Final Report:

Using Risk Models to Improve Safety with Dispensing High-Alert Medications in Community Pharmacies

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Abstract

Purpose: Determine if sociotechnical probabilistic risk assessment (ST-PRA) can create detailed risk models that predict the incidence of preventable adverse drug events (PADEs) with high-alert medications dispensed in community pharmacies.

Scope: This study involves PADEs associated with warfarin, methotrexate, fentanyl patches, and insulin analogs dispensed from a sample of 12,000 community pharmacies.

Methods: A model-building team was used to build 10 fault trees that predict the incidence of PADEs for the four targeted medications. The fault trees were populated with team estimates of human error and at-risk behaviors, validated, analyzed to determine unique risk pathways, and evaluated to determine the impact of recommended interventions on incidence rates.

Results: PADEs with the highest incidence include dispensing the wrong dose/strength of warfarin due to a data entry error (1.83/1,000 prescriptions), dispensing warfarin to the wrong patient (1.22/1,000 prescriptions), and dispensing an inappropriate fentanyl patch dose due to a prescribing error (7.30/10,000 prescriptions). PADEs with the lowest incidence include dispensing the wrong drug when filling a warfarin prescription (9.43/1 billion prescriptions). Increased patient counseling, conducting a second data entry verification process during product verification, using barcoding technology, and using hard computer alerts that can't be bypassed easily provided the largest quantifiable reductions in risk.

Key Words
Sociotechnical probabilistic risk assessment (ST-PRA), high-alert medication, failure mode and effects analysis (FMEA), root cause analysis (RCA), fault tree, preventable adverse drug event (PADE)

Purpose

The purpose of this study was to determine if sociotechnical probabilistic risk assessment (ST-PRA) can create detailed risk models identifying process failures and behavioral elements that produce preventable adverse drug events (PADEs) involving high-alert medications dispensed in community pharmacies and whether the models can be used to predict the effectiveness of interventions to prevent ADEs. To accomplish this, five objectives were set:

- Identify a list of high-alert medications dispensed from community pharmacies
- Develop a generic fault tree describing community pharmacy dispensing errors likely to reach patients
- Model selected PADEs for four high-alert medications using the generic fault tree as a template
- Identify specific error pathways with a high probability of occurrence for the four high-alert medications
- Identify and evaluate the impact of risk-reduction interventions with the four high-alert medications.

Scope and Significance

Preventable Adverse Drug Events in Community Pharmacies

Adverse drug events (ADEs), defined as injuries from drug therapy,[1] are among the most common causes of harm during the delivery of healthcare.[2,3,4] At least a quarter of these events are preventable.[1,5,6] On an annual basis, up to 450,000 inpatients experience a preventable adverse drug event (PADE),[7] which is a harmful medication error. PADEs lead to about 4% (range, 1.4-15.4%) of hospital admissions[8,9,10,11,12,13] and account for injuries in 3% of patients in their homes.[14]

Few prospective data detail the incidence of PADEs in ambulatory patients. In the modest studies that exist, the data are difficult to compare due to differing definitions of medication errors, ADEs, and PADEs; variable methodologies for detecting errors and ADEs; differing sources of information; variable populations and study periods; and questionable population estimates based on small sample sizes.[15,16,17] Four well-designed retrospective studies that examined community pharmacy dispensing errors using similar definitions, detection methods, and expression of incidence rates still reported a wide range of errors–from 1.7-24%.[18,19,20,21] Studies conducted between 1991 and 2000 reported higher error rates than more recent studies, likely reflecting improvements in dispensing systems and technology over time. However, the lowest dispensing error rate (1.7%) still translates to approximately four errors per 250 prescriptions per pharmacy per day, or 60 million errors during the dispensing of 4 billion prescriptions annually.[22,23]

Few studies have reported the frequency of harm caused by PADEs associated with medications dispensed from community pharmacies. Gandhi et al.[14] found that 5% of ambulatory patients experienced a PADE stemming from medications dispensed from community pharmacies. Gurwitz et al.[24] identified that almost half of the serious, life-threatening, or fatal ADEs related to medications dispensed from pharmacies were preventable. Several studies suggest that dosing errors occur frequently and have the highest rate of clinical significance among types of medication errors.[25,26,27] Conservative estimates suggest an annual cost associated with PADEs in the ambulatory setting, among older adults, of $887 million.[28] In the early 1990s, Johnson and Bootman estimated that an average of $76.6 billion ($30.1 billion to $136.8 billion) is spent annually in the ambulatory setting in the US to resolve drug-related problems, with drug-related hospitalizations as the largest cost.[29] An update to this estimate by Ernst and Grizzle in 2000 determined that hospital admissions accounted for $121.5 billion, or 70% of total costs of drug-related problems in the US.[30]

The drugs associated with the most harmful PADEs in acute care settings were first coined “high-alert” medications by the Institute for Safe Medication Practices (ISMP) in 1998.[31,32,33] Although high-alert medications are an essential component of drug therapy, they carry a significant risk of causing serious injuries or death to patients if misused. Errors with these drugs are not necessarily more common, but the consequences are more devastating. ISMP published the first list of high-alert medications for acute care settings in 1989[34] and has updated the list regularly.[35,36,37,38] Evidence summarized in Table 1 (Appendix A*) notes the characteristics, medications, and types of errors involved in patient harm from PADEs in the ambulatory setting. Until now, no formal list of high-alert medications dispensed from community pharmacies has been compiled.

Retrospective and Prospective Risk Assessment Tools

Traditionally, healthcare systems have relied on retrospective risk identification and assessment tools, such as event reporting, document review, and root cause analysis (RCA), to understand the risks involved in prescribing, dispensing, and administering medications.[39,40,41] RCA is typically a top-down, reactive process

used after a preventable adverse event occurs or nearly occurs to provide insight into system and process failures; however, RCA does not examine behavioral components of error, an important omission.

Recognizing the need for more prospective risk identification and analysis, healthcare providers began using failure mode and effects analysis (FMEA),[42,43,44,45,46] which has its roots in highly reliable industries such as commercial aviation and nuclear power.[47,48,49,50] It is a bottom-up analysis technique in which knowledgeable staff look at vulnerable processes by asking, "What can possibly go wrong?" and "What is the effect of each failure?" When a failure is identified, two options exist: reduce the probability of failure to an acceptable level, or add safety steps to mitigate the effects of failure.[51] In 1994, Cohen et al. were among the first to publish the benefits of using FMEA in healthcare. FMEA has since been endorsed by The Joint Commission as a prospective risk assessment tool that leads to action without having to learn through actual events.[52]

RCA and FMEA represent the most basic types of causal or risk analysis.[53,54,55] They both offer qualitative information about risk and error. Neither allows the analyst to quantify the level of risk or model the effects of combinations of failures.[56] Sociotechnical probabilistic risk assessment (ST-PRA) is a prospective risk assessment technique that advances the qualitative work of FMEA and RCA into a quantitative realm by estimating the probabilities of human error and the influence of behavioral norms on outcomes.[57] Table 2 (Appendix A) summarizes the advantages of ST-PRA over FMEA and RCA. The tool is used to model all possible combinations of failures.[58,59] Insights are obtained by breaking down the system into individual tasks or components for which estimated failure rates are determined. Combinations of failures of the different tasks/ components of the system are modeled in a fault tree, leading to a single adverse outcome.[60]

ST-PRA is derived from a probabilistic risk assessment (PRA) tool that originated in the mid 1970s in nuclear power plants to improve safety.[61,62,63,64] PRA has since been used in many complex, high-risk industries [65,66] because multiple failure modes can be considered in combination with one another. Although PRA is used to model predominantly mechanical systems (e.g., airplanes, cars, equipment), ST-PRA is used to model predominantly human systems. Thus, ST-PRA is the more appropriate tool for use in healthcare. Although its use in healthcare is still relatively new,[67,68,69,70,71] a previous study using ST-PRA to model medication system failures in long-term care strongly suggests that application of this process to high-alert medications dispensed from community pharmacies will be successful in assessing risks and gauging the impact of system and behavioral changes on these risks.

