Comparing the Effectiveness of Computerized Adverse Drug Event Monitoring Systems to Enhance Clinical Decision Support for Hospitalized Patients

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Keywords

Clinical decision support, pharmacy information systems, error management and prevention, data collection, system improvement

Summary

Objective: Performance of computerized adverse drug event (ADE) monitoring of electronic health records through a prospective ADE Monitor and ICD9-coded clinical text review operating independently and simultaneously on the same patient population for a 10-year period are compared. Requirements are compiled for clinical decision support in pharmacy systems to enhance ADE detection.

Methods: A large tertiary care facility in Utah, with a history of quality improvement using its advanced hospital information system, was leveraged in this study. ICD9-based review of clinical charts (ICD9 System) was compared quantitatively and qualitatively to computer-assisted pharmacist-verified ADEs (ADE Monitor). The capture-recapture statistical method was applied to the data to determine an estimated prevalence of ADEs.

Results: A total estimated ADE prevalence of 5.53% (13,420/242,599) was calculated, with the ICD9 system identifying 2,604 or 19.4%, and the ADE monitor 3,386 or 25.2% of all estimated ADEs. Both methods commonly identified 4.9% of all estimated ADEs and matched 62.0% of the time, each having its strength in detecting a slightly different domain of ADEs. 70% of the ADE documentation in the clinical notes was found in the discharge summaries.

Conclusion: Coupled with spontaneous reporting, computerized methods account for approximately half of all ADEs that can currently be detected. To enhance ADE monitoring and patient safety in a hospitalized setting, pharmacy information systems should incorporate prospective structuring and coding of the text in clinical charts and using that data alongside computer-generated alerts of laboratory results and drug orders. Natural language processing can aid computerized detection by automating the coding, in real-time, of physician text from clinical charts so that decision support rules can be created and applied. New detection strategies and enhancements to existing systems should be researched to enhance the detection of ADEs since approximately half are not currently detected.

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1. Introduction

Since previous studies have shown that a single gold standard to identify adverse drug events (ADEs) does not exist [1], and the most commonly used detection method of spontaneous reporting identifies only 5% of ADEs [2], multiple methods of detecting and treating ADEs are needed to enhance patient safety. Current computerized ADE monitoring of electronic health records includes prospective ADE monitoring and retrospective ICD9-coded review. Prospective surveillance requires algorithms to identify abrupt medication stop orders, antidote ordering, vital sign abnormalities and certain abnormal laboratory values resulting in alerts in the hospital and outpatient settings to facilitate timely interventions that assist in preventing serious ADEs [3, 24]. Retrospective review of unstructured clinical notes flags charts with one or more of a pre-determined list of codes that indicate a potential ADE [4-6]. Finally, pharmaceutical industry and health authority consortiums are focusing on applying new analytic methods to analyze and mine data from large administrative claims and electronic medical records (EMR) databases with the hope of being able to confirm existing safety signals and discover early indications of new safety concerns about marketed medicines [7, 8].

Although the relative accuracy of detecting ADEs has been established using computerized algorithms to send alerts, and International Classification of Diseases, Ninth Revision, Clinical Modification (ICD9) codes to identify ADEs, comparison of these two methods has been limited [9-11]. In addition to the varying accuracy of different detection methods, the incidence of ADEs has also differed widely depending on the detection method used to calculate the incidence of ADEs. According to a June 2001 Utah Department of Health report based on its hospital discharge database, approximately 25,000 discharges from a total of one million hospitalizations from the entire state of Utah contained ICD9 codes indicating possible incidence of up to 2.5% of hospitalized patients [12].

