Grant Final Report

Grant ID: HIT/UC1HS014882-03

Automated Adverse Drug Event Detection and Intervention

Inclusive dates: 09/01/04 - 08/31/08

Principal Investigator:
Jeffrey Ferranti, MD, MS, Duke University Health System

Team members:
Asif Ahmad*
Lynne Alexander, MS†
Heidi Cozart*
Julie Eckstrand*
Monica Horvath, PhD*
Andrea Long, PharmD*
Steve Pladna*
Ira Togo*
Julie Whitehurst, PharmD*
Lynn Whitt, PharmD‡
Gene Woodall§
Pete Woods*

* Duke University Health System
† Duke University Hospital
‡ Duke Durham Regional Hospital
§ Duke Raleigh Hospital

Performing Organization:
Duke University School of Medicine

Project Officer:
Jon White

Submitted to:
The Agency for Healthcare Research and Quality (AHRQ)
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Abstract

Purpose: Study the implementation and operational utility of an automated surveillance system to detect and mitigate adverse drug events (ADEs) in hospitalized patients. Methods were also expended to evaluate the contribution and challenge an automated ADE surveillance system brings to an organizational patient safety program.

Scope: The study included automated surveillance of patients admitted to two community-based hospitals and an academic medical center between November 1, 2004 and September 30, 2008.

Methods: The study utilized an internally developed computer system with a logic-based rules engine. The system focused on the detection and intervention of medication-related patient harm. Potential events detected by the system were subsequently reviewed by pharmacists for objective evidence or intervention. ADE rates per 1000 patient days and per 100 admissions were calculated for two community-based hospitals and an academic medical center.

Results: Over the four year period, over 100 rules were deployed. Adverse drug events, as detected by computerized surveillance were complementary to the existing voluntary method. Automated surveillance provides a quantitative method for monitoring medication safety performance over time. Leadership adoption and cultural change play foundational roles in the deployment and adoption of a computerized surveillance system.

Key Words: ADE, adverse drug event, surveillance, trigger

Final Report

Purpose

The primary purpose of the Automated Adverse Drug Event Detection and Intervention project was to reliably measure and reduce the incidence of adverse drug events (ADEs) suffered by hospitalized patients using a computerized system for ADE detection, reporting, and intervention. The initiative embodied collaboration between information technology resources, patient safety and clinical leadership and the Departments of Pharmacy at three partnering hospitals. The specific objectives were to 1) establish a baseline rate of the incidence of adverse drug events (ADEs) in hospitalized patients of the three hospital system, 2) study the implementation and operational utility of an automated surveillance system for detection and mitigation of ADEs, and 3) reduce the incidence of ADEs through process, or technology-based interventions. As a by-product of these objectives, effort was also directed at the operational challenges of integrating an automated ADE surveillance system into an organizational patient safety program.

Scope

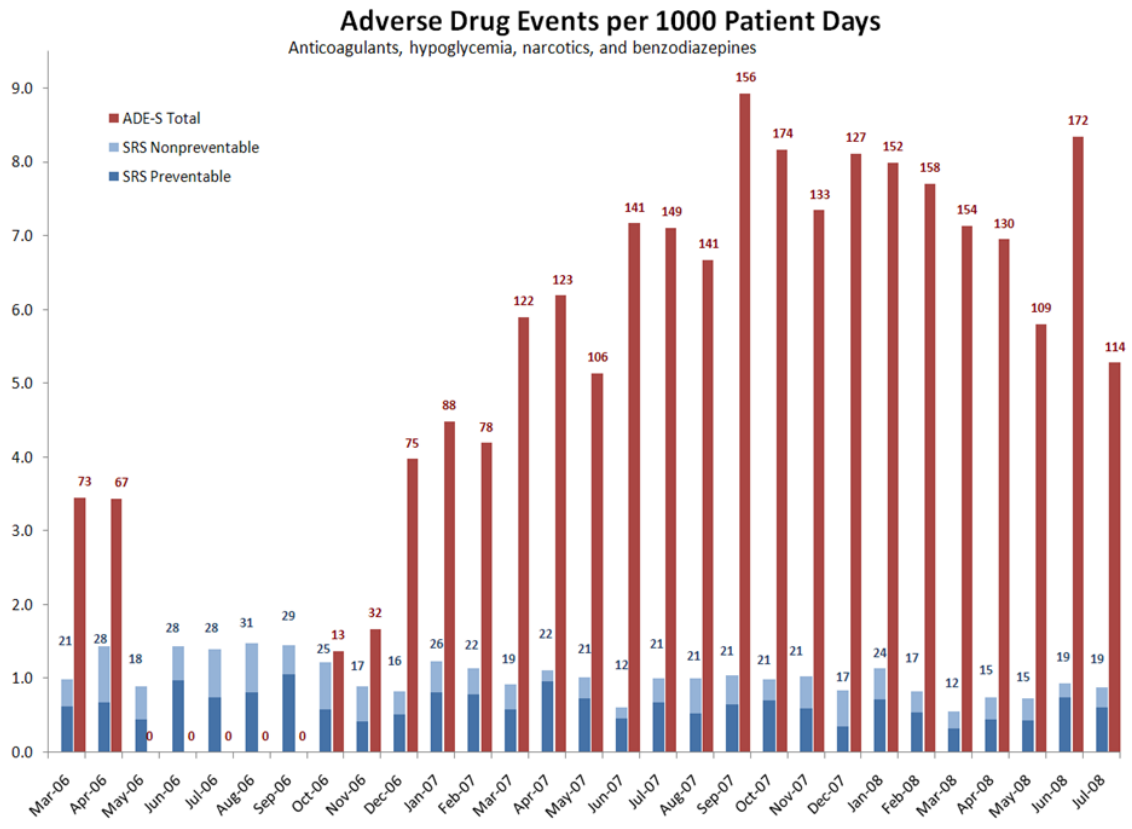
Background. Adverse drug event (ADE) detection is a national priority. In the landmark Harvard Medical Practice Study published in 1991, it was estimated that 3.7% of all hospitalized patients experienced an adverse event [1]. However, it was not until the Institute of Medicine (IOM) Report *To Err is Human* in 1999 that there was heightened interest in safety event analysis [2]. Most recently, the IOM Report *Preventing Medication Errors* emphasizes the use of voluntary reporting and computerized detection methods to capture information on harmful patient safety related events and subsequently employ this information to improve the safety of the health care delivery system [3]. Although it is clear that the detection of ADEs is critical to identify safety priorities and improve the quality of care, it is unclear which methodologies offer the greatest potential for recognizing ADEs and improving patient outcomes: manual chart review, voluntary reporting system, trigger tools, or computerized surveillance. This research focused on the development, implementation, and assessment of a computerized surveillance system to measure and monitor ADEs at a large academic medical center and two community based hospitals over a four year period.

Methods

Study Design

The study took place at a large, tertiary care-based health system which included an academic medical center and two community-based hospitals. The surveillance system leveraged technology and information systems already in place at each of the three entities, and included three unique vendor-based systems, a centralized, health system clinical data repository, and a mainframe based rules engine. The rules engine process was scheduled to run in batch once daily, at which time it received transactional patient, laboratory, and pharmacy data from the hospital information systems. Within the rules engine, specific rule logic was programmed to screen for "trigger" data that alone or in combination suggested the occurrence of an ADE. A subset of rules was also selected for immediate electronic communication to clinicians caring for the involved patient, permitting evaluation and intervention of a possible ADE, or an evolving unsafe condition. When the rule logic is met, a trigger is created in the surveillance database. A new web-based user interface was developed to assist with the daily trigger list review and evaluation data entry (Figure 1).

