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EDITORIAL / ÉDITORIAL

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Deprescribing Proton Pump Inhibitors

Peter J Zed

Deprescribing is the planned and supervised process of dose reduction or discontinuation of a medication that may cause harm or that may no longer be providing benefit to a patient.[1] Deprescribing reduces polypharmacy while minimizing the risk of adverse events caused by unnecessary medications. Although deprescribing strategies should be applied to all patients, older adults are often the target population because of their higher risk of adverse drug events.

Proton pump inhibitors (PPIs) are one of the most commonly prescribed classes of medication. They are used to treat a variety of gastrointestinal indications, including gastroesophageal reflux disorder, peptic ulcer disease, Barrett esophagus, esophagitis, and gastritis; they are also used as gastroprotection for patients receiving long-term therapy with nonsteroidal anti-inflammatory drugs. Although PPIs are a relatively safe class of medications, their use carries certain risks, particularly with long-term use. The risks of long-term PPI use include fractures, pneumonia, enteric infections, hypomagnesemia, acute interstitial nephritis, and vitamin B_{12} deficiency.[2] In a national modified Delphi consensus process, PPIs were selected as a target medication class for deprescribing strategies because of their high prevalence of both use and overuse.[3]

This issue of the *Canadian Journal of Hospital Pharmacy* includes 3 papers that highlight ongoing issues with PPIs and evaluate the impact for patients for whom PPIs are being prescribed and those who are using PPIs on a long-term basis. Chan and others[4] retrospectively evaluated the appropriateness of PPI use among patients in residential care facilities in British Columbia.[4] They found that among 407 PPI orders for 334 patients, 16% did not have any of the broad evidence-based indications for use, as defined by the study's authors, and 44% did not have a common evidence-based indication for use (i.e., gastroesophageal reflux disorder or peptic ulcer disease). Doell and others[5] retrospectively evaluated the charts of 147 residents of long-term care facilities to determine their eligibility for PPI deprescribing. In addition, they evaluated vitamin B_{12} deficiency and fall risk in the study population. They found that 63% of the residents were candidates for PPI deprescribing. Among those residents, 20% did not have any identifiable indication for PPI use. Although no causal relationship or consequences were established in this study, 9% of the residents had experienced a fall within the previous 30 days, and 36% were receiving vitamin B_{12} supplements or had low serum vitamin B_{12} levels. In the third study, Wan and others[6] characterized the appropriateness of PPI orders initiated or continued in a population of internal medicine and family practice inpatients. They also evaluated potential adverse events associated with PPI use and the impact of an educational intervention to improve prescribing. This chart review showed that 36% of the 258 patients did not have any indication for PPI. Community-acquired pneumonia and *Clostridium difficile* infections were the most common adverse events potentially associated with PPI use. Finally, the authors' survey of health care professionals showed that a multidisciplinary educational intervention improved PPI prescribing for more than half of respondents.

This important series of studies, conducted in 3 distinct patient populations, illuminates the issue of PPI deprescribing, and challenges pharmacists to play a role in appropriate use of these drugs. Every patient, in any setting, for whom a PPI is being prescribed and all those who are receiving a PPI on a long-term basis should undergo an assessment for appropriate use. A recently published evidence-based clinical practice guideline can help clinicians to make decisions about when and how to deprescribe PPIs.[7] In addition, a toolkit for deprescibing PPIs

has been developed by the Choosing Wisely Canada campaign.[8] Together, these resources are valuable tools for all health care providers, presenting details on the appropriate indications for and duration of PPI therapy, the long-term risks of using a PPI, strategies to engage patients and health care providers, and thorough deprescribing algorithms. In addition, the Choosing Wisely Canada toolkit provides useful and practical performance measures that hospitals and related health care settings can use to evaluate interventions associated with PPI prescribing and deprescibing.

Pharmacists are the optimal health care professionals to provide leadership in appropriate use of all medications. Although this issue of the Journal focuses on deprescribing PPIs, we should always be exploring opportunities to improve medication use and thereby enhance the health outcomes of our patients.

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Competing interests: None declared.

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CORRECTION

Successful Treatment of Stevens–Johnson Syndrome with Cyclosporine and Corticosteroid: Correction

A recent case report[1] in the *Canadian Journal of Hospital Pharmacy* (*CJHP*) included a table summarizing previously published evidence for the use of cyclosporine to treat Stevens–Johnson syndrome and/or toxic epidermal necrolysis. One of the articles summarized in that table was by Singh and others.[2] In the *CJHP* article,[1] the intervention column of Table 1 showed an incorrect starting dose for the cyclosporine therapy administered in the study by Singh and others.[2] The starting dose was 3 mg/kg, not 1 mg/kg as stated in the table.

Therefore, in the row for the study by Singh and others, the entry for the intervention column should read as follows:

> Cyclosporine 3 mg/kg daily orally in 3 divided doses for 7 days, then 2 mg/kg daily in 2 divided doses for 7 days (n = 11)

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Déprescription des inhibiteurs de la pompe à protons

par Peter J Zed

La déprescription est un processus planifié et supervisé de réduction de dose ou d'interruption d'un médicament qui pourrait être dommageable ou pourrait ne plus présenter d'avantage pour un patient[1]. La déprescription diminue la polypharmacie tout en réduisant les risques d'événements indésirables causés par l'utilisation superflue de médicaments. Bien que les stratégies de déprescription doivent être utilisées pour tous les patients, la population cible est souvent celle des personnes âgées à cause des risques plus élevés d'événements indésirables liés aux médicaments auxquels elles sont sujettes.

Les inhibiteurs de la pompe à protons (IPP) sont parmi les classes de médicaments les plus couramment prescrits. On les emploie pour traiter une gamme d'indications gastro-intestinales, notamment le reflux gastro-œsophagien, l'ulcère gastroduodénal, l'œsophage de Barrett, l'œsophagite et la gastrite. Ils sont aussi utilisés aux fins de protection gastrique pour les patients qui prennent un traitement à long terme d'anti-inflammatoires non stéroïdiens. Bien que les IPP soient une classe de médicaments relativement sécuritaire, leur utilisation comporte certains risques, particulièrement lorsqu'utilisés à long terme. Les risques d'utilisation à long terme d'IPP comptent les fractures, les pneumonies, les infections entériques, l'hypomagnésémie, les néphrites interstitielles aiguës et les carences en vitamine B_{12}[2]. Au cours d'un processus Delphi modifié d'établissement de consensus mené à l'échelle nationale, les IPP ont été choisis comme une classe de médicament cible pour les stratégies de déprescription à cause de leur prévalence élevée d'utilisation et d'abus[3].

Le présent numéro du *Journal canadien de la pharmacie hospitalière* contient trois articles qui mettent en lumière les enjeux actuels entourant les IPP et évaluent les conséquences pour les patients qui se voient prescrire des IPP et ceux qui reçoivent un traitement par IPP à long terme. Chan et collab.[4] ont fait une évaluation rétrospective de la pertinence d'une utilisation des IPP chez des patients de centres d'hébergement et de soins de longue durée en Colombie-Britannique[4]. Ils ont découvert que, parmi 407 ordonnances d'IPP pour 334 patients, 16 % ne s'appuyaient sur aucune des indications larges fondées sur des données probantes définies par les auteurs de l'étude et que 44 % ne reposaient pas sur une indication usuelle fondée sur des données probantes (c.-à-d. le reflux gastro-œsophagien ou l'ulcère gastroduodénal). Doell et collab.[5] ont fait une évaluation rétrospective des dossiers médicaux de 147 résidents de centres d'hébergement et de soins de longue durée afin de déterminer s'ils satisfaisaient aux conditions requises pour une déprescription d'IPP. De plus, ils ont évalué les cas de carence en vitamine B_{12} et les risques de chute dans la population à l'étude. Ils ont découvert que 63 % des résidents remplissaient les conditions requises pour une déprescription d'IPP. Parmi ces résidents, 20 % ne présentaient pas d'indication identifiable motivant l'utilisation d'IPP. Bien qu'aucun lien causal ou aucune conséquence n'aient été établis dans le cadre de cette étude, 9 % des résidents avaient subi une chute au cours des 30 jours précédents et 36 % recevaient des suppléments de vitamine B_{12} ou présentaient des faibles taux sériques de vitamine B_{12}. Dans la troisième étude, Wan et collab.[6] ont décrit la pertinence des ordonnances d'IPP, nouvelles ou renouvelées, dans une population de patients hospitalisés aux services de médecine interne et de médecine familiale. Ils ont aussi évalué les événements indésirables potentiels liés à l'utilisation d'IPP et les effets d'une intervention éducative visant à améliorer les pratiques de prescription. Cette analyse de dossiers médicaux a montré que 36 % des 258 patients n'avaient aucune indication motivant l'utilisation d'IPP. Les pneumonies extra-hospitalières et les infections à *Clostridium difficile* représentaient les événements indésirables les plus courants potentiellement liés à l'utilisation d'IPP. Finalement, l'enquête des auteurs auprès des professionnels de la santé a montré qu'une formation multidisciplinaire avait amélioré les pratiques de prescription d'IPP chez plus de la moitié des répondants.