Methods

To conduct this developmental study in 2007-2008, ISMP partnered with two chain pharmacies representing almost 12,000 community pharmacies of various size, prescription volumes, hours of operation, geographic locations, and populations served. These pharmacies represent a fifth of all community pharmacies in the 48 contiguous US states. From the two chains, a purposive sample of 22 pharmacies from three regions in the US was selected to participate in the study to ensure diversity in regards to setting, prescription volume, hours of operation, and population served. The study employs process and control mapping, FMEA, and ST-PRA to produce medication dispensing risk models that can be used to identify and quantify risk as well as predict the impact of interventions. It is the first study to apply ST-PRA to the community pharmacy dispensing process. The models were built by teams comprising pharmacists and pharmacy technicians who provided estimates of process failure and human error probabilities based on real-time experiences in community pharmacy practice. The study's focus on high-alert medications heightens its ability to impact the health and safety of consumers and provide meaningful insight into community pharmacy safety.

Model-building Sample

The modeling teams comprised two trained ST-PRA facilitators, one or two research staff, and six pharmacists/ three pharmacy technicians who volunteered to participate from nine of the sample of pharmacies. Informed consent was obtained from all participants. To conduct model-building sessions, all nine pharmacies where the participants worked were within a 50-mile radius in the West South Central region of the US. The participants' pharmacies ranged in weekly prescription volumes from less than 1,000 to greater than 3,000 per week. The pharmacies served both urban and suburban areas, and one was located in a small community setting. Pharmacy staffing patterns ranged from a single pharmacist on duty to multiple pharmacists and technicians on duty. One pharmacy was open 24 hours, and several offered drive-through service. The

participants had diverse ethnic backgrounds—African American, Asian, Hispanic, and Caucasian—and included both genders. Years of experience ranged from 5 to 18 years (median 10 years).

Model Validation Sample

Pharmacists from both chains who worked in 11 community pharmacies in the New England and Mid-Atlantic regions in the US participated in structured interviews to validate the risk models. As with the model-building sample, these pharmacies and participants were diverse, particularly in regards to experience levels (1.5-30 years, mean of 8 years), practice settings, average volume of prescriptions filled daily, and gender/ethnic backgrounds (including Asian, Indian, and Caucasian). Observations were also conducted by the research team at two pharmacies selected from a convenience sample, one from each chain, during validation of the models.

Identifying High-Alert Medications

A list of high-alert medications dispensed from community pharmacies was compiled using qualitative research methods, including analysis of data about PADEs from the following sources:

- ISMP Medication Errors Reporting System[72] and the Pennsylvania Patient Safety Reporting System[73]
- FDA MedWatch databases (national reporting system for harmful errors and adverse drug reactions)[74]
- Community pharmacy databases from participating pharmacies (quality data, prescription volume data)
- Community pharmacy survey data[75]
- Public litigation data[76] and review of the literature (see Table 1 in Appendix A).

The data were sorted into relevant categories based on the types of medications, severity of harm to the patient,[77] and frequency of prescribing.[78,79] Consensus was reached on which drugs to include on the community pharmacy high-alert medication list, based primarily on the risk of harm to the patient if the drug is misused. Four of these medications were selected for ST-PRA modeling.

Steps in the ST-PRA Model-Building Process

1) Recruit the Modeling Team

A voluntary modeling team was recruited using a noncoercive protocol approved by an Institutional Review Board. District managers from the pharmacy chains nominated pharmacists and technicians based on diversity of backgrounds and work experiences, knowledge of the dispensing system, and ability and willingness to communicate candidly about processes and behaviors that could lead to PADEs. The team did not include personnel with direct supervisory relationships to each other; all members were from different pharmacies.

2) Build a Process and Control System Map

The research team created a process and control map of the dispensing process. Observations and discussion verified that differences in the workflow between the two pharmacy chains were minimal, allowing agreement upon one standard map. The map shows how work inputs, outputs, and tasks are linked and how the embedded control systems can help prevent and detect errors.[80,81,82] Active control systems are deliberate steps in the process that specifically help manage the risk of errors, such as data entry verification. Passive controls are features inherent in the system that might help control risks but are not specifically set up for that purpose, such as differences in tablet appearance that may alert a pharmacist to an incorrect medication.

3) Identify Failure Modes

The researchers used an abbreviated FMEA process to identify individual failures (errors, at-risk behaviors, equipment failures) possible during the dispensing process and for each targeted high-alert medication. Table 3 (Appendix A) shows small cross-sections of the FMEAs related to warfarin and fentanyl transdermal patches.

4) Identify Top-level Events (PADEs)

The FMEAs were used to determine PADEs to be modeled for the targeted drugs. As described in Table 4 (Appendix A), six PADEs for warfarin, and one PADE each for fentanyl patches, methotrexate, and insulin analogs were identified. The scope of the study did not allow modeling of all significant PADEs for each medication. The PADEs became the top-level events in the risk models, which were expressed using a “per prescription” denominator. To calculate PADEs that reached patients, prescription volumes were obtained from participating pharmacies and augmented with national data when appropriate.

5) Build the Fault Trees

The primary tool of ST-PRA is the fault tree, a graphical quantitative risk model that represents the complex

relationships between system elements, organizational culture, human errors, equipment failure, behavioral norms, and undesirable outcomes. The structure of the fault tree is informed by the process and control system map and the FMEAs. Table 5 (Appendix A) summarizes the elements of fault trees. The fault tree is built from left to right, starting with an initiating error that could lead to a top-level event (PADE). The initiating error flows through the branches of the fault tree, which link basic events together. The basic events represent 1) exposure rates, or how often certain activities occur; 2) fundamental failures, such a human error, at-risk behavior, or equipment failure rates; or 3) capture opportunities, which help detect and correct errors. The basic events are combined by AND gates, in which all elements feeding the gate are required for the gate to be true, and OR gates, in which only one element feeding the gate is required for the gate to be true. These gates and basic elements are illustrated and described in detail in Figure 1 (Appendix B).

During February to April 2007, the modeling team met six times (5 to 7 hours each) and created 10 fault trees for the PADEs described in Table 4 (Appendix A). The fault trees went through multiple iterations until the team was satisfied that they captured the most important elements of the dispensing process.