Figure 1. Surveillance and voluntary incident reporting monthly trending report; rates expressed as number of ADEs per 1000 patient days

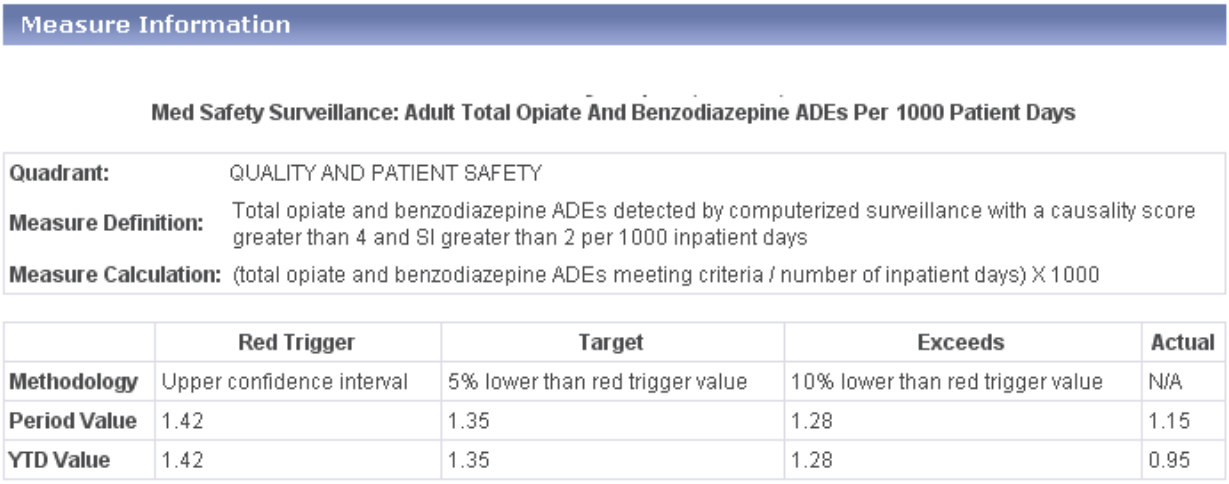


When the logic of a specific rule was met, alerts were triggered and compiled into a daily electronic report for evaluation by pharmacists trained in ADE investigation. Every triggering event was investigated in detail within 24 hours to determine whether it represents an ADE. The evaluation included review of the patient's chart and discussion with clinicians involved in the patient's care and if possible. If an adverse event was determined to have occurred, the pharmacist evaluated its causality, severity, and gathered event data specific to the incident. These electronic reports were entered into a database so they would be available for further analysis. In addition to permitting immediate intervention and mitigation of ADEs, the automated surveillance system also permitted the establishment of baseline statistics on the incidence and nature of ADEs at each of the three partnering hospitals. This will permit evaluation of the effectiveness of alert-generated interventions, as well as the effectiveness of other interventions currently in implementation to improve medication safety (for example, computerized physician order entry).

Data Sources/Collection/Measures

The surveillance system was moved into production within 4 months of initiation of the study at the academic medical center, and in March and July of 2005 at the two community-based hospitals. It has since been fully operationalized and continues to survey all of the inpatient medication and laboratory information against a set of 60+ clinical rules. The rules span 3 main categories: abnormal laboratory results, drug dispenses for known antidotes, and drug-laboratory combinations [5]. In the operational model when a rule condition is met, a trigger is fired and sent to a clinical pharmacist assigned to each of the three entities. The pharmacists perform a focused chart review of the daily trigger list to assess whether an ADE has occurred. The pharmacists assign a causality score using the algorithm of Naranjo et al [4] and a severity score using the internally developed 7-point scale (Figure 2). All of the events scored with a causality of 5 and a severity of 3 are considered true ADEs. Inter-rater reliability between the pharmacists completing surveillance trigger evaluations exceeded 0.88 (Kappa Statistic)[4,5] Secondary to their limited value, rules targeted at interventions in patient care processes at the academic medical center were turned off after the first 24 months of the study. This was suspected to be in part due to a combination of the limitations in original technology design, as well as the decentralized clinical pharmacist model deployed at the academic medical center. However, in the two community-based hospitals where a centralized pharmacist model exists, the pharmacists continue to evaluate the intervention-based rule to assess if changes in patient care may be necessary.

Figure 2. Med safety surveillance scorecard measure sample definition for fiscal year 2009



Measure Information

Med Safety Surveillance: Adult Total Opiate And Benzodiazepine ADEs Per 1000 Patient Days

Quadrant:	QUALITY AND PATIENT SAFETY
Measure Definition:	Total opiate and benzodiazepine ADEs detected by computerized surveillance with a causality score greater than 4 and SI greater than 2 per 1000 inpatient days
Measure Calculation:	(total opiate and benzodiazepine ADEs meeting criteria / number of inpatient days) X 1000

	Red Trigger	Target	Exceeds	Actual
Methodology	Upper confidence interval	5% lower than red trigger value	10% lower than red trigger value	N/A
Period Value	1.42	1.35	1.28	1.15
YTD Value	1.42	1.35	1.28	0.95

The surveillance rules catalog referenced in the study (Table 1) originated from a variety of sources. The initial rule set was developed based on previously published research [8,9]. However, assessments of individual rule performance were iteratively examined throughout the study. Rule revisions, as well as the integration of new electronic data sources into the surveillance system, typically occurred on a quarterly basis. Revisions were targeted to 1) improve rule performance for ADE detection or intervention, 2) enhance the detection profile to include the capture of new safety concerns as reported by the voluntary reporting system, 3) detect potential ADEs known to result from the use of new or high-risk medications, and 4) to fill known gaps in surveillance research.

Table 1. ADE rule performance [Positive Predictive Values (PPVs)]

Rule #	Rule name	Category	DRAH PPV (ADE)	DUH PPV (ADE)	DRH PPV (ADE)
76	ENOXAPARIN OR FONDAPARINUX & CR > 1.5 & RISE > .5	Anticoagulants	N/A	1.7%	1.2%
197	Heparin or DTI IV & 2 consec PTT>100 or 1 PTT>150	Anticoagulants	0.0%	4.4%	6.5%
58	Heparin Product and 2 PTT > 100	Anticoagulants	N/A	7.4%	4.3%
196	Heparin,Enox,Fonda PLT<100 24hr/drop>50% past 7dy	Anticoagulants	0.0%	1.9%	1.6%
118	HIT assay - PF4 (ERISA)	Anticoagulants	N/A	30.3%	71.4%
104	Lepirudin,Argatroban,Bivalirudin for HIT	Anticoagulants	N/A	8.5%	0.0%
63	platelets<80 & prior platelets within 7 days>=80	Anticoagulants	0.0%	10.5%	22.0%
82	Platlets < 50 & Aspirin, Clopidogrel, Toclo. NSAID	Anticoagulants	0.0%	0.6%	0.7%
92	Protamine Sulfate IV	Anticoagulants	3.8%	6.5%	0.0%
71	Ranitidine or Famotidine and Cr > 2.0	Anticoagulants	N/A	3.6%	0.2%
157	Sulfonamide & Coumadin	Anticoagulants	N/A	N/A	0.0%
112	Vitamin K (Phytonadione) and INR > 3	Anticoagulants	50.4%	21.4%	46.6%
99	Vitamin K and Warfarin	Anticoagulants	N/A	N/A	N/A
59	Warfarin and INR > 4	Anticoagulants	9.9%	6.3%	6.5%

Table 1. ADE rule performance [Positive Predictive Values (PPVs)] (continued)