2. Objective

This research was designed to quantify a more comprehensive and accurate understanding of ADEs by comparing and contrasting two separate mechanisms for ADE surveillance in a unique scenario at an institution with a history of focusing on patient safety improvement activities. The scenario is that computerized monitoring (through an ADE monitor) and unstructured clinical text review (through an ICD9 system) operated completely independently and simultaneously on the same patient population in the same institution for almost a decade. By directly comparing the methods during the same time period, the performance of each system was compared and an estimated prevalence of ADEs was calculated. An optimal detection strategy for ADEs can be understood through this type of comparison and tailored for other similarly sized and complex care facilities.

An advantage of the processes in place at the research location, a tertiary care medical center, is that between 1992 and 2001 the ADE monitor and ICD9 system were completely separate. ICD9 codes were collected and analyzed independent of the ADE data considered by the ADE monitor. Therefore, two independent systems to detect ADEs, with their respective retrospective datasets, were available for comparison. The strengths and weaknesses of the systems were examined to better understand how to potentially combine the features of both systems into an overarching detection capability. Evaluation of the two systems included comparing the process with which ADE data was collected and coded, reporting the quantity and quality of the ADE data, and estimating the total incidence of ADEs by considering both detection methods as having identified samples of a larger, complete set of ADEs.

3. Methods

3.1 Setting

The study took place at LDS Hospital, a tertiary care medical center and 520-bed tertiary-care teaching hospital. Located in Salt Lake City, Utah, it has an internally developed computerized information system which managed administrative, financial and clinical information since 1970 [13]. The study included 242,599 hospitalized adults whose clinical data were in an archived database at the tertiary care medical center between January 1, 1992 and December 31, 2001. Institutional Review Board (IRB) approvals were obtained from three IRBs, including the University of Utah, LDS Hospital, and the Utah Department of Health.

3.2 ICD9 System ADEs

Patient records in the medical center's archived database were selected by searching for inpatient hospitalizations that contained one or more of 446 ICD9 ADE codes taken from a larger patient safety event detection code set developed by an expert panel [14]. Patient records had an average of 14 and a maximum of 44 ICD9 codes per encounter. ▶Table 1 shows a summary of the 446 "E" and "N" ICD9 codes used to identify the patient records. Patient-identifiable data from the archived database were placed in a separate password-protected Oracle database behind the medical center's firewall. Patient encounter numbers (unique identifiers assigned to each patient) were used to sort the database tables and identify patient data.

Medical coders at the tertiary care medical center used 3M Corporation's Codefinder™ software to assign ICD9 codes to patient records after discharge, based on physician documentation of clinical events in the patient's chart [15]. The software offered prompts to allow the coders to assign adverse event and poisoning codes based on whether the clinical documentation noted a condition being due to a drug, medicinal or biological substance [10].

3.3 ADE Monitor ADEs

Another separate database of ADE monitor records that was developed in 1989, contained pharmacist-identified and documented ADEs [13, 16-18]. That documented record for each verified ADE contained the computerized alert, drug name, clinical manifestation, time of occurrence, and severity of the ADE. The ADE monitor was automatically activated when a clinical event (such as a nurse documenting that a patient experienced a mental status change while being prescribed morphine) caused a rule to become true (data driven) and was also activated once each day (time driven) to alert a clinical pharmacist of hospitalized patients who may be experiencing an ADE [16]. The alerts were based on pre-defined algorithms and rules that considered all relevant and coded patient data, such as drug orders, laboratory results, nurse charting and physiologic changes from the integrated clinical database [3, 19-21]. The pharmacist verified each ADE alert by determining which drug may have been associated with the clinical manifestation experienced by the patient [22]. All ADE monitor alerts were relayed to the prescribing physicians to ensure timely therapeutic action and the documentation was stored in a database within the Clinical Information System [3, 4, 19-21, 23-25].