6) Estimate Event Rates

Input from the modeling team was used to estimate the probability of failure or frequency of occurrence for each basic event in the fault trees. This is often the most difficult task in ST-PRA. Most healthcare practitioners do not have actual rate data for the underlying basic events. At best, data collection systems only capture the end result, with the rate of intermediate failures relatively unknown. Failures, at-risk behaviors, and adverse events are underreported, making any data source relying on reporting systems suspect. Thus, many ST-PRA fault trees are developed purely through modeling team experiences.

The modeling team was led by experts with knowledge of human factors, human reliability, probability theory, ST-PRA modeling, medication safety, and group dynamics. The pharmacists and technicians possessed deep domain knowledge of the pharmacy processes under assessment. With exposure rates, such as the percent of prescriptions entered by technicians, the chain pharmacies' corporate data sources verified the team's estimates. When estimating at-risk behavior rates, the pharmacists and technicians relied on their own work experiences and observations and came to a consensus regarding frequencies. When estimating rates of human error, mishap data from literature was referenced when applicable, and the team facilitators anchored the group estimates on human error rates reported in the literature. Table 6 (Appendix A) summarizes the human error probabilities that helped inform and verify team estimates.

Numerous sophisticated techniques have been employed since the early 1980s to estimate rates of human error, particularly in the aviation and nuclear power industry.[83,84,85,86,87,88,89,90,91] Although the formulas and tables for estimating human error probabilities vary from technique to technique, each factors in error type and performance shaping factors (PSF), such as those in Table 7 (Appendix A). PSFs have a positive or negative effect on performance. For example, staff training can influence performance either positively (e.g., when it emphasizes the appropriate response) or negatively (e.g., when absent). The modeling team referenced the FMEAs to uncover the most relevant PSFs before making estimates.

In very general terms, given a human performance limit for a single person operating in ideal conditions of 0.0001 (1/10,000), the modeling team often started with an error rate of 0.001 (1/1,000) to account for the negative influence of a single PSF, such as time constraints. Identification of additional PSFs (e.g., illegible prescriptions, look-alike product names, complex tasks, minimal training) was part of the group process. The number of PSFs and their degree of influence helped the team adjust its estimates upward or downward through an iterative process before deciding on a final probability of error. The team quickly gained comfort in the task of estimating error and at-risk behavior rates, which is typical of ST-PRA modeling teams. These team estimates are more accepted than rates from event data and are often more accurate than rates predicted by senior management.[92,93]

7) Compare Risk Models Against Group Expectations and Validate the Models

Observation. Two members of the research team visited one pharmacy from each of the participating chains to observe and ask questions regarding processes and workflow. The observations served to validate that the structure of the fault trees represented the "as-is" dispensing process at the participating pharmacies. Observations also confirmed the presence or absence of visible process risks (e.g., low frequency of patient counseling, bypassed computer alerts) and PSFs (e.g., time constraints, look-alike products near each other).

Interviews. A survey instrument for interviewing pharmacists was constructed and tested. The survey items were based on an analysis that indentified exposure rates, failures, and at-risk behaviors most predictive of the PADEs. The survey instrument touched upon more than half of all the basic events in the 10 fault trees, including all at-risk behaviors, two thirds of the exposure rates, and one third of the human error rates. The research team interviewed 11 pharmacists from the participating chains. At the beginning of the interview, the research team provided the pharmacists with a brief description of project and general human error rates and PSFs that were referenced during the modeling sessions to anchor estimates. Probabilities estimated by the modeling group were not shared with the validation group before they provided independent estimates. Interviewees were also asked to respond if system weaknesses and/or at-risk behaviors were present in their facilities; if present, to what extent; and if not present, the systems in place that guard against that at-risk behavior. Each interview took approximately 1 hour to complete.

Literature review. Well-constructed studies of drug mishaps were examined to provide, when possible, evidence to support the probability estimates derived for the PADEs and initiating errors in the fault trees.

8) Identify and Quantify the Impact of Risk-reduction Interventions (Sensitivity Analysis)
After validation of the fault trees, fault tree software[94] calculated combinations of failures and the total combined probability of occurrence of the PADE (top-level event). All unique failure combinations that could lead to the PADEs were identified and ranked in cut sets, producing a "portfolio of risk" for each fault tree. The cut sets were used to identify high-risk error pathways for the targeted high-alert medications. With input from an advisory group, these portfolios were used to identify interventions to reduce the probability of the initiating error; alter the human error, at-risk behavior, and exposure rates within the fault tree; or change the structure of the fault tree by building into the process opportunities for capture of errors. Once the interventions were identified, the fault trees were updated to reflect the relative influence of the interventions. Given new estimates of error with the proposed interventions in place, the models quantified the impact of the strategy.

Results

Community Pharmacy High-Alert Medications

Table 8 (Appendix A) lists the drugs that were identified as high-alert medications dispensed from community pharmacies. Warfarin, fentanyl patches, methotrexate, and insulin analogs were selected for ST-PRA modeling. Examples of risk factors with these drugs can be found in Table 9 (Appendix A).

Validation of Fault Trees

Based on observations and survey findings, two of 52 rates associated with at-risk behaviors were adjusted to reflect minor differences in estimates. No changes were made to 306 exposure rates or 211 failure rates, as the validation group provided the same or remarkably similar estimates as the modeling team. No changes to the fault trees occurred as a result of comparison to published studies about medication mishaps.[95,96,97,98,99,100,101,102,103] Data reported in the literature were not directly comparable to the predicted rates of occurrences in the fault trees. The incidence of PADEs for each of the targeted high-alert medications is not readily available. Most studies have identified general rates of error, ADEs, and/or PADEs. Direct comparisons using these studies were limited by differences in event definitions, event categories, study settings, detection methods, and outcomes evaluated. Furthermore, many studies do not distinguish between inpatient and outpatient prescriptions; errors, PADEs, and ADEs; types of errors with each drug; or forms of the drug involved in the errors (e.g., oral, parenteral, transdermal). These limitations made it difficult to compare published incidence rates to the probabilities in the fault trees. However, based on observations and validation surveys, there is sufficient evidence to support the conclusion that the fault trees are good representations of pharmacy dispensing systems in the two chains participating in the study.

Risk of PADEs Reaching Patients

This study produced 10 fault trees for PADEs associated with warfarin, fentanyl patches, methotrexate, and insulin analogs. Table 4 (Appendix A) lists the PADEs that were modeled and the rationale for selection. The fault trees begin with an initiating error and predict the ability of the pharmacy dispensing system to detect and correct the error before it reaches patients. Table 10 (Appendix A) shows the predicted rate of PADEs reaching patients for each fault tree. Estimates of the number of PADEs reaching patients annually are also provided. An analysis of each fault tree follows, along with the results of sensitivity analyses to evaluate the impact of selected risk-reduction interventions (see Table 11, Appendix A).

Wrong Patient Errors at the Point of Sale

Fault tree analysis. Pharmacies are vulnerable to dispensing correctly filled prescriptions to the wrong patient (or family member, friend, or caregiver) at the point of sale, a risk substantiated in the literature.[104,105,106] This PADE is not influenced by the attributes of a specific medication; thus, dispensing any prescription medication to the wrong patient at the point of sale carries a similar level of risk. Infrequent patient counseling and patient identification according to procedures were the most contributory factors that led to a predicted error rate of 1.22 per 1,000 prescriptions. Among 56,000[107] community pharmacies in the US, this error rate suggests that 332,755 prescriptions will be dispensed to the wrong patient each month, or six every month per pharmacy.

