INNOVATIONS in pharmacy

Volume 2 | Number 1 Article 36

2011

Pharmaceutical systematics: Description and preliminary investigation of an alternative method for structuring drug information

Mary E. Kiersma

Aleda M. H. Chen

Kristin R. Villa

Brian M. Shepler

Matthew M. Murawski

Pharmaceutical systematics: Description and preliminary investigation of an alternative method for structuring drug information

*Mary E. Kiersma, Aleda M. H. Chen, Kristin R. Villa, Brian M. Shepler, Matthew M. Murawski**
**Corresponding Author*

Author Identification:
Mary E. Kiersma, Pharm.D., M.S., Graduate Research Assistant (GRA), Purdue University, College of Pharmacy
Aleda M. H. Chen, Pharm.D., M.S., GRA, Purdue University, College of Pharmacy and Center on Aging and the Life Course
Kristin R. Villa, Pharm.D., GRA, Purdue University, College of Pharmacy
Brian M. Shepler, Pharm.D., Clinical Assistant Professor, Pharmacy Practice and Director, Advanced Pharmacy Practice Experiences, Purdue University, College of Pharmacy
Matthew M. Murawski, Ph.D., R.Ph., Associate Professor, Pharmacy Administration, Purdue University, College of Pharmacy

Acknowledgements: Thanks to Mary Roswarski, Christy Gorbach, and Matthew Jacobs for their assistance with data analysis in this project.
Funding: This research project was supported, in part, by a Lilly seed grant from the College of Pharmacy, Purdue University. Support for Aleda M. H. Chen was provided by the National Institute on Aging (T32AG025671) and the Purdue University Center on Aging and the Life Course.
Previous Presentation: Components of this project were presented as student posters at the American Society of Health Systems Pharmacists Annual Meeting, Las Vegas, Nevada, December 2009 and as a conference poster at the International Society for Pharmacoepidemiology, Brighton, United Kingdom, August 21, 2010.

Abstract
Objectives: *To identify the 30 most common adverse drug events or reactions (ADE/ADRs) within the top 200 medications: (1) by raw incidence, (2) weighted by prescription volume, (3) and weighted by retail dollars.*
Methods: *The Pharmacy Times Top 200 Medications (as ranked by prescription volume) was utilized to identify the top 200 medications in 2008. The ADE/ADRs for each medication were obtained from Facts and Comparisons, Micromedex, and Lexi-Comp and entered into a database. These ADE/ADRs were compiled and summed, identifying the number of times each appeared. These then were ranked to identify the 30 most common ADE/ADRs. The actual prescription volume and total retail dollars for each medication were obtained and listed next to each medication's ADE/ADR. The incidence of each ADE/ADR then was weighted by actual prescription volume and retail dollars to determine the top 30 most common ADE/ADRs.*
Results: *Initial evaluation resulted in 9829 individual ADE/ADRs and summed into 1477 distinct ADE/ADRs, after adjusting for interchangeable terminology. Examples of the 30 most common ADE/ADRs (raw incidence) included: dizziness/vertigo, headache, nausea, vomiting, and diarrhea/loose stools. The list remained the same after weighting by actual prescription volume. After weighting by retail dollars, the order of ADE/ADRs changed slightly.*
Conclusion: *Knowledge of ADE/ADRs is important for pharmacists in all healthcare settings. Consolidating ADE/ADRs for medications may enable pharmacists to recall the most common side effects and aid in earlier identification of ADE/ADRs, which may positively impact patient safety across practice settings.*

Introduction

The role of the community pharmacist and the nature of community pharmacy practice have undergone considerable evolution in recent decades as the number of medications consumed in addition to the spending on prescription drugs have markedly increased. Nearly 81 percent of older adults between the ages of 57 and 85 use at least one prescription medication and one in three older adults use at least five or more prescription medications.[1] Spending on prescription drugs has significantly increased from $51 billion in 1993 to an estimated $244.8 billion in 2009. These numbers are expected to increase to $453.7 billion by 2018, despite the current economic recession.[2] During this same period, the level of training and clinical expertise of the pharmacy practitioner has increased substantially with the implementation of a required Doctor of Pharmacy degree.[3] From 2000 to 2009, the percentage of licensed pharmacists with a Doctor of Pharmacy degree has increased from approximately 14 percent to nearly 22 percent.[40] Pharmacists are well-prepared to identify, address and

resolve drug-related problems their patients may be experiencing and can provide patients with important information about adverse drug reactions and adverse drug events.[4]