Rule #	Rule name	Category	DRAH PPV (ADE)	DUH PPV (ADE)	DRH PPV (ADE)
155	C Diff positive assay	C. difficile colitis	62.8%	72.2%	26.6%
115	Metronidazole,Vancomycin and Pos C. diff Tox Assay	C. difficile colitis	66.7%	N/A	62.1%
91	ORAL Metronidazole	C. difficile colitis	0.0%	N/A	13.6%
93	ORAL Vancomycin	C. difficile colitis	50.0%	N/A	11.0%
88	Dextrose 50%	DEPENDS ON EVALUATION	17.6%	43.3%	26.4%
186	(PEDS) Potassium > 7 meq/l	Hyperkalemia	N/A	0.0%	N/A
95	Polystyrene	Hyperkalemia	37.5%	13.9%	12.5%
54	potassium > 6.5	Hyperkalemia	9.6%	N/A	4.5%
102	Tacrolimus Result High > 20	Hyperkalemia	N/a	4.8%	0.0%
184	(PEDS) Insulin and BG <50 mg/dl	Hypoglycemia	N/A	61.0%	N/A
198	Blood Glucose < 50	Hypoglycemia	59.1%	N/A	N/A
75	METFORMIN AND CR > 1.5 AND RISE > .5	Hypoglycemia	N/A	0.0%	2.3%
195	Clozapine and no WBC or ANC within past 7 days	Intervention only	N/A	N/A	N/A
162	IV to PO Switch - Azithromycin	Intervention only	0.0%	0.0%	0.0%
163	IV to PO Switch - Ciprofloxacin	Intervention only	0.0%	0.0%	0.0%
164	IV to PO Switch - Famotidine	Intervention only	N/A	0.0%	N/A
165	IV to PO Switch - Fluconazole	Intervention only	N/A	0.0%	0.0%
166	IV to PO Switch - Folic acid	Intervention only	N/A	0.0%	0.0%
151	IV to PO switch - LEVOFLOXACIN	Intervention only	0.0%	0.0%	N/A
167	IV to PO Switch - Metronidazole	Intervention only	N/A	0.0%	0.0%
171	IV to PO Switch - Moxifloxacin	Intervention only	N/A	0.0%	0.0%
168	IV to PO Switch - Multivitamin	Intervention only	N/A	0.0%	0.0%
169	IV to PO Switch - Pantoprazole	Intervention only	N/A	0.0%	0.0%
170	IV to PO Switch - Ranitidine	Intervention only	N/A	0.0%	0.0%
156	Positive micro culture	Intervention only	N/A	N/A	0.0%
105	Voriconazole and Rifampin	Intervention only	N/A	0.0%	N/A
194	Warfarin and no INR in previous 24 hours	Intervention only	0.0%	N/A	N/A
185	(PEDS) Calcium ionized > 1.5 mg/dl	Miscellaneous	N/A	0.0%	N/A
189	(PEDS) Chloride < 80 meq/l	Miscellaneous	N/A	0.0%	N/A
190	(PEDS) Magnesium > 3.5 meq/l	Miscellaneous	N/A	0.0%	N/A
192	(PEDS) Sodium < 120 meq/dl	Miscellaneous	0.0%	0.0%	N/A
191	(PEDS) Sodium > 157 meq/l	Miscellaneous	N/A	0.0%	N/A
188	(PEDS) Total Bilirubin > 20 mg/dl	Miscellaneous	N/A	0.0%	N/A
187	(PEDS) Triglycerides > 500 mc/dl	Miscellaneous	N/A	0.0%	N/A
51	Activated Charcoal	Miscellaneous	28.6%	62.5%	42.9%
111	Allopurinol and Cr > 2.5	Miscellaneous	N/A	0.0%	0.7%
81	ALT up 20% > 450 & Ison./Pheny./Cyclo./Metho./Warf	Miscellaneous	28.6%	N/A	0.0%
173	Amiodarone & Statin	Miscellaneous	N/A	N/A	1.2%
153	Amiodarone and Coumadin	Miscellaneous	N/A	N/A	0.0%
106	Amiodarone and Digoxin	Miscellaneous	0.0%	0.0%	1.6%
113	Amitriptyline and Age > 65	Miscellaneous	3.9%	0.3%	1.0%
79	ATENOLOL AND CR > 1.5 AND RISE > .5	Miscellaneous	N/A	0.0%	0.9%
84	Carbamazepine > 12	Miscellaneous	21.4%	0.0%	35.3%
176	Cyclobenzaprine and age > 65 yrs	Miscellaneous	4.1%	N/A	N/A
107	Cyclosporine and previous Tacrolimus	Miscellaneous	N/A	0.0%	N/A
89	Digibind IV	Miscellaneous	0.0%	100.0%	50.0%
1	Digoxin > 2 ng/ml	Miscellaneous	24.2%	9.8%	11.4%
68	Digoxin and Cr > 1.5 in 1 day and Cr rise > 0.5	Miscellaneous	N/A	N/A	N/A
146	Dofetilide and Mg < 2 or K < 4	Miscellaneous	N/A	N/A	N/A
159	Flecainide & Digoxin	Miscellaneous	N/A	N/A	N/A
86	Gabapentin (Neurontin) and CR > 1.8	Miscellaneous	N/A	N/A	0.4%

Table 1. ADE rule performance [Positive Predictive Values (PPVs)] (continued)

Rule #	Rule name	Category	DRAH PPV (ADE)	DUH PPV (ADE)	DRH PPV (ADE)
70	Levofloxacin or Ciprofloxacin and Cr > 1.5 & r .5	Miscellaneous	N/A	N/A	0.7%
6	Lidocaine > 5 mcg/ml	Miscellaneous	N/A	N/A	0.0%
116	Lithium > 1.5	Miscellaneous	35.7%	46.2%	29.0%
161	Loop Diuretic & Lithium	Miscellaneous	N/A	N/A	0.0%
149	Methemoglobin > 10%	Miscellaneous	N/A	0.0%	N/A
110	Oxcarbazepine and Na < 130	Miscellaneous	N/A	0.0%	33.3%
5	Phenobarbital > 45 mcg/ml	Miscellaneous	N/A	1.7%	33.3%
7	Phenytoin (Dilantin) > 20mcg/ml	Miscellaneous	9.7%	1.7%	14.3%
103	Phenytoin > 18 and Albumin < 3.3	Miscellaneous	12.5%	0.0%	0.0%
3	Procainamide > 10 mcg/ml	Miscellaneous	N/A	N/A	N/A
158	Propafenone & Digoxin	Miscellaneous	N/A	N/A	N/A
4	Quinidine > 5 mcg/ml	Miscellaneous	N/A	50.0%	N/A
152	Quinidine and Digoxin	Miscellaneous	N/A	N/A	0.0%
80	SGOT up 20% >450 & Ison./Pheny./Cyclo./Metho./Warf	Miscellaneous	0.0%	10.3%	0.0%
119	Sodium Phosphate & CR>0.7 & rise>1.0 next 7 days	Miscellaneous	N/A	0.0%	0.0%
147	Sotalol and Mg < 2 or K < 4	Miscellaneous	N/A	0.0%	N/A
108	Tacrolimus and previous Cyclosporine	Miscellaneous	N/A	30.0%	N/A
2	Theophylline > 20 mcg/ml	Miscellaneous	N/A	0.0%	25.0%
154	Thiazide Diuretic & Lithium	Miscellaneous	N/A	N/A	0.0%
10	Valproic Acid > 120 mcg/ml	Miscellaneous	40.0%	0.0%	6.7%
160	Verapamil & Digoxin	Miscellaneous	N/A	N/A	0.0%
78	VORICONAZOLE AND CR > 3.5	Miscellaneous	N/A	0.0%	N/A
90	Flumazenil IV	Narcotics/Benzodiazepines	24.1%	19.5%	17.2%
69	Meperidine and Cr > 1.5	Narcotics/Benzodiazepines	N/A	0.0%	0.0%
109	Morphine and Cr > 1.5 and rise > 0.5	Narcotics/Benzodiazepines	N/A	1.0%	N/A
52	Naloxone IV	Narcotics/Benzodiazepines	40.1%	14.8%	39.3%
174	Naloxone-Periop	Narcotics/Benzodiazepines	N/A	15.6%	N/A
175	Propoxyphene and age > 65 yrs	Narcotics/Benzodiazepines	2.0%	1.1%	0.1%
66	Acyclovir,Pentamidine and Creatinine > 1.5 & r .5	Nephrotoxins and Increased CR	N/A	0.5%	3.9%
11	Amikacin > 30 mcg/ml POST	Nephrotoxins and Increased CR	N/A	0.0%	N/A
9	Amikacin > 5 (DUKE)/> 30 (DRH&DHRH) mcg/ml SPOT	Nephrotoxins and Increased CR	N/A	0.0%	N/A
8	Amikacin > 5 mcg/ml PRE	Nephrotoxins and Increased CR	N/A	0.0%	0.0%
65	Amikacin,Gentamicin,Tobramycin and Cr>1.5<3.5&r>.5	Nephrotoxins and Increased CR	N/A	N/A	N/A
72	AMPHO.,FOSCAR.,FLUCONA.,ITRACONA. AND CR > 1.5	Nephrotoxins and Increased CR	N/A	1.5%	0.7%
74	CARBO.,CISP.,IFOSFA. AND CR > 1.5 AND RISE > .5	Nephrotoxins and Increased CR	N/A	20.0%	0.0%
21	Cyclosporin > 500 ng/ml	Nephrotoxins and Increased CR	N/A	N/A	50.0%
17	Gentamicin> 10 mcg/ml POST	Nephrotoxins and Increased CR	N/A	0.0%	0.0%
16	Gentamicin> 2 (DUKE)/> 10 (DRH&DHRH) mcg/ml SPOT	Nephrotoxins and Increased CR	N/A	6.3%	0.0%
15	Gentamicin> 2 mcg/ml PRE	Nephrotoxins and Increased CR	0.0%	15.2%	3.7%
114	Imipenem,Meropenem and Cr > 1.5 and rise > 0.5	Nephrotoxins and Increased CR	N/A	1.0%	0.0%

