

Potentially Unintended Discontinuation of Long-term Medication Use After Elective Surgical Procedures

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Background: Transitions between health care settings represent vulnerable periods for medical error. Discontinuation of long-term medication use may occur during discharge from the hospital to the community.

Methods: We performed a population-based, cohort study using administrative records from Ontario, Canada, between April 1, 1997, and September 30, 2002. We studied all residents 66 years and older with continuous use of warfarin, 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins), or β -blocker ophthalmic drops for 1 or more years. Those who had an overnight hospitalization for selected elective surgical procedures were compared with 2 control groups: one that had an ambulatory procedure and one that had no procedures. All groups were assessed for the outcome of failure to renew the prescription within 6 months.

Results: Rates of drug treatment discontinuation after overnight hospitalizations, after ambulatory procedures, and after no procedures were 11.4%, 7.5%, and

4.8%, respectively, in the warfarin group; 4.0%, 3.9%, and 3.9%, respectively, in the statin group; and 8.4%, 8.9%, and 7.9%, respectively, in the ophthalmic drops group. The adjusted odds ratio (OR) was 2.6 (95% confidence interval [CI], 2.0-3.4) for discontinuation of warfarin therapy after overnight hospitalizations and 1.6 (95% CI, 1.4-1.7) after ambulatory procedures. In contrast, there was no increased risk of discontinuing treatment with either statins (OR for overnight hospitalization, 1.0 [95% CI, 0.9-1.2]; OR for ambulatory procedure, 1.0 [95% CI, 1.0-1.1]) or ophthalmic drops (OR for overnight hospitalization, 1.0 [95% CI, 0.8-1.5]; OR for ambulatory procedure, 1.1 [95% CI, 1.0-1.2]).

Conclusions: Patients prescribed long-term therapy with warfarin were at risk for potentially unintended medication discontinuation after elective procedures. Patients prescribed statins or β -blocker ophthalmic drops were not at increased risk.

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PATIENTS ARE VULNERABLE TO medical error during transitions between health care settings.¹⁻⁷ During these transitions, failure to communicate important information and to reconcile admission and discharge medications may result in adverse events.⁷ So-called errors of omission or failure to provide indicated treatment have also been identified as a threat to patient safety during care transitions.⁸ However, little is known about a specific omission error—the potentially unintended discontinuation of long-term medication use—that may place an individual at risk for preventable adverse events.⁹

Older adults may be particularly susceptible to long-term medication errors during care transitions.^{10,11} The elderly have a high burden of chronic illness: most individuals 65 years and older have 2 or more chronic conditions and use 3 or more prescription drugs yearly.^{12,13} In addition, elderly adults often receive care from

multiple providers in numerous care settings.¹⁴ This fragmentation can impair care coordination and lead to poor quality care.¹⁵

We sought to determine whether potentially unintended discontinuation of long-term medication use occurs after elective surgery. We examined continuity of care and patient safety in seniors, who are at highest risk for adverse drug events.

METHODS

STUDY OVERVIEW

This study used population-based administrative data for all 1.3 million residents of Ontario, Canada, aged 66 years and older, to select those with at least 1 year of continuous use of warfarin, 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor (statins), or β -blocker ophthalmic drops. Those who had an overnight hospitalization for elective surgical procedures were compared with 2 control groups: one that had an ambulatory

Table 1. Surgery and Procedure Codes³³

Procedure	CCP Code Number	OHIP Code	Database
Transurethral prostate resection	72.1	...	DAD
Hysterectomy	80.2, 80.3, 80.4	...	DAD
Total knee replacement	93.41	...	DAD
Total hip replacement	93.5	...	DAD
Lens extraction	27.4, 27.5, 27.6	E140	DAD + OHIP
Inguinal hernia repair	65.0, 65.1, 65.2, 65.3	S323	DAD + OHIP
Cholecystectomy	63.12, 63.14	S287	DAD + OHIP
Cystoscopy	01.34	Z606	DAD + OHIP
Colonoscopy	01.2	E747	DAD + OHIP
Esophagogastroduodenoscopy	01.1	Z399	DAD + OHIP

Abbreviations: CCP, Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures; DAD, Hospital Discharge Abstract Database; OHIP, Ontario Health Insurance Plan physician-billing database.

