June 2011

Adverse event reports : their role in detecting and preventing drug-drug interactions

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ADVERSE EVENT REPORTS: THEIR ROLE IN DETECTING AND PREVENTING DRUG-DRUG INTERACTIONS

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Presented to the Department of Medical Informatics and Clinical Epidemiology

and the Oregon Health and Science University School of Medicine

in partial fulfillment of the requirements for the degree of

Master of Biomedical Informatics

June 2011

School of Medicine

Oregon Health & Science University

CERTIFICATE OF APPROVAL

This is to certify that the Master's Capstone Project of

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"ADVERSE EVENT REPORTS: THEIR ROLE IN DETECTING AND PREVENTING DRUG-DRUG INTERACTIONS"

Has been approved

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Acknowledgements

I would like to recognize the guidance, wisdom and patience of my advisor, Dr. Judith Logan throughout her supervision and contributions to this project. I would also like to acknowledge Drs. Holly Jimison and Paul Gorman for their constructive comments on an early draft of the survey instrument and Dr. Howard Shiffman for pilot testing the survey instrument and providing valuable feedback. The faculty members of the Department of Medical Informatics and Clinical Epidemiology have helped to foster my interest in contributing to the informatics field.

Abstract

The FDA has received millions of reports of adverse events over the last ten years. Clinician ability to identify potential drug-drug interactions in routine practice, even when aided by decision support software, is limited. To date, the literature does not report any attempts to use FDA Adverse Event Reporting System (AERS) data in clinical decision support systems. Data availability of data elements for patient and administrative information, drug information, and diagnoses, reaction and outcomes, varies widely. The research question in this preliminary project is to determine if the data elements found in the FDA adverse event case reports were used and displayed by drug-drug interaction software, would that display be useful to clinicians in making prescribing or other therapeutic decisions?

We surveyed physicians thought to use drug-drug interaction software in routine clinical practice. Survey questions were constructed to confirm use and frequency of use of drug-drug interaction software and determine the relative importance to the respondents of access to a specific data element within a data category (e.g. administrative data, drug information, diagnoses). The survey instrument also attempted to elicit ways that adverse event report data elements could be presented, other than as a list of relevant case reports, to help clinicians in detecting or preventing adverse events. Clinicians feel that there are several FDA AERS data elements that would be important in the detection and prevention of drug-drug interactions. Unfortunately, we saw that for some of these elements, data availability is lacking. The most useful display of adverse event report data would enable quick access to concise sorted summaries of the relevant AERS

reports, though constrained by availability of data elements. We suggest that a future study include a sample illustration of how AERS reports may be presented to clinicians in a concise manner as this preliminary study indicated that clinicians do not have a strong affinity for viewing detailed AERS reports.

Introduction

Adverse events are a significant problem for healthcare as evidenced by the steady increase in adverse event reports to the Food and Drug Administration over the last 10 years, now aggregating several million case reports.[1] The Agency for Healthcare Research and Quality, in 2001, suggested that over 770,000 people are impacted by adverse drug events in hospital settings each year.[2] Estimates of the annual cost associated with adverse drug events are substantial, on the order of $177 billion in the United States[3]. While many people are impacted by adverse drug events, clinicians' ability to identify potential drug-drug interactions in routine practice, even when aided by decision support software, is limited[4,5]. This project assumes that the drug-drug interaction software that is being used to evaluate a clinical case could search the AERS database for reports with events or drug combinations similar to that case. The research question in this exploratory project is to determine which, if any, of the data elements found in an adverse event report, if used and displayed by drug-drug interaction software, would be useful to clinicians in making prescribing or other therapeutic decisions?

Background

Clinical decision support systems that attempt to identify potential drug-drug interactions (DDIs) are limited in the source of substantiating data[6,7]. Sources of information consist of results from the original clinical trials, packaging inserts, reports in the biomedical literature, and on occasion advisories from the FDA. Parameters used by DDI software may include but are not limited to an

interaction's severity level (e.g. major, moderate or minor), the quality of studies or documentation supporting the interaction, and speed of onset. For those interactions that have supporting evidence in the biomedical literature, the evidence reported is commonly limited to one or possibly a few case reports.

The FDA's Adverse Event Reporting System (AERS) and the World Health Organization's Vigibase systems each contain millions of adverse event reports.[1,8] The FDA AERS data is available to the public from the FDA website. This project will attempt to leverage the data elements of the experiential databases of the FDA and the WHO in order to suggest relevant content for decision support software and drug information systems. Drug-drug interactions are common, complex, and frequently result in disastrous outcomes, and thus require decision support systems. However, there can be clinical dissatisfaction with the alerts generated by DDI software as they often do not provide sufficient supporting evidence to the alerts generated[6].

Some clinical decision support systems include functionality to identify possible drug-drug interactions. To illustrate the different displays available to a user consider an interaction between a macrolide antibiotic such as ciprofloxacin and a QT prolonging drug such as an antifungal. Appendix 1[9] illustrates how Lexi-Comp, a clinical decision support system, has displayed interaction information for this drug combination to the end user. This system, typical of drug-drug interaction software, provides a risk rating, severity classification and reliability rating all according to the software manufacturers rating scales. The system also displays a short monograph and literature references.

In contrast to clinical decision support systems, spontaneous reporting systems, such as the FDA's Adverse Event Reporting System, contain case-specific information including detailed demographic, drug, reaction, outcome, therapy and indication for use data (Appendix 2[10]). The challenge here is to identify which, if any, adverse event reporting system data elements might be useful to clinicians that are already using a drug information or clinical decision support system. In this preliminary project we propose what may be a novel approach to enhancing the quantum of data points available to clinical decision support systems. This project will propose an enhancement to the typical supporting evidence by suggesting data elements to be used when referencing relevant cases from spontaneous reporting systems such as the FDA's adverse event reporting system.

Examples can be found in the literature of how FDA AERS data has been used. A PubMed search for all years up to 2011 conducted on April 28, 2011 using the keyword search "Adverse Event Reporting System" or "AERS" identified 475 articles. Review of the abstracts to these articles suggested that 46 of the studies used FDA AERS data to identify the frequency of specific drug-event combinations. Examples of this use of the FDA data for drug-event combinations were studies for itraconazole and congestive heart failure[11], natalizumab and liver injury[12], and telithromycin and hepatoxicity[13] To identify studies about drug-drug interactions, the abstracts were then searched using the keywords "interaction" or "concomitant". Only twelve abstracts indicated the use of FDA AERS data to identify the frequency of specific drug-drug-event combinations (i.e. interactions). Examples of these articles were studies on simvastatin, CYP3A4 inhibitors and rhabdomyolysis[14] and on topiramate, valproic acid and hypothermia.[15] Of the 475

abstracts reviewed, none made mention of using FDA adverse event report data in clinical decision support systems. Several articles examined the utility of the FDA data however.[16,17] Harpaz et al[18] suggested a method in which natural language processing could be used to identify multi-drug-event combinations within the FDA data.

