive and negative predictive value, a physician-led expert	Classen DC, Resar R, Griffin F, Federico F, Frankel T, Kimmel N, Whittington JC, Frankel A, Seger A, James BC. "Global Trigger Tool" Shows That Adverse Events In Hospitals May Be Ten Times Greater Than Previously Measured. *Health Aff (Millwood)*. 2011;30(4):581-589. doi:10.1377/hlthaff.2011.0190.[39]

	review team independently conducted complete hospital record reviews for all patients included in the study from one of the hospital sites. The three methods combined detected 393 AEs. The IHI GTT methodology identified 354 AEs (90.1% of total AEs; 94.9% sensitivity, 100% specificity), voluntary hospital reporting identified 4 AEs (1%; 0% sensitivity, 100% specificity), and the PSIs identified 35 AEs (8.99%; 5.8% sensitivity, 98.5% specificity).	
Cross-Sectional Study	Investigators used an automated electronic health record adverse event (AE) detection system to identify and categorize hypoglycemia-related AEs in pediatric inpatients. Hypoglycemia-related triggers (glucose level ≤50 mg/dL) that were generated over a 1-year period at Children's National Medical Center were retrospectively reviewed. Data were collected from the Emergency Department (ED) and all inpatient clinical areas. An AE was defined as hypoglycemia that resulted from medical therapy or lack of appropriate medical therapy. The electronic health records of all patients admitted to the hospital from September 2007 to August 2008 were reviewed; however, weekend days from September 2007 to February 2008 were excluded due to investigator resource limitations. AE rates were calculated using data from March to August 2008. A total of 1,254 triggers were detected, of which 198 were determined to be AEs (positive predictive value (PPV) 15.8%). The 198 AEs were attributed to 68 patients. The majority of AEs occurred in the neonatal intensive care unit (13.4 AEs per 1000 patient-days; 28.2 AEs per 100	Dickerman MJ, Jacobs BR, Vinodrao H, Stockwell DC. Recognizing hypoglycemia in children through automated adverse-event detection. *Pediatrics*. 2011;127(4):e1035-1041. doi:10.1542/peds.2009-3432.[75]

	patient admissions).	
Cross-Sectional Study	Investigators compared computerized surveillance, which used triggers, and voluntary reporting of adverse drug event (ADE) detection. For each system, they also analyzed the number of ADEs resulting from medications most likely to cause harm. The study population consisted of adult inpatients at a large, tertiary care academic medical system from December 1, 2006 to June 30, 2007. Medication safety pharmacists evaluated and scored ADEs from that period, and investigators calculated ADEs/1,000 patient days. Computerized surveillance detected 710 ADEs and voluntary reporting 205 ADEs. 40 ADEs were found by both systems. The two systems showed significantly different ADE rates for different drug categories. Computerized surveillance mostly detected hypoglycemia-related ADEs (68.2%) while voluntary reporting were detected "miscellaneous" ADEs (49.8%). Computerized surveillance is better at estimating the ADE rate, but voluntary reporting provides qualitative details not available from computerized surveillance.	Ferranti J, Horvath MM, Cozart H, Whitehurst J, Eckstrand J, Pietrobon R, Rajgor D, Ahmad A. A Multifaceted Approach to Safety: The Synergistic Detection of Adverse Drug Events in Adult Inpatients. J Patient Saf. 2008;4(3):184-190. doi:10.1097/PTS.0b013e318184a9d5.[56]
Cross-Sectional Study	Investigators developed and tested a trigger tool for the detection of adverse events (AEs) among surgical inpatients. In 2003, the initial surgical trigger tool was tested in five hospitals that had prior experience with the Institute for Healthcare Improvement (IHI) trigger tools, resulting in a final tool with 23 triggers. The resulting tool was tested in 31 hospitals from October 2003 to October 2004. 11 hospitals provided de-identified patient-level data. A total of 854 records were reviewed from these 11 hospitals.	Griffin FA, Classen DC. Detection of adverse events in surgical patients using the Trigger Tool approach. *Qual Saf Health Care*. 2008;17(4):253-258. doi:10.1136/qshc.2007.025080.[53]

	Over the course of one year, AEs were identified in 125 medical records (138 AEs total), resulting in a rate of 16 surgical AEs per 100 patients. Many participating hospitals reported that the trigger tool was more effective at identifying surgical AEs than existing reporting systems.	
Cross-Sectional Study	Investigators evaluated the utility of a trigger tool to assess and classify adverse events (AEs) compared to voluntary reporting. The study population consisted of 60 randomly selected intensive care patients from a pediatric university hospital. Two independent investigators classified each AE detected by the trigger tool as insignificant, minor, moderate, major, or catastrophic. Each record took an average of 40 minutes to review. A total of 98 AEs (59.9 AEs per 100 patient days) were identified. Investigator 1 found 66 AEs, and Investigator 2 found 93 AEs, (inter-rater reliability Kappa = 0.63). Of the 61 AEs identified by both investigators, the agreement for severity classification was very good (Kappa = 0.89).	Hooper AJ, Tibballs J. Comparison of a Trigger Tool and voluntary reporting to identify adverse events in a paediatric intensive care unit. *Anaesth Intensive Care*. 2014;42(2):199-206.[54]
Cross-Sectional Study	Investigators used an enhanced version of the Institute for Healthcare Improvement's (IHI) Global Trigger Tool (GTT) to report five years of adverse events (AEs) in a large health care system. The study population consisted of a random sample of adults (≥18 years) admitted to eight Baylor Health Care System acute care hospitals from 2007 to 2011 with a minimum length of stay of three days. A total of 9,017 records were reviewed by professional nurse reviewers. Medical record/account numbers were matched to	Kennerly DA, Kudyakov R, da Graca B, Saldaña M, Compton J, Nicewander D, Gilder R. Characterization of Adverse Events Detected in a Large Health Care Delivery System Using an Enhanced Global Trigger Tool over a Five-Year Interval. *Health Serv Res*. 2014. doi:10.1111/1475-6773.12163.[44]