(same-day) procedure and one that had neither an ambulatory procedure nor an overnight hospitalization and surgical procedure. All 3 groups were assessed for the outcome of drug discontinuation within 6 months after discharge following the procedure. The study was approved by the ethics committee of the Sunnybrook Health Sciences Centre. We used protocols of the Institute for Clinical Evaluative Sciences in Ontario to maintain data confidentiality.

SETTING AND DATABASES

We conducted a retrospective cohort study of multiple health databases in Ontario between April 1, 1997, and September 30, 2002. Data on individuals from 4 separate databases were linked using an encrypted unique identifier. The Ontario Drug Benefit (ODB) database records data on all prescription medications dispensed to patients older than 65 years.¹⁶ The Canadian Institute for Health Information Discharge Abstract Database (DAD) contains information on all hospitalizations and procedures in Ontario hospitals. There is excellent agreement between administrative hospitalization data and chart audit.¹⁷ The Ontario Health Insurance Plan physician-billing database (OHIP) records information on physician services, including procedures and surgical procedures. The Registered Persons Database contains demographic and vital status information for each patient in Ontario. There is little basic information missing in these databases.¹⁷ Analyses are considered population-based because of the comprehensive nature of universal health insurance in Ontario.

PATIENTS AND MEDICATIONS

To allow ascertainment of a full year of prior use, all community-dwelling patients 66 years and older who were prescribed warfarin, statins, or ophthalmic drops continuously for 1 or more years, as identified through the ODB, were included. The "day supply" variable allowed us to estimate the intended duration of each prescription. A 100-day supply is the maximum allowable quantity of drug that can be dispensed. If subjects were dispensed a drug prior to the end of the day supply period, the excess drug supply was carried over to the next prescription's day supply estimation. Subjects were allowed a 150% grace period on the previous day supply to refill the next prescription. For the warfarin analysis, a 200% grace period was allowed to account for possible alterations in dose due to laboratory monitoring. For example, a patient given a 30-day statin prescription would have 45 days to refill the prescription to be considered "continuously" exposed, and a patient given a 30-day

warfarin prescription would have 60 days to obtain a refill. If patients did not refill their prescription for the study drug within these successive time windows, they were not considered continuous users.

We selected the long-term medications in this study because they are commonly prescribed for the elderly and represent medications in which adherence has been estimated in large populations of seniors.¹⁸⁻²³ Also, the medications have established records of long-term efficacy.²⁴⁻²⁷ Moreover, the use of each medication drew on different aspects of our conceptual framework.^{28,29} Patients taking warfarin usually require active discontinuation of the drug prior to surgery because of increased bleeding risk.^{30,31} Failure to continue therapy with warfarin after hospital discharge therefore represents a failure to restart therapy with the medication after an intentional discontinuation. In contrast, statins do not require discontinuation prior to surgery.³² Thus, failure to continue therapy with a statin after hospital discharge represents a failure to continue therapy with the medication. Ophthalmic drops represent a different group of medications that are largely managed (initiated and doses modified) by ophthalmologists, who are generally not actively involved in the hospital care of patients admitted for nonophthalmologic procedures. We included this group as a control and did not anticipate observing differences in adherence because the therapy is not systemic and hospital-based physicians do not typically focus on these medications.

EXPOSURES

In each of the 3 medication-based cohorts (warfarin, statins, and ophthalmologic drops), we identified 3 groups of patients: those who had an overnight hospitalization for an elective surgical procedure, those who had a same-day surgical procedure, and those who had neither an overnight hospitalization nor a same-day surgical procedure. We studied both inpatient and ambulatory procedures to separate the effect of hospitalization from the procedure itself. During hospitalization, prescribed medications are usually provided to the patient. For outpatient procedures, medication continuity is generally the responsibility of the patient. The third group provided an estimate of the baseline rate of medication discontinuation.