The modeling team identified two initiating errors that most often led to this PADE: errors when placing filled prescriptions into a bag for customer pick-up (0.4/1,000 prescriptions) and errors when retrieving the medications at the point of sale (3/1,000 prescriptions). Bagging errors often stem from working on more than one patient's prescriptions at a time during the verification and bagging process. Because the bag is not opened at the point of sale, these errors are rarely captured before the customer leaves the pharmacy.

A flawed or absent patient identification process most often led to errors when retrieving the medications at the point of sale. Although patient verification is expected at the point of sale, the modeling team reported difficulty obtaining a birth date when prescriptions are picked up by caregivers, family, or friends. Using an address as a second identifier was felt to be suboptimal, as patients with the same last name often live together. Forgetting to carry out a verification process or skipping it when busy was considered a failure point. Modeling team members who worked in stores with lower prescription volumes felt they were able to visually identify most patients; however, they were also more likely to skip a formal verification process.

Unless patient counseling occurs at the point of sale, dispensing a prescription to the wrong patient is associated with a single pathway failure, meaning there are no significant opportunities to capture the error from the time it is made until it reaches the patient.

Sensitivity analysis. The team determined the impact of four interventions on the incidence of dispensing medications to the wrong patient. A simple process change such as opening the bag at the point of sale to view all the filled prescriptions yielded improvement, from 1.22 to 0.534 errors per 1,000 prescriptions. We modeled this process change with only a modest improvement in both the pharmacy staffs' and patients' abilities to capture the error; yet the intervention was very effective in reducing the risk of an error.

The modeling team estimated that pharmacy staff followed a patient identification process at the point of sale only half the time. The identification process included verification of the patient's last name along with one other unique identifier—birth date or address. With a modest increase from 50% to 80% in the frequency of carrying out the patient identification process at the point of sale, the incidence of dispensing a prescription to the wrong patient decreased from 1.22 to 0.804 errors per 1,000 prescriptions. Combining 80% compliance with following the patient identification process with opening the bag at the point of sale lowered the incidence of this error more, from 1.22 to 0.233 errors per 1,000 prescriptions, representing an 81% improvement.

Increasing the frequency of counseling patients who pick up prescriptions from 30% to 50% changed the incidence of the error from 1.22 to 0.899 per 1,000 prescriptions. Adding this intervention to the previous two interventions—opening the bag and following the identification process 80% of the time—resulted in a reduction to 0.169 per 1,000 prescriptions. Reducing the at-risk behavior of working on more than one patient's medications during product verification lowered the incidence of bagging errors from 0.4 to 0.1 per 1,000 prescriptions, which yielded a reduction in dispensing medications to the wrong patient from 1.22 to 1.11 per 1,000 prescriptions. When combined with the three interventions previously described, the risk is reduced more to 0.154 per 1,000 prescriptions.

Wrong Patient Data Entry Errors

Fault tree analysis. Entering a prescription into the wrong patient profile was estimated to occur in five per 1,000 prescriptions. Of these, the fault tree predicts that the error would not be captured, and the medication would be dispensed to the wrong patient in 0.052 per 1,000 prescriptions (5.2 per 100,000 prescriptions). This PADE was also applicable to any medication, not just the high-alert drugs under study. On a national level, this computes to dispensing medications to 14,183 wrong patients per month, or once every 4 months per US pharmacy. The team did not model the potential omission of the prescribed medication for the correct patient.

Wrong patient data entry errors were estimated to occur and reach patients less often than data entry errors involving selection of the wrong dose of warfarin or the wrong insulin analog. One factor driving this difference is that the patient selected in error during data entry of the prescription must come into the pharmacy to pick up other prescription medications in order for the erroneous medication to be dispensed. Assigned a 50% chance that the patient will never enter the pharmacy to pick up the erroneous prescription, the PADE only reaches about half of its possible victims. Assuming that all patients will initiate the process of picking up the erroneous prescription, the frequency of the adverse event almost doubles (0.103 per 1,000 prescriptions), bringing it more in line with a data entry error involving selection of the wrong insulin analog.

During data entry, once the wrong patient profile has been selected, it is very unlikely for pharmacy staff to notice they are entering the prescription into the wrong profile. During data entry verification, capture of the error had a high failure rate (nine failures per 10 prescriptions) if the pharmacist conducting the verification also made the error while entering the order. Self checks conducted immediately after work completion are prone to dependency errors[108] and are unreliable.[109] An independent check by another pharmacist who did not make the data entry error was estimated to have a much lower failure rate (1/100 prescriptions).

The primary at-risk behavior identified with this PADE was a rushed or inattentive data entry verification process, with an estimated rate of occurrence of one in 10 prescriptions. Among the modeling team, it was agreed that, although the data verification process was not simply bypassed, careful attention during the task did not always occur given competing demands for the pharmacists' attention. If the order entry error was not caught during data entry verification, it had little opportunity for capture while filling the prescription.

Counseling patients, particularly if the prescription bottle is opened to view the tablets, offered another opportunity to capture the error, with a nominal risk of failure set at just one in 100 prescriptions. However, a 30% counseling rate—supported in the literature[110,111,112,113,114]—makes this an unreliable capture opportunity.

Sensitivity analysis. We determined the impact of five interventions on the incidence of dispensing a filled prescription to the wrong patient after entering a prescription into the wrong patient profile. The first intervention evaluated improvements in the environment to support a consistent, cognitive checking process during data entry verification. Remote data entry verification or shifting work in high-volume pharmacies to low-volume pharmacies are examples of interventions to help reduce time pressures during the dispensing process and, thus, reduce the frequency of inattentive data entry verification. By decreasing the risk of inattentive data entry verification, failure to capture the error decreased from one in 10 to five in 100 prescriptions.

Increasing the frequency of counseling patients from 30% to 50% changed the incidence of the PADE from 0.052 to 0.037 per 1,000 prescriptions. We also evaluated process changes to increase verification of prescriptions entered by one pharmacist by another pharmacist (independent verification). These process changes included remote data entry verification and staffing patterns that result in more than one pharmacist on duty per shift. However, increasing the frequency of an independent verification of prescriptions entered by pharmacists from 50% to 90% resulted in little improvement, because only 10% of prescriptions are entered by pharmacists. In pharmacies where pharmacists enter more prescriptions, the impact could be larger.

Another process change modeled was including a second redundant data entry verification step during the product verification step. The fault tree is structured with data entry verification occurring after the data entry process and before filling the prescription. This more closely models the process in one of the two participating chain pharmacies. The other chain pharmacies conduct data entry verification during the product verification step, after the prescription has been filled. Because a scanned image of the prescription is available in the computer in both pharmacy chains, we modeled a structural change of including data entry verification both before filling the prescription and again after filling the prescription. A downward-adjusted capture rate was calculated for the second data entry verification process compared with the first data entry verification process, because repeated redundancies are prone to dependency errors and their effectiveness tends to decrease.[9] By adding the second data entry verification process, the risk of dispensing a medication to the wrong patient due to a data entry error declined from 0.052 to 0.007 per 1,000 prescriptions, an 87% improvement.