	identify overlapping voluntary reports or the Agency for Healthcare Research and Quality's (AHRQ) Patient Safety Indicators (PSIs). A total of 3,430 AEs were identified. AE rates were estimated to be 61.4 AEs per 1,000 patient days. Of the hospital-acquired AEs, a majority were deemed to be possibly preventable. Of the 1,186 hospital-acquired AEs identified by the GTT between October 2008 and December 2011, 42 (3.5%) were identified via voluntary reporting, and 18 (1.5%) had a PSI detected via analysis of administrative data.	
Cross-Sectional Study	Investigators sought to adapt the Institute for Healthcare Improvement's (IHI) Global Trigger Tool (GTT) for use as a sustainable monitoring tool. The study population consisted of patients from the Baylor Health Care System over a four-year period. To reduce costs, investigators limited the eligible patients to those with a length of stay >3 days, adapted the sample size and frequency of review, and used a single nurse reviewer followed by quality assurance review with the Office of Patient Safety. A total of 16,172 records were reviewed. 14,184 records had positive triggers, of which 17.1% were associated with adverse events (AEs). Most AEs were identified using the surgical and patient care trigger tool modules. Chart reviewers had fair to good agreement (Kappa = 0.62).	Kennerly DA, Saldaña M, Kudyakov R, da Graca B, Nicewander D, Compton J. Description and evaluation of adaptations to the global trigger tool to enhance value to adverse event reduction efforts. *J Patient Saf*. 2013;9(2):87-95. doi:10.1097/PTS.0b013e31827cdc3b.[45]
Cross-Sectional Study	Investigators evaluated the utility of the Institute for Healthcare Improvement's (IHI) Global Trigger Tool (GTT) for adverse event (AE) detection in pediatric populations. The study population consisted of randomly	Kirkendall ES, Kloppenborg E, Papp J, White D, Frese C, Hacker D, Schoettker PJ, Muething S, Kotagal U. Measuring adverse

	selected patients from Cincinnati Children's Hospital Medical Center, a large, urban, academic tertiary care center. A total of 240 charts were reviewed by nurses, followed by a physician validation check for the presence of AEs. Inter-rater reliability was assessed on a 3-month sample of charts. Nurse reviewers had an inter-rater reliability of Kappa = 0.63 for the presence of AEs, and the agreement between nurse and physician reviewers was Kappa = 0.85. A total of 404 triggers and 88 AEs were identified, resulting in a mean rate of 36.7 AEs per 100 patients and 76.3 AEs per 1,000 patient days. Twenty-nine of the identified AEs (33%) were discovered without a particular GTT trigger being identified (an "Other" trigger), indicating that many pediatric AEs are not captured by adult triggers and that additional pediatric triggers may be required. No AEs were detected by triggers from the Emergency Department (ED), Intensive Care, and Perinatal modules. Modifications to the GTT to address pediatric-specific issues could increase its test characteristics.	events and levels of harm in pediatric inpatients with the Global Trigger Tool. *Pediatrics*. 2012;130(5):e1206-1214. doi:10.1542/peds.2012-0179.[13]
Cross-Sectional Study	Investigators developed and tested a trigger tool to identify errors and adverse events (AEs) that affect pediatric otolaryngology (ORL) patients. The study population consisted of 48 patients who were randomly selected from the ORL service discharge list at Boston Children's Hospital. The trigger tool was used by two non-clinicians to screen charts. Detailed chart reviews performed by two board-certified otolaryngologists served as the gold standard for error and AE detection. Chart review using the trigger tool took approximately 25 minutes per chart. A total	Lander L, Roberson DW, Plummer KM, Forbes PW, Healy GB, Shah RK. A trigger tool fails to identify serious errors and adverse events in pediatric otolaryngology. *Otolaryngol--Head Neck Surg Off J Am Acad Otolaryngol-Head Neck Surg*. 2010;143(4):480-486. doi:10.1016/j.otohns.2010.06.820.[59]