In order to obtain a benchmark for completeness of FDA data, publicly available data files for the 2009 calendar year were accessed on the FDA website.[19] A total of 491,699 adverse event reports were filed for 2009, summarized in Table 1. The data summary is divided into patient or administrative information, drug information, reaction, outcome and diagnoses data elements. Twenty-one data elements were reported; overall availability of those data elements was 54%. Table 1 illustrates that availability of specific data elements varied widely from 1% to 100%.

There is a wide range of completion for patient or administrative data elements (9% to 100%). As may be expected, 100% of adverse event reports included the date that the FDA received the report, of which 93% of reports included the date the manufacturer received the report in question (the reminder were submitted to the FDA by non-manufacturers). Only 68% of reports included the date the adverse event occurred or began. The patient's age, gender and weight, were recorded in only 47%, 91% and 31% of reports respectively. The occupation of the reporter of the adverse event was noted in 85% of cases. While the date the patient died was only recorded in 9% of all reports, this is misleading. Since 13.5% of adverse event reports specified death as the patient outcome, the implication is that the date of

Table 1 – 2009 Data Summary

Patient or Administrative Data	Data Element	Total Count	Missing Count	Available	Missing (%)	Availability (%)
Date the adverse event occurred or began	EVENT_DT	491,699	156,898	334,801	32%	68%
Date the drug manufacturer first received an initial or follow-up report	MFR_DT	491,699	34,227	457,472	7%	93%
Date the FDA received the report	FDA_DT	491,699	0	491,699	0%	100%
The patient's age at the time of the event	AGE, AGE_COD	491,699	262,615	229,084	53%	47%
The patient's gender	GNDR_COD	491,699	41,918	449,781	9%	91%
The patient's weight	WT, WT_COD	491,699	339,108	152,591	69%	31%
The occupation of the reporter of the adverse event	OCCP_COD	491,699	74,841	416,858	15%	85%
The date the patient died	DEATH_DT	491,699	449,101	42,598	91%	9%
Drug Information Data						
Whether the drug was reported to be the primary cause of the event, a cause of the event but not the primary cause, a concomitant or an interacting drug	ROLE_COD	1,925,345	0	1,925,345	0%	100%
The name of the medicinal product	DRUGNAME	1,925,345	648	1,924,697	0%	100%
The route of drug administration	ROUTE	1,925,345	949,589	975,756	49%	51%
Whether the reaction was reduced in degree or intensity when drug therapy was stopped	DECHAL	1,925,345	1,802,633	122,712	94%	6%
Whether the reaction recurred when drug therapy was restarted	RECHAL	1,925,345	1,806,504	118,841	94%	6%
The lot number of the drug	LOT_NUM	1,925,345	1,700,348	224,997	88%	12%
The expiration date of the drug	EXP_DT	1,925,345	1,911,732	13,613	99%	1%
The date therapy was started (or re-started) for the drug	START_DT	798,821	53,708	745,113	7%	93%
The date therapy was stopped for the drug	END_DT	798,821	393,434	405,387	49%	51%
The duration of the therapy for the drug	DUR, DUR_COD	798,821	625,299	173,522	78%	22%
Reaction/Outcome/Diagnoses Data						
Description of the reaction or event using medical terminology	PT	1,758,876	0	1,758,876	0%	100%
Patient's outcome	OUTC_COD	491,699	18,247	473,452	4%	96%
Patient diagnoses using medical terminology	INDI_PT	962,210	0	962,210	0%	100%

death was recorded in 9%/13.5% or 67% of reports that had death as the patient outcome.

There is also a wide range of completion for drug information data elements (1% to 100%). A single adverse event report may include multiple drug records, one for each drug reported in the subject ADR. The 491,699 reports in 2009 included 1,925,345 drug records. The name of the medicinal product was recorded in 100% of the drug records supporting an adverse drug reaction. The role of the drug (whether the drug was reported to be the primary cause of the event, a cause of the event but not the primary cause, a concomitant or an interacting drug) was recorded in 100% of the drug records (primary suspect – 26%, secondary suspect – 19%, concomitant – 55%, interacting – 0%). The route of drug administration was recorded in 51% of the drug records. The date that therapy was started (or restarted) for a specific drug was noted in 93% of drug records. The date that therapy was stopped was recorded in 51% of drug records. Dechallenge (whether the reaction was reduced in degree or intensity when drug therapy was stopped) and rechallenge (whether the reaction recurred when drug therapy was restarted) were each recorded in 6% of the drug records with the majority of those being "does not apply". The duration of drug therapy was recorded in 22% of the records. Lot number and expiration date were recorded in 12% and 1% of drug records respectively.

A description of the reaction or event as well as patient diagnoses using medical terminology were recorded for 100% of the adverse event reports. Patient outcomes were reported for 96% of the adverse event reports (death – 13%, life-threatening – 5%, hospitalization – initial or prolonged – 33%, disability – 3%, congenital anomaly – 1%, other - 40%, required intervention to prevent permanent impairment/damage – 1%).

In the current project we conducted a small survey of physician clinicians in order to determine whether, if drug-drug interaction software could display select AERS data elements, that display would be of use in clinical decision-making. As human subjects were involved, Oregon Health and Science University Institutional Review Board approval was first obtained.

Methods

In order to determine whether display of AERS data elements by drug-drug interaction software would be useful to clinician decision-making, a survey method was chosen. Participants were recruited via a recruitment email (Appendix 3). The goal was to recruit at least 5 and up to 10 study subjects. Sampling was to be augmented as necessary to recruit additional participants by asking for referrals from existing participants. Participants were clinicians thought to use drug-drug interaction software in routine practice and were known to the investigator. Recruitment emails were sent to 9 prospective respondents during April 2011. The survey was designed to take approximately 10-15 minutes for each participant to complete.

Prior to creation of the survey instrument, the data elements captured by the FDA and WHO systems were reviewed. Data elements common to the two systems formed the basis for the survey questions. An initial draft of the survey instrument was provided to two experts in survey design for critique. The initial survey used a five point Likert scale. Though the center item is usually neutral, the initial survey would have biased the results to saying things are important, since the middle item response was initially "important". As recommended by one of the experts, the survey was amended to incorporate a four point Likert scale. With a four point scale, and without a natural neutral point, respondents were forced to make a choice. Even with the four point scale, the survey instrument was subject to central tendency bias and social desirability bias. Central tendency bias would result in responses closer to the middle of the scale ("somewhat important" or "very important") as opposed to responses at the ends of the scale ("not important" or "essential"). Social desirability bias may result in respondents replying in such a way that their answers may be viewed as favourable. The other main expert recommendation was to conduct a pilot test with individuals similar to the intended respondents to ensure that respondent interpretation of the survey questions was as intended. Accordingly, the investigator met with a family physician and pilot-tested the survey instrument. Trialing the survey elicited some useful comments and resulted in three changes to question wording (Appendix 4).

