

The effect of pharmacist-led medication review in high-risk patients in the emergency department: an evaluation protocol

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Abstract

Background: Adverse drug events are unintended and harmful events related to medication use. They are a leading cause of visits to the emergency department, unplanned admissions to hospital and death. Adverse drug events can be misdiagnosed in the emergency department, resulting in treatment delays. Our objective was to describe a process to evaluate the effect of pharmacist-led medication review in high-risk patients in the emergency department on the number of days these patients subsequently spent in hospital within 30 days of their index visit.

Methods: We describe the evaluation of a prospective multicentre quality improvement program. During the evaluation period, triage nurses will flag incoming patients to the emergency department at high risk for adverse drug events by applying a clinical decision rule consisting of 4 variables (comorbid conditions, antibiotic use within 7 days, medication changes within 28 days and age). Consecutive eligible patients will be enrolled in the study and systematically allocated to either a pharmacist-led medication review group or a control group. In the intervention group, pharmacists will collect best-possible medication histories, review the patient's medications for appropriateness and adverse drug events, and communicate the results of their medication review to patients, caregivers and physicians. In the control group, nurses will start medication reconciliation by collecting best-possible medication histories, and physicians will refer patients to onsite pharmacists for specific medication management questions as needed. Health outcomes will be assessed using anonymized data linkage to administrative health databases. The primary outcome will be the percent days spent in hospital over a 30-day period.

Interpretation: This protocol describes the methods for evaluating the effect of pharmacist-led medication review in high-risk patients in the emergency department on use of health services, and highlights the methodological challenges that will be encountered. We plan to disseminate the results of this evaluation through articles published in peer-reviewed journals, presentations at scientific meetings and briefing notes to institutional, provincial and national stakeholders.

Prescription and over-the-counter medications make up the second-largest category of health care spending in Canada and incurred direct costs of \$31 billion in 2010.¹ Additional indirect costs occur when patients have adverse drug events — unintended and harmful effects of medications.² Adverse drug events reduce the treatment benefit of medications, increase drug therapy costs and are a leading cause of ambulatory care visits, emergency department presentations, hospital admissions and death.³⁻¹⁰ Unfortunately, physicians do not attribute the symptoms of adverse drug events to medication use in as many as 40% of emergency department presentations, which results in missed diagnoses and delays in treatment.^{11,12}

Medication review is a structured critical examination of a patient's medications that is usually done by a pharmacist or a physician. Medication review entails obtaining an accurate medication history, reaching agreement with the patient about the goals of treatment, reviewing the medications to optimize

their effectiveness, and identifying and addressing medication-related problems including any adverse drug events.¹³ Research trials to evaluate the effect of pharmacist-led medication review among patients in hospital are limited in number; to the best of our knowledge, none have been conducted in the setting of the emergency department.¹⁴

In Canada, many acute care institutions have implemented medication reconciliation — an intervention to reduce medication errors and adverse drug events resulting from inaccurate medication information at care transitions.^{15,16} As implemented

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in Canada, medication reconciliation is generally initiated by nurses with minimal involvement of pharmacists and focuses on improving the accuracy of the patient's medication history. However, a recent systematic review of hospital-based medication reconciliation practices failed to identify an effect on patient-oriented outcomes, except when the intervention targeted high-risk patients and was performed by pharmacists who also assessed medications for appropriateness and adverse drug events — features associated with medication review.¹³

Our aim is to describe the evaluation of the effect of pharmacist-led medication review compared with nurse- or physician-led medication reconciliation on use of health services in a cohort of high-risk patients in the emergency department who are enrolled in a quality improvement program. We hypothesize that pharmacist-led medication review will decrease the downstream use of health services by reducing misdiagnosed adverse drug events and by contributing to earlier and more appropriate drug therapy.

Methods

Design

This protocol describes the evaluation of a prospective multi-centre quality improvement program in which pharmacist-led medication review was implemented for high-risk patients in the emergency department. The Adverse Drug Event Screen-

ing Program is a quality-improvement program that aims to reduce the number of missed adverse drug events in emergency departments and ensure early appropriate drug therapy by expanding access to pharmacist-led medication review. Within this program, triage nurses identify patients at high-risk for adverse drug events using a clinical decision rule that classifies patients into high- and low-risk groups based on their comorbid conditions, recent medication changes, antibiotic use and age (Figure 1).¹⁷ Clinical pharmacists (subsequently termed “medication review pharmacists”) review the medications of patients deemed high-risk and recommend changes in drug therapy.