	of 236 triggers were identified. Inter-rater reliability, assessed using Kappa statistics, ranged from 0.35 (Admission trigger category) to 0.90 (Medication trigger category). Physician review identified 587 errors or AEs (553 errors and 34 AEs). The trigger tool identified 92 errors and AEs. The trigger tool had a sensitivity of 17% (95% CI 14% to 20%), a specificity of 82% (95% CI 79% to 84%), a positive predictive value of 39% (95% CI 33% to 46%), and a negative predictive value of 59% (95% CI 56% to 62%).	
Cross-Sectional Study	Investigators used the Canadian Paediatric Trigger Tool to determine incidence, type, severity, and preventability of adverse events (AEs) among children admitted to academic and community hospitals in Canada. The study population consisted of randomly selected patients from 0 to 18 years old. A 2-stage review process was used to screen medical records. A nurse or health record technologist first reviewed charts for triggers. A physician then reviewed all the charts in which a trigger was identified. Inter-rater reliability was assessed on a sample of 19 anonymized charts during the chart review training process. The percent agreement among nurses for the presence of a trigger was 87% (95% CI 83% to 90%). The percent agreement among physician reviewers for AEs was 66% (95% CI 57% to 76%). Overall, 9.2% of children admitted to the hospital experience AEs.	Matlow AG, Baker GR, Flintoft V, Cochrane D, Coffey M, Cohen E, Cronin CMG, Damignani R, Dubé R, Galbraith R, Hartfield D, Newhook LA, Nijssen-Jordan C. Adverse events among children in Canadian hospitals: the Canadian Paediatric Adverse Events Study. *Can Med Assoc J* 2012;184(13):E709-718. doi:10.1503/cmaj.112153. [19]
Cross-Sectional Study	Investigators examined the inter-rater reliability of the Institute for Healthcare Improvement's (IHI) Global Trigger Tool (GTT) and explored the value of individual	Naessens JM, O'Byrne TJ, Johnson MG, Vansuch MB, McGlone CM, Huddleston JM. Measuring hospital

	triggers. The study population consisted of 1,138 randomly selected adult patients who had been discharged from three Mayo Clinic practices. Charts were reviewed by two nurse reviewers, with final reconciliation performed by a physician. Review of each record was capped at 20 minutes. The positive predictive value of triggers varied. For triggers identified in at least 20 cases, 80.6% of cases with the "Return to Surgery" trigger had an adverse event (AE), while 25.5% of cases with the "X-Ray intra-op or in PACU" trigger had an AE. Overall agreement between nurse reviewers on the presence of any trigger (Kappa = 0.63; 95% CI 0.58 to 0.68) was higher than overall agreement between nurse reviewers on the presence of AEs (Kappa = 0.51; 95% CI 0.45 to 0.57). The overall agreement between nurse and physician assessment of AEs was higher (Kappa = 0.71; 95% CI 0.68 to 0.74).	adverse events: assessing inter-rater reliability and trigger performance of the Global Trigger Tool. *Int J Qual Health Care J Int Soc Qual Health Care ISQua*. 2010;22(4):266-274. doi:10.1093/intqhc/mzq026.[57]
Cross-Sectional Study	Investigators examined the rate of adverse events (AEs) using a trigger tool specific to intensive care units (ICUs). The study population consisted of adult (≥18 years) patients with an inpatient stay >48 hours. Patients were randomly selected from 62 ICUs in 54 U.S. academic and community hospitals participating in the Institute for Healthcare Improvement (IHI) critical care collaboratives between 2001 and 2004. A total of 12,074 charts were reviewed. Analyses were also conducted on a subgroup of 1,294 charts from 13 pilot ICUs in 10 hospitals. The prevalence of AEs across all 62 ICUs was 11.3 events per 100 ICU days (range 3.2 to 27.36 AEs). The AE prevalence in the pilot subgroup was 16.4 events per 100	Resar RK, Rozich JD, Simmonds T, Haraden CR. A trigger tool to identify adverse events in the intensive care unit. *Jt Comm J Qual Patient Saf Jt Comm Resour*. 2006;32(10):585-590.[58]

	ICU days. Among the pilot subgroup, 10 of 23 triggers were associated with 1,064 of 1,450 AEs. The positive blood culture trigger had the highest percent yield for AE detection. A small number of triggers led to the detection of a majority of the AEs.	
Cross-Sectional Study	Investigators developed and tested a trigger tool to identify adverse drug events (ADEs). The primary objectives were to: (1) assess the feasibility of training individuals to use the tool; (2) clarify training requirements; and (3) describe the extent and scope of ADEs in inpatient settings. The study population consisted of patients with a minimum hospital stay of two days who were discharged from 86 hospitals in four different medication safety collaboratives. Hospitals were recruited over an 18-month period starting in June 1999. A total of 2,837 charts were reviewed using a tool that comprised 24 triggers. Training new reviewers took approximately 30 to 60 minutes. An average of 2.68 ADEs per 1000 doses of medication was identified. In a subset of 1,704 charts, the trigger with the highest percentage yield was “abrupt medication stop”, which was found 248 times and was associated with 86 ADEs. In another subset of hospitals, only 5 of 274 (1.8%) ADEs found using the trigger tool were identified using traditional reporting methods.	Rozich JD, Haraden CR, Resar RK. Adverse drug event trigger tool: a practical methodology for measuring medication related harm. *Qual Saf Health Care*. 2003;12(3):194-200. doi:10.1136/qhc.12.3.194. [41]
Cross-Sectional Study	Investigators developed and tested a neonatal intensive care unit- (NICU) specific trigger tool designed to identify adverse events (AEs). The study population consisted of patients who were hospitalized for a minimum of two days and were discharged, transferred out, or died between November 1, 2004 and	Sharek PJ, Horbar JD, Mason W, Bisarya H, Thurm CW, Suresh G, Gray JE, Edwards WH, Goldmann D, Classen D. Adverse events in the neonatal intensive care unit: development, testing, and findings of an NICU-