The survey instrument provided some brief background to the topic followed by a use case for respondents to consider. The scenario presented was constructed to resonate with the respondents since they were believed to currently use drug-drug interaction software in routine clinical practice, Figure 1.

Figure 1 – Survey Scenario

Dr. Smith is refilling a prescription for a calcium channel blocker, amlodipine, for Mr. Jones. Mr. Jones is also taking an antifungal, fluconazole, and has had some problems with hypotension. Dr. Smith wants to see if there are reports of an interaction of those two drugs that might cause this symptom. He asks his provider order entry software to check for FDA reports on an interaction between these drugs. The system shows a list of relevant case reports (the most recent 20 of 526 related reports), with the ability to look at others, if desired. Dr. Smith sees that there are a number of other cases with a similar case history to the one he is concerned about, and chooses, therefore, to change the drug prescribed.

The first two survey questions confirmed use and frequency of use of drug-drug interaction software, Figure 2.

Figure 2 – Use and Frequency of DDI Software

1. **Do you use drug-drug interaction software to detect drug-drug interactions in your routine practice? This would include use of a Clinical Decision Support system embedded in an Electronic Health Record or a drug information system.**

   ○ Yes ○ No

2. **If yes, which phrase below best describes how frequently you use that software to detect drug-drug interactions, on average?**

   ○ Once per month ○ Once per week ○ Once per day ○ More than once per day

The next five survey questions were constructed to determine the relative importance to the respondents of access to a specific data element within a data category (e.g. administrative data, drug information, diagnoses), Figure 3. All had the same response scales: Not important, Somewhat important , Very important or Essential.

Figure 3 – Importance of Specific Data Elements

3. **When viewing AERs, how important would it be for you to have access to each of the following types of patient demographic and administrative information?**

Date the adverse event occurred or began
Date the drug manufacturer first received an initial or follow-up report
Date the FDA or WHO received the report
The patient's age at the time of the event
The patient's gender
The patient's weight
The occupation of the reporter of the adverse event (e.g. physician, pharmacist, etc.)
The date the patient died

4. **When viewing AERs, how important would it be for you to have access to each of the following types of drug information for each involved drug?**

Whether the drug was reported to be the primary cause of the event, a cause of the event but not the primary cause, a concomitant or an interacting drug
The name of the medicinal product
The route of drug administration
Whether the reaction was reduced in degree or intensity when drug therapy was stopped
Whether the reaction recurred when drug therapy was restarted
The lot number of the drug
The expiration date of the drug
The date therapy was started (or re-started) for the drug
The date therapy was stopped for the drug
The duration of the therapy for the drug

5. **When viewing AERs, how important would it be for you to have access to a description of the reaction or event using medical terminology (e.g. cardiac arrhythmia)?**

6. **When viewing AERs, how important would it be for you to have access to the patient's outcome?**

7. **When viewing AERs, how important would it be for you to have access to the patient's diagnoses using medical terminology?**

The final question was a free text question intended to elicit ways that adverse event report data elements could be presented, other than as a list of relevant case reports, to help clinicians in detecting or preventing adverse events, Figure 4.

Figure 4 – Alternative Ways AERS Data Elements Could Be Presented

8. **Are there some ways (other than a list of relevant case reports) that the AER data may be presented that might help you in detecting or preventing drug-drug interactions?**

Survey data was collected via an Internet-based collection tool, SurveyMonkey (surveymonkey.com, Palo Alto, United States). Personal information such as name, address, etc. was not collected during the survey. The survey collection tool was set not to retain IP addresses. The survey results were analyzed using descriptive statistics to determine points of central tendency. Given the limited data set, variability and correlation were not analyzed. Spreadsheets and the built-in graphics capability of the collection tool were used to assess the importance of access to the data elements as reported by the survey participants. Tabulated results were then compared to the data available in the FDA's Adverse Event Reporting System (AERS) so that the viability of displaying specific FDA AERS data elements could be assessed.

Results

The recruitment email was sent to nine clinicians. Each of the prospective respondents were physicians known to the investigators and thought to use drug-drug interaction software in routine clinical practice. Seven participants completed the on-line survey. One response was excluded from the data analysis as that respondent indicated that drug-drug interaction software was not used in routine practice. One respondent indicated use of drug-drug interaction software once per

month, one indicated use once per week and four indicated use more than once per day. Detailed survey results are in Appendix 5.

The importance of each data element to the survey respondents in detecting or preventing adverse events was calculated by averaging the responses to each question. The average importance for each element, weighted by the rating per four point scale (1 – not important, 2 – somewhat important, 3 – very important, 4 – essential) is detailed in Table 2 and shows the percentage of AERS reports which contained that element.

Of the patient or administrative data elements, no elements had a weighted importance of "very important" or 3.0 on the scale of 1-4. The most highly rated patient or administrative data elements were the patient's age at the time of the event (2.67), the patient's gender (2.33) and the occupation of the reporter of the event (2.17). While patient age and gender were both weighted between "somewhat important" and "very important" (between 2.0 and 3.0 on the 4 point scale), patient age data was available in the FDA AERS (for 2009) in slightly less than half (47%) and patient gender was available in almost all (91%) of the 2009 FDA AERS reports. Patient weight was thought to be slightly less than "somewhat important" (1.83) and was available in 31% of the FDA reports. The lowest rated patient or administrative data elements were each ranked between "not important" and "somewhat important" (between 1.0 and 2.0 on the 4 point scale) and had variable data availability as follows: the date the manufacturer first received an initial or follow-up report (1.33, 93%), the date the patient died (1.33, 9%) and the date the FDA received the report (1.67, 100%).