An adverse drug reaction (ADR) is typically defined as "harm directly caused by a drug at normal doses,"[5] while an adverse drug event (ADE) is "harm caused by the use of a drug."[5] An example of an ADR could be myopathy from the usage of a statin, while an example of an ADE could be hepatic failure from inappropriate overdosing of an opioid combination product. Together, ADEs and ADRs are estimated to result in more than 100,000 deaths each year, are between the fourth and sixth leading cause of death in the United States, and are estimated to account for nearly 10 percent of all hospital admissions.[6, 7] The cost of drug-related morbidity and mortality creates a significant economic burden, with the cost in the United States health care system estimated to exceed $177 billion each year.[8] ADE/ADRs are reported to be common in the ambulatory population, with many instances resulting in hospitalization.[6,7,9] Serious and fatal ADEs reported to the U.S. Food and Drug Administration (FDA) more than doubled from 1998 to 2005;[7] however, ADE/ADRs are underreported.[10-12] According to a systematic review, incidence of ADE/ADRs are estimated to be 94 percent higher than actually reported.[11] Many of the ADE/ADRs reported tend to be considered serious and/or life-threatening.[7] There is little information available regarding the prevalence and incidence of "tolerable" ADE/ADRs that may reduce patients' quality of life and decrease medication adherence but do not reach a minimum threshold of "reportability."

Previous research has demonstrated pharmacists' ability to reduce ADEs, primarily in the institutional setting. In one study including pharmacists on a pediatric rounds team, 94 percent of ADEs were prevented.[13] Similar results in other studies have substantiated the value of pharmacists in reducing ADEs, mainly in the inpatient setting.[14-22] In a study by Thomsen and colleagues (2007), medication errors resulting in preventable ADEs occur in the prescribing and monitoring stage of the medication use process.[23] These studies clearly demonstrate that pharmacists have the capability to effectively influence the incidence of ADE/ADRs. To date, however, the reduction of ADE/ADRs has primarily been accomplished in closely-monitored and controlled patient populations in institutional settings.[4,14-22] While this type of patient care is an extremely vital component of the health care system, there is substantial unmet need to monitor patients in the ambulatory population for the existence of ongoing ADE/ADRs.[20]

Community pharmacy practice differs substantially from practice in institutional settings, where pharmacists can provide feedback through chart reviews and patient rounds.[4,14-22] Community pharmacists are more likely to contend with the consequences of medication therapy and often have less influence on medication therapy choices. However, community pharmacists, by virtue of their training and accessibility, are uniquely positioned in the health care system to address the issue of ongoing ADE/ADRs in ambulatory patients. Indeed, community pharmacist counseling interventions have been found to improve outcomes by decreasing ADEs in cardiovascular patients.[20] The Institute for Safe Medication Practices (ISMP) agrees, believing that pharmacist counseling improves medication use in the ambulatory population and bridges the communication gap between healthcare providers and patients.[38]

Community pharmacists often have difficulty engaging in lengthy patient communication activities due to the time constraints of modern practice. Approximately 72 percent of community pharmacist time is spent in medication dispensing activities and managerial duties, allotting less time for patient counseling activities.[39] As a result, during a patient counseling session, the community pharmacist must discover ADE/ADRs a patient is experiencing as rapidly as possible and determine which medication is responsible. While knowledge of ADE/ADRs is essential for pharmacists in all settings, recollection of every potential ADE/ADR for each medication under such circumstances may prove daunting.

The current method of classifying, learning, and recalling ADE/ADRs is based on structuring medication knowledge within each particular therapeutic class. This method of organizing medication knowledge by pharmacological or therapeutic classification provides an efficient approach to the prescribing process, since the ADE/ADRs can be analyzed prospectively. Pharmacists can effectively use their knowledge to aid in the prospective evaluation process of proposed prescribing using this framework.[14-22] However, in the community setting, pharmacists typically deal with prescriptions retrospectively; when problems occur (i.e. are presented with an ADE/ADR), they must work backward to determine which medication from the patient's regimen is responsible. The manner by which drug information has traditionally been organized and taught can make this process cumbersome when done retrospectively.

