Inappropriate Prescribing Practices: The Challenge and Opportunity for Patient Safety

Laurel K. Taylor, Yuko Kawasumi, Gillian Bartlett and Robyn Tamblyn

Abstract

Adverse clinical events related to inappropriate prescribing practices are an important threat to patient safety. Avoidance of inappropriate prescribing in community settings, where the majority of prescriptions are written, offers a major area of opportunity to improve quality of care and outcomes. Electronic medication order entry systems, with automated clinical risk screening and online alerting capabilities, appear as particularly promising enabling tools in such settings. The Medical Office of the Twenty First Century (MOXXI-III) research group is currently utilizing such a system that integrates identification of dosing errors, adverse drug interactions, drug-disease and allergy contraindications and potential toxicity or contraindications based on patient age.

This paper characterizes the spectrum of alerts in an urban community of care involving 28 physicians and 32 pharmacies. Over a consecutive nine-month period, alerts were generated in 29% of 22,419 prescriptions, resulting in revised prescriptions in 14% of the alert cases. Drug-disease contraindications were the most common driver of alerts, accounting for 41% of the total and resulting in revised prescriptions in 14% of cases. In contrast, potential dosing errors generated only 8% of all alerts, but resulted in revised prescriptions 23% of the time. Overall, online evidence-based screening and alerting around prescription of medications in a community setting demands confirmation in prescribers' clinical decision making in almost one-third of prescriptions and leads to changed decisions in up to one-quarter of some prescribing categories. Its ultimate determination of clinical relevance to patient safety may, however, have to await more detailed examination of physician response to alerts and patient outcomes as a primary measure of utility.

Patient safety is an increasingly recognized challenge and opportunity for stakeholders in improving health care delivery. It involves many issues, including delayed diagnosis and treatment, as well as inappropriate undertreatment and overtreatment. The common denominators, however, are that care and outcomes could be better, and there is a role for patients, providers and policy makers in making improvements.

THE CHALLENGE

Adverse events related to medication use are a leading cause of patient morbidity and mortality in North America (Lazarou et al. 1998). There are numerous contributing causes of the overall adverse event rates, including errors in dispensing, monitoring and adherence to medications (Avery et al. 2002). They may drive up to a quarter of all hospital admissions (Grymonpre et al. 1988; Hurwitz 1969; Ives et al. 1987; May et al. 1977), and this problem will likely be magnified by the increasing prevalence of chronic comorbidities in an increasingly aged population who also live in a culture of widespread over-the-counter medication use and acceptance of polypharmacy.

Changing the prescribing behaviour of physicians, particularly for complex aspects of care, can be a formidable challenge. Proven tools to facilitate recognition and closure of care gaps are few and even fewer offer a real time capability for matching problem identification to corrective action.

Recent work suggests that electronic prescription order entry systems with automated evidence-based risk-screening and alerting capabilities offer promise as tools in decreasing inappropriate prescribing patterns and related adverse clinical events (Bates et al. 1999; Bates et al. 2001; Bates et al. 2003; Bates and Gawande 2003; Kaushal and Bates 2002). At least theoretically, physicians consider an alerting system a worthwhile ingredient to improve prescribing safety (Ashworth 2002). However, despite the potential advantages offered by such tools, their effective acceptance and utilization has been slow (Aydin and Rice 1991; Bates and Gawande 2003; Tamblyn et al. 2003). Studies to assess why this is so have indicated several potential causes, including variable technical performance and the "back box" nature of some tools, which make it difficult to obtain reliable data to allow cause and effect analyses (Hazlet et al. 2001; Oren et al. 2003). Perhaps more importantly, there is also a physician perception of narrow clinical applicability, or inadequate general clinical relevance, of the parameters screened and alerts generated by these tools (Gurwitz et al. 2003; Hsieh et al. 2004; Monane et al. 1998).