Table 2 – Data Element Importance

Patient or Administrative Data	Data Element	Availability	Importance
Date the adverse event occurred or began	EVENT_DT	68%	**2.00**
Date the drug manufacturer first received an initial or follow-up report	MFR_DT	93%	**1.33**
Date the FDA received the report	FDA_DT	100%	**1.67**
The patient's age at the time of the event	AGE, AGE_COD	47%	**2.67**
The patient's gender	GNDR_COD	91%	**2.33**
The patient's weight	WT, WT_COD	31%	**1.83**
The occupation of the reporter of the adverse event	OCCP_COD	85%	**2.17**
The date the patient died	DEATH_DT	9%	**1.33**
Drug Information Data			
Whether the drug was reported to be the primary cause of the event, a cause of the event but not the primary cause, a concomitant or an interacting drug	ROLE_COD	100%	**3.17**
The name of the medicinal product	DRUGNAME	100%	**3.50**
The route of drug administration	ROUTE	51%	**3.17**
Whether the reaction was reduced in degree or intensity when drug therapy was stopped	DECHAL	6%	**3.00**
Whether the reaction recurred when drug therapy was restarted	RECHAL	6%	**3.17**
The lot number of the drug	LOT_NUM	12%	**2.33**
The expiration date of the drug	EXP_DT	1%	**2.33**
The date therapy was started (or re-started) for the drug	START_DT	93%	**2.17**
The date therapy was stopped for the drug	END_DT	51%	**2.17**
The duration of the therapy for the drug	DUR, DUR_COD	22%	**2.83**
Reaction/Outcome/Diagnoses Data			
Description of the reaction or event using medical terminology	PT	100%	**3.33**
Patient's outcome	OUTC_COD	96%	**3.67**
Patient's diagnoses using medical terminology	INDI_PT	100%	**3.50**

Of the drug information data elements, several elements reached a weighted importance of between "very important" or 3.0 and "essential" or 4.0 on the scale of 1-4. The most highly rated drug information data elements were the name of the medicinal product (3.50), the route of drug administration (3.17), whether the reaction recurred when drug therapy was restarted (3.17), whether the drug was reported to be the primary cause of the event, a cause of the event but not the primary cause, a concomitant or interacting drug (3.17), whether the reaction was reduced in degree or intensity when drug therapy was stopped (3.0). Data for the

name and role of the drug were available in 100% of reports. The route of drug administration was available in just over one half, 51%, of reports. While dechallenge and rechallenge responses were thought to be "somewhat important", or slightly higher in the case of rechallenge, these data elements were only available in 6% of reports. The lowest rated drug information data elements were each ranked between "somewhat important" and "very important" (between 2.0 and 3.0 on the 4 point scale) and had variable data availability as follows: the duration of the therapy for the drug (2.83, 22%), the lot number of the drug (2.33, 12%), the expiration date of the drug (2.33, 1%), the date therapy was started (or re-started) for the drug (2.17, 93%) and the date therapy was stopped for the drug (2.17, 51%).

The reaction, outcome, and diagnoses data elements, had weighted ratings of 3.33, 3.67 and 3.50 respectively, placing those elements between "somewhat important" and "essential" in importance. The reaction, outcome, and diagnoses data elements had availability of 100%, 96%, and 100% respectively.

Responses to the free text question intended to elicit comment as to ways in which adverse event report data elements could be presented to help clinicians in detecting or preventing adverse events are per Table 3.

Discussion

Although the survey sample was limited, this preliminary study is instructive in several ways. As we saw in the data, clinicians feel that there are several FDA AERS

Table 3 – Free Text Responses

Respondent	**Response**
Respondent 1	Summaries of published studies based on administrative or other drug data that assessed possible drug-drug interactions with references for the study.
Respondent 2	Alerts that that show up when both drugs are prescribed.
Respondent 3	If not already being done place the list of adverse reactions in order of prevalence not alphabetical order.
Respondent 4	Summary data, preferably from an expert, from all the appropriate AER reports would be most helpful, with an option or link to the actual report. Maybe something with the tone, brevity and direct style of say The Medical Letter. As an ER doctor, I may not have time to read individual reports in detail in many cases but would like to retain the option if needed.
Respondent 5	Having a medication reconciliation process so that the patient's medication list is current to compare against for any drug-drug interactions on new potential medications.
Respondent 6	I think the most useful way drug-drug interaction function in EHR is to clinicians is that it alerts physicians to potential interactions and the degree of severity/serious of the interaction. i think currently software that then gives clinician option to click on the potential action and obtain more detailed information about the nature of the interaction to be able to make a clinical decision whether the potential interaction is relevant in the particular situation he/she faces. beyond that, i think having much more information would be excessive as clinicians are often using this functionality on the go or in situations when they do not have too much time to review large amounts of data. thus data best kept succinct and to the point

data elements that would be important in the detection and prevention of drug-drug interactions. Unfortunately, we saw that for some of these data elements, data

availability is lacking. There is a belief that the most useful display of adverse event report data would enable quick access to concise sorted summaries of the relevant AERS reports. Brevity of the information displayed is thought to be key as clinicians do not have a lot of time to search through volumes of data and narrative.

A lot may be learned from the responses to the free text question which was intended to elicit ways adverse event report data elements could be presented to help clinicians in detecting or preventing adverse events. A common theme is that clinicians would prefer to see a concise sorted presentation that is summarized by frequency, and that would allow clinicians to link to additional detail whether in the form of an individual case report or literature references, while highlighting the impact of newly administered drugs. However, not all respondents actually understood the intent of the question. Some respondents were either thinking of the base functionality provided by existing drug-drug interaction software or desired to integrate medication reconciliation to drug-drug interaction software. Overall, the main sentiment expressed was that the information should be summarized and sorted for conciseness and ease of access.

Given the variability of data completion for the AERS data elements noted above, a proposed presentation format for AERS reports is accordingly constrained. While patient age and gender, and drug role and route of administration are relatively available, dechallenge and rechallenge data are not. Using the scenario presented in the preamble to the survey - concomitant administration of amlodipine and

fluconazole with the symptom of hypotension - a sample illustration for presentation could be as in Figure 5.

Figure 5 – Sample Presentation of AERS Data

Input by Clinician

Drugs - Amlodipine, Fluconazole, … Drug N

Diagnosis – Hypotension (clinician may input Diagnosis or Reaction)

Output to Clinician

AERS report numbers/percentages (sorting Reactions by frequency of reaction)

Reaction	Outcome
QTc prolongation 255/70% (avg. age – 34, male – 48%, primary suspect – fluconazole – 76%)	Death – 15/5%, Hospitalization – 240/95%, Disability – 0/0%
Torsade de pointes 33/10% (avg. age – 32, male – 45%, primary suspect – fluconazole - 85%)	Death – 9/28%, Hospitalization – 24/72%, Disability – 0/0%
…	
Diagnosis N #/% (avg. age – xx, male – xx%)	Death – #/xx%, Hospitalization – #/%, Disability – #/xx%
Total 360/100% (avg. age – 33, male – 47%, primary suspect – fluconazole – 81%)	Death – 24/6%, Hospitalization – 270/75%, Disability – 0/%

The study had several limitations. With only seven responses, we did not have a sufficient sample for statistical significance and did not compute measures of variability beyond that of the mean importance of data elements. That said, this preliminary study was intended to garner only a feel for clinician assessment of the importance of data elements, as opposed to statistical significance. Increasing the sample size may not have necessarily resulted in better information. We also limited the study respondents to physician clinicians as opposed to surveying other relevant disciplines such as pharmacists or nurses which might have yielded a variety of perspectives. We did not refer to other years of FDA AERS data and

assumed that the 2009 reports were sufficient on which to base a measure of data completeness. The survey instrument itself was subject to central tendency bias and social desirability bias.