Rather than using the current approach, which relies on recall of all possible ADE/ADRs for each medication, the development of a classification system based on ADE/ADRs would provide a list of potential "suspect" medications to the

pharmacist allowing for more efficient identification of the causal agent and enable them to effectively recall the most frequently occurring side effects, improving patient safety and outcomes.

Objective

The objectives of this study were to identify the 30 most common adverse drug events or reactions (ADE/ADRs) within the top 200 medications: (1) by raw incidence, (2) weighted by prescription volume, (3) and weighted by retail dollars.

Methods

The *Pharmacy Times* Top 200 Drugs of 2008 list was used to identify the prescription medications most commonly used within the ambulatory population during 2008. The *Pharmacy Times* listing ordinally ranks the top 200 medications according to prescription volume, combining both brand and generic medications into a single ranked list, using data from IMS Health.[24] There are other publicly-available lists compiled by *Drug Topics* (using data from SDI/Verispan), but these contain two separate top 200 drug lists, one for brand-name medications and another for generic medications.[25, 26]

Once the *Pharmacy Times* list was obtained, a database using Microsoft Excel® was created by entering the top 200 medications. The medications then were categorized and sorted according to pharmacologic class. Pharmacologic class determinations were made using the most recent version of *Drug Facts and Comparisons* (July 2009). After the top 200 medications were sorted into pharmacologic classes within the database, the adverse drug experiences and adverse drug reactions (ADE/ADRs) for each medication were obtained from July 2009 to September 2009 from drug information resources (*Drug Facts and Comparisons, Lexi-Comp,* and *Micromedex*) and listed next to each medication in the database. These drug information resources were used to create an exhaustive list of all the ADR/ADEs for the top 200 prescription medications. Estimates of frequency of ADE/ADR occurrence and frequency vs. placebo, when available, also were obtained and entered into the database.

After the list of ADE/ADRs was compiled and entered into the database for each medication, another list of ADE/ADRs was compiled for each pharmacological class. Common ADE/ADRs which occurred for each medication within the pharmacologic class were identified and sorted within the database. After entry, the resulting ADE/ADR database for a specific pharmacologic class included ADE/ADRs common to all medications of the pharmacologic class as well as those specific to individual medications.

When the ADE/ADR lists for all identified pharmacologic classes were completed, a master list of all ADE/ADRs found within the top 200 medications was created and sorted according to specific ADE/ADRs. The resulting master list of ADE/ADRs then was analyzed to identify any terms that could be considered interchangeable, in order to consolidate the list and retain only unique ADE/ADRs. Terms that were identified as interchangeable were verified through a primary literature review in Medline, which indicated that the terms were used interchangeably in the literature. Pharmacist clinical judgment (by authors Kiersma and Chen) also was used, and there were no disagreements regarding the list of interchangeable terms. If, according to the literature and clinical judgment, two terms were considered interchangeable then the ADE/ADRs were combined. For example, one such interchangeable set of ADE/ADRs identified was dyspnea and shortness of breath. A list of similar terms that were consolidated can be found in Table 1.

After the final list was completed, the number of instances in which each ADE/ADR occurred within the top 200 medications was tabulated to rank the most common ADE/ADRs. The final list of ADE/ADRs was weighted by the prescription volume for each drug using the prescription drug volumes contained in the *Drug Topics* Top 200 drugs of 2008 list.[25, 26] The prescription drug volume list was sorted and ranked to determine the most common ADE/ADRs weighted by prescription volume. The same method also was used to generate the list weighted by retail dollars, using the values contained in the *Drug Topics* list.[36,37] Weighting by prescription volume or retail dollars corrects for the difference in relative magnitude between all 200 medications, since the original top 200 list provides only the rank of each medication. For example, information regarding the magnitude between the medications at the twenty-fourth and twenty-fifth positions as opposed to the twenty-sixth and twenty-seventh positions.