Table 1. ADE rule performance [Positive Predictive Values (PPVs)] (continued)

Rule #	Rule name	Category	DRAH PPV (ADE)	DUH PPV (ADE)	DRH PPV (ADE)
193	Ketorolac administration > 5 days	Nephrotoxins and Increased CR	14.3%	N/A	N/A
83	NSAID, COX inh. and CR > 1.5 & risen .5	Nephrotoxins and Increased CR	N/A	6.5%	2.4%
13	Tobramycin > 10 mcg/ml POST	Nephrotoxins and Increased CR	N/A	3.9%	0.0%
14	Tobramycin > 2 (DUKE)/> 10 (DRH&DHRH) mcg/ml SPOT	Nephrotoxins and Increased CR	N/A	1.3%	N/A
12	Tobramycin > 2 mcg/ml PRE	Nephrotoxins and Increased CR	N/A	4.5%	0.0%
20	Vancomycin > 20 (DUKE)/> 40 (DRH&DHRH) mcg/ml SPOT	Nephrotoxins and Increased CR	0.0%	7.2%	25.0%
18	Vancomycin > 20 mcg/ml PRE	Nephrotoxins and Increased CR	14.5%	7.2%	4.8%
19	Vancomycin > 40 mcg/ml POST	Nephrotoxins and Increased CR	16.7%	20.0%	N/A
67	Vancomycin and Cr > 1.5 in 1 day and Cr rise > .5	Nephrotoxins and Increased CR	N/A	N/A	1.5%

Three clinical pharmacists (kappa 0.88) manually examine all of the ADEs detected by the surveillance system, score the event, and assign an event category. Positive predictive values for the rules were calculated as the proportion of surveillance triggers that were deemed ADEs, or when an intervention occurred as a result of the pharmacists' evaluation over the total number of evaluations completed [6]. For the surveillance system, any ADE found by a trigger was counted in the numerator of the calculation even if that ADE was not what the trigger was originally designed to detect [6]. ADE rates detected by the surveillance system were calculated as either the number of ADEs detected per 1000 patient-days or the number of ADEs detected per 100 admissions.

Midpoint through the study, there were major refinements to the triggers and to the overall surveillance model strategy. The focus of these refinements was two-fold: establish a long-term, sustainable surveillance model that could be utilized for monitoring medication safety performance beyond the funding of the project, and ensure maximum utility of the surveillance system by accommodating the unique medication safety profiles of the three individual hospitals.

Up until this point in time in the project, the surveillance system focused on the detection of all ADE categories. This model was beneficial for estimating true ADE incident rates, as detected by surveillance, at two community hospital and an academic medical center. The broad scope of this model was beneficial for gauging internal performance, as well as for comparison of this performance to similar, previously published studies. However, the downsides of this model were the clinical pharmacist resources required to complete trigger evaluations each day, and the repetitiveness of their work. The three pharmacists funded by the project spent the majority of their time completing trigger evaluations and chart reviews. Although this approach detected considerable numbers of ADEs, it left little time for the pharmacists to assist quality leaders with making improvements based on these findings.

Therefore, in year three of the project the surveillance process was first revised at the academic medical center, where surveillance evaluations accounted for 2 pharmacist FTEs. The process was adjusted to only include the top three high-risk drug categories: anticoagulants, hypoglycemia, and narcotic/benozodiazepines. This reduced the research funded pharmacist FTE

allocation down to one, freeing the other pharmacist to work with the P&T committee, and medication safety and quality leaders across the organization to apply these data to quality improvement efforts. However, despite these labors there continued to be minimal support for surveillance within the medication safety program at the academic medical center. This was thought to be due to the absence of leadership adoption and a long-standing medication safety culture which solely relied on qualitative data, as reported by the voluntary reporting system, for safety issue prioritization and on-going measurement of their performance. At the close of the study, internally funded resources have yet to be allocated to trigger evaluations at the academic center, despite having 3 pharmacist FTEs dedicated to review of voluntary incident reports. Secondary to this absence of organizational support, surveillance evaluations were further reduced to include only narcotic/benzodiazepine and warfarin-related triggers. At the time of discontinuation of grant funding for the project, the research pharmacist responsible for the academic center's surveillance evaluations is funded by the health system.

Similar to the academic medical center, the larger community based hospital followed suit by shortening their rules list to include anticoagulants, hypoglycemia, narcotic/benozodiazepines, nephrotoxins and *C.Diff.* Due to the trivial volume of triggers generated at the smaller community based hospital, they continued to evaluate all ADE categories and are still doing so at the close of the study.

Unlike the academic mediation center, the pharmacy department leadership at the two community-based hospitals embraced the contribution surveillance made to their medication safety programs. As such, they internally funded pharmacy resources in year three of the project in an effort to sustain the program long-term. Only health system technical, analytical and quality assurance services will need to be provided to the community-based hospitals to maintain the surveillance system within their organizations beyond the grant period.

Sound leadership adoption, as well as an openness for cultural and medication safety transformation, were observed to be key elements to the deployment of a sustainable surveillance system model. The long-standing leadership and cultural barriers observed at the academic center were felt to be limitations of the study. Interestingly, these barriers were not observed at the two community-based hospitals and as such, the significance of this observation should not be underscored.

In addition to the resource allocation concerns, the original surveillance model also targeted the detection of ADEs and interventions similarly across all three entities, despite there being significant variances in patient acuity, technology implementation, clinical practice models, and medication use processes. Consequently, it became apparent that the potential adverse drug events and interventions experienced by the patients at each of the entities were also exceedingly different. To enhance the overall utility of the surveillance system, a midpoint release solely focused on addressing the local surveillance needs at each entity. As a result of this analysis, intervention-based rules at the academic center were mostly turned off, whereas these intervention alerts where expanded at the two community-based hospitals. The practice variances and surveillance rule performance at each study site are being provided to AHRQ as a supplement to this report, as well as being made available on our project web-site. Collective performance of the rules focused ADE detections across all three hospitals are shown in Table 1.