The final intervention evaluated was aimed at preventing the data entry error rather than detecting and correcting it. In inpatient settings, patient verification using two unique identifiers is required before drug administration. If a similar risk-reduction strategy were employed during data entry of prescriptions—that is,

requiring search/entry by name *and* birth date—we estimated a decrease in the incidence of entering a prescription into the wrong patient profile from five to one per 1,000 prescriptions. This reduces the risk of dispensing a prescription to the wrong patient from 0.052 to 0.010 per 1,000 prescriptions, an 81% improvement. This practice change would require the patient's birth date on all prescriptions.

Incorrect or Inappropriate Dose of Fentanyl Patches Dispensed Due to a Prescribing Error

Fault tree analysis. Prescribing an incorrect or inappropriate dose of fentanyl patches was estimated to occur in one per every 1,000 fentanyl patch prescriptions. Inappropriate doses included prescriptions for fentanyl patches that were prescribed for acute pain and/or opioid-naïve patients. Of these errors, the fault tree calculated that the wrong dose would be dispensed to the patient at a rate of 0.730 per 1,000 prescriptions.

This fault tree shows that the dispensing system in participating pharmacies is largely unreliable in its ability to detect this prescribing error; only 27% of the errors were estimated to be captured and corrected. The modeling team suggested this low rate of capture is primarily associated with inadequate knowledge about the patient's prior opioid use and the type of pain for which the patch has been prescribed. Fentanyl patch is classified by the Drug Enforcement Agency (DEA) as a Class II drug and, as such, requires a new prescription for it to be dispensed. Thus, pharmacy staff cannot tell if the prescription is new or a continuation of previously prescribed fentanyl—which might help determine opioid tolerance. The modeling team agreed it is not routine practice or considered a duty to review the patient's entire drug profile before entering a prescription. Pharmacy technicians, who typically receive the prescription, cannot conduct medication management activities, such as asking the patient about prior opioid use. Furthermore, the patient's relatives, who often drop off and pick up these prescriptions, may be unreliable historians regarding the patient's prior opioid use.

Drug utilization review (DUR) and patient counseling are the two process steps for which fentanyl patch prescribing errors may be captured, but with very limited success. The acceptable dose range for fentanyl patches is wide, from 12.5 mcg/hour to 100 mcg/hour or more, depending on the patient's opioid tolerance and pain level. Doses up to 300 mcg/hour are recommended for patients with a 24-hour intake history of oral morphine in doses ranging from 1,035-1,124 mg/dL.[115] Thus, an out-of-range dose alert would occur in just one in 100 prescriptions, as the computer cannot detect an inappropriate dose within an acceptable therapeutic range. If the computer issues an out-of-range dose alert, the modeling team estimated that the error would be detected 98% of the time, but the low rate of dose alerts makes this an unreliable capture opportunity.

The frequency of patient counseling was estimated to be 10%, because many patients on fentanyl patches did not pick up their own prescriptions, and counseling was often declined by the caregiver or friend picking up the prescription. When counseling occurred, the focus on how to use the patch correctly, rather than assuring the appropriateness of the dose, led to capture of just 10% of dosing errors. Given these limitations, the fault tree for this PADE differed from every other fault tree in that there was a zero probability or a very high rate of failure to capture the error during steps in the dispensing process. Thus, this prescribing error resembles a single pathway failure more often seen with drug administration errors, with little or no opportunity for capture.

***Sensitivity analysis*.** We determined the impact of two interventions on the incidence of dispensing an inappropriate dose of fentanyl patch due to a prescribing error. Both strategies involved obtaining a history of opioid use from the patient or healthcare provider. In the first case, we added a process step during receipt of the prescription for pharmacists to request information from patients, caregivers, and/or the patient's healthcare provider about the patient's prior opioid use and for pharmacists to review the information (and the patient's drug profile, as necessary) before the prescription is entered into the computer. The team estimated a 40% capture rate for inappropriately prescribed doses. Even with this modest capture rate, the process change allowed capture of 56% of the prescribing errors.

The second intervention involved collecting an opioid history during face-to-face or phone counseling. We increased the frequency of patient counseling from 10% to 80%, and the ability to detect an incorrect or inappropriate dose during the counseling session increased—from 10% to 80%—using a checklist and added a redundant review of the patient's intake history obtained when the prescription was received in the pharmacy (if available). This process change reduced the probability of errors reaching patients from 0.730 to 0.263 per 1,000 prescriptions. This represents a prescribing error capture rate of 74%. Combining both interventions improved the probability of capturing the prescribing error from 27% to 84%.

Methotrexate Dispensed with Directions to Take Daily Due to a Prescribing Error

Fault tree analysis. Prescriptions for methotrexate with directions to take the drug daily instead of a weekly dosing schedule were estimated to occur in one per 1,000 prescriptions. Of these, the fault tree predicted that 0.0009 errors per 1,000 prescriptions (9.64 per 10 million prescriptions) will actually reach patients.

A methotrexate prescription intended for nononcologic use was the focus of the modeling team. However, given that methotrexate doses for oncologic use do not typically exceed courses of 5 days repeated after a week with no therapy, the fault tree includes all prescriptions for methotrexate that were prescribed daily for more than one consecutive week. This fault tree demonstrates that pharmacies in our study have a robust dispensing process that captures and corrects 99.9% of methotrexate prescriptions with directions to take the drug daily. The reasons for a high capture rate include effective computer alerts and heightened pharmacy staff awareness of this error. Such conditions may not exist in other pharmacies.

The fault tree demonstrates multiple opportunities to capture the prescribing error with varying success. For example, a pharmacist was estimated to capture more errors during data entry than a technician, although only 10% of the prescriptions are entered by pharmacists. As with most prescribing errors, the DUR step offers the greatest opportunity for capture, particularly because an alert always reminds the pharmacist to investigate the daily directions for use. The ability to capture the error is 98% if the prescription is for an existing patient who has been taking methotrexate in the correct dose and the pharmacist reviews the patient's drug profile.

Capture opportunities are also predicted when a duplicate therapy alert is evaluated (80% capture) and during the product verification step (50% capture). The duplicate therapy alert is less effective than the dose alert, because staff tend to bypass duplicate therapy alerts 30% of the time. If the error gets through the dispensing process without detection, it may be captured during counseling; however, only 30% of patients are counseled.

Sensitivity analysis. We determined the impact of three interventions on the incidence of dispensing methotrexate with directions to take daily due to a prescribing error. Because knowing the indication for use could increase detection of a methotrexate prescription with the wrong directions for use,[116,117] we measured the impact of including an indication for the drug on the prescription. Estimating an 80% prescribing compliance rate with including the drug's indication on the prescription, and estimating modest increases (50% or less) in pharmacy staffs' ability to detect the error from the time receiving the prescription until the DUR process, the rate of the PADE was reduced from 0.0009 to 0.0007 per 1,000 methotrexate prescriptions.

We also modeled the effect of enhancing the computer alert by making it a hard stop that does not allow entry of methotrexate prescriptions with daily dosing for more than one consecutive week. The effect of this change occurred primarily in the order entry process section of the fault tree, when the risk of overlooking the prescribing error was reduced to one per 100,000 prescriptions. This lowered the incidence of dispensing methotrexate with directions for daily use to once every 100 billion prescriptions.