Although the *Pharmacy Times* Top 200 of 2008 list was used to identify the prescription medications,[24] it was necessary to utilize the *Drug Topics* Top 200 of 2008 drug list to generate the actual prescription volume and retail dollars for individual agents as complete information for all 200 medications was unavailable in the *Pharmacy Times* list .[24-26, 35, 36] The *Drug Topics* Top 200 drug list did not include a prescription volume or retail dollars for amlodipine,[25,35] which was listed in the *Drug Topics* top 200 list. However the *Pharmacy Times* Top 200 drug list did provided a prescription volume for amlodipine.[24] The ADE/ADRs associated with amlodipine were not weighted by retail dollars, as the information was unavailable.

Results

Evaluation of the master list of all ADE/ADRs contained within the top 200 prescription medications resulted in the identification of 9,829 ADE/ADRs. After consolidation of interchangeable terms, 1,477 unique ADE/ADRs remained.

The top five ADE/ADRs (prior to weighting by retail dollars and prescription volume) occurring in top 200 drugs were: 1) nausea, 2) dizziness/vertigo, 3) headache, 4) vomiting, and 5) rash/skin eruption. The top five most common ADE/ADRs weighted by prescription volume were: 1) dizziness/vertigo, 2) headache, 3) nausea, 4) diarrhea/loose stools, and 5) vomiting, After weighting ADE/ADRs by retail dollars, the top five ADE/ADRs were: 1) dizziness/vertigo, 2) fatigue, 3) vomiting, 4) nausea, and 5) headache.

Overall, the top 30 unweighted and weighted ADE/ADR lists were similar, but there were some differences (see Table 2). Results for the top 30 unweighted and weighted by retail dollars ADE/ADR lists included angioedema, fever, and anaphylaxis, but were not reported in the top 30 list weighted by prescription volume. The unweighted list also did not include the ADE/ADRs of angina/chest pain, xerostomia/dry mouth, and taste perversion/dysguesia which were included on lists weighted by retail dollars and prescription volume. Table 2 presents the results of the top 30 ADE/ADRs unweighted, weighted by prescription volume, and weighted by retail dollars. Also, the 30 most common ADE/ADRs weighted by prescription volume were similar for the tabulations including and excluding amlodipine, with only the ranking of ADE/ADRs differing.

Discussion

The intention of this study was to provide preliminary data for the future development of an alternative method that would provide more information regarding the prevalence and aid in identification of unintended consequences (ADE/ADRs) associated with medication utilization. In 2008, approximately 2,329,957 top 200 prescription medications were dispensed.[25,26] This research project provided information on the frequency of the most common ADE/ADRs patients are most likely to experience when taking one of the top 200 medications, allowing for an estimate of the actual incidence of the ADE/ADRs in the ambulatory population based on the published literature.

There are several alternate methods whereby this study could have been structured. For example, other publications listing the top 200 medications could have been chosen. However, there are few other reliable listings of top 200 medications are publicly-available, and *The Pharmacy Times* and the *Drug Topics* lists are comprehensive, publicly-available, and utilize data generated by reliable sources, i.e. IMS Health and SDI/Verispan.[24-26] The *Pharmacy Times* list was selected to generate the top 200, since it was used more frequently in the literature[27-31] and combined both brand and generic medications.

Also, medications were organized according to pharmacologic category or class in view of the fact that both practice and the literature routinely utilize this method of classification to compartmentalize similar medications within pharmacological class that tend to share similar therapeutic use and ADE/ADRs. *Facts and Comparisons* was selected for classification purposes due to its utilization in other studies as a source of accurate and reliable information.[32, 33] This study employed a unique approach to ADE/ADR classification by categorizing the top 200 prescription medications by ADE/ADR. To develop an initial list of all possible ADE/ADRs experienced within the top 200 medications, three different reference software programs (*Facts and Comparisons, Lexi-Comp*, and *Micromedex*) were employed for identification of ADE/ADRs due to their demonstrated ability to provide comprehensive and accurate information.[32-35]

Information regarding the incidence, prevalence, and frequencies of ADE/ADRs for individual medications and placebo was gathered and entered into the database, when available. However, for a number of medications, ADE/ADR incidence and prevalence data was not readily available. Many of those medications for which information was not available included those which have been on the market for a lengthy period of time (e.g., prednisone and amitriptyline). Similarly, information regarding the medication versus placebo ADE/ADR incidence was frequently unavailable. Therefore, our estimates of the most common 30 ADE/ADRs could not be adjusted for actual incidence (e.g. 10 percent incidence of placebo-induced nausea versus 50 percent incidence of medication-induced nausea) due to limitations of the data sources. Further research is needed to determine the actual prevalence of ADE/ADRs for many of these medications in the ambulatory population.