We feel that with the current study, although not definitive in nature, we gained enough insights to proceed to future work. However, given the results of the free text question, it would seem that not all respondents were aligned with the investigators' line of query. Further work should demonstrate how AERS reports should be presented. A subsequent study may also need to survey additional clinicians and could include a qualitative interview. We suggest that a future study include a sample illustration of how AERS reports may be presented to clinicians in a concise manner as this preliminary study indicated that clinicians do not have a strong affinity for viewing detailed AERS reports.

Conclusion

This preliminary study suggests, if drug-drug interaction software could display the data elements found in an FDA adverse event report, that clinicians would prefer a concise, sorted summary of relevant adverse event reports to detect or prevent adverse events. A presentation using adverse event report data is constrained by the availability of data for specific data elements. Future study should examine how AERS reports should be presented.

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APPENDIX 1 – Sample DDI Software Display

Lexi-Comp ONLINE™ Interaction Analysis

Customize Analysis

View interaction detail by clicking on link.

Ciprofloxacin (Ciprofloxacin) [C] Fluconazole (QTc-Prolonging Agents)

Fluconazole (Fluconazole) [C] Ciprofloxacin (Ciprofloxacin)

Date November 16, 2010

Displaying interactions with a risk rating of Rist Filter A, B, C, D and X

Disclaimer Readers are advised that decisions regarding drug therapy must be based on the independent judgment of the clinician, changing information about a drug (eg, as reflected in the literature and manufacturer's most current product information), and changing medical practices.

Lexi-Comp ONLINE™ Interaction Monograph

Title **QTc-Prolonging Agents / Ciprofloxacin**

Risk Rating C: Monitor therapy

Summary Ciprofloxacin may enhance the QTc-prolonging effect of QTc-Prolonging Agents. **Severity** Major **Reliability Rating** Fair

Patient Management If ciprofloxacin is used in combination with other drugs known to affect the QT interval, or in patients in which other risk factors for ventricular arrythmias (such as congenital long QT syndrome, hypokalemia) are present, exercise caution and monitor patient. However, based on the rare reports of QTc prolongation/TdP relative to an extensive usage history, the likelihood of clinically-significant events for the vast majority of patients seems low.

QTc-Prolonging Agents Interacting Members Amiodarone; Amitriptyline; Amoxapine; Apomorphine; Arsenic Trioxide; Artemether; Asenapine; Azithromycin; Azithromycin (Systemic); Bepridil [Off Market]; ChlorproMAZINE; Cisapride; Citalopram; Clarithromycin; ClomiPRAMINE; Dasatinib; Degarelix; Desipramine; Disopyramide; Dofetilide; Dolasetron; Domperidone; Doxepin; Doxepin (Systemic); Doxepin (Topical); Dronedarone; Droperidol; Erythromycin; Erythromycin (Systemic); Escitalopram; Flecainide; Fluconazole; FLUoxetine; Flupenthixol; Foscarnet; Gadofosveset; Halofantrine; Haloperidol; Ibutilide; Iloperidone; Imipramine; Indapamide; Isradipine; Lapatinib; Levofloxacin; Levofloxacin (Systemic); Loxapine; Lumefantrine; Maprotiline; Mefloquine; Mesoridazine; Methadone; Methotrimeprazine; Moxifloxacin; Moxifloxacin (Systemic); Nilotinib; Norfloxacin; Nortriptyline; Octreotide; Pazopanib; Pentamidine; Perflutren Lipid Microspheres; Pimozide; Probucol; Procainamide; Propafenone; Protriptyline; QUEtiapine; QuiNIDine; Ranolazine; Risperidone; Romidepsin; Saquinavir; Sotalol; Sparfloxacin; Sunitinib; Tacrolimus; Tacrolimus (Systemic); Telavancin; Telithromycin; Tetrabenazine; Thioridazine; Thiothixene; Toremifene; Trimipramine; Voriconazole; Vorinostat; Ziprasidone; Zuclopenthixol

Discussion Among the fluoroquinolones, ciprofloxacin is widely recognized as imparting minimal effects on the QT interval. This assessment is based on standardized *in vitro* methods (eg, Purkinje fiber and HERG channel blockade measurements) used to evaluate the effects of quinolones (and other agents) on cardiac action potentials,[1,2,3] as well as clinical experience data documenting little to no QTc prolongation with standard treatments.[4,5,6,7] Estimates for ciprofloxacin's effects on the QT interval range from no effect to minimal changes of 3-5 milliseconds in healthy adults,[5,6,7] well below the level of >30-60 milliseconds proposed (but somewhat contested) as the threshold for clinical concern within the cardiology community.[4] However, despite the strong *in vitro* and clinical evidence that ciprofloxacin is generally considered non-arrythmogenic, there are documented rare reports of torsades de pointes (TdP, estimated at 0.3 cases per 10 million prescriptions[8]) and a handful of case reports noting QTc prolongation, some progressing to TdP, temporally associated with the use of ciprofloxacin. However, a number of potentially confounding variables were evident.

Of the more recent case reports, one details a 70-year-old female treated for suspected respiratory illness who developed QTc prolongation and premature ventricular complexes after 3 days of intravenous ciprofloxacin and furosemide therapy.[9] The patient, who presented with underlying bundle branch block, borderline prolongation of QTc, and normal electrolytes, was also on several maintenance medications, including olanzapine. The QTc interval gradually returned to baseline several days after discontinuation of ciprofloxacin. The authors commented on the possibility of ciprofloxacin inhibiting CYP1A2-mediated metabolism of olanzapine as a potential explanation for this observation, although drug levels were not determined.

Another case involved a 22-year old male treated for respiratory distress.[10] On the second day of multiple antibiotic therapy, including ciprofloxacin, he developed ventricular ectopy progressing to episodes of TdP 10 and 14 hours after discontinuation of ciprofloxacin. The patient had normal potassium and magnesium levels during these events, but a previous history revealed syncopal episodes suggestive of a possible arrythmogenic propensity. An implanted defibrillator was placed due to the apparent congential nature of his QT prolongation.