3.4 Matching Drugs and Codes

Approximately half of all the patients' records that were present in both ICD9 system and ADE monitor datasets over the 10 years were randomly chosen to compare data from the systems. Two of the physician authors (GNP and YK) compared the ICD9 codes with the ADE drug names and reached consensus on which categories to match the records. For example, the category "Complete Match" corresponded to an ICD9 code that exactly matched the ADE monitor drug name ("E935.2" indicated an opiate and "Meperidine" was an opiate). An initial comparison between the two datasets consisted of establishing a matching criterion for categorizing the information present

in the ICD9 system code assigned by the medical coder and the ADE monitor drug name assigned by the pharmacist.

3.5 Chart Review Validation

Although the details of the chart review are part of a separate paper to be submitted in parallel with the current study, 187 randomly selected records identified through the ICD9 system were used to validate the ICD9 codes. The review found that hospital-acquired ADEs occurred in 23%, while the remainder of records indicated a community-acquired ADE, intentional outpatient poisoning, coding error or ambiguous documentation [26]. An independent study conducted in the same time period [4] also found that about a quarter of ICD9-flagged patients had hospital-acquired ADEs. The patient records with hospital-acquired ADEs were categorized to determine the location of the relevant documentation in the chart, the frequency of documentation of the drug name, the clinical manifestation and the severity of the ADE.

3.6 Capture-Recapture Method

To ensure consistent quantitative comparison with only hospital-acquired ADEs, 23% of the total ICD9 ADEs were used in the calculations with the ADE monitor findings using the Capture-Recapture method [27]. Capture-Recapture is a statistical method for indirectly estimating prevalence. The overlap created between two or more random samples from two or more independent data sources, such as the ICD9 system and the ADE monitor, allow for a more accurate calculation of the prevalence of hospital-acquired ADEs. Accuracy is extremely important in ADE surveillance because no gold standard exists and quality management and clinical research activities over the past decade have reported a wide range of prevalence of ADEs. Since many ADEs are not reported or detected through either spontaneous reporting, ICD9, or ADE monitor systems, the Capture-Recapture method can give a more complete picture of ADE occurrence.

4. Results

As shown in ▶Table 2 during the 10-year period from January 1, 1992 through December 31, 2001, the ICD9 system identified 11,977 alerts with 2,604 (23% of 11,977) estimated as hospital-acquired ADEs, and the ADE monitor generated 40,025 computerized alerts with 3,386 (8.5% of 40,025) validated as hospital-acquired ADEs. Using the Capture-Recapture method the total prevalence of ADEs in the hospitalized patient population was 13,420 (2,604*3,386/657) over the 10 years, for a total estimated ADE rate of 5.53% (13,420/242,599). As shown in ▶Figure 1, the ICD9 system identified 2,604 or 19.4% of all estimated ADEs and the ADE monitor identified 3,386 or 25.2%, while the 657 patients identified by both methods accounted for 4.9% of the total.

Although a detailed analysis of the documented clinical manifestations and their frequencies in the ICD9 system is the subject of a separate study, a brief description is presented here. Mental status change, nausea/vomiting and allergic reaction were the most common manifestations with analgesic, anti-infective and cardiovascular drugs responsible for over half of all hospital-acquired ICD9 system ADEs. Seventy percent of the ADE-related documentation was located in the Discharge Summary and 30% in the Progress Notes, the History and Physical, or the Consultation Notes.

▶Table 3 shows the four categories and ▶Table 4 shows the results from the comparison study to match drugs and codes for the patients commonly identified by the ICD9 system and ADE monitor. The records indicating an ADE were categorized according to ▶Table 3. A "Complete Match" occurred in 51.8% (177/342) and a "Partial Match" in 10.2% (35/342) for a total match rate of 62.0% (212/342). "No Match" occurred in 32.2% (110/342) and "Drug Not Specified" occurred in 5.9% (20/342) for a total unmatched rate of 38.0% (130/342). The benefits and limitations of both detection methods are summarized in ▶Table 5.