	January 31, 2005. The trigger tool was used to retrospectively review 749 randomly selected charts of patients discharged from 15 NICUs (14 in the U.S. and 1 in Canada). Chart reviews revealed a total of 2,218 triggers (2.96 triggers per patient) and 554 unique AEs (0.74 AEs per patient). Only 6.1% of the unique AEs identified did not have an associated trigger. Of the 554 detected unique AEs, only 8% were identified by voluntary occurrence reports. The NICU trigger tool resulted in a median chart review time of 15 minutes, a mean chart review time of 20.5 minutes, and had a mean positive predictive value (PPV) of 0.38 (range of PPVs for each individual independent trigger 0.08 to 1.0). The most common AEs identified were nosocomial infections, catheter infiltrates, and abnormal cranial imaging.	focused trigger tool to identify harm in North American NICUs. *Pediatrics*. 2006;118(4):1332-1340. doi:10.1542/peds.2006-0565.[15]
Cross-Sectional Study	Investigators assessed the performance characteristics of the Institute for Healthcare Improvement's (IHI) Global Trigger Tool (GTT) to determine its reliability at regional and national levels. Chart reviews were conducted at 10 stratified, randomly selected acute care hospitals in North Carolina. Eligible patients were ≥18 years on admission and were discharged between January 1, 2002 and December 31, 2007. A total of 2,400 randomly selected charts (240 per hospital: 10 per hospital per quarter) were reviewed by internal (hospital-affiliated) and external (unaffiliated) reviewers. Additionally, an expert review team reviewed a 10% random sample of charts. A total of 202 charts were reviewed by all three review teams. The trigger tool's reliability to detect the	Sharek PJ, Parry G, Goldmann D, Bones K, Hackbarth A, Resar R, Griffin FA, Rhoda D, Murphy C, Landrigan CP. Performance characteristics of a methodology to quantify adverse events over time in hospitalized patients. *Health Serv Res*. 2011;46(2):654-678. doi:10.1111/j.1475-6773.2010.01156.x.[50]

	presence, number, and severity of adverse events (AEs) ranged from Kappa = 0.4 to 0.6. The internal reviewers, external reviewers, and expert reviewers identified 49, 32, and 74 AEs, respectively. Using the expert team as a comparison group, the internal review team had a higher sensitivity and specificity (49% and 94%, respectively) than did the external review team (34% and 93%, respectively).	
Cross-Sectional Study	Investigators from the Automated Adverse Event Detection Collaborative (AAEDC), a group of academic pediatric organizations that conduct research on automated adverse event (AE) detection, compared data from two academic children's hospitals' use of an automated trigger tool system. Records were pulled from September 2007 to October 2010 for Children's National Medical Center, and from July 2006 to October 2010 for Cincinnati Children's Hospital Medical Center. Medical records flagged with triggers by the EHR system were manually reviewed to determine whether an AE had occurred, and if it had occurred, the event's preventability and severity. Triggers associated with opioid and benzodiazepine toxicity, intravenous infiltration, hypoglycemia, coagulation disturbances, and renal dysfunction had good positive predictive values. Reviewers identified a total of 3,264 AEs, of which 57.3% were preventable. The automated system proved to be more accurate than traditional voluntary reporting, which only accounted for 492 AEs.	Stockwell DC, Kirkendall E, Muething SE, Kloppenborg E, Vinodrao H, Jacobs BR. Automated adverse event detection collaborative: electronic adverse event identification, classification, and corrective actions across academic pediatric institutions. J Patient Saf. 2013;9(4):203-210. doi:10.1097/PTS.0000000000000055.[46]
Cross-Sectional Study	Investigators developed and tested a pediatric-specific trigger tool for adverse drug event (ADE) detection, adapted from	Takata GS, Mason W, Taketomo C, Logsdon T, Sharek PJ. Development,

	the existing adult Institute for Healthcare Improvement (IHI) ADE tool. The study population consisted of patients selected from 12 freestanding U.S. children's hospitals, who were in the hospital for a minimum of two days and were discharged, transferred out, or died between March 18 and May 28, 2002. The first 30 days of hospitalization from a total of 960 randomly selected charts (80 per site) were reviewed. A total of 2,388 triggers and 107 ADEs were identified, producing a mean rate of 2.49 triggers per patient and 11.1 ADEs per 100 patients (95% CI 2.39 to 2.59 and 9.13 to 13.5, respectively), 15.7 ADEs per 1,000 patient days (95% CI 12.9 to 19.0), and 1.23 ADEs per 1,000 medication doses (95% CI 1.01 to 1.49). The positive predictive value (PPV) of individual triggers ranged from 0% to 20%, with a PPV of 3.7% for the trigger tool overall. 18 of 107 identified ADEs (16.8%) did not have an associated trigger. The trigger tool specifically identified 89 of the total 107 ADEs (83.2%), while hospital occurrence reports identified 4 ADEs (3.7%). The trigger tool identified approximately 22 times more ADEs than occurrence reports.	testing, and findings of a pediatric-focused trigger tool to identify medication-related harm in US children's hospitals. *Pediatrics*. 2008;121(4):e927-935. doi:10.1542/peds.2007-1779.[9]
Cross-Sectional Study	Investigators assessed the incidence and type of adverse events (AEs) and negligent AEs in Utah and Colorado. The study population consisted of 15,000 randomly selected non-psychiatric patients who were discharged from 28 hospitals in Utah and Colorado in 1992. Trained nurse reviewers screened a total of 14,700 records (4,943 from Utah; 9,757 from Colorado) for 1 of 18 criteria associated with AEs. Physicians reviewed records in which at least one criteria was present. To	Thomas EJ, Studdert DM, Burstin HR, Orav EJ, Zeena T, Williams EJ, Howard KM, Weiler PC, Brennan TA. Incidence and types of adverse events and negligent care in Utah and Colorado. *Med Care*. 2000;38(3):261-271.[47]