Setting

The program was implemented in consecutive 6- to 8-week pilot phases at each site in 3 British Columbian emergency departments, including 1 tertiary care referral centre (Vancouver General Hospital) and 2 urban community hospitals (Lions Gate Hospital and Richmond General Hospital). After the initial pilot phase, a 12-month evaluation period began at each site between November 2011 and February 2013. These departments have a combined annual census of 185 000 patient visits. Before the implementation of the program, the emergency departments had limited clinical pharmacist manpower, which was available only on weekdays during business hours, and most patients did not receive medication review. Given

ADVERSE DRUG EVENT CLINICAL DECISION RULE	
Have you taken any medications in the past 2 weeks?	
<input type="checkbox"/> Yes <input type="checkbox"/> No →	Enter Low Risk into PCIS → STOP
↓	
Do you either:	
Have any pre-existing medical problems? OR	
Have you taken antibiotics in the past 7 days?	
<input type="checkbox"/> Yes <input type="checkbox"/> No →	Enter Low Risk into PCIS → STOP
↓	
Are you 80 years or older? OR	
Have you stopped, started or changed any of your medications in the past 28 days?	
<input type="checkbox"/> Yes <input type="checkbox"/> No →	Enter Low Risk into PCIS → STOP
↓	
	Enter High Risk into PCIS
Medications: _____	

Figure 1: The modified adverse drug event clinical decision rule used to identify patients at high-risk for adverse drug events in the emergency department.¹⁷ After consultation with nursing managers and triage nurses, we modified the rule by incorporating the most important inclusion criterion for its application, medication use within 2 weeks, into the algorithm. PCIS = patient care information system.

the dual standard of existing pharmacy care, and the limited resources available through the program that would allow for an estimated 30% of high-risk patients to receive medication review, we deemed it ethical to create a control group for the purposes of evaluation. The University of British Columbia Clinical Research Ethics Board deemed our protocol to be an evaluation of quality improvement and waived the need for informed consent.

Participants

During the evaluation period, triage nurses classified all incoming patients to the emergency department as being at high or low risk for adverse drug events using a clinical decision rule implemented into existing triage algorithms (Figure 1). Consecutive high-risk patients aged 19 years or older who presented when a medication review pharmacist was on duty were eligible for enrolment. During the first month of implementation and after triage nurses started flagging incoming patients as high or low risk for adverse drug events, we identified the highest volume times of the day and days of the week, and scheduled medication review pharmacists based on those data. Pharmacist coverage was expanded from 0 hours to 8 hours per day on weekends and holidays at all sites, and from a baseline of 8 hours up to 12 hours (2 sites) and 16 hours per day (1 site) on weekdays. We allowed pharmacist coverage to fluctuate by time of day and day of the week to maximize coverage (providing double and triple coverage) during the busiest hours and days of the weeks (e.g., Monday evenings), while not providing any coverage during consistently low volume hours and days of the week (e.g., Thursday nights). We excluded patients with a Canadian Triage Acuity Score (CTAS) of 1, because they required immediate resuscitation,¹⁸ as well as those presenting for multisystem trauma (e.g., penetrating trauma), scheduled visits (e.g., for intravenous administration of antibiotics), sexual assaults, postsurgical or pregnancy-related complications or social problems (e.g., those presenting for homelessness or failure to cope with no acute medical problem), and those for whom we could not link data to administrative records (e.g., out-of-province patients).

Study enrolment and group allocation

Given the aim of the quality improvement program to expand access to medication review without providing sufficient resources to offer it to all patients, we designed a patient enrolment and allocation algorithm that enabled pharmacists to complete as many interventions as possible while creating 2 comparable groups of patients. Three factors created a variable rather than fixed demand for medication review interventions: (i) a variable influx of high-risk patients into emergency departments; (ii) a constant pressure to discharge patients that created an egress of lower-acuity patients, sometimes while medication review was ongoing and (iii) a variable amount of time required to complete the intervention. Given a fixed number of available pharmacists, these factors created a random availability of pharmacists at any given point in time.