The overnight hospitalization group comprised patients who had 1 of 4 elective surgical procedures: transurethral resection of the prostate, hysterectomy, total knee replacement, and total hip replacement (**Table 1**). We selected these elective surgical procedures because they are performed commonly in seniors and involve diverse specialties. We excluded surgical procedures with complications (such as myocardial infarction, stroke, or major hemorrhage) or prolonged lengths of stay (>10 days) to avoid

situations in which the discontinuation of the medication may have been intentional. The same-day procedure group comprised patients who had uncomplicated outpatient procedures not requiring overnight hospitalization. These included intraocular lens extraction, inguinal hernia repair, cholecystectomy, cystoscopy, colonoscopy, and esophagogastroduodenoscopy (Table 1). This group also represented diverse providers. Because many of these procedures occur outside the hospital setting, both the hospitalization and physician billings databases were used to identify this group. The third group served as a comparator and included patients who were not hospitalized and did not undergo any of these procedures during the study period. This group was identified with the drug benefit database, and their absence of procedures and hospitalizations was verified with the hospital and physician billings databases.

INDEX DATES

Index dates were chosen for each of the 3 procedure categories. The index date for patients having an overnight hospitalization for elective surgery was the date of hospital discharge. The index date for patients having same-day procedures was the procedure date. For the group having neither an overnight hospitalization for elective surgery nor a same-day procedure, the index date was randomly assigned from the study period.

EXCLUSIONS

To isolate the effect of the exposure of interest, patients who had any overnight hospitalization or ambulatory procedure in the 6 months prior to or after the index date were excluded. Patients were also excluded if they died within 6 months following the index date or resided in long-term care facilities. Patients could be included more than once in the study.

OUTCOMES

All 3 of our selected drugs are evidence-based therapies used to decrease the risk of adverse outcomes.²⁴⁻²⁷ Therefore, we considered the discontinuation of these medications to represent a potential adverse event. Drug discontinuation, as defined by the absence of any prescription renewals in the drug benefit database within 6 months after the index date, was our primary outcome measure.³⁴ A within-class change of medication (eg, between different types of statins) was not considered an outcome event. Similarly, postoperative changes in medication dose would not be considered an outcome.

COVARIATES

We controlled for confounding factors that might influence drug discontinuation. These patient-level factors included age, sex, low-income status as measured in the drug benefit program to determine copayment, and comorbid disease burden. We used the number of distinct drugs dispensed in the year prior to cohort entry as a measure of comorbidity.^{35,36} Models also included the number of primary care and internal medicine specialist physician contacts subsequent to the index date as a covariate to account for differences in the intensity of ambulatory care and the potential for intentional discontinuation.

STATISTICAL ANALYSIS

Separate analyses were performed for each of the 3 selected medication cohorts. In the primary analysis, we compared the risk of drug discontinuation among (1) patients who had overnight hospitalizations for surgery and (2) patients who had am-

bulatory procedures. The baseline rate was estimated by persons who had neither a hospitalization nor ambulatory procedure. Multivariate logistic regression was used to model the effect of hospitalization for elective surgery on drug discontinuation in each of the 3 medication cohorts and to adjust for the effect of confounding variables. The effects of exposures on the risk of drug discontinuation were expressed as odds ratios (ORs) and 95% confidence intervals (CIs). All reported *P* values are 2-tailed. Statistical analyses were performed with SAS statistical software version 8.2 (SAS Institute Inc, Cary, NC).

SENSITIVITY ANALYSES: WARFARIN

For the cohort of subjects taking warfarin, sensitivity analyses were performed with and without persons having total hip and knee replacements, colonoscopy, cystoscopy, and esophagogastroduodenoscopy because these procedures may affect the decision to continue anticoagulation.

RESULTS

Over the 6-year period, 45 220 persons were included in the warfarin group, 156 172 were included in the statin group, and 32 386 were included in the β -blocker ophthalmic drops group (Table 2). The median age was 77 years (interquartile range [IQR], 73-82 years) in the warfarin group, 74 years (IQR, 71-77 years) in the statin group, and 77 years (IQR, 73-82 years) in the ophthalmic drops group. Just over half of the persons in the warfarin group were men (23 609/45 220 [52%]). Women composed the majority of the statin (85 186 of 156 172 [55%]) and ophthalmic drops (19 618/32 386 [61%]) groups.