One problem that arose was clinically similar ADE/ADRs with slight differences in terminology. Several ADE/ADRs were grouped (as seen in Table 1) using both a primary literature review and pharmacist clinical judgment due to differences in terminology used in the drug information databases. Grouping decisions were determined on the basis of scientific knowledge regarding medications provided by literature and the pharmacists' educational background. In future research other ADE/ADRs groupings could be determined, since many terms describe ADE/ADRs in different ways. However, for purposes of this study, the research team elected to allow the

separation of ADE/ADRs unless the definitions were entirely interchangeable according to the primary literature and clinical judgment.

In this study, the number of occurrences of ADE/ADRs was weighted by retail dollars and by prescription volume and compared. The *Drug Topics* listing of the top 200 medications does contain complete information by retail dollars and prescription volume for both brand and generic name.[25,26,36,37] Both listings were selected, analyzed, and presented to avoid systematic bias based on cost differences between prescription medications, which could occur if the rankings were based solely on retail dollars. In addition, comparison of the list of ADE/ADRs created using both prescription volume and retail dollars top 200 rankings provided a method for assessing the sensitivity of our methods in creating the ADE/ADR lists. Arguably, our approach to constructing a list of the most common ADE/ADRs should be sufficiently "sensitive" to be able to discern the differences in ADE/ADR incidence in lists generated according to the criteria of prescription volume and of dollar volume, which each of our lists changed according to the different criteria. We consider the difference in ADE/ADR incidence according to prescription volume and retail dollars as evidence for the validity of our method of developing the ADE/ADR list.

Limitations

There were some limitations to this project. There was limited publicly-available information regarding which medications comprise the top 200 list. *The Pharmacy Times* list,[24] while widely-utilized and reliable, does not contain the prescription volume for all 200 medications. It also does not contain information regarding the retail dollars for the top 200 medications.[24] Due to this fact, the *Drug Topics* list had to be used to generate the prescription volume[25,26] and retail dollars[35,36] for the top 200 prescription medications. Additionally, the *Drug Topics* list[25,26,35,36] does not include amlodipine, which is present in the top 200 medications reported in *The Pharmacy Times* list.[24] No information was available regarding this omission. These limitations have been acknowledged and accounted for throughout the project using conservative methods of analysis and reporting of results.

Conclusion

Pharmacists are well-prepared to identify, address and resolve pharmaceutical therapy-related problems their patients may be experiencing while providing patients with important information about adverse drug reactions. Unfortunately due to time constraints, today's highly trained pharmacy practitioner often has difficulty engaging in lengthy patient communication activities that are of vital importance to a patient's well-being due to medication dispensing functions and managerial activities that take up over 70 percent of their time daily.[39] Given the limited amount of time remaining for patient counseling, the exchange of information and problem discovery that occurs during the pharmacist-patient interactions needs to be as efficient as possible. Consolidating the ADE/ADRs for the top 200 medications, each drug class, and eventually all medications may enable pharmacists to recall the most common side effects and aid in earlier identification of ADE/ADRs a patient may be experiencing, which may positively impact patient safety across healthcare settings. When comparing an ADE/ADR to a patient's medication list, organizing medications by ADE/ADR also may aid in efficiently identifying the causal medication for a reported ADE/ADR. Again, while organizing medications according to pharmacological class is useful to identify potential ADE/ADRs during prospective drug evaluation, it may not be the best method for identification of ADE/ADRs in the community pharmacy setting.