Medication review pharmacists started their shifts by sorting the emergency department census by the time of patient

arrival to identify the number and sequence of patients presenting within the past hour (Figure 2). We assumed that the sequence of patient presentation to emergency departments within any 1-hour period was random, and that a 1-hour delay from patient arrival to study enrolment would allow for the registration and triage process. While blinded to patient characteristics, the medication review pharmacist counted the number of high-risk patients available for enrolment who presented within the past hour and estimated the ratio of patients for whom they would be able to complete the intervention to the number of patients they would not have the

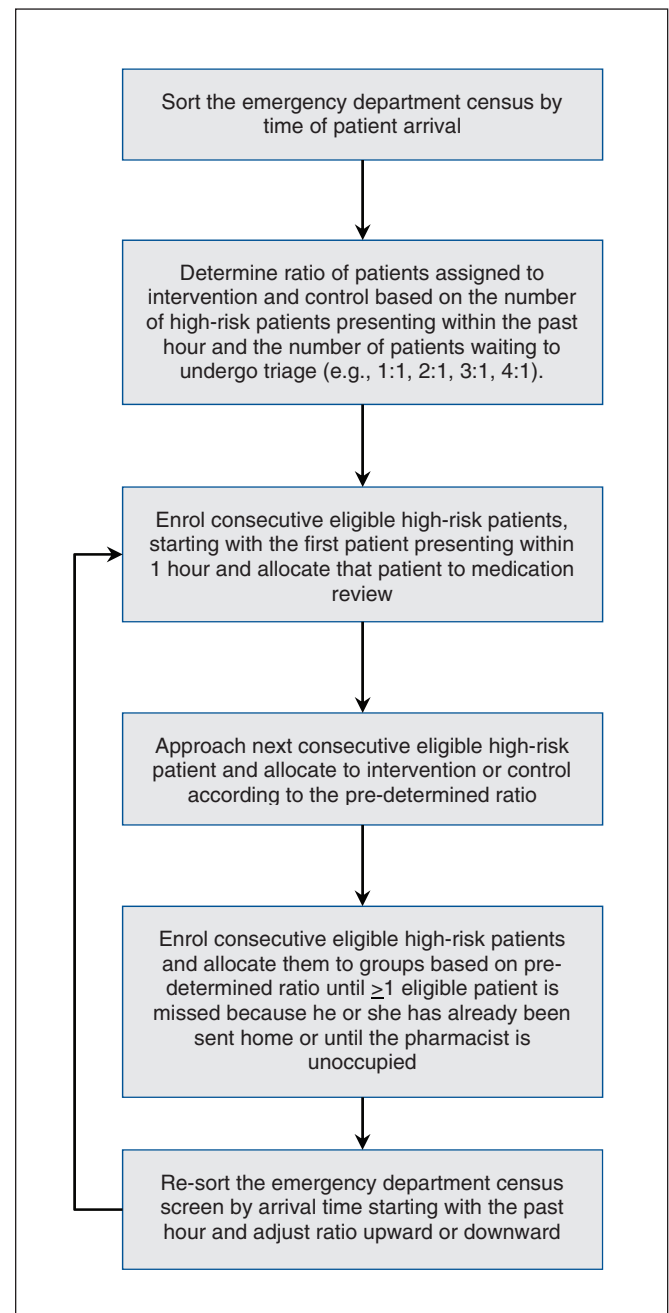


Figure 2: Algorithm used to systematically allocate emergency department patients to medication review or control.

time to see and designated as control. We allowed pharmacists to determine this ratio at the start of their shift, varying it from 1:1 to 4:1. The medication review pharmacist then approached consecutive eligible patients, starting with the first patient who presented within the past hour, and assigned consecutive eligible patients to the intervention or control arm according to the predefined ratio. The pharmacist adjusted the ratio as soon as more than one consecutive high-risk eligible patient had left the emergency department before being enrolled, to ensure that the number of missed eligible patients is minimized.

This algorithm enabled us to avoid the development of queues, thereby minimizing the selection bias that would have occurred if patients who were less sick were preferentially discharged from the medication review group, and limiting the number of incomplete interventions. The predictable sequence of allocation optimized the workflow of pharmacists, allowing them to follow-up with patients (e.g., access results from laboratory investigations and diagnostic tests) during intervals when patients in the control group were enrolled.

Intervention

Pharmacist-led medication review was defined as a structured, critical examination of a patient's medications with the objective of reaching agreement with the patient about treatment, optimizing the medications' effect and minimizing the number of medication-related problems and adverse drug events.¹⁹ Patients' medication histories were prepopulated with the data from PharmaNet, British Columbia's outpatient medication dispensing database (Figure 3). The medication history was confirmed with the patient, caregivers or outpatient care providers. The medication review pharmacist then conferred with the patient about the goals of drug therapy and reviewed the medications for appropriateness and adverse events. Medication review pharmacists had access to hospital records and results from laboratory investigations and diagnostic tests; they reviewed all suspected adverse drug events that required treatment in person or over the phone with emergency or admitting physicians and documented such events in patient charts. For nonurgent events, pharmacists documented in charts and sent notes to family physicians (Figure 4). Pharmacists carried a pager and responded to emails and could be contacted by physicians through either means.