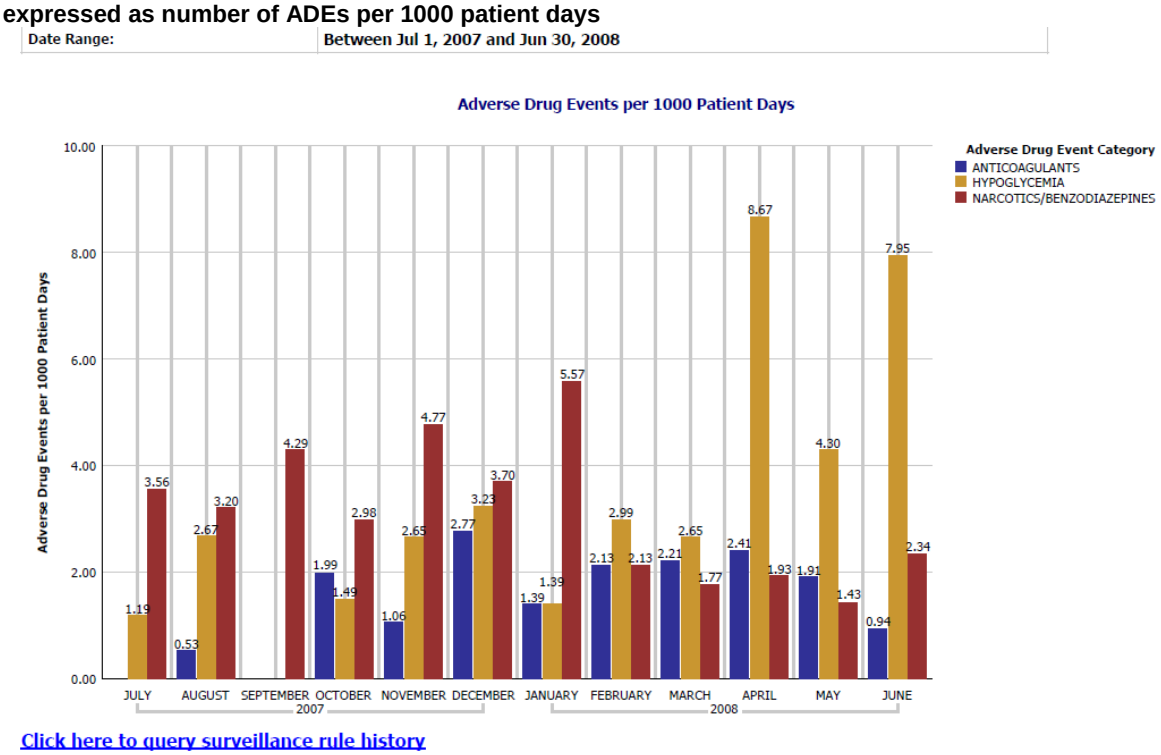
Results

Principal Findings/Outcomes/Discussion

The priority outcomes and themes from this study are shared below in summary form.

ADE Surveillance Implementation. The computerized adverse drug event (ADE) surveillance system was fully deployed and operational in our academic medical center by December 2004, and the two community based hospitals by early 2005. The programming and implementation phase of the project was completed 6-12 months ahead of the intial projected project timeine. Over the entire course of the study more than 100 surveillance rules were protoytped and tested. At the time of this report, the system currently operates 70 distinct rules, which continue to use a combinations of drug, laboratory, and demographic data extracted from the centralized clinical data repository, pharmacy system database, and patient information databases. The surveillance system focuses on the detection of ADEs in high-risk drug categories. The ADE rates per 1000 patient days for these combined categories are shared in Figures 3-5.

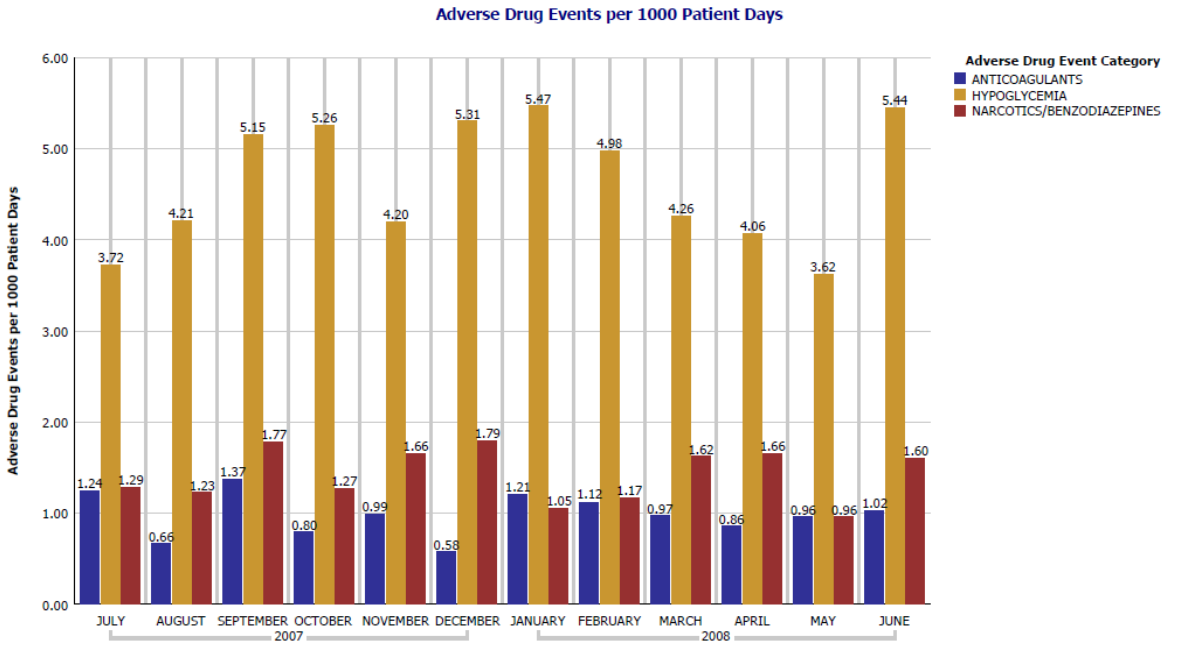
Figure 3. Monthly surveillance trending report for study hospital 1 using Business Intelligence; rates expressed as number of ADEs per 1000 patient days



Click here to query surveillance rule history

Figure 4. Monthly surveillance trending report for study hospital 2 using Business Intelligence; rates expressed as number of ADEs per 1000 patient days