The proportion of low-income patients in the groups ranged from about one quarter to one third. Patients in the warfarin group had the most contact with primary care providers and internal medicine specialists in the 6 months subsequent to the index date.

DRUG DISCONTINUATION

In the warfarin group, 11.4% of patients who had an overnight hospitalization for elective surgery experienced the primary outcome compared with 7.5% of patients who had an ambulatory procedure and 4.8% of patients who did not have any procedure. In the statin group, 4.0% of patients who had an overnight hospitalization for elective surgery experienced the primary outcome compared with 3.9% of patients who had an ambulatory procedure and 3.9% of patients who did not have any procedure. In the β -blocker ophthalmic drops group, 8.4% of patients who had an overnight hospitalization for elective surgery experienced the primary outcome compared with 8.9% of patients who had an ambulatory procedure and 7.9% of patients who did not have any procedure.

ADJUSTED ANALYSES

Warfarin

Patients prescribed long-term warfarin therapy who had an overnight hospitalization and surgical procedure had an adjusted OR of 2.6 (95% CI, 2.0-3.4) for the primary outcome. Patients taking warfarin who had an ambula-

Table 2. Characteristics of Patients Continuously Prescribed Warfarin, Statins, and β -Blocker Ophthalmic Drops for More Than 1 Year

Characteristic	Warfarin Group			Statin Group			β -Blocker Ophthalmic Drops Group		
	Overnight Admission Surgery (n = 527)	Outpatient Surgery (n = 17 052)	No Procedure (n = 27 641)	Overnight Admission Surgery (n = 3392)	Outpatient Surgery (n = 57 008)	No procedure (n = 95 772)	Overnight Admission Surgery (n = 466)	Outpatient Surgery (n = 11 716)	No Procedure (n = 20 204)
Age at index date, median (IQR), y	75 (71-79)	77 (73-81)	77 (73-82)	73 (70-76)	73 (70-77)	74 (71-78)	76 (72-80)	77 (73-82)	78 (73-83)
Female sex, No. (%)	241 (46)	7343 (43)	14 027 (51)	2050 (60)	29 035 (51)	54 101 (56)	297 (64)	6674 (57)	12 647 (63)
Low-income status, No. (%)*	121 (23)	4675 (27)	8663 (31)	800 (24)	14 606 (26)	27 925 (29)	106 (23)	3312 (28)	6331 (31)
No. of drugs prescribed in year prior to the index date, median (IQR)	11 (8-14)	12 (8-17)	10 (7-14)	10 (7-14)	10 (7-15)	8 (5-12)	10 (7-13)	10 (7-14)	8 (5-12)
Primary care visits in 6 mo after the index date, median (IQR), No.	10 (6-15)	10 (6-14)	8 (5-13)	5 (3-9)	5 (2-8)	4 (2-6)	5 (3-10)	4 (2-8)	3 (2-6)
Internal medicine and subspecialist visits in 6 mo after the index date, median (IQR), No.	1 (0-3)	2 (0-6)	1 (0-4)	0 (0-2)	1 (0-3)	0 (0-2)	0 (0-1)	1 (0-2)	0 (0-1)
Drug discontinuation, No. (%)	60 (11.2)	1275 (7.5)	1326 (4.8)	136 (4.0)	2198 (3.9)	3713 (3.9)	39 (8.4)	1038 (8.9)	1558 (7.9)

Abbreviation: IQR, interquartile range

*Low-income status was classified as individual income below \$16 018 or couples income below \$24 175

tory procedure had an adjusted OR of 1.6 (95% CI, 1.4-1.7) for the primary outcome (**Table 3**).

Statins and β -Blocker Ophthalmic Drops

Patients prescribed either statins or ophthalmic drops had no increased risk of drug discontinuation with hospitalization for elective surgery or an ambulatory procedure. Patients prescribed long-term statin therapy who had an overnight hospitalization for elective surgery had an adjusted OR of 1.0 (95% CI, 0.9-1.2) for the primary outcome. The adjusted OR was 1.0 (95% CI, 1.0-1.1) for patients who had an ambulatory procedure. Patients prescribed ophthalmic drops who had an overnight hospitalization had an adjusted OR of 1.0 (95% CI, 0.8-1.5) for the primary outcome. The adjusted OR was 1.1 (95% CI, 1.0-1.2) for patients who had an ambulatory procedure (Table 3).