One practical manifestation of this sense of clinical irrelevance is that physicians' frequently override, or ignore, drug alerts (Glassman et al. 2002; Magnus et al. 2002). This may also suggest an element of alert fatigue or information overload, further encouraging physicians to view alerts as a burden or hindrance to improving practice quality rather than as a decision support tool to improve quality of prescribing. If we are going to optimize the use of these systems to optimize patient safety, we need to understand four fundamental issues: the alerts these systems are producing, their clinical relevance, the physicians' response, and the reasons the physicians are responding in this manner. It is only with this information that we can improve the utility of these decision aids to reduce drug-related morbidity.

At this point, the purpose of this research was identify what alerts physicians are seeing in outpatient settings, to and to build a better understanding of their perceptions of the value of alert systems. We took advantage of a community-based trial to conduct a novel investigation of the type of drug-related alerts in primary care.

THE OPPORTUNITY

The Medical Office of the Twenty First Century (MOXXI-III) is a group of academic and community-based health care stakeholders interested in improving care and outcomes for patients. As part of the research program, this partnership has developed a comprehensive, evidence-based and integrated drug management system designed to reduce prescription errors. Briefly, the system provides an electronic prescription, drug and disease management system for primary care physicians, community-based pharmacists and their patients. It is unique in several ways. It has the ability to identify dosing errors, drug interactions and duplications, as well as possible drug-disease contraindications, drug-allergy reactions, potential toxicity and contraindications due to patient age. The system also electronically documents the clinical rationale used by the physician in prescribing decisions at the point-of-care, including starting, stopping and renewing medications and response to drug alerts.

Participating physicians utilize a personal digital assistant (PDA) that includes a dynamic prescription pad that displays treatment indications and allows participating pharmacies to electronically retrieve the prescription. The content for the electronic prescription drug alerts was provided by Vigilance Santé Inc. via their Rx Vigilance therapeutic advisor. A drug profiler on the PDA allows the physician to view a graphic representation of each patient's prescription medication(s) for the prior 12 months, including drugs prescribed by other physicians via access to linked data from the provincial health database. The PDA alert system also flags drug interactions, therapeutic duplications, contraindications for specific allergies or diseases and verifies drug dosage against the base of continually updated evidence for these variables. A specific message is automatically generated on the PDA providing a summary of the situation and allowing the physician to respond in an autonomous manner. The physician's response to the alert is also captured in the system.

The MOXXI approach to assessing prescription-associated errors has been undergoing pilot testing in representative communities of care. One project was carried out in the West Island area of Montreal and involved 28 community physicians, 32 community pharmacies and approximately 12,500 patients between June 2003 and February 2004. The primary purpose was to gain an overview of the prevalence of prescribing problems, by type of prescribing error and disease and therapeutic category, in a large community care setting. A subsid-

iary purpose was to develop a sense of the clinical relevance of such data, particularly as it was used by physicians to alter their decision making. The early findings of this project are summarized below.

WHERE WE ARE NOW

During a nine-month period, a total of 6,428 alerts were generated by 22,419 prescriptions, an overall alert rate of 29%. The overall revision rate (prescriptions revised on the basis of alert information received) on the alerted prescriptions was 14%. Six categories of potential error or inappropriateness accounted for 99% of the alerts. They were: drug-disease contraindication; drug duplication; drug-drug interaction; toxicity; dosing error; and age-related contraindications, displayed in **Table 1**. Drug-disease contraindications generated the greatest number of alerts; dosing errors, the least. However, dosing errors drove the highest rate of prescription revisions, 23%. Interestingly, age-related alerts were both infrequent and low drivers of revision.

The most prevalent drug classes associated with alert generation for each of the prescribing error categories are displayed in **Table 2**. Antidepressants were the most frequently involved class of drugs, accounting for 13% of all alerts and making the top three list of prevalence in five of the six alert categories (Table 2). A close second was the nonsteroidal anti-inflammatory drug class (NSAIDs), underlying 12% of all alerts and making the top three list for three alert categories.