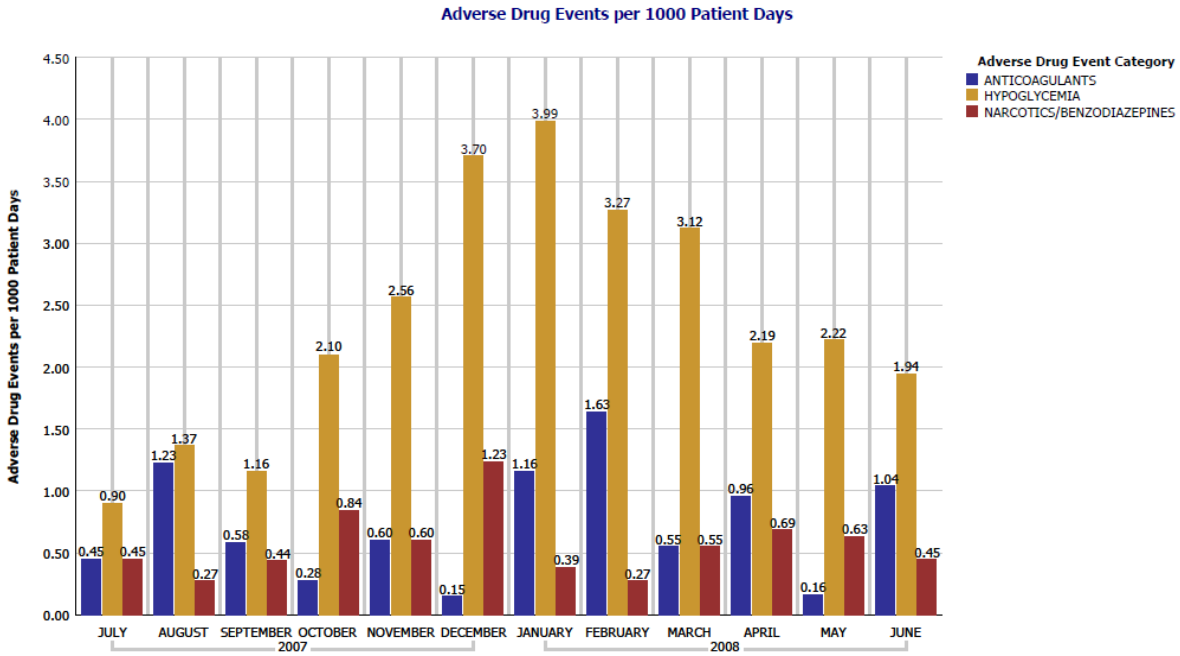
Date Range:	Between Jul 1, 2007 and Jun 30, 2008



Click here to query surveillance rule history

Figure 5. Monthly surveillance trending report for study hospital 3 using Business Intelligence; rates expressed as number of ADEs per 1000 patient days

Date Range:	Between Jul 1, 2007 and Jun 30, 2008



Click here to query surveillance rule history

This project provided the funds necessary to study the deployment, as well as the challenges, of introducing a computerized surveillance system into the medication safety programs of a three hospital health system. The detailed findings from this research have provided a more comprehensive view of the pulse of our medication safety programs, as well its complementary detection profile when compared to well -established methodologies already deployed across our organization. It also provided the opportunity to closely study the unique contributions a surveillance system provides to the community-based hospital versus the academic medical center environments.

Similar to other organizations we approached the pharmacist evaluation task by concentrating all responsibilities on dedicated pharmacy resources.(3) This approach had the advantage of better standardization and higher quality of evaluations; its principle disadvantage is the greater difficulty of making care interventions, as the dedicated resource is not a member of the patient care team and must work through others to recommend an intervention. We have subsequently deployed a combined approach, leaving interventions to clinical pharmacists but concentrating ADE detection among a smaller group of dedicated pharmacists.

As a result of the integrity of these findings, the organization became committed to working towards a long-term sustainable model so surveillance could exist beyond the grant period. As described above, the clinical resources required by the initial surveillance deployment model solely focused on grant-funded resources. Since this time, the system has been fully operationalized at the two community based hospitals, whereby internally funded pharmacists complete the surveillance evaluations, ADE scoring, and any potential interventions in patient care that may be necessary. Pharmacy leadership at these entities actively review the surveillance ADE data in an effort to identify potential quality improvement opportunites. Aggregate surveillance ADE trending data is also presented out to various safety and quality committees at these organizations.

Surveillance evaluations at the academic medical center are currently limited to ADE detection of narcotic/benzodiazepine and a subset of anticoagulants. The system is not currenly being used for any clinical pharamacy interventions. Presently, ADE detection evaluations are still being completed by one of the research pharmacists. However, training is underway to transition this effort to hospital-funded pharmacy resources. The proposed model will be for frontline pharmacists to complete the initial surveillance evaluation, and then kappa trained medication safety pharmacists finish the ADE scoring component. It is unclear if the integrity of the ADE data will be compromised with this model. We currently plan to have the research pharmacist monitor the quality assurance of the evaluations for several months beyond the end of the grant to ensure success.

ADE Surveillance System Performance. As an output of the data collected by the surveillance system and these evaluation processes, we complete on-going analysis of: number of triggers fired per rule; number of ADEs detected per rule and total (specifically, events resulting in harm to the patient per severity score AND Naranjo causality score of Probable or Definite ADE); and number of therapeutic interventions recommended by pharmacists per rule. Data from ADE surveillance are also compared with data gathered by traditional voluntary "incident reporting" on a monthly basis.

Studies of system performance based on these data have provided the ability to calculate the positive predictive value (PPV) for each rule and thereby determine which rules are of greatest value in detecting ADEs or intervention opportunities, and which are lowest yield. Combined

rule performance for the three hospitals has been provided in Table 1. These PPVs reflect rule performance for ADEs and were calculated based on the most recent data available for a given rule. Low level PPVs are in keeping with the “safety net” concept of ADE detection and result in a large number of false positives in order to find one "true" ADE. Additional findings from these analysis are being shared as an addendum to this report and have also been published elsewhere. (5,7,10)

A Surveillance System is Complementary to Other ADE Detection Methodologies. As part of this study, we completed a comparison of two fully operational ADE detection methods: computerized surveillance and voluntary reporting. This analysis underscored the synergistic nature of these two approaches. While surveillance provides quantitative data to estimate the true rate of ADEs, voluntary reporting contributes qualitative evidence to inspire future trigger development and to identify potential areas of emerging risk. We further analyzed the medications most likely to cause harm, evaluated each system’s strengths, and proposed a synergistic strategy for monitoring medication safety performance. Detailed descriptions of these study findings and analysis have been published in the literature.(7)

Clinical Pharmacy Practice Deployment Models May Affect the Overall Safety Contribution and Value of a Computerized Surveillance System. As previously discussed in this report, we are aware of the challenges of influencing clinician behavior and in successfully achieving adoption of the surveillance system by clinicians. Our initial model proposed using clinical pharmacists on care teams to complete the trigger evaluations on their patients, documenting ADEs and recommending interventions.(2) Although this has proven to be successful at the community-based hospital, we have since migrated to mixed evaluation model at the academic medication center as previously described above. This effort has required a more comprehensive strategy for educational processes, extensive one-on-one teaching and assistance, continuous feedback and evaluation, and centralized health system monitoring of evaluation performance. Nonetheless, this mixed model will be a new task for all pharmacists involved, and resistance and misunderstandings are still to be expected.

Interventions to Prevent Adverse Drug Events. We no longer track intervention rates as part of the initial surveillance implementation secondary due poor clinican adoption and lack of timely alert notifications generated from a once daily batch process. However, application and analysis of data collected by our retrospective ADE surveillance system, highlighted the clinical necessity of implementing new real-time, prospective surveillance alerts to warn health care providers of evolving unsafe patient conditions.

The current surveillance design is a stand-alone computerized patient safety system with the primary function of detecting and quantitatively measuring the incidence of ADEs in the acute care setting. However, to construct safer clinical care processes through intervention, it was apparent we needed to reconsider the IT design of the original system. In the original design, the rules could only be configured to be retrospective, i.e. runs once daily in a batch process for prior 24 hours. However, this configuration did not support the development of prospective trigger rules which ideally targeted the prevention of patient harm. In addition, triggers were only currently accessible for review by clinical pharmacists. These findings helped support the natural progression of any technology implementation, which is continuous improvement. Therefore, we completed a pilot surveillance project of "just in time" alerts for anticoagulants. These

new surveillance alerts instantaneously notify the covering physicianwho is most suited to carry out the interventional action. Physicians are notified via alpha numeric page when an alert files. The design details of this pilot were shared in a poster presentation at the AHRQ 2008 Annual Conference. (Long et al.)