SENSITIVITY ANALYSIS: WARFARIN

When total hip and knee replacements, colonoscopy, cystoscopy, and esophagogastroduodenoscopy were excluded, the adjusted OR for the primary outcome was 2.8 (95% CI, 2.0-3.8) for patients hospitalized overnight and 1.3 (95% CI, 1.2-1.4) for patients who had ambulatory procedures.

COMMENT

We estimated the risk of potentially unintended drug use discontinuation after an overnight hospitalization for elec-

tive surgery or an ambulatory procedure among patients continuously prescribed warfarin, statins, or β -blocker ophthalmic drops. After controlling for confounding factors, patients prescribed warfarin were more than twice as likely to discontinue the drug after an overnight hospitalization for elective surgery and were more than 1½ times more likely to discontinue the drug after an ambulatory procedure compared with the general population. Having a procedure did not affect the risk of potentially unintended discontinuation of either statins or β -blocker ophthalmic drops.

Previous studies suggest that discontinuation of drug use after hospital discharge is common.^{7,37,38} However, these studies focused on changes in drug regimens rather than the discontinuation of long-term medication use. No study followed patients for longer than 1 month to determine if the drug regimens were restarted nor commented on whether the use of the drugs was intentionally discontinued for clinical indications.

Why did patients receiving warfarin have an elevated risk for medication discontinuation while patients receiving statins or ophthalmic drops did not? We believe that this may relate to differences in patients' medication-taking practices. Patients receiving warfarin are usually instructed to discontinue use of the medication prior to procedures because of concern about excessive bleeding.^{30,32,39} Also, there may be a period following the operation or procedure when anticoagulation with warfarin is intentionally not resumed. Restarting anticoagulation therapy then requires active participation of the patient and physician. Further miscommunication may ensue if the physician dis-

Table 3. Multivariate Odds Ratios for Patients Continuously Prescribed Warfarin, Statins, and β -Blocker Eye Drops for More Than 1 Year*

Group†	Unadjusted OR (95% CI)			Adjusted OR (95% CI)*		
	Warfarin Group	Statin Group	β -Blocker Ophthalmic Drops Group	Warfarin Group	Statin Group	β -Blocker Ophthalmic Drops Group
Overnight admission for an elective surgical procedure	2.6 (1.9-3.4)	1.0 (0.9-1.2)	1.1 (0.8-1.5)	2.6 (2.0-3.4)	1.0 (0.9-1.2)	1.0 (0.8-1.5)
Ambulatory procedure	1.6 (1.5-1.7)	1.0 (0.9-1.1)	1.1 (1.0-1.2)	1.6 (1.4-1.7)	1.0 (1.0-1.1)	1.1 (1.0-1.2)

Abbreviations: CI, confidence interval; OR, odds ratio.

*Adjusted for age, sex, patient income, number of prescribed drugs, number of primary care visits, and number of internal medicine and subspecialist visits.

†The referent category for both groups was patients with long-term medication use who had neither an overnight hospitalization nor an ambulatory procedure.

continuing the medication therapy is different from the one expected to reinstitute therapy.⁴⁰ Other medication therapies requiring active discontinuation and restarting in the perioperative period such as antiplatelet agents and other anticoagulants may also pose an elevated risk of discontinuation. In contrast, patients prescribed statins and ophthalmic drops are usually not instructed to discontinue therapy before procedures.³² Still, some of the observed differences may be attributable to specific characteristics of the drug itself rather than to the class it represents. However, the findings for warfarin nevertheless represent an important consideration for patient care.