Cette importante série d'études, menées auprès de trois populations distinctes de patients, met en lumière la question de la déprescription des IPP et appelle les pharmaciens à jouer un rôle dans l'utilisation pertinente de ces médicaments. Tous les patients, dans tous les milieux, à qui l'on prescrit des IPP et tous ceux qui reçoivent un traitement à long terme d'IPP devraient subir une évaluation afin de déterminer si l'utilisation est pertinente. Des lignes directrices de pratique clinique fondées sur des données probantes publiées récemment peuvent aider les cliniciens à décider quand et comment procéder à la déprescription des IPP[7]. De plus, une trousse à outils de déprescription des IPP a été mise au point par la campagne Choisir avec soin Canada[8]. Ensemble, ces ressources sont de précieux outils pour tous les fournisseurs de soins de santé, car elles présentent de l'information sur les indications pertinentes du traitement par IPP et sa durée, sur les risques à long terme de l'utilisation d'un IPP, sur les stratégies pour conscientiser les patients et les fournisseurs de soins de santé et sur des algorithmes détaillés de déprescription. En plus, la boîte à outils de Choisir avec soin Canada offre des mesures du rendement utiles et pratiques que les établissements de santé peuvent utiliser pour évaluer les interventions en lien avec la prescription et la déprescription d'IPP.

Les pharmaciens sont les professionnels de la santé les mieux placés pour faire preuve de leadership en ce qui touche à l'utilisation pertinente de tout médicament. Bien que le présent numéro du Journal se concentre sur la déprescription des IPP, l'on doit toujours chercher les occasions d'optimiser l'utilisation des médicaments et ainsi améliorer les résultats thérapeutiques.

[Traduction par l'éditeur]

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Is There a Reason for the Proton Pump Inhibitor? An Assessment of Prescribing for Residential Care Patients in British Columbia

Adriel Chan, Libby Liang, Anthony C H Tung, Angus Kinkade, and Aaron M Tejani

ABSTRACT

Background: The use of proton pump inhibitors (PPIs) may cause significant harm to patients in the residential care setting, as these patients are often frail with multiple morbidities. The extent of non–evidence-based use of PPIs in residential care sites of the Fraser Health Authority in British Columbia is unknown.

Objective: To determine the proportion of non–evidence-based use of PPI therapy for residential care patients of the Fraser Health Authority.

Methods: This retrospective cross-sectional study was conducted in 6 Fraser Health residential care facilities in British Columbia between April 1, 2015, and March 31, 2016. Two definitions of "evidence-based indications" were used. The first definition encompassed *broad* evidence-based indications for PPI use, specifically gastroesophageal reflux disease (GERD), peptic ulcer disease (PUD), gastritis, esophagitis, Barrett esophagus, and gastrointestinal protection from concurrent oral steroids, oral nonsteroidal anti-inflammatory drugs, antiplatelet agents, and anticoagulants. The second definition involved *common* evidence-based indications for PPI use, specifically GERD or PUD. Descriptive statistics were used to evaluate the primary outcome: the proportion of PPI orders without a documented broad or common evidence-based indication for PPI treatment.

Results: A total of 331 residential care patients and 407 PPI orders were assessed. The proportion of PPI orders without a documented broad evidence-based indication was 16.2% (66/407). The proportion of PPI orders without a documented common evidence-based indication was 43.7% (178/407). The most frequently documented reason for a PPI order was GERD (214/407 or 52.6%). PPI orders for patients with GERD and gastrointestinal bleeding had the longest duration of therapy during residential care admission, averaging 205.1 and 218.1 days, respectively.

Conclusion: About 1 in 6 PPI orders for Fraser Health residential care patients did not have a documented broad evidence-based indication, and about 2 in 5 PPI orders did not have a documented common evidence-based indication. These results indicate a need to assess the appropriateness of therapy for every patient with an active PPI order in residential care facilities.

Keywords: evidence-based care, proton pump inhibitor, residential care

RÉSUMÉ

Contexte : L'emploi d'inhibiteurs de la pompe à protons (IPP) peut causer des torts importants aux patients qui résident en centre d'hébergement et de soins de longue durée, car souvent ces personnes sont fragiles et souffrent de multiples maladies. On ignore quelle est la proportion d'utilisation d'IPP ne reposant pas sur des données probantes dans les centres d'hébergement et de soins de longue durée de la Fraser Health Authority en Colombie-Britannique.

Objectif : Déterminer la proportion d'utilisation de traitement par IPP ne reposant pas sur des données probantes chez les patients en centre d'hébergement et de soins de longue durée de la Fraser Health Authority.

Méthodes : Cette étude rétrospective transversale a été menée dans six centres d'hébergement et de soins de longue durée de la Fraser Health en Colombie-Britannique, entre le 1er avril 2015 et le 31 mars 2016. Deux définitions du terme « indications fondées sur des données probantes » ont été utilisées. La première définition englobait des indications *larges* fondées sur des données probantes appuyant l'utilisation d'IPP, plus particulièrement : pour traiter le reflux gastro-œsophagien, l'ulcère gastroduodénal, la gastrite, l'œsophagite et l'œsophage de Barrett ainsi que pour fournir une protection gastrique contre les effets indésirables de la prise de médicaments anti-inflammatoires oraux stéroïdiens ou non stéroïdiens, d'antiplaquettaires et d'anticoagulants. La seconde définition comprenait les indications *usuelles* fondées sur des données probantes pour appuyer l'utilisation d'IPP, plus précisément : le reflux gastro-œsophagien ou l'ulcère gastroduodénal. Des statistiques descriptives ont été employées pour analyser le principal paramètre d'évaluation : la proportion d'ordonnances d'IPP pour lesquelles aucune indication, large ou usuelle, fondée sur des données probantes n'a été consignée.

Résultats : Au total, les dossiers de 331 résidents de centres d'hébergement et de soins de longue durée et 407 ordonnances d'IPP ont été évalués. La proportion d'ordonnances d'IPP pour lesquelles aucune indication large fondée sur des données probantes n'a été consignée était de 16,2 % (66/407). La proportion d'ordonnances d'IPP pour lesquelles aucune indication usuelle fondée sur des données probantes n'a été consignée était de 43,7 % (178/407). La raison la plus souvent consignée pour l'émission d'une ordonnance d'IPP était le reflux gastro-œsophagien (214/407 ou 52,6 %). Les ordonnances d'IPP destinées aux patients souffrant de reflux gastro-œsophagien ou d'hémorragie gastro-intestinale étaient celles pour lesquelles la durée du traitement était la plus longue au cours du séjour en centre d'hébergement et de soins de longue durée, soit respectivement de 205,1 et 218,1 jours en moyenne.

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Conclusion : Environ 1 ordonnance d'IPP sur 6 pour les patients de centres d'hébergement et de soins de longue durée de la Fraser Health ne reposait pas sur une indication large consignée et fondée sur des données probantes et environ 2 ordonnances d'IPP sur 5 ne s'appuyaient pas sur une indication usuelle consignée et fondée sur des données probantes. Les résultats révèlent la nécessité d'évaluer la pertinence des traitements par IPP pour chaque patient ayant une ordonnance active d'IPP dans les centres d'hébergement et de soins de longue durée.

Mots clés : soins basés sur les données probantes, inhibiteur de la pompe à protons, centre d'hébergement et de soins de longue durée

INTRODUCTION

Proton pump inhibitors (PPIs) are a class of drugs used to treat various gastrointestinal (GI) conditions, such as gastroesophageal reflux disease (GERD), peptic ulcer disease (PUD), *Helicobacter pylori* infections, Barrett esophagus, esophagitis, and gastritis.[1,2] PPIs work by selectively and irreversibly inhibiting hydrogen potassium ATPase on parietal cells, thereby leading to decreased gastric acid levels in the stomach.[3,4] PPIs are considered relatively safe, their most frequent adverse effects being headache and GI-related problems (nausea, abdominal pain, flatulence, constipation, and diarrhea).[4] Long-term use of PPIs is associated with serious complications such as *Clostridium difficile* infections, pneumonia, vitamin B_{12} deficiency, and calcium deficiency, the last of which increases the risk of osteoporosis and associated bone fractures.[4-6]

In a US study that assessed 355 600 nursing home residents aged 65 or older (representing 27% of the total population of such residents) who were receiving at least 1 PPI, 49% of those evaluated did not have a documented evidence-based indication for the drug.[1] No similar studies have been done within the residential care facilities of the Fraser Health Authority in British Columbia, such that the proportion of these patients without an evidence-based indication for PPI treatment is largely unknown. Residential care patients have more comorbidities than the general public and are therefore at increased risk of polypharmacy.[7] Inappropriate prescribing of PPIs is an issue associated with polypharmacy and puts residential care patients at increased risk of PPI-induced complications. Therefore, it is important to investigate the local proportion of inappropriate PPI use, to support PPI deprescribing efforts and potentially reduce the risk of complications.[6,8]

The primary objective of this study was to determine the proportion of PPI orders among Fraser Health residential care patients for which a broad evidence-based indication or a common evidence-based indication could not be identified. The secondary objectives were to determine the proportion of PPI orders with no documented indication of any kind, the proportion of PPI orders for patients with a history of PPI use before admission to residential care, the documented indications for PPI therapy, and the duration of PPI therapy.

METHODS

Study Design and Setting

This retrospective, cross-sectional study examined non–evidence-based use of PPIs at Fraser Health residential care sites between April 1, 2015, and March 31, 2016. The Fraser Health Authority is a large, publicly funded health authority in British Columbia that provides a variety of health care services in the Fraser region of the province, from Burnaby to Boston Bar. As part of this mandate, Fraser Health serves a total of 7760 residents at the following 6 publicly owned and funded residential care facilities (all of which maintain electronic medical records): Chilliwack General Hospital, Delta Hospital, Langley Memorial Hospital, Mission Memorial Hospital, Peace Arch Hospital, and Queen's Park Care Centre. Data from these facilities were collected for this study in June 2016.