Because the dispensing systems of the participating pharmacies were rather effective in detecting and correcting methotrexate prescribing errors before any interventions, we evaluated the reliability of the dispensing process to detect the error if the computer system did not warn pharmacy staff about daily dosing of methotrexate. Removing this important safety feature resulted in more than a 500% increase in risk, with the probability of capturing the error decreasing from 0.0009 to 0.006 events per 1,000 methotrexate prescriptions.

Wrong Insulin Analog Dispensed Due to Selecting the Wrong Drug During Data Entry

Fault tree analysis. Dispensing the wrong insulin analog due to a data entry error was estimated to occur in one per every 100 insulin analog prescriptions. The insulin analogs considered while building the fault tree were Humalog, Humalog Mix 75/25, Humalog Mix 50/50, NovoLog, NovoLog Mix 70/30, Apidra, Lantus, and Levemir. The dispensing processes of the participating pharmacies were capable of capturing 96.9% of these data entry errors, leaving 0.306 errors per 1,000 prescriptions to reach patients. The error rate for selecting the wrong insulin analog during order entry was estimated to be higher than a typical human error rate (see Table 6 in Appendix A) due to several well-known PSFs, including look- and sound-alike product names, similar strengths and mixtures, handwritten prescriptions susceptible to being misread as a similarly named insulin, and long pick lists in the computer from which to select the product.

Data entry verification is the most opportune time in the dispensing process to detect this error. During this step, the modeling team estimated that only 10% of the errors would be recognized if the same pharmacist

both entered and verified the entry of a prescription. The team estimated that 90% of the errors would be captured if an independent verification process occurred, still allowing for a 10% failure rate because the exogenous conditions that initially led to the data entry error, such as a handwritten prescription for Humalog that looks like NovoLog, would still exist. Ten percent of the time, the team estimated that the verification process was carried out in an inattentive manner due to PSFs (see Table 7 in Appendix A).

According to the fault tree, DUR is not a reliable way to capture this particular data entry error. Dosing ranges overlap, so out-of-range dose alerts occur infrequently. Duplicate therapy alerts are common and occur with about 80% of insulin prescriptions, because many patients with diabetes require more than one type of insulin. However, the frequency of duplicate therapy alerts with insulin led the modeling team to estimate a 30% rate of bypassing the alert, and the frequency of patients receiving more than one type of insulin led the team to estimate a 90% failure rate for detecting the error even if the alert is investigated.

The ability to detect the data entry error drops significantly after DUR unless the patient is counseled, which was estimated to occur with 30% of patients. The modeling team estimated that the ability to detect the data entry error would increase from 90% to 99% if the counseling session included visual inspection by the patient of the insulin carton, vial, or pen. To be effective, this requires counseling at the counter, not the drive through.

Sensitivity analysis. We evaluated the impact of four risk-reduction interventions on the incidence of dispensing the wrong insulin analog to a patient due to a data entry error. The first two actions aimed to reduce the incidence of the data entry error by changing PSFs. We evaluated the impact of increasing electronic or computer-printed prescriptions by 20% to reduce the risk of misreading handwritten prescriptions for insulins with similar names. This was estimated to lower the initiating error rate from 10 to eight per 1,000 prescriptions, yielding a reduction in data entry errors reaching patients from 0.306 to 0.245 per 1,000 prescriptions. We also evaluated the use of tall man letters to draw attention to the differences in insulin names (e.g., Huma**LOG**, Humu**LIN**, Novo**LOG**, Novo**LIN**) listed on computer screens, which lowered the initiating error rate of selecting the wrong insulin during data entry from 10 to five per 1,000 prescriptions. This action lowered the probability of dispensing the wrong insulin analog to a patient from 0.306 to 0.153 events per 1,000 prescriptions. Conducting a second data entry verification process during the product verification step had a similar effect.

Anticipating that a data entry error would occur in every 10 per 1,000 prescriptions, we evaluated the dispensing system's ability to capture the error by increasing the frequency of patient counseling from 30% to 80%. This increased the probability of capturing the error from 96.9% to 99%, which reduced the risk of dispensing the wrong insulin to a patient from 0.306 to 0.100 per 1,000 prescriptions. The probability of this error was further reduced to 0.014 per 1,000 prescriptions by employing all four of the interventions evaluated.

Wrong Drug or Dose Dispensed Due to a Selection Error While Filling a Prescription for Warfarin

Fault tree analysis. Selecting the wrong drug while manually filling a warfarin prescription was estimated to occur in one per 1,000 prescriptions. Mix-ups between warfarin and other medications during product selection have rarely been reported, although a risk exists with a branded warfarin product, Jantoven, which could be confused with Januvia or Janumet.[118] However, pharmacies often stock warfarin on shelves according to generic names, lessening the risk of such an error.

Selecting the wrong dose while manually filling a prescription for warfarin was estimated to occur more frequently—one in 10 prescriptions—because there are nine different tablet strengths available. This estimate is in line with a study that found more than 5% of medications first selected to fill a prescription were wrong.[119] Given nine different tablet strengths, the error rate was set higher for warfarin. The 1-mg and 10-mg strengths are also prone to mix-ups if a trailing zero is used to express the 1-mg dose (1.0 mg) on pharmacy or product labels.[120] The risk of selecting the wrong drug or dose while filling automated dispensing equipment that dispenses about 20% of warfarin prescriptions was estimated to be low, just 1 per 10,000 opportunities, because barcoding technology is used during the loading process.

The probability of the wrong drug or dose reaching the patient is 9.43 per 1 billion warfarin prescriptions for wrong drug errors and 9.25 per 10 million prescriptions for wrong dose errors. These low probabilities are due primarily to the use of barcoding technology while filling warfarin prescriptions and the availability of a pill image during the product verification step. We estimated that the technology would fail to capture the error in one of 100,000 opportunities to account for an occasional problematic barcode or scanner malfunction. If the

error is not picked up with barcoding technology, an image of the correct drug and dose on the screen during product verification facilitates capture of the error in one of 100 occurrences. The final opportunity to capture an error is during patient counseling, which was estimated to occur 30% of the time, mostly for patients with a new prescription or dose change. If the bottle label is viewed and the bottle is opened during the counseling session, the chance of capturing the error was estimated to increase from 80% to 99%.

Sensitivity analysis. We determined the influence of five interventions on the frequency of dispensing the wrong drug or dose of warfarin due to a selection error. Two tests appraised the impact of removing otherwise effective technologies; one test evaluated the impact of a technology workaround; the two remaining tests looked at the effect of increasing the frequency of existing safeguards to help detect and correct errors.

Our fault trees for warfarin drug and dose selection errors add evidence to existing knowledge regarding the effectiveness of employing barcoding technology during the dispensing process.[121,122,123] With the technology, 99.9% of selection errors were detected and corrected. However, without barcoding technology, the probability of dispensing the wrong drug increased from 9.43 per 1 billion to nine per 1 million, and the probability of dispensing the wrong dose of warfarin increased from 9.25 per 10 million to nine per 10,000. Similar increases in dispensing the wrong drug or dose were seen if an image of the correct warfarin tablet was not available during product validation. When both barcoding and pill imaging technology are absent, the probability of dispensing the wrong drug or dose is increased from 9.43 per 1 billion prescriptions to 4.2 per 100 thousand prescriptions and from 9.25 per 10,000,000 prescriptions to 24.2 per 1,000 prescriptions, respectively. We also evaluated an increase in automated dispensing of warfarin from 20% to 50% and an increase in patient counseling from 30 to 80%, which reduced the risk of allowing a dispensing error to reach the patient by 78%.