Multiple factors may contribute to errors of omission. First, a patient's medication regimen may be documented inaccurately before or after hospitalization.⁴¹⁻⁴⁶ Second, patient medications commonly change during hospitalization.^{38,47-49} Third, the hospital record and the discharge prescription conflict for many patients.⁵⁰⁻⁵² Fourth, communication between hospital physicians and primary care providers is often poor.^{53,54} To address this issue, quality improvement initiatives have identified continuity of care as a major threat to patient safety.⁵⁵⁻⁵⁷ Our findings call attention to the need to develop a framework that focuses on the unintended discontinuation of medications during care transitions.^{2,58-62} Initiatives such as the development of electronic medical records and medication reconciliation programs on admission and on discharge or models of care that facilitate communication and coordination between hospital- and community-based physicians may help reduce the risk of unintended drug discontinuation.^{55,57,62-65}

Our work has several limitations. First, we used administrative data that lacked clinical detail such as possible reasons for intended or appropriate medication therapy initiation and discontinuation. However, we do not believe that the observed medication discontinuation was intended. Specifically, the medication therapies we studied are usually long-term and lifelong. To exclude the possibility that patients discontinued medication use because a course of active treatment had been completed (eg, 6 months of warfarin therapy for deep vein thrombosis), we required 1 year of continuous use of the drug. This requirement also minimized any confounding from patient non-adherence. Also, we used a control group without any surgical procedures or hospitalization to estimate the baseline discontinuation risk. Some may contend that the higher

rate of discontinuation among the patients in the overnight hospitalization and elective procedures group could be explained by greater physician attention to the original indication for the drug and hence the drug discontinuation might be intentional. However, we excluded elective surgical procedures that were associated with postoperative complications that may result in intentional drug discontinuation. We also adjusted for internal medicine and primary care consultations. Moreover, we excluded those who were hospitalized for any reason within 6 months of the index date to avoid including patients with active medical issues. Furthermore, a sensitivity analysis that excluded patients with indications for warfarin prophylaxis yielded similar results. Finally, another study using structured implicit and explicit review of clinical data in the intensive care unit setting has also demonstrated the unintended discontinuation of many long-term medication therapies including warfarin, suggesting that our findings are not merely attributable to insufficient clinical detail.⁶⁶

Other limitations include our reliance on administrative data. However, the databases we used are accurate and have been used previously to study medication adherence.^{16,17,23,67} Second, since this was an observational study, the results are susceptible to bias or confounding. However, we took care to ensure the comparability of the patient groups. Our inclusion criteria, matching strategy, use of a control group, and covariate adjustment helped to account for baseline differences. Third, we studied the phenomenon of potentially unintended medication discontinuation in the specific context of hospitalizations for certain elective surgical procedures. The risk of potentially unintended medication discontinuation in other clinical settings may be different. Fourth, the specific procedures studied in the overnight hospitalization and ambulatory groups were different, and we cannot exclude the possibility that differences in medication discontinuation are related to the procedure studied. Finally, we did not measure the effect of medication discontinuation on long-term clinical outcomes. However, it is reasonable to believe that discontinuation of medication therapies with strong evidence of clinical effectiveness compromises optimal patient care and exposes patients to potential harm.

Transitions between settings of care are an area of vulnerability for patient safety.^{1,68} We found that patients prescribed long-term anticoagulants are at risk for potentially unintended drug discontinuation. These findings may

extend to other types of medications as well as the broader context of care transitions after hospitalization. Better communication strategies involving hospital-based physicians, pharmacists, and nurses, their counterparts in the community, as well as the patients themselves, may reduce the risk of this phenomenon. Hospitalization should provide an opportunity to encourage medication adherence and not be a contributor to its failure.

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Author Contributions: Dr Bell had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. **Study concept and design:** Bell, Bajcar, Bierman, Mamdani, and Urbach. **Acquisition of data:** Bell and Li. **Analysis and interpretation of data:** Bell, Bajcar, Bierman, Li, Mamdani, and Urbach. **Drafting of the manuscript:** Bell, Bajcar, Bierman, Li, Mamdani, and Urbach. **Critical revision of the manuscript for important intellectual content:** Bell, Bajcar, Bierman, Li, Mamdani, and Urbach. **Statistical analysis:** Bell, Li, Mamdani, Urbach. **Obtained funding:** Bell, Bajcar, Bierman, Mamdani, and Urbach. **Study supervision:** Bell and Mamdani.

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