Medication review pharmacists were residency-trained clinical pharmacists with a minimum of 2 years' experience in acute care hospitals. A total of about 30 trained pharmacists participated in the evaluation. They were oriented in a 2-week training and pilot period. They worked 20%–30% of their time in the emergency department during data collection shifts scheduled between 8 am and midnight, and the remainder of their hours were spent in other acute care areas.

Control

Patients in the control arm received nurse-led medication reconciliation using electronic forms that were prepopulated with the patient's outpatient medication record in PharmaNet (Figure 3). Patients in the control group only underwent assess-

ment by the emergency department pharmacist if they presented on weekdays during business hours and the emergency physician requested a consultation for specific medication management questions (e.g., antibiotic dosing in renal failure).

Evaluation

Outcome measures

We will assess the effect of medication review on subsequent health care use. Our primary outcome will be the percentage of days spent in hospital during the first 30 days after the index visit to the emergency department. We will follow patients for 30 days, because medication review in the emergency department is unlikely to influence admissions lasting more than 30 days, which typically result from intercurrent illness, prolonged disability and the need to wait for rehabilitation or long-term care. Secondary outcomes will include the number of patients whose time spent in hospital exceeds the expected length of stay within 30 days in addition to 3 outcomes determined during follow-up: unplanned visits to the emergency department within 7 days (defined as any unplanned visit unrelated to trauma, sexual assault, a postoperative or pregnancy-related complication or social problem), unplanned readmission (defined as any admission that occurs through the emergency department and is unrelated to trauma, sexual assault, a postoperative or pregnancy-related complication or social problem) and death from any cause. All study outcomes will be determined through patient-level anonymized linkages with administrative databases (Hospital Separations, Medical Services Plan Billing, Vital Statistics, Client Registry and PharmaNet) and will be collected without any knowledge about patients' group assignments. These data provide a uniform source of events that are reliably captured in all hospitals in British Columbia and are considered complete.

Confounding

Although we used a systematic patient-selection algorithm to generate comparable groups of patients, we will account for the possibility of imbalances between the groups at the analytical stage. We will use inverse probability-weighted propensity scores to balance patient characteristics between groups using the pretreatment variables age, sex, Canadian Triage and Acuity Scale score (proxy for acuity), the first 3 digits of the patient's postal code (proxy for socioeconomic status), and the number of active medications (proxy for comorbidity and health care access).^{20,21}

Sample size

During our pilot phase, the average percentage of days spent in hospital during the first 30 days after the index visit was 34% among high-risk patients (standard deviation 30%). The sampling distribution of this proportion is normal if sample size (N) is large and the true proportion (p) is not close to 0 or 1. The normal approximation is relevant if both Np and $N(1 - p)$ are greater than 10. We will require 2102 patients per group to detect a 3% difference in the mean percentage of days spent in hospital during the follow-up period (corresponds to 1 hospital day) with 90% power at a 2-sided 5% significance level.



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Figure 3: Forms used by clinical pharmacists to document best-possible medication histories.

Statistical analyses

We will summarize categorical variables using frequency distributions, and continuous variables using means with standard deviations or medians with interquartile ranges. We will

use linear regression to estimate the association between medication review and the primary outcome, as well as logistic regression to estimate the association between medication review and prolonged stay using patients who did not undergo



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Addressograph

Date: _____
 To: _____
 Phone: _____
 Fax: _____
 Number of pages including cover: _____

Dear Dr. _____

Your patient was seen by a pharmacist in our Emergency Department today as part of a regional adverse drug event screening program that has been implemented at Vancouver General Hospital.

We have identified medication-related problem(s) involving:

Please see the attached “ADE Screening Pharmacist – re: adverse drug event” section for more information.

Please do not hesitate to contact our team for further information. We also welcome your comment or feedback.

Our team can be reached as follows:
 Pharmacist: _____
 Pager: 604-632-0546
 Email: VGHADEPharmacist@vch.ca

Thank you for your attention to this matter.

Sincerely,
The ED Adverse Drug Event Screening Team

This report is for information purposes only, and does not imply error.