In the drug-disease contraindication alert category, the top three medication classes (NSAIDs, thyroid replacements and antidepressants) generated 47% of all the alerts. Thirty percent of the alerts were triggered by a contraindication due to the presence of asthma, while 66% were associated with underlying hypertension. The presence of cardiovascular disorders was associated with 99% of the alerts for thyroid replacement therapy. Likewise, 82% of the warning messages that physicians received for antidepressant medication flagged a possible contraindication due to the presence of a cardiovascular disorder.

HMG-CoA reductase inhibitors led the drug-drug interaction category of alerts, the majority flagged because of concern over concomitant use with calcium channel blockers (47%). In the case of beta-blockers, 17% of the drug-drug interaction alerts involved potentially negative interaction with an antidepressant medication, while 14% involved an alpha or beta agonist. Insulin was implicated in 29% of the interactions with an NSAID, with sulfonylurea agents involved in 26%.

Potential toxicity was principally associated with

antidepressant therapy, alerts warning of potential arrhythmias in 69% of the cases and of sedation in 31%. ACE inhibitors were associated with the potential for hyperkalemia in all cases, while benzodiazepines generated a warning of potential sedation in all cases. Antidepressants and benzodiazepines accounted for 58% of potentially inappropriate prescriptions among the older age patients.

Table 1. Prescription Alerts Generated and Revised, by Prescribing Error Category

Alert Category	Alerts Generated (n)	Alerts Revised	
		(n)	(%)
Drug Disease Contraindiction	2644	376	14
Drug-Drug Interactions	1522	207	14
Potential Toxicity	1022	137	13
Drug Duplication	731	120	16
Contraindicated for Patient Age	249	21	8
Potential Dosing Error	221	50	23
Other	39	8	21
Total	**6428**	**919**	**14**

Table 2. Most Prevalent Therapeutic Classes, by Alert Category

Alert Category	Top Three Therapeutic Medication Classes	Alerts Generated	
		(n)	(%)
Drug-Disease Contraindication	Antidepressants	225	9
	NSAIDs	192	7
	Thyroid Replacements	122	5
Drug-Drug Interactions	Beta-Blockers	81	5
	HMG CoA Reductase Inhibitors	77	5
	NSAIDs	65	4
Potential Toxicity	Antidepressants	314	31
	ACE Inhibitors	150	15
	Benzodiazepines	96	9
Drug Duplication	Antidepressants	136	19
	NSAIDs	128	18
	HMG CoA Reductase Inhibitors	56	8
Contraindicated for Patient Age	Antidepressants	13	5
	Benzodiazepines	6	2
	Thyroid Replacements	5	2
Potential Dosing Error	Antidepressants	33	15
	Restricted Medications*	24	11
	Thyroid Replacements	21	10

* Medication requiring physician pre-authorization

Potential dosing errors resulted in messages that alerted the prescribing physician that an initially prescribed medication dose was either too high or too low. All alerts associated with antidepressants and thyroid agents suggested too-high doses, while medications that required prior authorization by the prescribing physician warned of doses being too low.

THE VIEW GOING FORWARD

In summary, automated online medication screening and risk alerting appears to have significant potential to reduce inappropriate prescribing practices and improve patient outcomes.

The MOXXI III evidence-based system used in the community based general practice setting demanded confirmation in prescribers' clinical decision making for almost one-third of prescriptions and led to changes in ultimate prescribing decisions about 14% of the time, overall, but up to one-quarter of the cases in some prescribing categories; for example, dosing level.