Wrong Dose or Strength of Warfarin Dispensed Due to a Prescribing Error

Fault tree analysis. Prescribing the wrong dose or strength of warfarin tablets was estimated to occur in one of every 100 prescriptions. Of these, 0.569 errors per 1,000 prescriptions reached the patient. Despite what might appear to be a high rate of capture (94.3%), the fault tree shows that the dispensing system is not highly reliable for detecting these prescribing errors unless the warfarin dose/strength exceeds safe daily dosing limits (e.g., 10 mg or more) or is prescribed in a strength not available from manufacturers.

Unlike hospital pharmacists, community pharmacists rarely have the ability to access information about the patient, such as INR values, to assess the appropriateness of warfarin doses, particularly given that dosing changes may occur frequently. If the dose exceeds safe daily limits, the pharmacist has a 98% probability of capturing the error during DUR. However, only one in 100 dose/strength errors was estimated to exceed safe limits; most erroneous doses/strengths had a high probability of falling within safe limits.

Duplicate therapy alerts were estimated to occur with almost 90% of all warfarin prescriptions, because it is common for patients to have multiple strengths of warfarin tablets on their active drug profiles. However, alert fatigue led the modeling team to estimate that 30% of the alerts would be bypassed. The team also estimated the probability of capturing a dose/strength error at just 20% with a duplicate therapy alert. Again, the fault trees calculated a low probability of capturing the error during product verification unless the dose was out of range. Counseling the patient had limited value, because it occurred infrequently (30%) and carried an 80% failure rate for capturing the prescribing error, given that most doses were still within an acceptable range.

Sensitivity analysis. We determined the impact of one intervention on the incidence of capturing and correcting prescribing errors associated with the wrong warfarin dose or strength. By increasing the frequency of patient counseling to 80%, the risk of allowing the prescribing error to reach the patient is reduced by 52%, from 0.569 errors to 0.274 errors per 1,000 prescriptions. The prescribing error was captured most frequently if the vial was opened to view the tablets and the patient expected a different dose and/or tablet color than the prescribed dose. Without knowledge of the patient's laboratory monitoring results, no other interventions were deemed helpful in capturing a wrong dose prescribing error unless the dose was out of range.

Wrong Warfarin Dose Dispensed Due to a Data Entry Error

Fault tree analysis. The frequency of entering a wrong dose or strength of warfarin into the patient's profile during data entry was estimated to occur with one in 10 warfarin prescriptions. Of these, 1.83 data entry errors per 1,000 prescriptions reached patients. The fault tree shows that the dispensing system is particularly

vulnerable to this type of data entry error, given the nine different strengths of warfarin tablets from which to choose. These errors are rarely corrected if data entry verification and patient counseling do not occur.

During data entry, pharmacists and technicians have a greater chance of detecting the error if the patient has had previous warfarin prescriptions filled at that pharmacy. But failure to detect the error is still at 75%, given a 90% probability that these patients have more than a single strength of warfarin in their drug profile history.

An independent data entry verification process by a pharmacist who has not entered the prescription was estimated to capture up to 99% of errors if an out-of-range dose alert occurs and is not bypassed without notice. However, dose alerts are not likely if the wrong strength of tablets is selected during data entry. Duplicate therapy alerts occur during data entry with about 80% of warfarin prescriptions but are not reliable as a means of detecting a data entry error. Patient counseling was estimated to occur with 30% of patients. If the prescription bottle is opened during counseling, a patient who knows what color tablets to expect has a 99% chance of capturing the data entry error. However, the bottle is only opened about 30% of the time.

Sensitivity analysis. We determined the impact of four interventions on the incidence of dispensing the wrong warfarin dose due to a data entry error. Similar to other data entry errors modeled, we evaluated a reduction in inattentive data entry verification by 50%, an increase in patient counseling from 30% to 80%, more frequent (90%) independent verification by another pharmacist for prescriptions entered by pharmacists, and the addition of a second data entry verification process during the product verification step. The most effective interventions involved the second data entry verification process and patient counseling.

Increasing patient counseling to 80% resulted in a 67% reduction in the risk of dispensing the wrong warfarin dose due to a data entry error. In this case, the errors that would reach patients decreased from 1.83 to 0.600 per 1,000 prescriptions. Conducting a second data entry verification process during product verification by comparing the scanned prescription in the computer with the prescription label reduced the risk of this data entry error reaching patients by 80%. More frequent independent checks and less frequent inattentive checks during data entry verification reduced the risk of PADEs by 53% and 35%, respectively. All four interventions together lowered the risk of dispensing the wrong warfarin dose from 1.83 to 0.174 per 1,000 prescriptions.

Warfarin Prescription Dispensed with the Wrong Directions Due to a Prescribing Error

Fault tree analysis. Prescribing warfarin with incorrect directions for administration was estimated to occur in every two per 1,000 prescriptions. “Incorrect directions” included dosing schedules more frequent than daily (e.g., twice daily); directions to “take as directed,” though technically “incorrect,” were excluded. This fault tree demonstrated that the dispensing systems in the participating pharmacies are largely reliable, capturing 99.9% of these errors and allowing only 1.34 in 10 million to reach patients.

The factors most contributory to capturing this prescribing error are two fold. First, the error is typically caused by a mental slip on the part of the prescriber and is easily recognized by pharmacists and many experienced pharmacy technicians. Warfarin is a commonly prescribed medication that is typically administered in single, daily doses. Although alternating doses and days with no warfarin are also common, directions to take the drug more frequently than once daily are exceedingly rare and not according to the labeled dosage schedule.

Next, there are frequent opportunities during the dispensing process for the error to be captured, from data entry to the point of sale. For example, the modeling team estimated that a pharmacist would fail to capture the error in just one in 1,000 opportunities during DUR, given that an out-of-range dose alert was estimated to occur in more than half the warfarin prescriptions with dosing schedules of twice a day or more frequent. Even the insurance adjudication process and the sale of the prescription were deemed potential capture opportunities, particularly if the quantity of tablets dispensed are not as expected and/or have an impact on the cost of the prescription. If patient counseling occurs (30%), the probability of noticing the error was estimated at 90%.

Sensitivity analysis. We evaluated the impact of two risk-reduction interventions on the incidence of dispensing a warfarin prescription with the wrong directions (i.e., more frequent than daily dosing) due to a prescribing error. The dispensing system was already capturing 99.9% of these prescribing errors before interventions, but adding a computer alert regarding dosing schedules more frequent than daily, with a hard stop that required a pharmacist to intervene and document the reason for allowing the data entry to proceed, reduced the risk of failing to capture the prescribing error from 1.34 per 10 million prescriptions to one per 1 trillion prescriptions, virtually predicting that this type of error would be a “never” event. Patient counseling also

impacted the ability to capture the prescribing error. An increase in counseling from 30% to 80% of patients results in a 50% reduction in dispensing warfarin with erroneous directions to take more often than daily.