All of the publicly funded residential care facilities included in this study had an assigned clinical pharmacist. The clinical pharmacist is required to conduct a medication review every 6 months for every patient and also is expected to deal with medication-related problems on a daily basis. The average length of stay for patients in all facilities is 2.6 years, and the average frailty of patients at the time of this study, as measured by the Clinical Frailty Index,[9] was 7 (unpublished data). Medication reconciliation on admission is conducted at some sites but is not a requirement for all sites.

Study Sample

One investigator (L.L) identified all PPI orders during the study period and assigned them to 2 investigators (A.C., L.L.) for screening, application of inclusion and exclusion criteria, and data collection. Patients were identified through the pharmacy's order-entry system, Meditech, from a report of all PPI orders during the study period. Patients from the 6 Fraser Health–owned and operated residential sites were included if they had at least

1 PPI order during the study period. For patients with multiple courses of PPI treatment, a pair of PPI prescriptions was considered to represent separate courses of therapy if more than 7 days had elapsed between the 2 orders; conversely, a PPI order started within 7 days of discontinuation of another PPI order was considered to be a continuation of the earlier order. Patients for whom no electronic charts were available were excluded.

Some patients had received "pass medications", a supply of prescribed PPIs to take with them when they were away from their respective residential care sites (e.g., during a visit home). A pass PPI order was defined as a PPI order with a duration of 7 days or less that was prescribed concurrent with ongoing PPI therapy. These orders, identified in the patient charts, were excluded from the study because they were considered to be duplicate orders for patients who were receiving active PPI treatment while in residential care.

Data Sources and Measurement

The investigators collaborated to create an electronic data extraction form. The following data were collected from medical records and recorded using this electronic form: sex, residential care site, age at the start of PPI treatment during the study period, history of PPI use, start and end dates of PPI treatment, regimen (drug, dose, frequency, total daily dose) of the most recent course of PPI therapy, relevant concurrent medications (oral steroids, oral nonsteroidal anti-inflammatory drugs, antiplatelet agents, anticoagulants, bisphosphonates, histamine 2 receptor antagonists), documented indications for PPI therapy, and the date of the most recent upper or unspecified GI bleed, if applicable.

Data from the patient's entire electronic medical record (accessed through the local health records software) were extracted independently by the 2 investigators (A.C., L.L.) for an initial, randomly selected sample of 50 patient charts. Specific sections of the medical record that were reviewed included the prescriber progress notes, nursing notes, medication administration record, and physician orders. The 2 investigators compared their results to confirm consistency and accuracy of data collection. On the basis of this preliminary comparison, all investigators decided that A.C. and L.L. could each extract data for 50% of the remaining patients without independent duplication. Consultation with the other researchers (A.C.H.T., A.K., A.M.T.) was to occur if A.C. and L.L. encountered problems during data extraction.

For the purposes of the study, 2 definitions were developed, one for "broad evidence-based indications" for PPIs and the other for "common evidence-based indications" for PPIs (Table 1). To ensure that all possible indications were captured, 2 of the investigators (L.L, A.C.) included Health Canada–approved indications, as well as off-label, evidence-based indications mentioned in clinical practice guidelines and tertiary references. To give an optimistic estimate of usage within evidence-based indications, we did not consider duration of therapy in the primary assessment (i.e., a PPI order used beyond the approved duration for a particular indication included in one or both of the definitions was counted as having an evidence-based indication). The evidence used to support these indications was not scrutinized, and it was assumed that prescribing clinicians would use similar sources of information to guide their prescribing. This conservative approach would likely underestimate the proportion of PPI orders for which no evidence-based indication was documented. Furthermore, our categorization of indications was not validated nor was it used in other studies. The categorization was intentionally broad, to mimic the practical way in which clinicians might think about the indications for use of PPIs.

In instances where the documented indication met the criteria for both the "common" and "broad" evidence-based indications, the PPI order was counted in both categories. The reason for allowing this overlap was to assess both the number of PPI orders that met the strict criteria (i.e., common indications) and the number that met the less rigorous/more pragmatic criteria (i.e., broad indications). With regard to the dual aspects of the primary objective, the number of PPI orders without a clearly documented broad or common evidence-based indication was used as the numerator. For patients with multiple PPI orders, all orders were assessed individually. The proportions of PPI orders without broad or common evidence-based indications were then calculated by dividing the aforementioned numerators by the total number of PPI orders.

Table 1. Definitions of Evidence-Based Indications for Proton Pump Inhibitor Therapy

Category	Definition	Specific Details
Broad	Indications identified in the literature search* *PLUS* No clear documentation but the indication for PPI was presumed because of concomitant medication order	GERD,[8,10] PUD,[11,12] gastritis,[13] esophagitis,[14] Barrett esophagus[2] *PLUS* GI protection for concomitant use of NSAID, oral corticosteroid, or antiplatelet
Common	Indications most widely identified in the literature search* (from systematic reviews, clinical practice guidelines, and product monographs, including both Health Canada–approved and off-label indications)	GERD, PUD

GERD = gastroesophageal reflux disease, GI = gastrointestinal, NSAID = nonsteroidal anti-inflammatory drug, PUD = peptic ulcer disease.
*See Methods section for complete description.

The proportion of PPI orders for patients with a history of PPI use was determined by dividing the number of orders for these patients by the total number of PPI orders. A patient was deemed to have a history of PPI use if there was a record of PPI treatment during a previous hospital stay (either residential or acute care) or documentation of a history of PPI use anywhere in the electronic medical record. The average duration of PPI therapy during the residential care admission was calculated for all indications and for each indication separately using start and end dates. The average duration of PPI therapy for each indication was calculated by dividing the total duration of PPI therapy for the specified condition (e.g., sum of durations for all PPI orders for all patients with PUD; the numerator) by the total number of PPI orders for that indication (e.g., total number of PPI orders for all patients with PUD; the denominator). For patients who were taking PPIs before admission to any of the residential care facilities, we recorded only that prior PPI therapy had occurred; we did not assess the duration of such prior PPI therapy. Although the duration of PPI therapy before admission to residential care would have added important context, we did not have ready access to data for prescription drug use in the community.

Quantitative Variables and Statistical Methods

Descriptive statistics were used. Specifically, 95% confidence intervals (CIs) were calculated for all categorical variables (proportion of PPI orders for residential care patients at Fraser Health residential care sites with no evidence-based indication, proportion of PPI orders for patients who were taking PPIs before admission to residential care, and documented reasons for PPI therapy in the identified patients) to estimate the possible range of these outcomes across all Fraser Health residential care sites. The standard deviation (SD) was calculated for the continuous variable (duration of PPI treatment for each patient during the period of residential care).

RESULTS

Study Sample

A total of 674 PPI orders were initially identified by searching the Meditech system. After removal of pass medication orders, duplicate orders, and orders that were considered to be continuous with an earlier order, 410 PPI orders (for 334 patients) remained and were eligible for inclusion in the study. After the removal of orders for 3 patients who had no electronic charts available, 407 orders were considered in the final analysis.

Demographic Characteristics

The mean age of the patients in the study was 82 (SD 10) years. Of the initial 410 PPI orders, 154 (37.6%) were for men and 256 (62.4%) were for women. The reason for this difference between the sexes in number of PPI orders was not investigated, nor could it be easily explained by facility type; none of the residential care sites specifically caters to a particular population (e.g., a veterans' facility).

Outcomes

About 1 of every 6 PPI orders for Fraser Health residential care patients (16.2%) did not have a documented broad evidence-based indication for PPI therapy, and about 2 out of every 5 orders (43.7%) did not have a documented common evidence-based indication (Table 2).

A total of 138 (33.9%) orders had no documented indication at all. Overall, 357 orders (87.7%; 95% CI 83.8%–90.3%) involved patients who had a history of PPI use before their residential care admission. GERD was the most frequently documented reason for PPI therapy, with more than 50% of orders for patients with a documented history of this disease, followed by GI bleeding and PUD (Table 3). A smaller proportion of orders were for patients with a documented history of gastritis, esophagitis, or Barrett esophagus. PPI orders for patients with GERD and GI bleed had the longest duration of therapy, averaging 205.1 and 218.1 days, respectively (Table 4).

DISCUSSION

In this study, 16.2% of PPI orders for residential care patients did not have a documented broad evidence-based indication, and 43.7% did not have a documented common evidence-based indication. In addition, 33.9% of PPI orders did not have any documented indication at all. The average duration of PPI orders was about 190 days. These findings highlight some important problems and potential opportunities to improve the use of PPI, as discussed below.

Table 2. Proportion of PPI Orders at Fraser Health Residential Care Sites without Evidence-Based Indications of Various Types (*n* = 407 Orders)

Order Category	No. of Orders	% of Orders (95% CI for %)
No broad evidence-based indication	66	16.2 (12.6–19.8)
No common evidence-based indication*	178	43.7 (38.9–48.6)
No documented indication	138	33.9 (29.3–38.5)
Documented or inferred non–evidence-based indication	20	4.9 (2.8–7.0)

CI = confidence interval, PPI = proton pump inhibitor.
*Common evidence-based indications: gastroesophageal reflux disease, peptic ulcer disease.