5. Discussion

During the 10-year period studied, an estimated 5.53% of patients hospitalized experienced an ADE, twice as much as previously estimated by the Utah Department of Health. Previous studies have found that documentation in patient charts accounted for approximately 65% of all known ADEs, with voluntary reporting and computerized monitoring accounting for the remainder with a small overlap between known ADE detection methods [1]. The Capture-Recapture method showed that the performance of the two detection methods accounts for an estimated 44.7% (19.4% from the ICD9 system, 25.3% from the ADE monitor) of ADEs. If we add the 5% estimated prevalence of ADEs from spontaneous reporting, then we can conclude that about half (44.7% + 5%) of all ADEs are picked up by these 3 methods and half are undetected by these methods in their current form.

If half of all ADEs are currently undetected, enhancements to the current detection methods, or research into new detection methods are needed. Perhaps increased emphasis should be placed on detecting ADEs occurring in the community setting, which may give insight into how to better detect them in either outpatient or inpatient settings [29, 30, 32]. In addition, research into the collection of patient reported outcomes collected through the use of validated surveys from appropriately sized statistical samples of patients who are exposed to newly available medications on the market may serve to enhance detection.

Comparing the two databases for the patients identified by both methods determined how well the two systems matched with one another. The current ICD9 system identifies potential ADEs through codes that indicate the drug class or clinical manifestation documented as causing an ADE. The ADE monitor identifies potential ADEs through pre-determined alerts sent to a pharmacist to check the medical record and interview the patient to determine if any of the prescribed drugs are causing an ADE. The matching experiment showed that the records matched completely only half the time. Although the two methods identified the same patient as having an ADE, the physician documentation of the ADE in the chart often differed from the pharmacist documentation in the ADE monitor database. To explain this, the commonly identified patients may have had different documentation of the same ADE or there may have existed two different ADEs, one picked up by each method.

The balance between the benefits and limitations of each detection method should promote their incorporation into clinical decision support systems in health care facilities capable and willing to implement them. Each method identifies different types of ADEs with only a small overlap between them. The ADE monitor is optimized as an on-site detection system for prospective monitoring of patients while they are hospitalized. The ICD9 system is optimized for public health surveillance through retrospective analysis of patient records after patients are discharged from the hospital. Thus, in its current state the ICD9 system cannot be used to reduce the severity of ADEs. Optimum use of each system will depend on the existing infrastructure of the health care facilities implementing them. To best create a prospective alerting capability from the ICD9 system, and to enhance the rule set of the ADE monitor to include signs and symptoms documented by a physician through written or dictated documentation of the clinical notes, natural language processing (NLP) technology should be implemented to create structured medical concepts and codes from which decision support rules can be applied against and alerts generated for a pharmacist or physician to review [31]. Consideration of unstructured clinical text, such as that found in discharge summaries and progress notes, enhances the ability to identify certain ADEs such as mental status changes which are important to monitor medications like analgesics, and allows a pharmacist or physician to conduct a more detailed chart review and patient interview [33, 34].

Consideration of structured medication and lab information, such as those reviewed by the ADE monitor, are important to identify allergic and idiosyncratic ADEs such as nephrotoxicity causing renal impairment from anti-infectives, and rising serum creatinine, which can best monitor medications like anti-infectives and chemotherapies, respectively. Therefore, the two systems operate in a complementary manner, each having its strength in a slightly different domain of ADEs but with a small overlap. Spontaneous reporting may have its own strength and operate under a different manner, which should also be studied to best assess its comparative role.

6. Conclusions

Public health agencies such as State Departments of Health have the resources to implement surveillance systems by aggregating administrative data into discharge databases and search the databases for codes that indicate ADEs. Hospital administrations have the resources to implement patient safety initiatives to monitor computerized lab, vitals and pharmacy data for a prospective monitoring system similar to that used by the ADE monitor at the tertiary care medical center. Technology such as NLP for the real-time coding of physician text from clinical charts, and processes underlying better quality monitoring should be investigated so that methods such as the ICD9 system and ADE monitor can operate simultaneously and accumulate knowledge on ADEs to prevent future ADEs.