	test for reliability, 500 records were chosen for re-review. AEs were identified in 418 records in Colorado (21.1% of records reviewed by both nurses and physicians) and 169 records (20.1% of records reviewed by both nurses and physicians) in Utah. Operative AEs comprised 44.9% of the total AEs, while drugs, especially antibiotics and cardiovascular agents, were the second leading cause of AEs (19.3%). The percent agreement for AEs during the re-review was 79% (Kappa = 0.4, 95% CI 0.3 to 0.5).	
Cross-Sectional Study	Investigators evaluated the feasibility and capability of two retrospective chart review methods (the Harvard Medical Practice Study [HMPS] and the Institute for Healthcare Improvement's [IHI] Global Trigger Tool [GTT]) to detect adverse events (AEs) in orthopaedic inpatients. The study population consisted of a random sample of 350 adult orthopaedic admissions in 2009 at a Swedish university hospital. Two teams, each consisting of a registered nurse and two physicians, were assigned to each chart review method. Primary reviews were conducted by nurses. Records with suspected AEs were sent to the physicians, who independently reviewed the charts In total, 160 unique AEs were identified in 105 records. The median record review time was three (range 1 to 35) versus eight (range 1 to 20) minutes for the HMPS and GTT methods, respectively. Both tools demonstrated a learning curve for nurse reviewers. The positive predictive value for HMPS criteria and GTT triggers ranged from 0% to 80% and 0% to 100%, respectively.	Unbeck M, Schildmeijer K, Henriksson P, Jürgensen U, Muren O, Nilsson L, Pukk Härenstam K. Is detection of adverse events affected by record review methodology? an evaluation of the "Harvard Medical Practice Study" method and the "Global Trigger Tool." *Patient Saf Surg*. 2013;7(1):10. doi:10.1186/1754-9493-7-10.[60]

Cross-Sectional Study	Investigators reported on the adverse event (AE) detection method used in the 1994 Quality in Australian Health Care Study commissioned by the Commonwealth Department of Human Services and Health. The study population consisted of patients from 31 acute care hospitals in Australia. Medical record review teams comprised registered nurses and medical officers. Chart reviews occurred in a 2-stage process. In stage 1, nurses screened charts for at least 1 of 18 criteria that were indicators of potential AEs. In stage 2, medical officers reviewed charts with at least one criteria and made final determinations regarding the presence of AEs. Of the 18 criteria, return to the operating theatre had the highest odds ratio (OR 14.5) for association with an AE. Nurse reviewers had 84% agreement regarding the presence of positive criteria in patient charts (Kappa = 0.67; standard error [SE] 0.02). Nurses and medical officers had 98.7% agreement regarding the presence of positive criteria in patient charts. The sensitivity and specificity of the nurse screening process were 97.6% (95% CI 94.4% to 99.1%) and 67.3%, respectively. There was 80% agreement between medical officers regarding the presence of AEs (Kappa = 0.55). There was 58% agreement for preventability of the AEs (Kappa = 0.33).	Wilson RM, Runciman WB, Gibberd RW, Harrison BT, Newby L, Hamilton JD. The Quality in Australian Health Care Study. *Med J Aust*. 1995;163(9):458-471.[48]
Structured Review	Investigators reviewed several methodologies for identifying adverse events (AEs) using information technology, which are more timely and cost-effective compared to manual chart review. They also reviewed studies using these methodologies and study results for certain AE types, with a focus on nosocomial	Bates DW, Evans RS, Murff H, Stetson PD, Pizziferri L, Hripcsak G. Detecting Adverse Events Using Information Technology. J Am Med Inform Assoc. 2003;10(2):115-128.