Table 3. Documented Reasons for PPI Therapy (*n* = 407 Orders)

Reason	No. of Orders*	% of Orders (95% CI for %)
GERD	214	52.6 (47.7–57.4)
GI bleeding (upper or unspecified)	56	13.8 (10.4–17.1)
PUD	50	12.3 (9.1–15.5)
Gastritis	26	6.4 (4.0–8.8)
Esophagitis	9	2.2 (0.8–3.6)
Barrett esophagus	6	1.5 (0.3–2.6)

CI = confidence interval, GERD = gastroesophageal reflux disease, GI = gastrointestinal, PPI = proton pump inhibitor, PUD = peptic ulcer disease.
*Some orders had more than one documented reason for PPI therapy, and a total of 138 orders had no documented reason.

Table 4. Duration of PPI Treatment for Orders during Residential Care Stay

Indication	Duration of Therapy (Days) (Mean ± SD)
All orders (*n* = 407)	189.7 ± 260.9
GERD (*n* = 214)	205.1 ± 292.6
GI bleeding (*n* = 56)	218.1 ± 270.5
PUD (*n* = 50)	133.6 ± 172.2
Gastritis (*n* = 26)	181.8 ± 260.3
Esophagitis (*n* = 9)	184.0 ± 161.1
Barrett esophagus (*n* = 6)	143.3 ± 127.3

GERD = gastroesophageal reflux disease, GI = gastrointestinal, PPI = proton pump inhibitor, PUD = peptic ulcer disease, SD = standard deviation.

According to our definition of broad evidence-based indications, the findings of this study showed a lower proportion of non–evidence-based PPI use for residential care patients than was reported by Rane and others.[1] However, the current findings presumably reflect what would be found at other, privately owned residential care sites within the Fraser Health region, given that these sites implement similar practices and protocols with regard to patient care and medication review.

There could be several reasons for the difference in results between our study and that of Rane and others.[1] First, since 2004, the year in which Rane and others[1] conducted their analysis, there has been increasing research and awareness about the serious risks associated with PPI use, which may have led to more judicious use of PPIs in the Fraser Health facilities. Another reason could be the existence of regular medication review at Fraser Health residential care sites. It is mandatory that all residential care facilities in British Columbia have a medication safety and advisory committee, consisting of a pharmacist and other health care professionals involved in direct patient care. These committees conduct interdisciplinary meetings to assess medical conditions and drug therapy for all patients (every 6 months for each patient, on a staggered schedule).[15]

GERD was the most frequently documented reason for PPI therapy, with more than 50% of patients having a documented history of this disease, followed by 13.8% with GI bleeding and 12.3% with PUD. Given that GERD and GI bleeding were the 2 most frequently documented indications for PPI use and given that patients with these conditions had the longest average duration of PPI therapy (205.1 and 218.1 days, respectively), health care providers may be able make the biggest initial impact on reducing inappropriate PPI use by monitoring and assessing the duration of therapy for patients with a history of either of these 2 conditions. The long durations of PPI treatment for GERD and GI bleeding in this study suggest that some patients' PPI therapy was continued much longer than recommended by guidelines. For example, for the management of symptomatic GERD, the recommended duration of PPI treatment is 4 to 8 weeks; if the patient has an adequate response, the regimen can be changed to an as-needed basis or tapered until discontinuation.[6,12] Patients with a long duration of PPI therapy (e.g., more than 8 weeks) should be reassessed and monitored, with a view to tapering the medication.

Notably, the proportion of orders for patients with a history of PPI use before residential care admission was high (357 orders, 87.7%). This number may be an underestimate because PharmaNet records were inaccessible for the purposes of this study. PharmaNet is a data network that links all pharmacies in British Columbia, allowing pharmacists to access patients' comprehensive medication history. The large proportion of orders involving patients with a history of PPI therapy may suggest that prescribers were simply continuing courses of PPI therapy based on patients' previous medication histories, without proper assessment of therapy appropriateness. As a result, it is likely that the duration of therapy for a certain proportion of the PPI orders was longer than recommended by guidelines, and the large standard deviation for duration of PPI orders is likely due to several orders with durations of about 1 year or longer. However, given the retrospective nature of this study, we could not assess the appropriateness of therapy for PPIs initially prescribed before admission to residential care. In light of this high proportion of prior PPI utilization, we suggest that health care providers assess each patient's PPI therapy thoroughly at the time of residential care admission and consider discontinuation, dose tapering,

or careful monitoring of the drug. Our findings show that a significant portion of patients received long-term PPI therapy because of a distant diagnosis of conditions such as GI bleeding. In such cases, continuing the use of PPIs may not be the best clinical or therapeutic decision. From a practical perspective, our recommendation could be applied in the clinical setting with little difficulty, as several guidelines exist to provide useful advice for monitoring and deprescribing of PPIs.[6,8,16]

One finding of particular interest was that 33.9% of PPI orders did not have any documented indication. The absence of a documented indication raises the question of how the clinical team will assess the effectiveness, safety, or appropriateness of therapy. It is imperative that all medications have a clearly documented indication (evidence-based or not) if appropriate monitoring is to take place. This problem can be easily solved with indication-based prescribing.[17] According to this approach, when the order for a PPI is written, the indication should be included in the directions for use (e.g., "Take 1 tablet once daily for reflux"). If the indication is mentioned in the directions, the pharmacy will then include this information on the label, and it will also appear in the medication administration record, which becomes part of the patient's medical record. Additionally, if, after investigation by the clinical team, no indication can be found for an active PPI order, this may be the perfect target for deprescribing in an effort to reduce polypharmacy, especially for those without a documented indication and no symptoms.[18]

The results of this study can be discussed with policy-makers of the Fraser Health Authority to explore ways to improve the quality of patient care, such as development of a screening tool to be used by physicians and clinical pharmacists to ensure appropriate PPI prescribing. This study investigated only the presence or absence of documented evidence-based indications to determine the appropriateness of PPI therapy, but future studies investigating the regimen and duration specific to the medical condition being treated could help to further optimize PPI prescribing in residential care facilities. It would also be important to evaluate the reasons why indications for PPIs are not being documented in patients' charts. As mentioned previously, a policy that makes indication-based prescribing the standard would go a long way toward solving the documentation problem.

Limitations

The definitions for what constitutes an evidence-based indication (either broad or common) were intentionally chosen. This approach would likely underestimate the proportion of PPI orders with truly evidence-based indications.

Several patients had limited or no documentation in their electronic medical records. Poor documentation in patient charts made it difficult to identify the condition the PPI was meant to treat. Inconsistent documentation was also a potential source of bias in this study. For example, a nurse might have documented a patient as having a history of GERD, whereas for the same patient a physician might have documented a history of GI bleeding. Such discrepancies could mask the true indication for PPI treatment. Misinterpretation of clinical events could lead to another potential source of bias. For example, a patient with dyspepsia might have received a diagnosis of GERD. This would be a significant error, as the evidence for PPI treatment in dyspepsia is limited and weaker than the evidence for PPI treatment of GERD.[8,19] Another example might be a patient with upper or unspecified GI bleeding for whom the date on which the bleeding stopped was not documented. In this situation, it would not be possible to determine the appropriateness of the duration of PPI therapy.

We identified numerous PPI orders for which no documented reason/indication could be found in the patient's chart. It would be unfair to conclude that this absence of a documented indication is definitive evidence of inappropriate PPI use. Rather, it would be more appropriate to highlight the lack of clear documentation in the residential care setting. We did not plan to investigate the reasons for poor documentation practices, but this is an important issue that requires further study. Possible questions arising from such an investigation could be, "Why are reasons for medications not documented by health care workers?" and "What is the actual reason that patients with no documented indication for PPI therapy are taking drugs from this class?" These questions were beyond the scope of the current study.

Access to outpatient records was not possible with the resources available. Thus, patients' complete history of PPI use was unknown. For some patients, completed medication reconciliation forms were included in the electronic medical records, which gave a comprehensive medical history, whereas others had incomplete forms or no forms at all. Also, many patients were taking their own medications, which were not specified in medication lists in their electronic medical records. These medications may have included PPIs or relevant concurrent medications such as nonsteroidal anti-inflammatory drugs or steroids.

Pilot testing with a sample of orders was conducted before data collection for the study began. Two investigators collected data from the same 50 orders and discussed their findings thoroughly to ensure consistency and accuracy of data collection. A more comprehensive method of data collection would have been to have both investigators collect data from all patients independently and compare data to ensure consistency and accuracy. However, because of time limitations, this approach was not possible. Periodic meetings were held with the other researchers involved in the study to resolve any issues regarding data collection.

We calculated the proportion of PPI orders without documented indications, not the proportion of patients who had a PPI order without a documented indication. This approach was

useful for patients who had multiple PPI orders for different indications. However, it would lead to overestimation of the proportion of orders without a documented indication if there were multiple orders for the same indication.

CONCLUSION

About 1 in every 6 patients who was receiving a PPI at Fraser Health residential care sites did not have a documented broad evidence-based indication for the drug (16.2%), and about 2 in every 5 did not have a documented common evidence-based indication (43.7%). Equally concerning was that 33.9% of orders for PPIs did not have any documented indication at all. These findings indicate the need to assess the appropriateness of PPI therapy for every patient with an active PPI order in residential care facilities. Although the results of this study cannot be generalized beyond Fraser Health residential care facilities, the methods used and the findings obtained may be useful for similar assessments in other jurisdictions.

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ORIGINAL RESEARCH

Quantifying Candidacy for Deprescribing of Proton Pump Inhibitors among Long-Term Care Residents

Alanna Doell, Ashley Walus, Jaclyn To, and Allison Bell

ABSTRACT

Background: Proton pump inhibitors (PPIs) are a commonly prescribed drug class used to inhibit gastric acid secretion. They are prescribed for both treatment and prophylaxis of several gastrointestinal conditions. Although PPIs can be used safely in the short term, several serious adverse effects have been reported following long-term use, including increased risk of falls and fragility fractures. Long-term care home (LTCH) residents represent a population in which the long-term adverse effects of PPIs can be significant and PPI deprescribing should be considered when appropriate.