Implications of results for practitioners and/or consumers

Safer health care can be achieved by providing practitioners with relevant and timely data on patients who may be experiencing ADEs. The integration and implementation of multiple adverse event systems, such as the ICD9 system and ADE monitor can advance the knowledge base in ADE detection and create a safer environment for patients. Health care delivery that includes methods like NLP to automatically structure clinical notes and make the structured data available for clinical decision support to flag potential ADEs could soon play a pivotal role in the global surveillance and detection strategies for ADEs.

Conflict of Interest

Research presented here was completed as part of Gerasimos Petratos' post-doctoral research at the University of Utah prior to his employment at Hoffmann-La Roche, his current affiliation. The authors declare that they have no conflicts of interest in the research.

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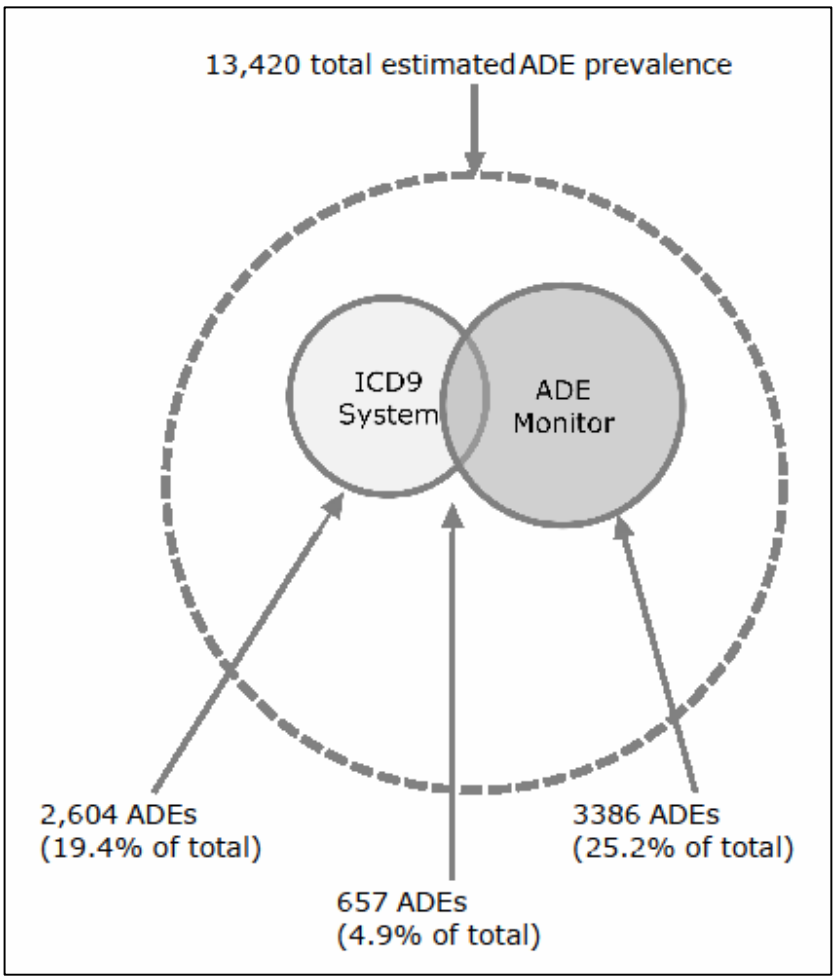

Fig. 1 Prevalence of ADEs estimated by the Capture Recapture method

Table 1 Summary of the 446 "E" and "N" ICD9 codes used to create ICD9 system alerts