Discussion

This study demonstrates important and largely correctable community pharmacy dispensing system vulnerabilities, identified by the people who work within those systems. The sociotechnical fault trees represent the impressions and best estimates of pharmacists and pharmacy technicians. Building these trees and estimating the probabilities of events leading to potentially serious PADEs involving four high-alert medications provide insights into the deep systems and human factors issues that define medication dispensing risks. The fault trees defined thousands of pathways of process failures and behavioral elements leading to each PADE, describing how each error was initiated and capture opportunities. This level of detail, unavailable from any other source, clearly showed examples of systems issues and the remarkable ability of the pharmacy dispensing process to detect and correct errors before reaching patients.

Prescribing errors. With prescribing errors, the fault trees suggest that community pharmacy dispensing systems may be designed to capture straightforward mistakes—such as prescribing warfarin twice a day—more often than errors associated with inappropriate drugs or doses—such as prescribing fentanyl patches for an opioid-naïve patient or warfarin in a dose not appropriate for the patient based on INR values. Detecting the former type of error associated with straightforward mistakes requires knowledge about the drug and/or system safeguards, such as computer alerts, to help capture these errors. Detecting the latter type of error related to appropriateness of drugs and doses requires knowledge of the drug and the patient's medical history, information that is rarely available or accessible in community pharmacies (but should be). Accordingly, it is not surprising that the fault trees demonstrated a 99.9% capture rate for prescribing errors associated with warfarin directions for use and a 27% capture rate for prescribing errors associated with the dose of fentanyl patches, which is highly dependent on the patient's type of pain and prior opioid tolerance.

The modeling team agreed that community pharmacists have a duty to capture wrong dose prescribing errors only if the dose falls outside a typical safe range. If the dose falls within a safe range but requires an adjustment based on medical information about the patient, such as acute and chronic diagnoses, weight, laboratory monitoring results, prior medication history, or renal/liver impairment, this type of clinical information is seldom available. Sensitivity analysis identified that more frequent and effective patient counseling will reduce prescribing errors that reach patients by as much as 64%. ISMP has previously commented on the need for community pharmacy access to clinical patient information and reimbursement systems that compensate the time pharmacists spend on clinical review of prescriptions and counseling.[124]

Dispensing errors. Community pharmacies in the study exhibited highly reliable systems for preventing and detecting drug or dose selection errors when filling prescriptions for warfarin. Reliability was driven by technologies available in the pharmacies studied, including barcoding, automated dispensing, and computer pill images. The wrong drug selection fault tree model predicted one of these errors would reach a patient every 14 years. On the other hand, wrong dose selection errors were predicted to reach a patient seven times each year. Increasing automated dispensing of warfarin to 50% and the frequency of patient counseling to 80% lowered the probability of wrong drug selection errors to once every 70 years and wrong dose selected and dispensed to once every 1.5 years in the 12,000 pharmacies participating in the study.

Community pharmacies in the study were vulnerable to wrong drug and wrong dose data entry errors, a finding consistent with the literature.[125] Sensitivity analysis revealed that conducting a second data entry verification process at the time of product verification reduced this risk by half (50%) for wrong insulin analog data entry errors and by 80% for wrong warfarin dose data entry errors.

Wrong patient errors also stood out as a risk in the dispensing process with about five per 100,000 errors originating from data entry into the wrong patient's profile and one per 1,000 errors originating at the point of sale. This finding is higher than reported rates in the literature, although errors captured at any point after the patient walked away from the counter were included in the incidence rates in the fault trees, even before the patient took the wrong medication. Based upon our analysis, opening the bag at the point of sale to view the prescription vials reduced the risk of this type of error by more than half (56%). In practice, confidentiality concerns and the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule will impact the degree to which this intervention can be applied.

Significance
This study focuses on identifying interventions to reduce PADE involving four high-alert drugs implicated in serious patient harm: warfarin, methotrexate, insulin analogs, or fentanyl patches. Using ST-PRA, our team has identified multiple heretofore unrecognized pharmacy dispensing systems pathways prone to process and/or behavioral failures. Study findings are important because they quantify, for the first time, human error probabilities and at-risk behavior frequencies that combine and contribute to dispensing system failures as well as the overall incidence of PADEs with these four high-alert medications.

The fault trees reveal important systems relationships, unintended consequences of behavioral choices, and valuable risk-reduction interventions that can guide and accelerate community pharmacy safety improvements. They serve as visible diagrams for shared understanding of the failure pathways that lead to harm, facilitating communication, shared goals, trust, and agreement between all stakeholders, because everyone owns the same risk model. The fault trees and interventions have the potential to become the foundation of safety improvement programs in community pharmacies. This study demonstrates the strength and value of ST-PRA and its application in healthcare, its advantages over current qualitative risk assessment methods, its capabilities to forecast combinations of risk leading to preventable adverse events, and its abilities to facilitate development and implementation of high-leverage changes that improve medication safety.

Most important, the fault trees are dynamic, living models of risk designed to evolve as data from new studies, industry standards, or system changes are used to refine probability estimates and subsequent predictions of risk. The tool also allows providers to identify which system attributes and failures have the highest impact on errors so that they can focus their resources on interventions most likely to benefit patients. Practice sites are more willing to adopt proposed interventions because they can appreciate the causes of errors and perceive the utility, in quantifiable terms, of the recommended interventions and best practices. The fault trees, in the end, are a management tool; a critical element in the decision-making process and allocation of resources.

Limitations
This study produced fault trees that are representations of the dispensing systems in the two pharmacy chains participating in the study. Results are not generalizable to all community pharmacies due to potential differences in process steps, work aids such as technology, the frequency staff engage in at-risk behaviors, and PSFs that increase or decrease risk. The four high-alert medications modeled were not selected at random but on the basis of potential harm to patients if misused. The model-building and validation samples required a purposive sample given the necessity of recruiting team members who were willing and able to honestly discuss practices that impact risk. The modeling sessions required a manageable number of participants, limiting the sample size. Constraints associated with bringing the modeling team together necessitated a convenience sample from a single geographic location. In an attempt to ensure diversity among the model-building and validation samples, staff who represented minorities may have been overrepresented. Thus, the probabilities of PADEs could differ in pharmacies not in the study; however, the fault trees are living models of risk that can accommodate changes in probabilities from pharmacy to pharmacy.

Conclusions
The ST-PRA models created during the study are exceptionally robust for identifying risks, predicting adverse outcomes, and evaluating the effectiveness of interventions. The techniques required to model human behavioral risks with ST-PRA are still advancing, and the process can be lengthy and complex and can require expert facilitation. But the alternative to ST-PRA is to assume the system is safe, wait for events to happen, investigate, and remove the newly seen risk. This study demonstrates that ST-PRA, even with its uncertainties, can lead to learning and improvements not achievable by current risk assessment processes or retrospective event investigations. Though it may not be practical for every community pharmacy to conduct its own ST-PRA modeling, application of the lessons learned from these existing models can lead to widespread improvement in community pharmacies nationwide. There is reason to believe that the fault trees will be useful across a broad range of community pharmacies, as they inform pharmacists about the systems design and behavioral elements that can produce or prevent a dispensing error. We anticipate that the results of this study will contribute greatly to the growing body of knowledge about the application of ST-PRA in healthcare and lead to further exploration regarding how the process can be demystified and used as a practical tool in healthcare settings.

*Contact the grantee institution for appendices or more information.

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