Objectives: To determine the proportion of LTCH residents with PPI prescriptions who were eligible for PPI deprescribing, and to examine vitamin B_{12} deficiencies and fall risk in the study population.

Methods: This cross-sectional, multisite chart review involved LTCH residents who had an active PPI prescription during October 2016. A convenience sample of 150 charts was randomly selected, and the appropriateness of PPI deprescribing was determined using Canadian guidelines. Descriptive statistics were used to examine demographic characteristics, PPI dosing and indication, vitamin B_{12} supplementation, fall history, and fall risk.

Results: Three of the selected charts were excluded because of missing information. Of the 147 residents included in the chart review, 93 (63%) were candidates for deprescribing. PPI use for gastroesophageal reflux disease for more than 8 weeks without a deprescribing attempt in the past year was the most frequently observed opportunity for deprescribing (49/93 [53%]). Twenty-nine residents (20%) had no documented indication for PPI use. Thirteen residents (9%) had had a fall within the past 30 days, and 53 (36%) had a prescription for vitamin B_{12} supplements and/or had low serum vitamin B_{12} levels.

Conclusions: A majority of the residents whose charts were reviewed were candidates for PPI deprescribing. This finding suggests an opportunity for clinicians who care for LTCH residents to increase their deprescribing efforts.

Keywords: proton pump inhibitors, elderly patients, deprescribing, long-term care

RÉSUMÉ

Contexte : Les inhibiteurs de la pompe à protons (IPP) sont des médicaments couramment prescrits pour inhiber la sécrétion d'acide gastrique. Ils sont prescrits comme traitement et comme prophylaxie pour plusieurs troubles gastro-intestinaux. Bien que les IPP puissent être utilisés de façon sécuritaire à court terme, plusieurs effets indésirables graves ont été signalés à la suite d'une utilisation à long terme, notamment une augmentation des risques de chutes et de fractures de fragilité. Les résidents de centres d'hébergement et de soins de longue durée (CHSLD) représentent une population chez qui les effets indésirables d'un traitement à long terme par IPP peuvent être significatifs et la déprescription des IPP doit être envisagée lorsque cela est approprié.

Objectifs : Déterminer la proportion de résidents de CHSLD ayant une ordonnance d'IPP qui satisfaisaient aux conditions requises pour une déprescription des IPP. De plus, examiner au sein de la population à l'étude les carences en vitamine B_{12} et les risques de chutes.

Méthodes : La présente étude transversale menée dans plusieurs centres comportait une analyse des dossiers médicaux de résidents de CHSLD qui avaient une ordonnance active d'IPP en octobre 2016. Un échantillon de commodité de 150 dossiers médicaux a été choisi au hasard et la pertinence d'une déprescription des IPP a été déterminée à l'aide des lignes directrices canadiennes. Des statistiques descriptives ont été employées pour analyser les caractéristiques démographiques, les posologies et les indications des IPP, la prise de suppléments de vitamine B12, les antécédents de chute et les risques de chute.

Résultats : Trois des dossiers sélectionnés ont été exclus parce qu'il y manquait des renseignements. Des 147 résidents dont les dossiers ont été analysés, 93 (63 %) satisfaisaient aux conditions requises pour une déprescription. L'emploi d'IPP pour traiter le reflux gastro-œsophagien pendant plus de huit semaines sans qu'il y ait eu de tentative de déprescription dans la dernière année représentait l'occasion la plus fréquemment observée pour procéder à une déprescription (49/93 ou 53 %). Vingt-neuf résidents (20 %) utilisaient des IPP sans qu'une indication apparaisse aux dossiers. Treize résidents (9 %) avaient subi une chute au cours des 30 derniers jours et 53 (36 %) avaient une prescription pour des suppléments de vitamine B_{12} ou affichaient des taux sériques faibles de vitamine B_{12}.

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Conclusions : La majorité des résidents dont les dossiers ont été examinés remplissaient les conditions requises pour une déprescription des IPP. Ce résultat suggère qu'il y a là une occasion pour les cliniciens qui prennent soin de résidents de CHSLD d'accroître leur travail de déprescription.

Mots clés : inhibiteurs de la pompe à protons, patients âgés, déprescription, soins de longue durée

INTRODUCTION

With US$26 billion spent worldwide in 2011, proton pump inhibitors (PPIs) are one of the most commonly prescribed classes of drugs.[1] PPIs prevent basal and stimulated gastric acid secretion from the parietal mucosa cells of the stomach by inhibiting the hydrogen potassium pump, which results in highly effective acid suppression. These agents are used to treat and prevent several disease states in which gastric acid suppression is required. They are usually indicated for short-term use (less than 8 weeks). PPIs have become widely used because of their efficacy, low cost, and acceptable adverse effect profile.

Although PPIs can be used safely in the short term, several serious adverse effects associated with long-term use have been described in the literature, including increased fracture risk, reduced absorption of some medications and nutrients (including vitamin B_{12}), pneumonia, *Clostridium difficile* infections, and death.[2-7] Several epidemiological studies and meta-analyses have described a modest, dose-dependent association between long-term PPI use and increased incidence of hip, vertebral, and all-type fractures.[8-15] Despite the association with fracture risk, there has been a lack of evidence demonstrating radiological changes in bone mineral density among PPI users.[16-19] However, long-term PPI use may be associated with an increased incidence of falls and resulting fracture, secondary to paresthesia caused by vitamin B_{12} deficiency.[20]

The incidence of PPI use without documented indication is estimated at about 50% and has been described as occurring among both inpatients and outpatients.[21-23] Overprescribing of PPIs also extends to long-term care homes (LTCHs), although the literature for this setting is much more limited.[24,25] Given the accumulating literature regarding serious adverse effects with prolonged use, the evidence appears to support regular re-evaluation of PPI therapy after an appropriate length of treatment.

Deprescribing is defined as the process by which drugs whose harm may outweigh their benefits in individual patients are identified and subsequently discontinued.[26] Deprescribing is especially important for elderly patients because this population is at higher risk of drug-related adverse effects and associated morbidity, mortality, and health care utilization.[27] Choosing Wisely Canada has created a toolkit for PPI deprescribing, which includes an algorithm and guideline to aid clinicians in making evidence-informed decisions regarding PPI discontinuation.[28] This algorithm clearly delineates a process for identifying patients who are suitable candidates for PPI deprescribing, options for deprescribing, and recommendations for monitoring and follow-up.

Despite the recent focus in the literature, it is unclear whether PPI deprescribing is being practised consistently for long-term care residents in Winnipeg. The primary objective of this study was to determine the proportion of PPI users in a group of LTCHs who were candidates for deprescribing, according to documented indications, duration of therapy, and past deprescribing attempts. The secondary objectives were to evaluate fall rates and factors relating to vitamin B_{12} deficiency, to determine whether any patterns could be identified among PPI users.

METHODS

A cross-sectional, multisite, chart review was conducted in 5 LTCHs in Winnipeg, Manitoba. Residents of the LTCHs were included if they were over the age of 65 years, had a prescription for a PPI at the time of the chart review, and had undergone at least 1 interdisciplinary quarterly medication review (QMR) since the PPI was initiated. Residents were excluded if they had resided in the LTCH for less than 6 months or they had died or been transferred to a different facility between the time when the pharmacy list was generated for the study and actual data collection.

A convenience sample of 150 health records from the 5 LTCHs with the largest volumes of PPI use was generated using reports from the pharmacy information system, which identified residents with an active PPI prescription during the month of October 2016. For each of the 5 participating sites, the list of residents taking PPIs was randomized using a random number generator, and the health records of 30 residents meeting the inclusion criteria were selected for review from this randomized list. Data were collected by a single investigator (A.D.); a second investigator (A.B.) independently validated the data collected from the first 5 health records at each facility.

Data are presented in aggregate using descriptive statistics. Descriptive parameters, including frequencies, medians, and ranges, were calculated using an Excel spreadsheet (Microsoft Inc, Redmond, Washington). This research was conducted in accordance with the ethical standards of the Helsinki Declaration. The data were collected as a non-interventional quality assurance audit; therefore, the Government of Canada's Interagency

Advisory Panel on Research Ethics involving humans exempts this project from ethics approval by the University of Manitoba's Bannatyne Campus Health Research Ethics Board. The project was reviewed by the Pharmacy Quality Council of the Winnipeg Regional Health Authority, which waived the need for informed consent.

Data were collected for the following characteristics of LTCH residents: age, sex, length of stay in current LTCH, number of QMRs since the resident started PPI therapy, and total number of prescribed medications. Concurrent medications associated with PPI use were recorded, including nonsteroidal anti-inflammatory drugs (NSAIDs), antiplatelet agents, glucocorticoids, and anticoagulants.