Pharmacist medication review and counseling have reduced the rate of ADEs, thereby improving patient outcomes, primarily within the inpatient setting.[14-22] In addition, increased identification of ADE/ADRs and subsequent counseling in the community setting may lead to greater reporting of pertinent ADE/ADRs to the FDA database, which can lead to changes in both practice and regulation that improve patient safety.[10] This project has derived the approximate estimates of the incidence of ADE/ADRs in the ambulatory population based on published literature. We have used the database to estimate that given the opportunity to ask a patient 30 questions related to the 30 most common ADE/ADRs, without any prior knowledge regarding the specific medications the patient is using, we would be able to identify nearly 30 percent of ADE/ADRs. Future research can utilize these lists to create instruments for the top 200 medications that better estimate the true prevalence of ADE/ADRs in the ambulatory patient population, and ultimately, develop tools to improve patient medication safety.

References

1. Qato DM, Alexander GC, Conti RM, Johnson M, Schumm P, Lindau ST. Use of prescription and over-the-counter medications and dietary supplements among older adults in the United States. *JAMA: Journal of the American Medical Association.* 2008;300(24):2867-2878.
2. Sisko A, Truffer C, Smith S, et al. Health spending projections through 2018: Recession effects add uncertainty to the outlook. *Health Affairs.* 2009;28(2):w346-357.
3. Accreditation Council for Pharmacy Education. *Accreditation standards and guidelines for the professional program in pharmacy leading to the doctor of pharmacy degree.* Chicago, IL: Accreditation Council for Pharmacy Education; 2006.
4. Svarstad BL, Bultman DC, Mount JK. Patient counseling provided in community pharmacies: Effects of state regulation, pharmacist age, and busyness. *Journal of the American Pharmacists Association.* 2004;44(1):22-29.
5. Nebeker JR, Barach P, Samore MH. Clarifying adverse drug events: A clinician's guide to terminology, documentation, and reporting. *Annals of Internal Medicine.* 2004;140(10):795-801.
6. Phillips J, Beam S, Brinker A, et al. Retrospective analysis of mortalities associated with medication errors. *American Journal of Health Systems Pharmacy.* 2001;58(19):1835-1841.
7. Moore TJ, Cohen MR, Furberg CD. Serious adverse drug events reported to the Food and Drug Administration, 1998-2005. *Archives of Internal Medicine.* 2007;167(16):1752-1759.
8. Field TS, Gilman BH, Subramanian S, Fuller JC, Bates DW, Gurwitz JH. The costs associated with adverse drug events among older adults in the ambulatory setting. *Medical Care.* 2005;43(12):1171-1176.
9. Ernst FR, Grizzle AJ. Drug-related morbidity and mortality: Updating the cost-of-illness model. *Journal of the American Pharmaceutical Association.* 2001;41(2):192-199.
10. Wysowski DK, Swartz L. Adverse drug event surveillance and drug withdrawals in the United States, 1969-2002: The importance of reporting suspected reactions. *Archives of Internal Medicine.* 2005;165(12):1363-1369.
11. Hazell L, Shakir SAW. Under-reporting of adverse drug reactions: A systematic review. *Drug Safety.* 2006;29(5):385.
12. Mayer MH, Dowsett SA, Brahmavar K, Hornbuckle K, Brookfield WP. Reporting adverse drug events. *U.S. Pharmacist.* 2010;35(4): HS-15-HS-19.
13. Kaushal R, Bates DW, Landrigan C, et al. Medication errors and adverse drug events in pediatric inpatients. *JAMA: Journal of the American Medical Association.* 2001;285(16):2114-2120.
14. Leape LL, Cullen DJ, Clapp MD, et al. Pharmacist participation on physician rounds and adverse drug events in the intensive care unit. *JAMA.* 1999;282(3):267-270.
15. Folli HL, Poole RL, Benitz WE, Russo JC. Medication error prevention by clinical pharmacists in two children's hospitals. *Pediatrics.* 1987;79(5):718-722.
16. Broyles JE, Brown RO, Vehe KL, Nolly RJ, Luther RW. Pharmacist interventions improve fluid balance in fluid-restricted patients requiring parenteral nutrition. *Annals of Pharmacotherapy.* 1991;25(2):119-122.
17. Kilroy R, Lafrate R. Provision of pharmaceutical care in the intensive care unit. *Critical Care Nursing Clinics of North America* 1993;5:221-225.
18. Montazeri M, Cook DJ. Impact of a clinical pharmacist in a multidisciplinary intensive care unit. *Critical Care Medicine.* 1994;22(6):1044-1048.
19. Schnipper JL, Kirwin JL, Cotugno MC, et al. Role of pharmacist counseling in preventing adverse drug events after hospitalization. *Archives of Internal Medicine.* 2006;166(5):565-571.
20. Murray MD, Ritchey ME, Wu J, Tu W. Effect of a pharmacist on adverse drug events and medication errors in outpatients with cardiovascular disease. *Archives of Internal Medicine.* 2009;169(8):757-763.
21. Wang JK, Herzog NS, Kaushal R, Park C, Mochizuki C, Weingarten SR. Prevention of pediatric medication errors by hospital pharmacists and the potential benefit of computerized physician order entry. *Pediatrics.* 2007;119(1):e77-85.
22. Rivkin A, Yin H. Evaluation of the role of the critical care pharmacist in identifying and avoiding or minimizing significant drug-drug interactions in medical intensive care patients. *Journal of Critical Care.* 2010;In Press, Corrected Proof.
23. Thomsen LA, Winterstein AG, Sondergaard B, Haugbolle LS, Melander A. Systematic review of the incidence and characteristics of preventable adverse drug events in ambulatory care. *Annals of Pharmacotherapy.* 2007;41(9):1411-1426.