Another publication noted two additional cases.[11] One involved a 67-year-old female with no previous cardiac history, who, within 12 hours of receiving ciprofloxacin for a urinary tract infection, developed two episodes of extended TdP requiring resuscitative efforts. Additional factors in this case included the initiation of both amiodarone and furosemide therapy 3 days previously, as well as hypokalemia noted on day 3. The other case involved a 44-year old female treated with ciprofloxacin for pyelonephritis. She had a history of paroxysmal atrial fibrillation managed with sotalol therapy. Hours after receiving a 1000 mg loading dose, the patient returned to the ER with syncopal spells and TdP requiring defibrillation. Baseline data prior to initiation of ciprofloxacin revealed a slightly prolonged QT interval. Again, discontinuation of ciprofloxacin (and sotalol) led to a resolution of symptoms within 2 days.

Given the background incidence of TdP and the reports discussed above, one cannot exclude the possibility that ciprofloxacin may contribute to a small increase in the risk of QTc prolongation and/or ventricular arrhythmia in certain patients, albeit to a much lesser extent than other quinolones. However, these cases also highlight the potentially confounding circumstances surrounding arrythmogenesis, namely electrolyte imbalances, concomitant therapy with known QTc-prolonging agents, and/or underlying cardiac conduction pathologies, all of which must be considered in the final causation analysis. Nevertheless, the severity of this effect may warrant caution if ciprofloxacin is used in conjunction with predisposing risk factors and/or other drugs known to prolong the QTc interval.

Footnotes

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APPENDIX 2 - FDA Case Specific Information

1) DEMOGRAPHIC file (DEMOyyQq.TXT)

NAME	DESCRIPTION
ISR	Unique number for identifying an AERS report. (See End Note 1.) This is the primary link field (primary key) between data files. (example: 3123456)
CASE	Number for identifying an AERS case. (Again, see End Note 1.) A case consists of one or more reports (ISRs). If correctly linked, a followup report will have the same CASE number as the initial report. (See End Note 2.)
I_F_COD	Code for initial or followup status of report, as reported by manufacturer. (See table below and End Note 2.)

CODE	MEANING_TEXT
I	Initial
F	Followup

FOLL_SEQ	The sequence number of a followup report, as reported by manufacturer. For initial reports, there will be no data for this field. (A small number of reports may have "bad" data for this number, such as alphabetic or special characters.) (See End Note 2.)
IMAGE	Identifier for an AERS report image. Character field consisting of the ISR number, a dash, and a check digit or letter. (ex: 3123456-X) See End Note 3.
EVENT_DT	Date adverse event occurred or began. (YYYYMMDD format)
MFR_DT	Date manufacturer first received initial (or follow-up) information. (YYYYMMDD format)
FDA_DT	Date FDA received report. (YYYYMMDD format)
REPT_COD	Code for the type of report submitted. (See table below.) Also, see End Note 4.

CODE	MEANING_TEXT
EXP	Expedited (15-Day)
PER	Periodic
DIR	Direct

MFR_NUM	Manufacturer's unique report identifier. (See Revision History, Jan - Mar 2002.)

MFR_SNDR Verbatim name of manufacturer sending report. (See End Note 5.)

AGE Numeric value of patient's age at event.

AGE_COD Unit abbreviation for patient's age. (See table below.)

CODE	MEANING_TEXT
DEC	DECADE
YR	YEAR
MON	MONTH
WK	WEEK
DY	DAY
HR	HOUR

GNDR_COD Code for patient's sex. (See table below.)

CODE	MEANING_TEXT
UNK	Unknown
M	Male
F	Female
NS	Not Specified

E_SUB Whether (Y/N) this report was submitted under the electronic submissions procedure for manufacturers.

WT Numeric value of patient's weight.

WT_COD Unit abbreviation for patient's weight. (See table below.)

CODE	MEANING_TEXT
KG	Kilograms
LBS	Pounds
GMS	Grams

REPT_DT Date report was sent. (YYYYMMDD format)

OCCP_COD Abbreviation for initial reporter's type of occupation.

CODE	MEANING_TEXT
MD	Physician
PH	Pharmacist
OT	Other health-professional
LW	Lawyer
CN	Consumer

DEATH_DT Date patient died. (YYYYMMDD format)

TO_MFR Whether or not (Y/N) voluntary reporter also notified manufacturer (blank for manufacturer reports).

CONFID Whether or not (Y/N) voluntary reporter stated that his identity should not be disclosed to the product manufacturer (blank for manufacturer reports).

REPORTER_COUNTRY Reporters are asked to give us their addresses. This
                  Is usually the country the event occurred in

2) DRUG file (DRUGyyQq.TXT)

NAME	DESCRIPTION
ISR	Number that uniquely identifies an AERS report. Primary link field between data files.
DRUG_SEQ	Unique number for identifying a drug for an ISR. To link to the THERyyQq.TXT data file, both the ISR number (primary key) and the DRUG_SEQ number (secondary key) are needed. (For an explanation of the DRUG_SEQ number, including an example, please see End Note 6.)
ROLE_COD	Code for drug's reported role in event.(See table below.)

CODE	MEANING_TEXT
PS	Primary Suspect Drug
SS	Secondary Suspect Drug
C	Concomitant
I	Interacting

DRUGNAME	Name of medicinal product. If a "Valid Trade Name" is populated for this ISR, then DRUGNAME = Valid Trade Name; if not, then DRUGNAME = "Verbatim" name, exactly as entered on the report. For the great majority of reports, there is a "Valid Trade Name." (See End Note 5.)
VAL_VBM	Code for source of DRUGNAME.(See table below.)

CODE	MEANING_TEXT
1	Validated trade name used
2	Verbatim name used

ROUTE	The route of drug administration.
DOSE_VBM	Verbatim text for dose, frequency, and route, exactly as entered on report.
DECHAL	Dechallenge code, indicating if reaction abated when drug therapy was stopped. (See table below.)

CODE	MEANING_TEXT
Y	Positive dechallenge
N	Negative dechallenge
U	Unknown
D	Does not apply

RECHAL	Rechallenge code, indicating if reaction recurred when drug therapy was restarted. (See table below.)

CODE	MEANING_TEXT
Y	Positive rechallenge
N	Negative rechallenge
U	Unknown
D	Does not apply

LOT_NUM Lot number of the drug.

EXP_DT Expiration date of the drug. (YYYYMMDD format)

NDA_NUM Verbatim NDA number, exactly as reported.

3) REACTION file (REACyyQq.TXT)

NAME	DESCRIPTION
ISR	Number that uniquely identifies an AERS report. Primary link field between data files.
PT	"Preferred Term" level medical terminology describing the event, using the Medical Dictionary for Regulatory Activities (MedDRA). The order of the terms for a given event does not imply priority. In other words, the first term listed is not necessarily considered more significant than the last one listed.