Much is Known About the Safety Role of a Surveillance System in Adult Patient Populations; However its Utility in Specialized Patient Populations, Such as Pediatrics, Remains Uncertain. Pediatric patients are at exceptionally high risk for medication-related adverse events. Therefore, we undertook an analysis of data from a one year period to compare the detection rates of two common adverse drug event (ADE) discovery strategies, voluntary reporting and computerized surveillance, in pediatric inpatients at a large, academic medical center. We assessed the primary drugs that generated ADEs in this specialized patient population, as well as made recommendations as to which may identify the most opportunities for intervention and reduce patient harm. We concluded that computerized ADE surveillance underperformed compared to detection rates seen in adult systems, suggesting that tailored rule sets are necessary to accommodate the unique needs of a high risk pediatric patients. A full description of this study has been published in *Pediatrics. (1)* The results of this study also prompted the development of series of pediatric-specific surveillance rules. The performance and findings from these pediatric specific rules will be shared in a future publication.

A Long-Term Surveillance Model Mandates it be Aligned With the Organization's Medication Safety Performance Infrastructure. If we were to encourage the widespread use of the data collected by the surveillance system in quality improvement efforts, it became apparent that significant effort needed to be expended to engage and educate health system leadership on its operational utility. The primary focus of these discussions and presentations was to ensure all leaders were familiar with the two-pronged approach to ADE detection at our organization and the limitations and benefits of each method. Although extensive leadership adoption and cultural change were observed at the community based hospitals, barriers to widespread adoption of the surveillance system at the academic medical center remain.

These barriers to adoption, as well as educational deficits, further necessitated the addition of surveillance ADE rate data to the Quality and Patient Safety quadrant of the health system Balanced Scorecards. The goals of score carding were two-fold: establish a new *quantitative* measure that would enhance the ability to monitor our medication safety performance over time, and elevate the acceptance and utility of the surveillance system within our organization. The details of the new Medication Safety Performance Metrics for the Acute Care Division FY09 were as follows:

- Enhance Scorecard to include a Quantitative Measures for Medication Safety Performance

- Addition of Narcotic/Benzodiazepine Events Rate per 1000 patient days as detected by Surveillance

- Continue all Current Medication Safety Measures in Parallel

The final proposal to only add Narcotic/Benzodiazepine ADEs, as detected by surveillance, to the scorecard, was based on that fact that narcotic/benzodiazepine related events occur in almost all care units across our health system and were the least controversial in terms of identifiable patient harm.

This initiative required extensive internal effort on the project team's part, including development of the measure definition, measure calculation, the methodology, as well as assigning values for both target and exceeds. This included definitions at the clinical service unit, entity and health system levels. With no available ADE benchmarks in the literature or at the national level for setting ADE target rates for score carding purposes, our measure values (target & exceeds) were set based on the historical ADE rates per 1000 patient days by using the upper 90% CI value minus 5% (target) and 10% (exceeds). We took a conservative approach to ensure the measure values set in the first year were fair and took into account variances in ADE rates across the different care areas. As we collect additional data in the coming fiscal year, we are optimistic we will be able to utilize more advanced statistical methods, such time series, to set more accurate ADE targets on future scorecard cycles. Final FY09 measure details were approved by health system executive leadership in July 2008. The details of a med safety surveillance ADE scorecard measure for the upcoming fiscal year has been provided in Figure 5.

Engagement of Quality Improvement Officers, Patient Safety Leaders, and Frontline Clinical Staff in the Analysis of Safety Data Collected by the ADE Surveillance System is Essential. In order to improve the safety profile of the health system it is essential safety leaders have prompt and accurate access to aggregate safety reports generated from the ADE surveillance system. Given the critical nature of patient safety data and with the introduction of the new scorecard measure, dissemination of aggregate safety metrics needed to be achieved in a validated and consistent manner. The existing surveillance reporting structure did not have the ability to schedule and automatically distribute aggregate reports to a specific group of users. This was a barrier to the effective sharing of patient safety data with health system leadership, clinical managers and quality improvement personnel. It also limited the utilization of this mission critical data for quality improvement initiatives.

With the support of our AHRQ grant, we integrated ADE surveillance data into our enterprise data warehouse. We also integrated business intelligence (BI) tools to directly empower unit leaders with real time and context specific access to their aggregate patient safety data.[11] These combined tools now allow clinicians to ask dynamic questions about their safety and quality issues. Providing this level of direct access to patient safety data also encourage the operational leadership to take ownership of the critical safety issues detected by the surveillance system, rather than it be exclusively viewed as a research initiative. Engagement of hospital and medication safety leadership at the academic center remained limited. Pharmacy leadership and the medication safety pharmacists at the community based hospitals actively engaged in the monthly review and analysis of these surveillance data.

As part of this process, it was also important to recognize users of the data had varying levels of technical expertise, as well as different reporting requirements. As a result, we decided to develop multiple portals from which patient safety leaders and QI officers could access the same standardized ADE surveillance reports. Health system leadership frequents the our Performance Services web site for all current safety and performance reporting, therefore integrated surveillance BI reports into this web portal. Frontline staff and QI clinical leaders, on the other

hand, spend most of their time within the voluntary reporting system dashboard and seldom access the Performance Services web site. To accommodate their daily workflow, we developed a tab within the voluntary system that serves as the portal for distribution of secured surveillance reports to these users. The security access procedures for these reports are currently being finalized with the patient safety office and risk management. The extent to which Risk Management should be involved in granting safety data access for internal quality improvement purposes remains controversial within our organization.

Transparency of Safety Data across Detection Methodologies is Essential to its Adoption and to Understand its True Utility in Improving the Medication Safety Profile of an Organization. Adverse drug events are currently being detected in our health system using two parallel yet disparate methodologies, voluntary reporting and trigger detection via the surveillance system. Potential events identified in both systems undergo parallel evaluations by specially trained medication safety pharmacists. Of the adverse drug events detected via the surveillance system, there is a percentage of overlap with events reported voluntarily, thus, resulting in duplication of efforts and inefficient use of expensive pharmacist resources.

Unlike voluntary reporting, the events detected via the surveillance system are primarily textual based and do not undergo a peer-review process. As a result of this deficit, the level of granularity necessary to identify process improvement opportunities is currently lacking in surveillance data. Events detected by surveillance are also stored in a separate database from voluntary reports and individual event stories are not readily available to the broader clinician workflow for trending, monitoring, and intervention. Therefore we engaged in a pilot to study the barriers and design requirements to integrate surveillance events into the operational medication safety incident review workflow. Because our internally developed voluntary system already provided the infrastructure to electronically communicate and share events with clinical leaders, we chose to use it as the portal for this pilot.

Understanding the underlying factors that contribute to harmful events is integral to the sustainability of any safety event detection methodology. A successful patient safety model must be multi-dimensional: Capture ADE counts or rates for trending and provide safety leaders with the granular information they need to drive quality improvements. We are optimistic the surveillance integration pilot project will allow us to assess the long-term feasibility of a medication safety solution that integrated the combined value of each individual methodology. We hope it will serve as a model for other organizations wishing to identify local process failures and deficits which contribute to safety events, yet collect the quantitative metrics necessary to assess the overall performance of the organization. Our descriptive findings from this pilot will be shared in a future manuscript.

Conclusions

A surveillance system provides a vital safety net to detect and monitor for potentially harmful patient safety events within any organization or hospital size. Unlike the capabilities of current and future technology solutions which focus on the measurable reduction of medication errors, such as barcode administration and computerized physician order entry, the surveillance system solely focuses on the detection and measurable reduction of events which cause patient harm. These are critical distinctions which must be acknowledged and expansively understood. A comprehensive health IT deployment strategy must include some level of computerized

surveillance to monitor medication safety performance and progress overtime. Additionally, this system provides the capability for an organization to detect and monitor for potentially harmful patient events at any stage in the medication management process. Unfortunately, surveillance technology with the level of sophistication detailed in this study in not readily available for wide scale deployment.