	infections, adverse drug events (ADEs), and injurious falls. The investigators found that computerized tools like event monitoring and natural language processing are cost-effective ways to detecting AEs, especially nosocomial infections and ADEs. For instance, the sensitivity for computerized surveillance of nosocomial infections versus manual surveillance was higher (90% vs. 76%). The computerized surveillance system identified infections quickly and lessened the reviewer time burden by >60%. As more hospitals adopt the latest technology, these tools may be adjusted to detect a wider range of AEs.	doi:10.1197/jamia.M1074.[63]
Office of the Inspector General Report	Investigators assessed the utility of various adverse event (AE) detection methods in a population of hospitalized Medicare beneficiaries. The study population consisted of a random sample of 278 Medicare beneficiary hospitalizations selected from all Medicare discharges from acute care hospitals in two selected U.S. counties during a 1-week period in August 2008. AEs were identified using a two stage review process. First, one of five methods was used to screen for possible AEs. Physicians then reviewed the medical records for which at least one screening method indicated a potential AE. The following five screening methods were used: (1) review of medical records by registered nurses using the Institute for Healthcare Improvement's (IHI) Global Trigger Tool (GTT), (2) analysis of present on admission (POA) indicators in billing data, (3) phone interviews with Medicare beneficiaries or their family members, (4) hospital incident reports, and (5) application of Agency for Healthcare Research and Quality's (AHRQ) Patient Safety Indicator	Levinson DR. *Adverse Events in Hospitals: Methods for Identifying Events*. Washington, DC: Office of the Inspector General, Department of Health and Human Services; 2010.[55]

	(PSI) software program to administrative billing data. The five screening methods identified 662 flags for potential AEs in total, of which 256 were determined to be associated with events by physician review. The 256 flags detected a total of 114 AEs. Nurse reviews identified 93 of 120 events (78%), POA analysis identified 61 events (51%), interviews identified 22 events (18%), incident reports identified 8 events (7%), and PSI analysis identified 8 events (7%).	
Relationship Between Patient Harm and Other Aspects of Quality		
Prospective Study	Investigators examined potential associations between evidence-based care and the occurrence of adverse events (AEs) in heart failure and chronic obstructive pulmonary disease (COPD) patients. The study population consisted of patients >50 years old who were discharged from five Emergency Departments (EDs) between September 2007 and April 2010 with a final diagnosis of heart failure or acute exacerbation of COPD. An expert panel of experienced staff emergency physicians created a list of evidence-based clinical practice guidelines for ED care. Trained data abstractors analyzed health records for guideline adherence. AEs were defined as the following outcomes associated with the index ED admission: return to the ED within 14 days with subsequent discharge, admission, or death. Trained emergency physicians reviewed patient case summaries to identify AEs. Overall, 21.1% of patients returned to the ED within 14 days. 12 AEs were identified, all of which were deemed to be preventable. Heart failure patients who died were significantly less likely to have	Calder L, Tierney S, Jiang Y, Gagné A, Gee A, Hobden E, Vaillancourt C, Perry J, Stiell I, Forster A. Patient safety analysis of the ED care of patients with heart failure and COPD exacerbations: a multicenter prospective cohort study. *Am J Emerg Med*. 2014;32(1):29-35. doi:10.1016/j.ajem.2013.09.013.[65]

	received guideline-adherent care (p=.02).	
Cross-Sectional Study	Investigators examined "never event" (as defined by the Center for Medicare and Medicaid Services) complications occurring after radical cystectomy. The study population consisted of adults >40 years who had undergone radical cystectomy. Data from 2002 to 2009 were obtained from the Nationwide Inpatient Sample (NIS). The main outcomes were in-hospital mortality, length of stay, and total hospital costs. A length of stay or total cost ≥ 90th percentile was considered prolonged or increased, respectively. A total of 12,451 patients who underwent radical cystectomy for bladder cancer were identified in the NIS. 2.42% of all patients experienced at least one never event. The presence of at least one never event was associated with a prolonged length of stay (OR 8.76; 95% CI 7.89 to 9.76), greater odds of in-hospital mortality (OR 3.48; 95% CI 2.91 to 4.18), and increased total costs (OR 7.49; 95% CI 6.65 to 8.26).	Joice GA, Deibert CM, Kates M, Spencer BA, McKiernan JM. "Never events": Centers for Medicare and Medicaid Services complications after radical cystectomy. *Urology*. 2013;81(3):527-532. doi:10.1016/j.urology.2012.09.050.[66]
Cross-Sectional Study	Investigators assessed the quality of care for surgical patients. Patient data were obtained from Medicare files from seven states. The four surgical procedures studied were coronary artery bypass grafting, coronary angioplasty, cholecystectomy, and prostatectomy. Postoperative adverse event (AE) rates ranged from 6.9% to 33.3%. 30-day mortality rates ranged from 1.0% to 6.6%. Compared to those with no AEs, coronary artery bypass graft patients with AEs had longer hospital stays (18.5 ± 13.2 days vs. 13.2 ± 6.2 days; p<.001) and increased mortality rates (15.2% vs. 2.6%; p<.001).	Rosen AK, Geraci JM, Ash AS, McNiff KJ, Moskowitz MA. Postoperative adverse events of common surgical procedures in the Medicare population. *Med Care*. 1992;30(9):753-765.[67]