To assess the primary objective, the PPI agent, dosing regimen, and indication from the most recent QMR were recorded. The algorithm in the Choosing Wisely Canada toolkit was used to assess PPI appropriateness and eligibility for deprescribing.[28] Residents with any of the following characteristics were not considered to be candidates for deprescribing: concurrent NSAID therapy and moderate to high risk for gastroduodenal injury; dual antiplatelet therapy; history of gastrointestinal ulcer, esophagitis, or Barrett esophagus; *Helicobacter pylori* eradication therapy administered for less than 14 days; or a failed deprescribing attempt in the past year. All documented gastrointestinal ulcers were presumed to be bleeding ulcers. Risk of gastrotoxicity in residents taking NSAIDs was determined with the American College of Cardiology Foundation Task Force consensus documents.[29] Candidates for deprescribing included those with no documented indication for PPI use, those receiving a PPI for gastroesophageal reflux disease (GERD) for longer than 8 weeks, those with twice-daily dosing for any indication other than *H. pylori* eradication, and those with inappropriate indications for PPI use. Residents whose only risk factor for gastrotoxicity was long-term use of low-dose acetylsalicylic acid (ASA) were considered candidates for deprescribing because of a lack of convincing evidence that PPIs confer benefit for this population.[30]

To assess the secondary objectives, the most recent serum vitamin B_{12} level was recorded. Levels were recorded as low (less than 220 pmol/mL), normal to high (greater than or equal to 220 pmol/mL), or not measured within the past 12 months. Fall risk was recorded as low, medium, or high, based on the most recent assessment of fall risk. Four of the LTCHs used the Fracture Risk Assessment Tool (FRAT),[31] whereas the fifth LTCH used the Morse Fall Scale.[32] History of a fall within the past 30 days was determined from LTCH incident records and progress notes in the residents' charts.

RESULTS

Of the 150 charts selected, 3 were omitted from analysis because information necessary to complete the review was missing; therefore, a total of 147 charts were analyzed. The study population had a mean age of 87 years, and most of the residents (113 [77%]) were women; other baseline characteristics are presented in Table 1. Pantoprazole was the most commonly used PPI (96 residents [65%]) because of institutional automatic substitution policies (Table 2). Most of the residents (118 [80%]) had been taking a PPI for longer than 1 year since admission. Of note, only 99 (67%) of the residents had been taking a PPI at the time of admission to the LTCH. The most common indication was GERD (79 [54%]); 29 residents (20%) had no documented indication for PPI therapy.

Candidacy for deprescribing is detailed in Table 3. Overall, 93 residents (63%) were potential candidates for deprescribing. Extended duration of PPI therapy (longer than 8 weeks) during treatment for GERD was the most frequently observed opportunity for deprescribing (49/93 [53%]). Pharmacists in the LTCHs had noted deprescribing opportunities on the QMR forms of 13 residents (9%). However, in each of these cases, the PPI had not been discontinued. For an additional 14 residents (10%), the PPI dose had been successfully reduced since admission to the LTCH.

More than half of the study population was considered to be at high risk for falls (Table 4). For 70 residents (48%), vitamin B_{12} had not been measured in the past year (Table 4). Fifty-three residents (36%) were receiving oral or intramuscular vitamin B_{12} supplementation and/or had low serum vitamin B_{12} levels.

DISCUSSION

This chart review showed that the majority of residents in the study population were candidates for PPI deprescribing. Current provincial standards dictate that long-term care residents undergo interprofessional medication reviews every 3 months. These QMRs involve the systematic evaluation of each resident's medication therapy and are attended by the prescriber, a pharmacist, and a nurse. If the QMRs are conducted in accordance with national guidelines, all residents who are taking a PPI would have an appropriate and documented indication for the drug. However, despite the opportunity to evaluate PPI appropriateness during QMRs, the current study suggests that this may not be done routinely for every resident.

Table 1. Characteristics of the Study Population

Characteristic	No. (%) of Patients* (*n* = 147)
Age (years), median (range)	87 (66–102)
Length of stay in LTCH (months), median (range)	30 (6–132)
Sex	
Men	34 (23)
Women	113 (77)
No. of medications, median (range)	12 (5–26)
Prescription for PPI on admission to LTCH	
Yes	99 (67)
No	48 (33)

LTCH = long-term care home, PPI = proton pump inhibitor.
*Except where indicated otherwise.

Table 2. Characteristics of PPI Use

Characteristic	No. (%) of Residents (*n* = 147)
PPI medication	
Pantoprazole	96 (65)
Omeprazole	48 (33)
Esomeprazole	2 (1)
Rabeprazole	1 (1)
Lansoprazole	0 (0)
Duration of PPI therapy since admission	
< 1 month	1 (1)
1 to 3 months	3 (2)
3 months to 1 year	25 (17)
1 to 3 years	75 (51)
> 3 years	43 (29)
PPI dosing schedule	
Daily	129 (88)
Twice daily	15 (10)
Three times per week	3 (2)
Documented indications	
Appropriate	
GERD	79 (54)
Peptic ulcer disease (active or history)	28 (19)
Long-term NSAID use with risk of bleeding	10 (7)
Inappropriate	
Corticosteroid use	2 (1)
Low-dose ASA use (81 mg)	10 (7)
Aggressive behaviour	1 (1)
No indication	29 (20)

ASA = acetylsalicylic acid, GERD = gastroesophageal reflux disease; NSAID = nonsteroidal anti-inflammatory drug, PPI = proton pump inhibitor.

Table 3. Evaluation of PPI Deprescribing Appropriateness

Variable	No. (%) of Residents (*n* = 147)
Candidate for deprescribing	
No	54 (37)
Yes	93 (63)
Reason for noncandidacy	*n* = 54
NSAID use	14 (26)
History of ulcer	30 (56)
Unsuccessful deprescribing attempt in past year	5 (9)
Dual antiplatelet therapy	5 (9)
Reasons for candidacy	*n* = 93
Twice daily dosing for indication other than *Helicobacter pylori* eradication	15 (16)
GERD treatment for > 8 weeks	49 (53)
Inappropriate indication	12 (13)
No documented indication	29 (31)

GERD = gastroesophageal reflux disease, NSAID = nonsteroidal anti-inflammatory drug, PPI = proton pump inhibitor.

Table 4. Fall Risk and Vitamin B_{12} Status

Characteristic	No. (%) of Residents (*n* = 147)
Fall risk	
Low	30 (20)
Medium	38 (26)
High	79 (54)
Vitamin B_{12} supplementation	
Intramuscular	7 (5)
Oral	43 (29)
None	97 (66)
Vitamin B_{12} level (within the past year)	
Low (< 220 pg/mL)	9 (6)
Normal or high (≥ 220 pg/mL)	68 (46)
Not measured	70 (48)
History of a fall in past 30 days	
Yes	13 (9)
No	134 (91)

These results are consistent with other studies that have considered PPI appropriateness in LTCHs. In a chart review conducted in Pennsylvania, 61% of patients transferred from hospital to an LTCH were taking a PPI.[24] The authors defined appropriate diagnoses as GERD, upper gastrointestinal bleeding, peptic ulcer disease, or empiric treatment of "heme-occult positive stool", but did not include ulcer prophylaxis with NSAID use. Using this list, they determined that PPIs had been prescribed with an appropriate diagnosis for only 50% of PPI users. A large-scale review of PPI use across LTCHs in 22 US states found that 24% of patients were taking PPIs without an appropriate indication, and 47% had no documented indication.[25] The authors of that review may have observed a lower rate of inappropriate use because they defined a wider range of indications as appropriate compared with other studies.

When deprescribing is considered, it is important to know relevant past medical conditions and medication indications. Documentation is important in this context, because the Choosing Wisely PPI deprescribing tool considers PPI therapy without a documented indication as a reason for deprescribing candidacy.[28] This chart review found incomplete documentation of past medical history and medication indications in the medical records at the LTCHs, in particular, limited documentation of medical conditions such as esophagitis or bleeding ulcers that could justify long-term PPI use. Without documented evidence to rule out these conditions as indications for PPI use, clinicians may be more hesitant to consider deprescribing. One of every 5 residents in the study population did not have a documented indication for PPI use, a rate much lower than what has been reported in other studies (about 50% of cases of PPI use without a documented indication[21-23]). This finding may be explained by the QMRs, which provide an ideal setting and opportunity for updating medical records and documenting indications for drug therapy appropriately.

The chart review identified opportunities for clinicians to reassess long-term PPI use for the treatment of GERD. Treatment for GERD for longer than 8 weeks without deprescribing attempts in the past year accounted for 53% of identified deprescribing candidates. Evidence suggests that among individuals using PPIs for GERD, decreasing the dose does not increase

the risk of symptom return, and 90% of individuals who discontinue the PPI and use it on demand will not have return of symptoms.[28] These data suggest that these are both reasonable strategies that could be used for residents who are being treated for GERD on a long-term basis. For residents with cognitive impairment, it might be difficult to implement and monitor on-demand use; therefore, this approach needs to be evaluated on a case-by-case basis.

Inappropriate documented indications in this chart review included concurrent use of low-dose ASA or a corticosteroid. There is unconvincing evidence that either of these medications require concomitant PPI therapy in the absence of other risk factors for gastrointestinal toxicity.[30] The chart review also identified a single resident for whom the documented indication for PPI use was aggressive behaviour. The authors are unaware of any literature to support this indication.

Forty-eight residents (33%) were not receiving a PPI at the time of admission to the LTCH. In this subgroup, the PPI had to have been started by the LTCH clinician or during a hospital stay occurring after transition to the LTCH. One opportunity for future study involves determining how many residents had PPIs started during a hospital stay and whether the appropriateness of PPI therapy was evaluated upon return to the LTCH.

The chart review identified residents with active PPI therapy during the study period; therefore, capturing the number of residents whose PPI was appropriately discontinued upon admission or during a previous QMR was beyond the scope of the study. However, this study did provide some insight on deprescribing efforts by pharmacists. As documented in the QMR records, pharmacists identified 13 residents who were potential candidates for deprescribing, but the reasons for not attempting deprescribing were not documented. Possible influencing factors include prescriber attitudes and beliefs, family or caregiver resistance, and discussion of reasons for noncandidacy that were not documented in QMR records. Further research is needed to identify barriers to deprescribing in this population and to design strategies that target those barriers with a goal of increasing deprescribing efforts.