A potential weakness of all current alert systems, however, is that they address only part of the problems facing the prescribing physician in the real-world primary care setting. Each patient presents a unique set of clinical conditions and risks that the physician must incorporate into treatment decisions. For example, antidepressants are among the most frequently dispensed drugs in Canada and the most common alert-generating medication. As well, they are among the four most frequently involved classes of medication implicated in adverse drug events in malpractice claims (Rothschild et al. 2002). Risk of adverse events from antidepressants increases as patient's age and the number of comorbid diseases and associated coprescriptions increase. But in an individual patient all of these factors may be counterbalanced by some other risk-reducing factor, like the patient whose genetically determined drug metabolism is more rapid. Current automatic alert systems are not refined enough to take these patient-specific characteristics into account. If the failure to account for these clinical conditions produces many false positive alerts, physicians will be overloaded with information and be unlikely to respond to true high-risk safety situations. This issue is not easily addressed. Current systems make an effort to reduce false positives by instituting modifiable severity alert levels, as is the case with the MOXXI system. However, these classifications are based on theoretical risk, low-levels of empirical evidence, and fail to consider patient-specific risk profiles.

Thus, what these systems don't do is identify and relay information that allows the physician to assess the balanced level of total risk, and they cannot, at the present time, remove the need for, and value of, clinical judgment. Finding the best criteria for alert threshold that provides a high degree of certainty that a positive alert is truly positive in the sense it truly identifies risk requiring action will require more study and investigation in multiple clinical settings. Nonetheless, the MOXXI III results suggest that the system, even with its current sensitivity and positive predictive value characteristics, may be seen as providing a measure of clinically relevant assistance for prescription decision making and lend itself to widespread adoption in general practice settings with modifications based on further analysis.

Its ultimate determination of clinical relevance to patient safety may, however, have to await the results of other studies, particularly randomized clinical trials, with patient outcomes as the primary measure.

References

Ashworth, M. 2002. "Re: GPs' Views on Computerized Drug Interaction Alerts." *J.Clin. Pharm. Ther.* 27(5): 311–312.

Avery, A. J., A. Sheikh, B. Hurwitz, L. Smeaton, Y. F. Chen, R. Howard, J. Cantrill and S. Royal. 2002. "Safer Medicines Management in Primary Care." *Br. J. Gen. Pract. 52 Suppl.* S17–S22.

Aydin, C. E. and R. E. Rice. 1991. "Social Worlds, Individual-Differences, and Implementation - Predicting Attitudes Toward A Medical Information System." *Information & Management* 20(2): 119–136.

Bates, D. W., M. Cohen, L. L. Leape, J. M. Overhage, M. M. Shabot and T. Sheridan. 2001. "Reducing the Frequency of Errors in Medicine Using Information Technology." *J. Am. Med. Inform. Assoc.* 8(4): 299–308.

Bates, D. W., R. S. Evans, H. Murff, P. D. Stetson, L. Pizziferri and G. Hripcsak. 2003. "Detecting Adverse Events Using Information Technology." *J. Am. Med. Inform. Assoc.* 10(2): 115–128.

Bates, D. W. and A. A. Gawande. 2003. "Improving Safety With Information Technology." *N. Engl. J. Med.* 348(25): 2526–2534.

Bates, D. W., J. M. Teich, J. Lee, D. Seger, G. J. Kuperman, N. Ma'Luf, D. Boyle and L. Leape. 1999. "The Impact of Computerized Physician Order Entry on Medication Error Prevention." *J. Am. Med. Inform. Assoc.* 6(4): 313–321.

Glassman, P. A., B. Simon, P. Belperio and A. Lanto. 2002. "Improving Recognition of Drug Interactions: Benefits and Barriers to Using Automated Drug Alerts." *Med. Care* 40(12): 1161–1171.

Grymonpre, R. E., P. A. Mitenko, D. S. Sitar, F. Y. Aoki and P. R. Montgomery. 1988. "Drug-Associated Hospital Admissions in Older Medical Patients." *Journal of the American Geriatrics Society* 361092–1098.

Gurwitz, J. H., T. S. Field, L. R. Harrold, J. Rothschild, K. Debellis, A. C. Seger, C. Cadoret, L. S. Fish, L. Garber, M. Kelleher and D. W. Bates. 2003. "Incidence and Preventability of Adverse Drug Events Among Older Persons in the Ambulatory Setting." *JAMA* 289(9): 1107–1116.