Cross-Sectional Study	Investigators examined the impact of experiencing an Agency for Healthcare Research and Quality's (AHRQ) Patient Safety Indicator (PSI) event on the likelihood of readmission. The study population consisted of acute care discharges from Veteran Affairs (VA) hospitals from October 2002 to September 2007. The final sample included 1,807,488 index hospitalizations and 262,026 readmissions. Data were abstracted from the VA Patient Treatment File and the VA Vital Status File. AHRQ PSI software was used to generate risk-adjusted PSI rates for individual PSIs and composite PSIs reflecting technical care and continuity of care. The primary outcome was 30-day all-cause readmission. The odds of readmission were 23% higher for index hospitalizations with any PSI event compared with those with no event (95% CI 1.19 to 1.26). For the composites, the biggest difference in readmission rates occurred when comparing patients with and without PSIs in the continuity of care composite (OR 1.37; 95% CI 1.26 to 1.50).	Rosen AK, Loveland S, Shin M, Shwartz M, Hanchate A, Chen Q, Kaafarani HMA, Borzecki A. Examining the impact of the AHRQ Patient Safety Indicators (PSIs) on the Veterans Health Administration: the case of readmissions. *Med Care*. 2013;51(1):37-44. doi:10.1097/MLR.0b013e318270c0f7.[68]
Cross-Sectional Study	Investigators assessed the quality of surgical oncology care by examining national trends in hospital-acquired adverse events (AEs) after major cancer surgery. Data for adult patients (≥18 years) who underwent one of eight major cancer surgeries in the U.S. between 1999 and 2009 were obtained from the Nationwide Inpatient Sample datasets. The Agency for Healthcare Research and Quality's (AHRQ) Patient Safety Indicators (PSIs) were used to identify potentially preventable AEs in medical records. 12.9% of all patients studied experienced at least one AE. AE rates after major cancer	Sukumar S, Roghmann F, Trinh VQ, Sammon JD, Gervais M-K, Tan H-J, Ravi P, Kim SP, Hu JC, Karakiewicz PI, Noldus J, Sun M, Menon M, Trinh Q-D. National trends in hospital-acquired preventable adverse events after major cancer surgery in the USA. *BMJ Open*. 2013;3(6). doi:10.1136/bmjopen-2013-002843.[69]

	surgery increased over the study period time frame (estimated annual percentage change 3.5%; 95% CI 2.8% to 4.1%; p<.001). Patients with one or more AEs experienced higher rates of in-hospital mortality (OR 19.38; 95% CI 18.44 to 20.37; p<.001), prolonged length of stay (OR 4.43; 95% CI 4.31 to 4.54; p<.001), and excessive hospital charges (OR 5.21; 95% CI 5.10 to 5.32; p<.001).	
Measuring Patient Safety to Drive Quality Improvement		
Prospective Study	Investigators examined the impact of computerized adverse drug event (ADE) surveillance on the ability to prevent future ADEs. Signals for potential ADEs were monitored using the LDS Hospital information system, installed in May 1989, which constantly monitors patients for potential ADEs. In the first year of computerized surveillance, physicians were only notified of verified ADEs that were considered severe or life-threatening. In the second year of surveillance, physicians were notified of all verified ADEs. In the first year of surveillance, 15% of identified ADEs were due to allergic or idiosyncratic reactions. In the second year, during which physicians received notification of drug allergies, only 1.4% of ADEs were due to allergic or idiosyncratic reactions, indicating a significant reduction (p<0.001). Timely identification of ADEs allowed physicians to intervene before the ADE became severe.	Evans RS, Pestotnik SL, Classen DC, Bass SB, Burke JP. Prevention of adverse drug events through computerized surveillance. *Proc Annu Symp Comput Appl Sic Med Care Symp Comput Appl Med Care*. 1992:437-441.[70]
Prospective Study	Investigators assessed the impact of a hospital based patient safety program on adverse drug event (ADE) rates. The study population consisted of patients discharged from Missouri Baptist Medical	Garrett PR Jr, Sammer C, Nelson A, Paisley KA, Jones C, Shapiro E, Tonkel J, Housman M. Developing and implementing a

	Center, a non-teaching community hospital. Data were collected from January 2001 to December 2003 via manual review of randomly selected charts using a trigger tool. The patient safety program intervention included formation of a patient safety council, hiring of a full-time patient safety specialist, new event reporting systems, as well as additional interventions recommended by the Institute for Safe Medication Practices, the American Society of Health System Pharmacists, the Institute for Healthcare Improvement, the Joint Commission for the Accreditation of Healthcare Organizations, and the Agency for Healthcare Research and Quality. The transition period (time during which interventions were instituted) lasted from July 2001 to March 2002. Median ADEs per 1000 doses of medication declined from 2.04 to 0.65 (p<.001) from the baseline to post-intervention period. Similarly, median ADEs per 100 patient days declined from 5.07 to 1.30 (p<.001). There was a threefold reduction in risk of an ADE (p<.001) comparing the baseline and post-intervention period. The incidence of category F-I harms as defined by the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) declined eightfold from the baseline to post-intervention period (p<.001).	standardized process for global trigger tool application across a large health system. *Jt Comm J Qual Patient Saf Jt Comm Resour*. 2013;39(7):292-297.[74]
Prospective Study	Investigators measured occurrences of unplanned extubations in pediatric critical care units and assessed the impact of coordinated interdisciplinary interventions on unplanned extubation rates. The study population consisted of patients in the cardiac intensive care unit (CICU) and pediatric intensive care unit (PICU) at Children's Hospital Colorado, a free-standing pediatric academic center. From	Kaufman J, Rannie M, Kahn MG, Vitaska M, Wathen B, Peyton C, Judd J, Quinby Z, da Cruz EM, Dobyns E. An interdisciplinary initiative to reduce unplanned extubations in pediatric critical care units. *Pediatrics*. 2012;129(6):e1594-1600.