ICD9 Class	ICD9 Codes	Description	Example
AN: Adverse Effect "N" Codes	909, 244.2, 292, 668, 692-693, 760, 763, 779	No single description	292: Drug Psychosis
PN: Poisoning "N" Codes	960-979	Poisoning by drugs, medicinal and biological substances	960.0: Poisoning by penicillins
PE: Poisoning "E" Codes	E850-E858	Accidental poisoning by drugs, medicinal and biological substances	E850.3: Accidental poisoning by salicylates
AE: Adverse Effect "E" Codes	E930-E949	Drugs, medicinal and biological substances causing adverse effects in therapeutic use	E931.0: Sulfonamides causing adverse effect in therapeutic use

Table 2 Frequency of alerts and estimated ADEs in the ICD9 system and ADE monitor

ADE System	Frequency of ADE Alerts	Frequency of Hospital-Acquired ADEs
ICD9	11,977	2,604
ADE Monitor	40,025	3,386

Table 3 Four categories and examples used in the comparison between the ICD9 system and ADE monitor common patient records

Category	ICD9 System		ADE Monitor	
	ICD9 Code	Description of ADE Code	ICD9 Code	Description of ADE Code
1. Complete Match	E935.2	Other opiates and related narcotics causing adverse effect in therapeutic use	Meperidine 300 MG/30 CC Syringe	Meperidine is an opiate; Drug name matches completely with the ICD9 code
2. Partial Match	E935.8	Other specified analgesics and antipyretics causing adverse effect in therapeutic use	Morphine	Morphine is an opiate, so the ideal code should be E935.2; Drug name matches correctly to the first 3 digits of the ICD9 code
3. Drug Not Specified	E947.9	Unspecified drug or medicinal substance causing adverse effect in therapeutic use	Morphine	Morphine is an opiate; ICD9 does not indicate any drug name
4. No Match	E934.2	Anticoagulants causing adverse effect in therapeutic use	Amoxicillin	Amoxicillin is an anti-infective, not anticoagulant; ICD9 indicates a completely different drug class

Table 4 Matching results between the ICD9 system and the ADE monitor databases.

Category	Number of Records	Percentage of 342 Total Records	Summary Percentages
Complete Match	177	51.8%	62.0% Matched
Partial Match	35	10.2%	
No Match	110	29.8%	38.0% Unmatched
Drug Not Specified	20	5.9%	

Table 5 Benefits and limitations of the ICD9 system and ADE monitor detection methods

Surveillance Method	Benefits	Limitations
ICD9 System	1 Physician documentation is coded from the medical record with little additional cost 2 Can be used for statewide ADE surveillance for hospital and community-acquired ADEs 3 Can be used to confirm suspected ADEs by focusing review of unstructured physician text to look for symptoms representative of ADEs such as mental status changes caused by analgesics	1 Information obtained from the codes is limited to the drug class involved and can be non-specific 2 Without being enhanced by real-time natural language processing, codes are generated after a patient leaves the hospital 3 Misses ADEs detected through patterns of lab value results
ADE Monitor	1 ADEs can be validated by a clinician at or near the time of occurrence to prevent and limit the harmful impact of ADEs 2 Computerized alerts often give an indication of the potential ADE prior or during it actually occurring 3 Most of the rules can be applied with an event monitor linked to a lab and pharmacy information system	1 An information system that includes laboratory and pharmacy data is needed 2 There can be a significant cost of technology, personnel and commitment from a clinician 3 Does not capture serious outpatient and symptom-based ADEs