Engagement of organizational leadership early on in the project is essential if the goal is to utilize the data collected by surveillance for quality improvement rather than exclusively for research purposes. Secondary to differences in leadership strategies of the PIs leading the study, significant effort was expended in the second half of the study period to get health system buy-in for the system, rather than at the onset of the project. The absence of having operational champions, who are responsible for safety and quality, engaged early on may have detracted the study team from gaining an understanding of the full potential a surveillance system may play in an organization's medication safety program. The leadership and safety culture differences in academic versus community based hospitals observed as a corollary of this study must be acknowledged. Furthermore, future research to better understand the influence these factors have on the deployment of a quantitative methodology to measure an organization's medication safety performance may be warranted.

ADE detection methodologies appear to be synergistic and complementary. When used in combination with each other, multiple detection methods may give us additional clarity on the scope of our medication safety issues. The surveillance system from this study focused on quantitative measurement succinct set of events which cause patient harm, whereas the established voluntary reporting system captured a broader range of events and provided more qualitative data for reducing medication use process errors. Any hospital medication safety program should consider using multiple ADE detection methods, if resources permit.

The next stage in this project will be to monitor the overall progress of the scorecard measure, as well as continue to education safety leaders on the operational utility of the data collected by the surveillance system. Additional work will also continue to define and deploy "just in time" surveillance system which solely focused on monitoring for unsafe patient conditions across the medication use continuum.

Significance

Our findings are significant in a) showing the feasibility of implementing and operating automated surveillance across multiple entities in a health system with disparate IT environments; b) demonstrating the ability of such a system to yield side-by-side comparative data on ADE incidence between academic and community hospitals (never before published); c) demonstrating the ability of such a system to detect changes in ADE incidence based on a specific intervention (e.g., reduction in antibiotic-associated colitis following implementation of safety measures). While we continue to reassess the technology requirements for pharmacist and provider interventions in patient care based upon the incidence of ADEs, the community-based pharmacists routinely detect and intervene in high-risk scenarios that would otherwise have gone undetected. Thus, both as a source of baseline metrics for medication safety and as a mechanism for ADE prevention, the ADE surveillance system have proven to exceed our initial expectations particularly at the community-based hospitals. However, the challenges and obstacles encountered throughout the duration of the project should not be minimized. Additional research

on the feasibility and wide scale deployment of automated surveillance systems to quantitatively measure an organization's medication safety performance over time are warranted.

References

1. Brennan TA, Leape LL, et al. Incidence of Adverse Events and Negligence in Hospitalized Patients: Results of the Harvard Medical Practice Study I. NEJM. 1991;324:370-376

2. Institute of Medicine. To err is human. Building a safer health system. Washington, DC, National Academy Press, 1999

3. Institute of Medicine. *Preventing Medication Errors: Quality Chasm Series*. Washington, DC, National Academy Press, 2006

4. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther.* 1981;30(2):239–245

5. Kilbridge PM, Campbell UC, Cozart HB, et al. Automated surveillance for adverse drug events at a community hospital and an academic medical center. *J Am Med Inform Assoc.* 2006;13(4):372–377

6. Ferranti J, Horvath MM, Cozart H, et al. Re-evaluating the safety profile of pediatrics: A comparison of computerized adverse drug event surveillance and voluntary reporting in the pediatric environment. *Pediatrics*: 2008;121;e1201-e1207

7. Ferranti J, Horvath MM, Cozart H, et al. (2008). A multifaceted approach to safety: The synergistic detection of adverse drug events in adult inpatients. *J Patient Saf* 2008;4:184-190

8. Classen DC, Pestotnik SL, Evans RS, et al. Computerized surveillance of adverse drug events in hospital patients. *JAMA*. 1991;266:2847-2851.

9. Jha AK, Kuperman GJ, Teich JM, et al. Identifying adverse drug events: development of a computer-based monitor and comparison with chart review and stimulated voluntary report. *J Am Med Inform Assoc*. 1998;5:305Y314.

10. Kilbridge PM, Alexander L, Ahmad A. Implementation of a system for computerized adverse drug event surveillance and intervention at an academic medical center. *JCOM* 2006; 13:94-100.

11. Horvath MM, Cozart H, Ferranti J, et al. Sharing Adverse Drug Event Surveillance Results Using Business Intelligence Technology. *J Patient Saf*; Accepted.

List of Publications and Products

Publications

Ferranti J, Horvath MM, Cozart H, et al. Re-Evaluating the Safety Profile of Pediatrics: A Comparison of Computerized Adverse Drug Event Surveillance and Voluntary Reporting in the Pediatric Environment. *Pediatrics*. 2008.121(5):e1201-7.

Ferranti J, Horvath MM, Cozart H, et al. A multifaceted approach to safety: The synergistic detection of adverse drug events in adult inpatients. *J Patient Saf* 2008; 4:184-190.

Horvath MM, Cozart H, Ferranti J, et al. Sharing Adverse Drug Event Surveillance Results Using Business Intelligence Technology. *J Patient Saf*; Accepted.

Kilbridge PM, Alexander L, Ahmad A. Implementation of a system for computerized adverse drug event surveillance and intervention at an academic medical center. *JCOM* 2006; 13:94-100.

Kilbridge PM, Campbell UC, Cozart HB, et al. Automated surveillance for adverse drug events at a community hospital and an academic medical center. *J Am Med Inform Assoc*. 2006; 13(4):372–377

Long A, Cozart H, Horvath M, Ferranti J. Patient Safety in Perioperative Care: Computerized Detection of Opioid Related Adverse Drug Events in an Academic Medical Center. *Am J Health-Syst Pharm*. In draft.

Eckstrand J, Cozart H, Horvath M, Ferranti J. Implementation of Pediatric Specific Triggers: Modification of a Computerized Adverse Drug Event Surveillance System. *Qual Saf Health Care*. In draft.

Presentations & Posters

Jeffrey Ferranti, MD, MS. Bridging the Gap: Empowering Caregivers with Real Time Access to Aggregate Patient Safety Data. AHRQ 2007 Annual Conference. September 2007. Washington, DC.

Heidi Cozart. Using Informatics and Basic Research to Improve Medication Safety. ASHP 2008 Midyear Clinical Meeting and Exhibition. December 7-11, 2008. Orlando, FL.

Horvath M, Cozart H, Ferranti J. Sharing Adverse Drug Event Surveillance Results Using Business Intelligence Technology. 2008 AMIA Spring Congress. May 29-31, 2008. Phoenix, AZ.

Cozart H, Horvath M, Ferranti J. Developing an Innovative Patient Safety System to Improve Healthcare Quality: Operational Integration of Computerized Adverse Event Surveillance. 2008 AMIA Spring Congress May 29-31, 2008. Phoenix, AZ.

Judy Wu. Using Information Technology to Detect Ambulatory Adverse Events Related to Anti-diabetic Drug Therapy. SERC presentation. April 2008

Tania Vila. Impact of the Institute for Healthcare Improvement Global Trigger Tool Compared to Current Adverse Event Monitoring Systems at a Large Teaching Hospital. SERC presentation. April 2008.

Long A, Cozart H, Eckstrand J, Ferranti J. Implementation of Anticoagulant-Focused "Just-in-Time" Alerts in an Academic Medical Center. AHRQ 2008 Annual Conference. September 8-10, 2008. Washington, DC.

Other Products

Computerized Patient Safety Project Website: http://cpsi.dhts.duke.edu/