24. Lamb E. Top 200 drugs of 2008. *Pharmacy Times.* May 2009. [accessed June 1, 2009] http://www.pharmacytimes.com/issue/pharmacy/2009/2009-05/RxFocusTop200Drugs-0509.
25. 2008 top 200 generic drugs by total prescriptions. *Drug Topics.* May 2009. [accessed June 1, 2009] http://drugtopics.modernmedicine.com/drugtopics/data/articlestandard//drugtopics/222009/599844/article.pdf.
26. 2008 top 200 branded drugs by total prescriptions. *Drug Topics.* May 2009. [accessed June 1, 2009] http://drugtopics.modernmedicine.com/drugtopics/data/articlestandard//drugtopics/222009/599845/article.pdf.
27. Smith RG. Fall-contributing adverse effects of the most frequently prescribed drugs. *Journal of the American Podiatric Medical Association.* 2003;93(1):42-50.
28. Lada P, Idrees U. Toxicity of oral agents used to treat diabetes. *Journal of Pharmacy Practice.* 2005;18(3):145-156.
29. Hersh EV, Pinto A, Moore PA. Adverse drug interactions involving common prescription and over-the-counter analgesic agents. *Clinical Therapeutics.* 2007;29(11, Supplement 1):2477-2497.
30. Chermak TE, Lambert BL. Descriptive analysis of primary package labels from commercially available prescription solid oral dosage form drugs. *Journal of the American Pharmacists Association.* 2009;49(3):399-406.
31. Pitman SK, Sorofman B. Medication use as evidence for pharmacotherapeutics curriculum content. *American Journal of Pharmaceutical Education.* 2009;73(8):(Article 148).
32. Hatfield C, May S, Markoff J. Quality of consumer drug information provided by four Web sites. *American Journal of Health-System Pharmacy.* 1999;56(22):2308-2311.
33. Belgado B, Hatton R, Doering P. Evaluation of electronic drug information resources for answering questions received by decentralized pharmacists. *American Journal of Health-System Pharmacy.* 1997;54(22):2592-2596.
34. Barrons R. Evaluation of personal digital assistant software for drug interactions. *American Journal of Health-System Pharmacy.* 2004;61(4):380-385.
35. Enders SJ, Enders JM, Holstad SG. Drug-information software for Palm operating system personal digital assistants: Breadth, clinical dependability, and ease of use. *Pharmacotherapy.* 2002;22(8):1036-1040.
36. 2008 top 200 generic drugs by retail dollars. *Drug Topics.* May 2009. [accessed June 1, 2009] http://drugtopics.modernmedicine.com/drugtopics/data/articlestandard//drugtopics/192009/597086/article.pdf. Published Last Modified Date|. Accessed Dated Accessed|.
37. 2008 top 200 branded drugs by retail dollars. *Drug Topics.* May 2009. [accessed June 1, 2009] http://drugtopics.modernmedicine.com/drugtopics/data/articlestandard//drugtopics/192009/597083/article.pdf.
38. Institute for Safe Medication Practices. (2007). A call to action: Protecting U.S. citizens from inappropriate medication use Retrieved October 7, 2010, from http://www.ismp.org/pressroom/viewpoints/CommunityPharmacy.pdf
39. Schommer JC, Pederson CA, Gaither CA, Doucette WR, Kreling DH. Pharmacists' desired and actual times in work activities: Evidence of gaps from the 2004 National Pharmacist Workforce Study Journal of the American Pharmacists Association. 2006;46(3):340-347.
40. Midwest Pharmacy Workforce Research Consortium. 2009 national pharmacist workforce survey. [accessed February 21, 2011] http://www.aacp.org/resources/research/pharmacymanpower/Documents/2009%20National%20Pharmacist%20Workforce%20Survey%20-%20FINAL%20REPORT.pdf.