References

1. Jha AK 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: 305-314.
2. Cullen DJ et al. The incident reporting system does not detect adverse drug events: a problem for quality improvement. Jt Comm J Qual Improv 1995; 21: 541-548.
3. Classen DC et al. Computerized surveillance of adverse drug events in hospital patients. JAMA 1991; 266: 2847-2851.
4. Hougland P et al. Performance of International Classification Of Diseases, 9th Revision, Clinical Modification codes as an adverse drug event surveillance system. Med Care 2006; 44: 629-636.
5. Bates DW et al. Detecting adverse events using information technology. J Am Med Inform Assoc 2003; 10: 115-128.
6. AHRQ. Reducing and Preventing Adverse Drug Events to Decrease Hospital Costs. Research in Action, Issue 1 2001; AHRQ Publication Number 01-0020.
7. http://imi.europa.eu/documents_en.html
8. http://omop.fnih.org/node/22
9. http://ftp.cdc.gov/pub/Health_Statistics/NCHS/Publications/ICD9 -CM/2001/Guide02.RTF. ICD9 Coding Guidelines (FY02), 2002.
10. ICD9 Coding Handbook. In: Brown F, ed: American Hospital Association 2002: 400.
11. McCarthy EP et al. Does clinical evidence support ICD9 diagnosis coding of complications? Med Care 2000; 38: 868-876.
12. Committee UHD. Adverse Events Related to Medical Care, Utah: 1995-99. Salt Lake City: Utah Department of Health, 2001.
13. Gardner RM, Pryor TA, Warner HR. The HELP hospital information system: update 1998. Int J Med Inf 1999; 54: 169-182.
14. The ICD9 Classification of Adverse Events, Version 2002. Salt Lake City, UT: The Utah/Missouri Patient Safety Project National Expert Panel, 2002.
15. 3M Codefinder Software. Vol. 2003: 3M Health Information Systems, 2003.
16. Pryor TA et al. The HELP system. J Med Syst 1983; 7: 87-102.
17. Haug PJ et al. Decision support in medicine: examples from the HELP system. Comput Biomed Res 1994; 27: 396-418.
18. Kuperman GJ, Gardner RM, Pryor TA. HELP: A Dynamic Hospital Information System. In: Orthner HF, ed. Computers and Medicine: Springer-Verlag, 1990.
19. Evans RS et al. Development of a computerized adverse drug event monitor. Proc Annu Symp Comput Appl Med Care 1991: 23-27.
20. Classen DC et al. Description of a computerized adverse drug event monitor using a hospital information system. Hosp Pharm 1992; 27: 774, 776-9, 783.
21. Evans RS et al. Prevention of adverse drug events through computerized surveillance. Proc Annu Symp Comput Appl Med Care 1992: 437-441.
22. Naranjo CA, Lanctot KL. Recent developments in computer-assisted diagnosis of putative adverse drug reactions. Drug Saf 1991; 6: 315-322.
23. Classen DC et al. Adverse drug events in hospitalized patients. Excess length of stay, extra costs, and attributable mortality. JAMA 1997; 277: 301-306.
24. Evans RS et al. Using a hospital information system to assess the effects of adverse drug events. Proc Annu Symp Comput Appl Med Care 1993: 161-165.
25. Evans RS et al. Preventing adverse drug events in hospitalized patients. Ann Pharmacother 1994; 28: 523-527.
26. Petratos GN. Masters Thesis Published by the University of Utah, 2003.
27. Martyn CN. Capture-recapture methods in surveys of diseases of the nervous system. J Neurol Neurosurg Psychiatry 1998; 64: 2-3.
28. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA 1998; 279: 1200-1205.
29. Hafner JW Jr et al. Adverse drug events in emergency department patients. Ann Emerg Med 2002; 39: 258-267.
30. Rothschild JM et al. Analysis of medication-related malpractice claims: causes, preventability, and costs. Arch Intern Med 2002; 162: 2414-2420.
31. Friedman C et al. Natural language processing in an operational clinical information system. Nat Lang Eng 1995; 1: 83-108.
32. Jha AK et al. Identifying hospital admissions due to adverse drug events using a computer-based monitor. Pharmacoepidemiol Drug Saf 2001; 10: 113-119.

33. Phansalkar S et al. Use of verbal protocol analysis for identification of ADE signals. AMIA Annu Symp Proc 2006: 1063.
34. Phansalkar S et al. Understanding pharmacist decision making for adverse drug event (ADE) detection. J Eval Clin Pract 2009; 15: 266-275.