The chart review found that 9% of residents had experienced a fall within the past 30 days. The Canadian Institute for Health Information has reported fall rates within the past 30 days of 19% for LTCHs in Winnipeg and 15.7% for LTCHs in all of Canada.[33] The lower incidence of falls in the current study population does not support the theory that an increase in fractures among PPI users occurs secondary to increased falls. However, because of inconsistencies in reporting falls across sites, the fall rate identified in the current chart review may not reflect the true incidence of falls in these 5 facilities. More than half of the residents were considered to have a high risk of falls; however, fall risk data for Winnipeg LTCHs are not available, and a comparison cannot be made with residents who did not have a PPI prescription.

This chart review also examined the rate of vitamin B_{12} deficiency and whether vitamin B_{12} deficiency was more prevalent among PPI users. Nine residents (6%) had a low serum vitamin B_{12} level. Unfortunately, 48% of the study sample had not had vitamin B_{12} serum level measured within the past 12 months, which made it difficult to comment on the prevalence of vitamin B_{12} deficiency for the study population as a whole; however, one-third of the study group was receiving exogenous vitamin B_{12}, which may be an indicator of the rate of deficiency.

Collecting data from 5 sites with multiple prescribers helped to capture a broad understanding of patterns of PPI use in Winnipeg LTCHs. QMRs were used for all residents and were of identical format across sites, which allowed for complete and uniform data collection. Medical records were easy to access, and records starting from admission were available, which allowed assessment of changes in therapy from the time of admission until data collection for this study. The authors were able to use Canadian and age-specific guidelines to determine PPI deprescribing candidacy. Use of the pharmacy information system to identify residents receiving a PPI resulted in all PPI users being randomized, which helped to ensure that the study sample accurately represented the population.

This chart review had a few limitations. Factors for not pursuing deprescribing that were unrelated to indication, such as resident or caregiver resistance to changing medications, could not be determined from the documentation available in the medical record. In addition, documentation of prior gastrointestinal bleeding or peptic ulcer disease was often missing or inconsistent among the 5 sites. Without verbal confirmation of medical history from the resident or caregiver, it is possible that the study overlooked residents with an undocumented history of gastrointestinal bleeding or peptic ulcer disease. There was also poor documentation of the reasons why PPI deprescribing attempts had failed. Another limitation was that the indication for each medication was not explicitly stated in the QMRs; as such, the indication for PPI therapy had to be inferred from concurrent medical conditions and medications listed on the QMR form. This situation leaves room for misinterpretation by the data collector.

CONCLUSION

In this chart review, the majority of LTCH residents in the study population were candidates for PPI deprescribing, which indicates opportunities for education and engagement of prescribers, pharmacists, nurses, residents, and family members. Long-term use of PPIs is associated with important adverse effects, and therapy must therefore be carefully re-evaluated at regular intervals. Clinicians should consider deprescribing, when appropriate, according to patient-specific factors. Further research is needed to evaluate strategies to encourage PPI deprescribing practice among clinicians.

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ORIGINAL RESEARCH

Evaluation of Prescribing Appropriateness and Initiatives to Improve Prescribing of Proton Pump Inhibitors at Vancouver General Hospital

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ABSTRACT

Background: Proton pump inhibitors (PPIs) have proven clinical efficacy for a variety of indications. However, there is emerging evidence of adverse events associated with their long-term use. The emergence of these adverse events has reinforced the need to regularly evaluate the appropriateness of continuing PPI therapy, and to use only the lowest effective dose for the minimally indicated duration.

Objectives: To characterize the appropriateness of PPI orders continued or initiated in the internal medicine and family practice units of Vancouver General Hospital, to detect adverse events associated with PPI use, and to explore the impact of multidisciplinary teaching and provision of educational resources on health care practitioners' views about PPI use.

Methods: A chart review was conducted for patients admitted (for at least 24 hours) between January 1 and December 31, 2015, for whom a hospital formulary PPI was prescribed. An educational initiative, which included interprofessional in-service sessions, a PPI prescribing infographic, a PPI prescribing card, and a patient counselling sheet, was implemented. The impact of these interventions was assessed using a qualitative survey of health care practitioners.

Results: Of the 258 patients whose charts were reviewed, 175 had a PPI prescription before hospital admission, and 83 were initiated on PPI therapy during their hospital stay. Overall, 94 (36%) of the patients were receiving PPIs without an appropriate indication. Community-acquired pneumonia and *Clostridium difficile* infections were the most common adverse events potentially associated with PPI use. In-service sessions and educational resources on PPI prescribing were reported to affect the clinical practice of 24 (52%) of the 46 survey respondents.

Conclusions: The results of this study emphasize the need for ongoing re-evaluation of long-term PPI therapy at the time of admission, during the hospital stay, and upon discharge. Implementing multidisciplinary teaching and providing educational resources may encourage more appropriate prescribing.

RÉSUMÉ

Contexte : Les inhibiteurs de la pompe à protons (IPP) ont prouvé leur efficacité clinique pour une gamme d'indications. Cependant, de nouvelles données sur leur utilisation à long terme leur imputent des événements indésirables. L'émergence de ces événements indésirables a renforcé l'idée qu'il est nécessaire d'évaluer régulièrement la pertinence d'un traitement prolongé par IPP et d'employer seulement la plus faible dose efficace pendant la durée indiquée la plus courte.

Objectifs : Offrir un portrait de la pertinence des ordonnances d'IPP, renouvelées ou nouvelles, dans les services de médecine interne et de médecine familiale de l'Hôpital général de Vancouver, détecter les événements indésirables liés à l'utilisation des IPP et étudier l'effet qu'ont une formation multidisciplinaire et une fourniture de ressources éducatives sur les points de vue des professionnels de la santé à propos des IPP.

Méthodes : Une analyse rétrospective de dossiers médicaux a été menée auprès de patients qui ont été admis (pendant au moins 24 heures) entre le 1er janvier et le 31 décembre 2015 et qui se sont vu prescrire un IPP inscrit sur la liste des médicaments de l'hôpital. On a mis en place un programme éducatif comprenant des séances de formation interprofessionnelles internes, un document infographique de prescription des IPP, une carte de prescription des IPP et une fiche de conseils aux patients. L'effet de ces interventions a été évalué à l'aide d'une enquête qualitative auprès des professionnels de la santé.

Résultats : Parmi les 258 patients dont le dossier a été examiné, 175 avaient une ordonnance d'IPP avant l'admission à l'hôpital et 83 ont amorcé un traitement par IPP pendant leur séjour. Dans l'ensemble, 94 (36 %) des patients recevaient un IPP sans indication pertinente. Les infections à *Clostridium difficile* et les pneumonies extra-hospitalières représentaient les événements indésirables les plus courants potentiellement liés à l'utilisation des IPP. On a signalé que les séances de formation interne et les ressources éducatives sur la prescription des IPP avaient eu un effet sur la pratique clinique de 24 (52 %) des 46 participants à l'enquête.

Keywords: proton pump inhibitors, prescribing initiatives, adverse events

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Conclusions : Les résultats de l'étude font ressortir la nécessité d'une réévaluation continuelle des traitements à long terme par IPP au moment de l'admission, pendant le séjour et lors du congé. La mise en place de formation multidisciplinaire et l'offre de ressources éducatives pourraient favoriser des pratiques de prescription plus adéquates.

Mots clés : inhibiteurs de la pompe à protons, programmes de formation sur les pratiques de prescription, événements indésirables

INTRODUCTION

Proton pump inhibitors (PPIs) are a class of medications that inhibit parietal cell hydrogen potassium ATPase pumps and suppress gastric acid secretion. Approved indications include severe gastroesophageal reflux disease (GERD), erosive and ulcerative esophagitis, gastric and duodenal ulceration, stress ulcer prophylaxis, prevention of ulceration induced by nonsteroidal anti-inflammatory drugs (NSAIDs), eradication of *Helicobacter pylori*, Barrett esophagus, and Zollinger–Ellison syndrome.[1-4] The recommended duration of use is usually short term (2–8 weeks), with few patients requiring long-term treatment.[5] Despite their capacity to provide clinically significant symptom management, prolonged use of PPIs has been associated with a plethora of adverse effects, including *Clostridium difficile* infections, hospital- and community-acquired pneumonia, dementia, osteoporosis and fracture, hypomagnesemia, hypoparathyroidism, and vitamin B_{12} deficiency.[1-3,6-13] Thus, it may be beneficial to regularly evaluate the appropriateness of PPI use for individual patients, and to treat only with the lowest effective dose for the minimally indicated duration.[14]

According to a 2016 report of the Canadian Institute for Health Information, PPIs accounted for more than $250 million dollars of annual spending on prescribed drugs, and ranked ninth among the top 100 drug classes used in British Columbia.[15] Regionally, this translated to 13 174 orders for oral PPIs at Vancouver General Hospital, with 2550 originating from the internal medicine and family practice inpatient units. PPIs are frequently used without a clear indication (e.g., in the absence of ulcer disease, esophagitis, or severe GERD), and inappropriate prescribing has been identified for about 50% of users.[3,16,17] In addition, PPI prescriptions are often automatically renewed, despite resolution of the original indication,[18] a process known as "prescribing inertia".[19,20] When compounded with their effectiveness in relieving dyspepsia and the lack of immediate adverse effects that would dissuade patients from using these drugs, PPI overprescribing is becoming more prevalent in clinical practice.[2,3,17,21,22]

For these reasons, PPI deprescribing initiatives are increasing, especially for older populations and patients who are taking more than 5 prescription medications daily.[18,23] At present, interventions to ameliorate PPI overprescribing that have been tried and reported in the literature include standardized guidelines on prescribing practice for patients not receiving PPIs at the time of hospital admission,[2] PPI deprescribing guidelines for long-term care,[8] an in-hospital pharmacist-managed program for stress ulcer prophylaxis,[24] and an in-hospital computerized clinical-decision support intervention.[25] Common among all of these interventions has been a significant decrease in the average number of PPIs ordered and re-ordered in both inpatient and outpatient settings; however, the overall practice of deprescribing has been difficult to maintain beyond the intervention period.[2,4,8,12,25] Cited barriers have included lack of access to a complete medical history following a transition of care, time limitations in reviewing the complete medical history and reassessing the patient, and malpractice concerns.[8,16,26]

The objective of this study was to first characterize the use of PPIs and detect adverse events associated with PPI use at Vancouver General Hospital, and to then develop, implement, and evaluate an intervention targeted toward improving PPI use.