Table 1. Similar Terms Combined Using Clinical Judgment

Dyspnea	Shortness of breath
Rash	Skin eruption
Dizziness	Vertigo
Dyspepsia	Indigestion
Diarrhea	Loose stools
Arthralgia	Joint pain
Myalgia	Muscle pain
Diplopia	Double vision
Ecchymyosis	Bruising
Cholelithiasis	Gallstones
Tremor	Shaking
Tinnitus	Ringing in ears
Dysgeusia	Taste disturbances
Pruritus	Itching
Urticaria	Hives
Angina	Chest pain
Xerostomia	Dry mouth

Table 2. Top 30 Adverse Drug Experiences/Adverse Drug Reactions (ADE/ADRs) in the Top 200 Drugs Unweighted, Weighted by Retail Dollars, and Weighted by Prescription (Rx) Volume

ADE/ADRs Unweighted	*ADE/ADRs Weighted by Retail Dollars*	*ADE/ADRs Weighted by Rx Volume*
1. Nausea	1. Dizziness/vertigo	1. Dizziness/vertigo
2. Dizziness/Vertigo	2. Fatigue	2. Headache
3. Headache	3. Vomiting	3. Nausea
4. Vomiting	4. Nausea	4. Vomiting
5. Rash/skin eruption	5. Headache	5. Diarrhea/loose stools
6. Diarrhea/loose stools	6. Rash/skin eruption	6. Rash/skin eruption
7. Constipation	7. Angina/chest pain	7. Constipation
8. Insomnia	8. Insomnia	8. Angina/chest pain
9. Abdominal pain	9. Diarrhea/loose stools	9. Fatigue
10. Dyspepsia/indigestion	10. Constipation	10. Insomnia
11. Pruritis/itching	11. Dyspepsia/indigestion	11. Abdominal pain
12. Fatigue	12. Abdominal pain	12. Thrombocytopenia
13. Urticaria/hives	13. Pruritus/itching	13. Dyspepsia/indigestion
14. Allergic reactions	14. Anaphylaxis	14. Pruritus/itching
15. Depression	15. Somnolence	15. Somnolence
16. Anaphylaxis	16. Xerostomia/dry mouth	16. Allergic reactions
17. Dyspnea/shortness of breath	17. Urticaria/hives	17. Dyspnea/shortness of breath
18. Tremor	18. Dyspnea/shortness of breath	18. Hypotension
19. Somnolence	19. Paresthesia	19. Xerostomia/dry mouth
20. Thrombocytopenia	20. Arthralgia/joint pain	20. Urticaria/hives
21. Arthralgia/joint pain	21. Depression	21. Depression
22. Palpitations	22. Tremors	22. Paresthesia
23. Paresthesia	23. Angioedema	23. Palpitations
24. Anxiety	24. Thrombocytopenia	24. Anorexia
25. Myalgia/muscle pain	25. Palpitations	25. Myalgia/muscle pain
26. Hypotension	26. Anxiety	26. Anxiety
27. Nervousness	27. Myalgia/muscle pain	27. Arthralgia/joint pain
28. Anorexia	28. Taste perversion/dysgeusia	28. Tremors
29. Fever	29. Cough	29. Taste perversion/dysgeusia
30. Angioedema	30. Fever	30. Nervousness