	January 2009 to December 2010, all incidences of unplanned extubations were documented by respiratory therapists and bedside nurses via electronic medical record. Interventions were implemented from October 2009 to May 2010. Interventions included: (1) standardized re-taping of endotracheal tubes for all patients admitted to the ICU; (2) standardized handoffs from the cardiovascular operating room to the CICU; (3) root-cause analysis of all unplanned extubations; (4) re-examination of sedation practices; and (5) public displaying of days since the last adverse event. The PICU had 21 events in the nine-month pre-intervention period, 14 events in the eight-month intervention period, and 5 events in the seven-month post-intervention period. The CICU experienced 11, 4, and 0 events in the pre-intervention, intervention, and post-intervention periods, respectively. Mean unplanned extubation rates per 100 patient days for each interval were 0.8, 0.5, and 0.29 for the PICU, and 0.74, 0.44, and 0 for the CICU.	doi:10.1542/peds.2011-2642.[71]
Prospective Study	Investigators examined the effect of an adverse drug event (ADE) alert system on cost and quality outcomes in community hospitals. The intervention involved implementation of an ADE alert system that is triggered in real time, allowing for immediate pharmacy intervention. The intervention study population consisted of medical and surgical patients admitted to one of seven Trinity Health hospitals. Patients admitted to these hospitals prior to the intervention served as an internal control group. Another set of hospitals without an ADE alert system served as the external control group.	Piontek F, Kohli R, Conlon P, Ellis JJ, Jablonski J, Kini N. Effects of an adverse-drug-event alert system on cost and quality outcomes in community hospitals. *Am J Health-Syst Pharm AJHP Off J Am Soc Health-Syst Pharm*. 2010;67(8):613-620. doi:10.2146/ajhp090056.[72]

	Primary outcomes included pharmacy department costs, variable drug costs, and mortality rates. Secondary outcomes included total hospitalization costs, length of stay, readmission rate, and case-mix index. Mean pharmacy department costs and drug costs decreased significantly from pre-implementation to post-implementation ($p<.001$), while these costs increased significantly in the external control group ($p=.029$). Statistically significant decreases in severity adjusted mortality and length of stay were only seen in the study group ($p<0.001$).	
Cross-Sectional Study	Investigators developed a centralized Institute for Healthcare Improvement's (IHI) Global Trigger Tool (GTT) process to generate uniform estimates of the number, type, and severity of adverse events (AEs) across a large health system. The study population consisted of adult patients (≥18 years) with a hospital stay >24 hours from 25 hospitals in the Adventist Health System (AHS) that used common electronic medical records. Investigators used a centralized web-based data collection system, which randomized patient charts from each hospital and selected charts for manual review using the IHI GTT. AHS sent quarterly reports and case studies of the worst harms to each participating hospital. Recipients of case studies were encouraged to identify opportunities for quality improvement. A total of 17,295 charts were reviewed between January 2009 and December 2011. Use of the GTT revealed a mean of 98 AEs per 1,000 patient days in the last six months of 2009 compared with a mean of 67 AEs in the last six months of 2011. System wide reduction in AEs rates were attributed to	Cohen MM, Kimmel NL, Benage MK, Cox MJ, Sanders N, Spence D, Chen J. Medication safety program reduces adverse drug events in a community hospital. *Qual Saf Health Care*. 2005;14(3):169-174. doi:10.1136/qshc.2004.010942.[73]

	safety improvement projects instituted by AHS.	
Cross-Sectional Study	The investigators applied the Agency for Healthcare Research and Quality's (AHRQ) Patient Safety Indicators (PSI) to hospital discharge data and examined prevalence of PSI events. They found that 16 of the 20 PSIs examined had rates of >100 pediatric cases per 10,000 pediatric discharges across the nation in 2000. PSIs also led to significant increases in length of stay, costs, charges, and in-hospital death. Furthermore, they discovered that PSI events happened more often among the very young (<1 year) and those on Medicaid insurance. Finally, the authors estimated that the events cost >$1 billion in extra charges for children in 2000.	Miller MR, Zhan C. Pediatric Patient Safety in Hospitals: A National Picture in 2000. *Pediatrics*. 2004;113(6):1741-1746.[24]
Institute of Medicine Report	The IOM identified patient safety as an area of national priority for quality improvement of the U.S. healthcare system. The IOM recommendations for improving patient safety comprise a four-tiered approach, which include (1) establishing a national focus to create leadership, research, tools and protocols to enhance the knowledge base about safety, (2) identifying and learning from errors through immediate and strong mandatory reporting efforts, as well as the encouragement of voluntary efforts, (3) raising standards and expectations for improvements in safety through the actions of oversight organizations, group purchasers, and professional groups, and (4) creating safety systems inside health care organizations through the implementation of safe practices at the delivery level. This level is the ultimate target of all the recommendations.	Kohn LT, Corrigan JM, Donaldson MS. *To Err Is Human: Building a Safer Health System*. Washington, DC: Institute of Medicine Committee on the Quality of Health Care in America;1999.[2]