4) OUTCOME file (OUTCyyQq.TXT)

NAME	DESCRIPTION
ISR	Number that uniquely identifies an AERS report. Primary link field between data files.
OUTC_COD	Code for a patient outcome. (See table below.)

CODE	MEANING_TEXT
DE	Death
LT	Life-Threatening
HO	Hospitalization - Initial or Prolonged
DS	Disability
CA	Congenital Anomaly
RI	Required Intervention to Prevent Permanent Impairment/Damage
OT	Other

5) REPORT SOURCE file (RPSRyyQq.TXT)

NAME DESCRIPTION

NAME	DESCRIPTION
ISR	Number that uniquely identifies an AERS report. Primary link field between data files.
RPSR_COD	Code for an initial source of the report. (See table below.)

CODE	MEANING_TEXT
FGN	Foreign
SDY	Study
LIT	Literature
CSM	Consumer
HP	Health Professional
UF	User Facility
CR	Company Representative
DT	Distributor
OTH	Other

6) THERAPY dates file (THERyyQq.TXT)

NAME	DESCRIPTION
ISR	Number that uniquely identifies an AERS report. Primary link field between data files.
DRUG_SEQ	Drug sequence number for identifying a drug for an ISR. To link to the DRUGyyQq.TXT data file, both the ISR number (primary key) and the DRUG_SEQ number (secondary key) are needed. (For an explanation of the DRUG_SEQ number, including an example, see End Note 6.)
START_DT	A date therapy was started (or re-started) for this drug. (YYYYMMDD)
END_DT	A date therapy was stopped for this drug. (YYYYMMDD)
DUR	Numeric value of the duration (length) of therapy
DUR_COD	Unit abbreviation for duration of therapy (see table below)

CODE	MEANING TEXT
YR	Years
MON	Months
WK	Weeks
DAY	Days
HR	Hours
MIN	Minutes
SEC	Seconds

7) INDICATIONS for use file (INDIyyQq.TXT)

NAME	DESCRIPTION
ISR	Number that uniquely identifies an AERS report. Primary link field between data files.
DRUG_SEQ	Drug sequence number for identifying a drug for an ISR. To link to the DRUGyyQq.TXT data file, both the ISR number (primary key) and the DRUG_SEQ number (secondary key) are needed. (For an explanation of the DRUG_SEQ number, including an example, see End Note 6.)
INDI_PT	"Preferred Term" level medical terminology describing the Indication for use, using the Medical Dictionary for Regulatory Activities (MedDRA).

APPENDIX 3 – Recruitment Email

Dear Clinician,

You are invited to participate in a study on the usefulness of data from adverse event reporting systems to clinicians who are trying to detect or prevent drug-drug interactions. There are millions of adverse event reports (AERs) in the FDA and World Health Organization databases. Drug-drug interaction software, whether in the form of clinical decision support systems or drug information systems, might be able to use the data from these AERs to help you detect or prevent drug-drug interactions.

You were selected as a possible participant because you were thought to use a clinical decision support system or drug information system in order to identify potential drug-drug interactions in routine clinical practice. If you do not use a system like this, then you do not qualify for the study.

If you qualify and choose to participate, you will be asked to complete an online survey that will take 10-15 minutes of your time. You will be asked to evaluate some of the data elements found in an FDA AER. If the drug-drug interaction software could display these elements, would that display be of use to you in clinical decision-making?

As an example:

Dr. Smith is refilling a prescription for a calcium channel blocker, amlodipine, for Mr. Jones. Mr. Jones is also taking an antifungal, fluconazole, and has had some problems with hypotension. Dr. Smith wants to see if there are reports of an interaction of those two drugs that might cause this symptom. He asks his provider order entry software to check for FDA reports on an interaction between these drugs. The system shows a list of relevant case reports (the most recent 20 of 526 related reports), with the ability to look at others, if desired. Dr. Smith sees that there are a number of other cases with a similar case history to the one he is concerned about, and chooses, therefore, to change the drug prescribed.

No personally identifiable information will be collected in this survey. Although we have made every effort to protect your identity, there is a minimal risk of loss of confidentiality. You do not have to join this or any research study, but if you do take the survey, you will not be able to withdraw from the study later, since we will not have a way to identify your responses. You will not benefit from being in this study. However, by serving as a subject, you may help us learn how to benefit patients in the future. If you have any questions regarding your rights as a research subject, you may contact the OHSU Research Integrity Office at (503) 494-7887.

Study title: Adverse Event Reports: Their Role in Detecting and Preventing Drug-Drug Interactions
Principle Investigator: Judith R. Logan, MD (503) 494-5902, loganju@ohsu.edu
Co-Investigator: Harry Enchin, (416) 460-7330, henchin@sympatico.ca

Oregon Health & Science University IRB # 7330, Study approval date: 03-23-2011

If you choose to participate, please click on the link below to begin the survey:

http://www.surveymonkey.com/s/PN9QTFB

Thank you, and please don't hesitate to contact us for any questions,

Harry Enchin
Master of Biomedical Informatics student
Oregon Health & Science University
Portland, Oregon

APPENDIX 4 – Survey Instrument

ADVERSE EVENT REPORTS: THEIR ROLE IN DETECTING AND PREVENTING DRUG-DRUG INTERACTIONS

There are millions of adverse event reports (AERs) in the FDA and World Health Organization (WHO) databases. Drug-drug interaction software, whether in the form of clinical decision support systems or drug information systems, might be able to use the data from these reporting systems to help you detect or prevent drug-drug interactions.

The purpose of this survey is to determine whether or not having access to AERs might benefit clinicians, and assumes that the drug-drug interaction software that is being used to evaluate a clinical case could search an AER database for reports with events or drug combinations similar to that case. You will be asked to evaluate some of the data elements found in an FDA AER. If the drug-drug interaction software could display these elements, would that display be of use to you in clinical decision-making?

As an example:

Dr. Smith is refilling a prescription for a calcium channel blocker, amlodipine, for Mr. Jones. Mr. Jones is also taking an antifungal, fluconazole, and has had some problems with hypotension. Dr. Smith wants to see if there are reports of an interaction of those two drugs that might cause this symptom. He asks his provider order entry software to check for FDA reports on an interaction between these drugs. The system shows a list of relevant case reports (the most recent 20 of 526 related reports), with the ability to look at others, if desired. Dr. Smith sees that there are a number of other cases with a similar case history to the one he is concerned about, and chooses, therefore, to change the drug prescribed.

This survey is conducted over the Internet via a web-based data collection tool. Personal information such as name, address, etc. will not be collected as part of this survey. The survey collection will not retain IP addresses. In this way, confidentiality of your answers is assured.

The survey will take approximately 10-15 minutes to complete.