Figure 4: Template used for communication with community-based care providers.

medication review as the reference group. We will use Poisson regression to estimate the association between medication review and all other secondary outcomes using time to occurrence of the outcome or the end of follow-up as the time at risk. We will apply weighting by inverse propensity scores to each observation entered into the regression analysis to balance patient and access-management characteristics in the study groups. The propensity score estimates the probability of being sampled in the intervention group according to these characteristics. We will conduct subgroup analyses for patients less than 80 years of age, patients aged 80 years and older, and by hospital site.

Interpretation

The implementation of a quality improvement program in the Vancouver Coastal Health Authority provides a unique opportunity to design the evaluation of medication review in high-risk patients in the emergency department. This process will address a gap in the evidence base on the effect of in-hospital medication review on health care use and will show how health services research methods may be applied to minimize bias in evaluating a quality improvement program.

Several studies have evaluated the effect of home-based medication review on patient outcomes; however, few studies have evaluated its effect in-hospital.¹⁹ Most studies enrolled small numbers of patients, were not blinded and used pharmacists with variable levels of training and clinical experience to conduct the interventions.²² We are not aware of any studies conducted in the emergency department setting. In previous studies, medication review was conducted on weekdays during business hours after patients were admitted to wards, which led to treatment delays for patients with nonelective admissions.^{19,22} Finally, patients in the control groups did not have their medications reconciled according to the standard of care in Canadian acute care hospitals.²³

In contrast to previous studies, we plan to evaluate the effect of in-hospital medication review in high-risk patients in the emergency department, allowing for the control group to receive medication reconciliation in the emergency department as part of standard care, with medication review by a clinical pharmacist in the control group only after the patient is admitted to a ward. Delivering the intervention in the emergency department has the benefit of identifying patients with otherwise unrecognized adverse drug events (estimated at 40%–50% of cases) who might be discharged.^{11,12} Medication review before emergency department discharge may become standard care for high-risk patients if it is shown to be clinically effective and economical.

Limitations

Medication review is a complex medical intervention that involves multiple stakeholders and encompasses elements of communication, interprofessional collaboration and workflow changes that we cannot capture. Our study cannot estimate any unintended effects that medication review may have on the upstream provision of care (e.g., by changing referral patterns

as a result of the new program), on downstream care (e.g., by reducing the need for ward-based pharmacists) or in low-risk patients (e.g., by reducing pharmacists available for these patients).

Defining appropriate outcome measures for medication review is difficult. The intervention is expected to add diagnostic information about adverse drug events, which will result in changes to drug therapy.²⁴ We expect the treatment effect to be most pronounced in patients whose adverse drug events would be missed by physicians.^{11,12} Although we would ideally capture the treatment effect in these patients, it is impossible to identify undiagnosed adverse drug events in control patients without conducting medication review, and unethical to not treat adverse drug events once diagnosed. Thus, we will compare high-risk patient groups in which the events are concentrated to improve the signal-to-noise ratio. Lack of reliable identification of adverse drug events within administrative data and within medical charts precludes accurate measures of adverse drug event–related emergency department revisits or hospitalizations.²⁵ Future work is needed in these areas to improve our understanding of adverse drug event epidemiology and our ability to measure medication review's effect.

Our proposed method of systematically allocating patients to groups to minimize selection bias falls short of that used in randomized trials to ensure balance between treatment groups. Although we will use statistical methods to minimize any baseline imbalances we see between groups, residual and unknown confounding may nonetheless bias the treatment effect.

It is possible that contamination between the control and intervention groups may occur as physicians, pharmacists and nurses practising at the study sites may be influenced by the ongoing quality improvement program and may incorporate aspects of medication review into their practice. This would make it more difficult to find differences between groups. Finally, we will not be able to adjust for medication review interventions that may be done after patients leave the emergency department (e.g., by ward pharmacists), as these types of interventions are not documented within administrative data.

Conclusion

In summary, we propose to evaluate the effect of medication review in high-risk emergency department patients and have proposed methods to address the challenge of selection bias created by a constant influx and egress of eligible patients from the study population. We provide an example of designing an evaluation nested within an existing quality improvement program. We plan to disseminate the results of this evaluation through articles in peer-reviewed journals, presentations at scientific meetings and briefing notes to institutional, provincial and national stakeholders. The results of this evaluation may support pharmacist manpower distribution within acute care hospitals and guide requirements for future hospital accreditation standards.

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