Hazlet, T. K., T. A. Lee, P. D. Hansten and J. R. Horn. 2001. "Performance of Community Pharmacy Drug Interaction Software." *J. Am. Pharm. Assoc.* (Wash.) 41(2): 200–204.

Hsieh, T. C., G. J. Kuperman, T. Jaggi, P. Hojnowski-Diaz, J. Fiskio, D. H. Williams, D. W. Bates and T. K. Gandhi. 2004. "Characteristics and Consequences of Drug Allergy Alert Overrides in a Computerized Physician Order Entry System." *J. Am. Med. Inform. Assoc.* 11(6): 482–491.

Hurwitz, N. 1969. "Predisposing Factors in Adverse Reactions to Drugs." *British Medical Journal:* 1536–539.

Ives, T. J., E. J. Bentz and R. E. Gwyther. 1987. "Drug-Related Admissions to a Family Medicine Inpatient Service." *Arch. Intern. Med* 147(6): 1117–1120.

Kaushal, R. and D. W. Bates. 2002. "Information Technology and Medication Safety: What Is the Benefit?" *Qual. Saf Health Care* 11(3): 261–265.

Lazarou, J., B. H. Pomeranz and P. N. Corey. 1998. "Incidence of Adverse Drug Reactions in Hospitalized Patients: a Meta-Analysis of Prospective Studies." *JAMA* 279(15): 1200–1205.

Magnus, D., S. Rodgers and A. J. Avery. 2002. "GPs' Views on Computerized Drug Interaction Alerts: Questionnaire Survey." *J. Clin. Pharm. Ther.* 27(5): 377–382.

May, F. E., R. B. Stewart and L. E. Cluff. 1977. "Drug Interactions and Multiple Drug Administration." *Clinical Pharmacology and Therapeutics:* 22322.

Monane, M., D. M. Matthias, B. A. Nagle and M. A. Kelly. 1998. "Improving Prescribing Patterns for the Elderly Through an Online Drug Utilization Review Intervention: a System Linking the Physician, Pharmacist, and Computer." *JAMA* 280(14): 1249–1252.

Oren, E., E. R. Shaffer and B. J. Guglielmo. 2003. "Impact of Emerging Technologies on Medication Errors and Adverse Drug Events." *Am. J. Health Syst. Pharm.* 60(14): 1447–1458.

Rothschild, J. M., F. A. Federico, T. K. Gandhi, R. Kaushal, D. H. Williams and D. W. Bates. 2002. "Analysis of Medication-Related Malpractice Claims: Causes, Preventability, and Costs." *Arch. Intern. Med.* 162(21): 2414–2420.

Tamblyn, R., A. Huang, R. Perreault, A. Jacques, D. Roy, J. Hanley, P. McLeod and R. Laprise. 2003. "The Medical Office of the 21st Century (MOXXI): Effectiveness of Computerized Decision-Making Support in Reducing Inappropriate Prescribing in Primary Care." *CMAJ.* 169(6): 549–556.

About the Authors

Laurel K. Taylor, PhD, is a Postdoctoral Fellow in the Department of Medicine, McGill University, QC.

Yuko Kawasumi, MSc, is a PhD Candidate in the Department of Epidemiology and Biostatistics, McGill University, QC.

Gillian Bartlett, PhD, is an Assistant Professor in the Department of Medicine and an FRSQ funded Chercheur-Boursier.

Robyn Tamblyn, PhD, is a Professor in the Department of Medicine and the Department of Epidemiology and Biostatistics at McGill University, Faculty of Medicine. She is a Canadian Institutes of Health Research (CIHR) scientist and a McGill University William-Dawson scholar. She also holds a position as Medical Scientist at the McGill University Health Center Research Institute.

Corresponding Author: Laurel K. Taylor, PhD, Clinical and Health Informatics Research Group, McGill University, 1140 Pine Avenue West, Montreal, Quebec, H3A 1A3, Canada., Tel: (514) 934-1934 ext. 32968; Fax: (514) 843-1551; Email: laurel.taylor@mcgill.ca