1. **Do you use drug-drug interaction software to detect drug-drug interactions in your routine practice? This would include use of a Clinical Decision Support system embedded in an Electronic Health Record or a drug information system.**

   ○ Yes ○ No

2. **If yes, which phrase below best describes how frequently you use that software to detect drug-drug interactions, on average?**

   ○ Once per month ○ Once per week ○ Once per day ○ More than once per day

3. **When viewing AERs, how important would it be for you to have access to each of the following types of patient demographic and administrative information?**

Date the adverse event occurred or began

○ Not important ○ Somewhat important ○ Very important ○ Essential

Date the drug manufacturer first received an initial or follow-up report

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

Date the FDA or WHO received the report

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

The patient's age at the time of the event

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

The patient's gender

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

The patient's weight

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

The occupation of the reporter of the adverse event (e.g. physician, pharmacist, etc.)

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

The date the patient died

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

4. When viewing AERs, how important would it be for you to have access to each of the following types of drug information for each involved drug?

Whether the drug was reported to be the primary cause of the event, a cause of the event but not the primary cause, a concomitant or an interacting drug

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

The name of the medicinal product

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

The route of drug administration

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

Whether the reaction was reduced in degree or intensity when drug therapy was stopped

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

Whether the reaction recurred when drug therapy was restarted

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

The lot number of the drug

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

The expiration date of the drug

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

The date therapy was started (or re-started) for the drug

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

The date therapy was stopped for the drug

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

The duration of the therapy for the drug

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

5. **When viewing AERs, how important would it be for you to have access to a description of the reaction or event using medical terminology (e.g. cardiac arrhythmia)?**

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

6. **When viewing AERs, how important would it be for you to have access to the patient's outcome?**

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

7. **When viewing AERs, how important would it be for you to have access to the patient's diagnoses using medical terminology?**

◯ Not important ◯ Somewhat important ◯ Very Important ◯ Essential

8. **Are there some ways (other than a list of relevant case reports) that the AER data may be presented that might help you in detecting or preventing drug-drug interactions?**

Thank you for participating in this survey.

Appendix 5 – Detailed Survey Results

ADVERSE EVENT REPORTS: THEIR ROLE IN DETECTING AND PREVENTING DRUG-DRUG INTERACTIONS

1. Do you use drug-drug interaction software to detect drug-drug interactions in your routine practice? This would include use of a Clinical Decision Support system embedded in an Electronic Health Record or a drug information system.

Answer Options	Response Percent	Response Count
Yes	100.0%	6
No	0.0%	0
answered question		6
skipped question		0

2. If yes, which phrase below best describes how frequently you use that software to detect drug-drug interactions, on average?

Answer Options	Response Percent	Response Count
Once per month	16.7%	1
Once per week	16.7%	1
Once per day	0.0%	0
More than once per day	66.7%	4
answered question		6
skipped question		0

3. When viewing AERs, how important would it be for you to have access to each of the following types of patient demographic and administrative information?

Answer Options	Not important	Somewhat important	Very Important	Essential	Response Count
Date the adverse event occurred or began	1	4	1	0	6
Date the drug manufacturer first received an initial or	4	2	0	0	6
Date the FDA or WHO received the report	3	2	1	0	6
The patient's age at the time of the event	0	3	2	1	6
The patient's gender	1	3	1	1	6
The patient's weight	2	3	1	0	6
The occupation of the reporter of the adverse event	2	2	1	1	6
The date the patient died	4	2	0	0	6
answered question					6
skipped question					0

4. When viewing AERs, how important would it be for you to have access to each of the following types of drug information for each involved drug?

Answer Options	Not important	Somewhat important	Very Important	Essential	Response Count
Whether the drug was reported to be the primary	0	1	3	2	6
The name of the medicinal product	0	0	3	3	6
The route of drug administration	0	1	3	2	6
Whether the reaction was reduced in degree or	0	1	4	1	6
Whether the reaction recurred when drug therapy was	0	1	3	2	6
The lot number of the drug	1	3	1	1	6
The expiration date of the drug	1	3	1	1	6
The date therapy was started (or re-started) for the	1	3	2	0	6
The date therapy was stopped for the drug	1	3	2	0	6
The duration of the therapy for the drug	0	2	3	1	6
				answered question	6
				skipped question	0

5. When viewing AERs, how important would it be for you to have access to a description of the reaction or event using medical terminology (e.g. cardiac arrhythmia)?

Answer Options	Response Percent	Response Count
Not important	0.0%	0
Somewhat important	16.7%	1
Very Important	33.3%	2
Essential	50.0%	3
answered question		6
skipped question		0

6. When viewing AERs, how important would it be for you to have access to the patient's outcome?

Answer Options	Response Percent	Response Count
Not important	0.0%	0
Somewhat important	0.0%	0
Very Important	33.3%	2
Essential	66.7%	4
answered question		6
skipped question		0

7. When viewing AERs, how important would it be for you to have access to the patient's diagnoses using medical terminology?		
Answer Options	**Response Percent**	**Response Count**
Not important	0.0%	0
Somewhat important	0.0%	0
Very Important	50.0%	3
Essential	50.0%	3
answered question		6
skipped question		0

8. Are there some ways (other than a list of relevant case reports) that the AER data may be presented that might help you in detecting or preventing drug-drug interactions?	
Answer Options	**Response Count**
	6
answered question	6
skipped question	0

Number	Response Date	Response Text
1	Apr 5, 2011 1:09 AM	summaries of published studies based on administrative or other drug data that assessed possible drug-drug interactions with references for the study.
2	Apr 5, 2011 1:35 PM	Alerts that that show up when both drugs are prescribed.
3	Apr 6, 2011 7:35 AM	If not already being done place the list of adverse reactions in order of prevalence not alphabetical order.
4	Apr 6, 2011 8:12 AM	Summary data, preferably from an expert, from all the appropriate AER reports would be most helpful, with an option or link to the actual report. Maybe something with the tone, brevity and direct style of say The Medical Letter. As an ER doctor, I may not have time to read individual reports in detail in many cases but would like to retain the option if needed.
5	Apr 7, 2011 3:37 AM	having a medication reconciliation process so that the patient's medication list is current to compare against for any drug-drug interactions on new potential medications.
6	Apr 11, 2011 5:38 AM	i think the most useful way drug-drug interaction function in EHR is to clinicians is that it alerts physicians to potential interactions and the degree of severity/serious of the interaction. i think currently software that then gives clinician option to click on the potential action and obtain more detailed information about the nature of the interaction to be able to make a clinical decision whether the potential interaction is relevant in the particular situation he/she faces. beyond that, i think having much more information would be excessive as clinicians are often using this functionality on the go or in situations when they do not have too much time to review large amounts of data. thus data best kept succinct and to the point