METHODS

Phase 1

In this phase, a retrospective, single-centre study was conducted at a tertiary care teaching hospital located in Vancouver, British Columbia. The hospital pharmacy's computerized prescription database (Carecast patient care information system, IDX Systems Corporation) was used to identify patients who were admitted between January 1 and December 31, 2015, and who received a hospital formulary PPI (pantoprazole or esomeprazole for oral administration) during their admission. Inclusion and exclusion criteria were then applied. Patients had to have stayed in hospital for at least 24 h and had to have been admitted to one of the internal medicine or family practice units. The following selection process was used for randomization. Charts for eligible patients were numerically labelled; every third chart was selected, and then every sixth chart was removed from those that remained. Finally, a convenience sample of these randomly identified patients was selected for inclusion in the chart review. Baseline

characteristics, including age, sex, dates of admission and discharge, reason for admission, and medications before admission, were collected. Charts were reviewed to determine the timeframe of the PPI therapy (short-term or long-term). The indication for PPI use was recorded and classified as to appropriateness, according to predetermined criteria (Appendix 1, available at https://www. cjhp-online.ca/index.php/cjhp/issue/view/186/showToc). Adverse events potentially related to PPI use were also noted, based on documentation of adverse event criteria (as defined in Appendix 1). Ethics approval was obtained from the University of British Columbia's Clinical Research Ethics Board to conduct the chart review.

Phase 2

A multidisciplinary intervention targeting improvement in PPI prescribing was developed, based on a literature review and stakeholder input. The multifaceted intervention was implemented between January 23 and March 24, 2017, which represented two 4-week clinical rotations. An infographic directed toward health care professionals, which summarized PPI drug information and tapering regimens, was created (Figure 1). In addition, a PPI prescribing card (Appendix 2, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/186/showToc) was provided to all medical students, medical residents, physicians, and pharmacists in the internal medicine and family practice areas at the start of each rotation. A patient counselling sheet (Appendix 3, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/186/showToc), which outlined PPI discontinuation information, was also created; this sheet was provided to the patient during the hospital admission to initiate a discussion about PPI describing and/or to serve as a supplemental reference once PPI de-escalation was initiated. Multidisciplinary in-service sessions were carried out in all targeted units. Some staff members could not attend these sessions in person, so a 7-min online PowerPoint presentation with voiceover was also created, with the link being sent out via e-mail.

A qualitative survey was developed to solicit feedback from the medical, pharmacy, and nursing staff who had been exposed to the intervention; the survey was administered at the end of the data collection period. The survey collected data on awareness of the educational interventions and the impact of these resources on clinical practice, as reported by the participating medical students, medical residents, physicians, nurses, and pharmacists. The utility of the in-service sessions and the infographic, as perceived by the interprofessional team, was also assessed.

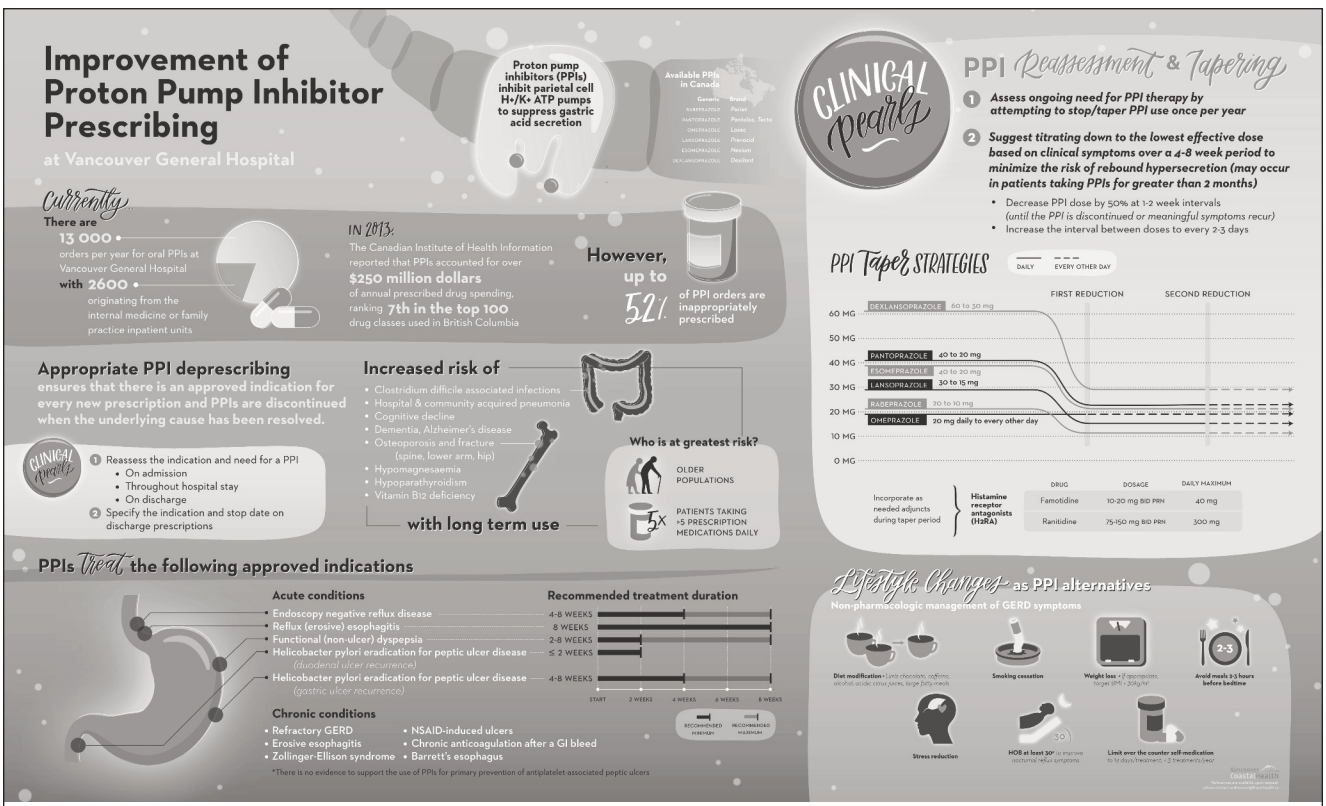

Figure 1. Infographic for prescribing proton pump inhibitors (PPIs). © 2016, Vancouver Coastal Health. Reproduced by permission.

Statistical Analysis

Descriptive statistics were used to assess outcomes in relation to the objectives listed above. Results are expressed as means and standard deviations (SDs) (with ranges), medians (with interquartile ranges), or proportions of the total number of patients.

RESULTS

Phase 1

A total of 13 174 patients were identified as having received a PPI during the study period. Of those, 3969 received treatment on one of the internal medicine or family practice units. After removal of duplicates, 2155 patients met the inclusion criteria, and a convenience sample of 258 charts was reviewed (Figure 2). The mean age of patients included in the chart review was 74 (SD 15) years, and 135 (52%) were men (Table 1). The median length of hospital stay was 9 days, with a majority of patients admitted to the internal medicine unit. On average, patients had 5 (SD 2) comorbidities (a majority being of either cardiac or gastrointestinal origin) and were taking 8 (SD 4) medications before hospital admission.

During the hospital stay, 235 (91%) of the patients received oral pantoprazole, and 23 (9%) received oral esomeprazole (Table 2). For 175 (68%) of the patients, the PPI orders were for continuation of a PPI initiated before admission, whereas the remaining 83 (32%) patients had PPI orders initiated during the hospital stay (Table 2). For PPI orders continued in hospital, the median duration of therapy before admission was 18 weeks, with an IQR of 0–31 weeks (Table 2).

Overall, 164 (64%) of the patients with PPI orders at Vancouver General Hospital had an appropriate indication (Figure 3). The most common indications were history of a bleeding gastrointestinal ulcer or refractory GERD (data not shown). Similarly, 109 (62%) of the 175 patients with PPIs continued on admission and 55 (66%) of the 83 with PPIs initiated during the admission had an appropriate indication (Figure 3). Of the 175 patients whose PPI therapy was continued upon hospital admission, 49 experienced adverse events potentially associated with long-term PPI use, with 44 of these 49 patients having taken a PPI for longer than 8 weeks. The most common adverse events were community-acquired pneumonia and *C. difficile* infection (Table 3).

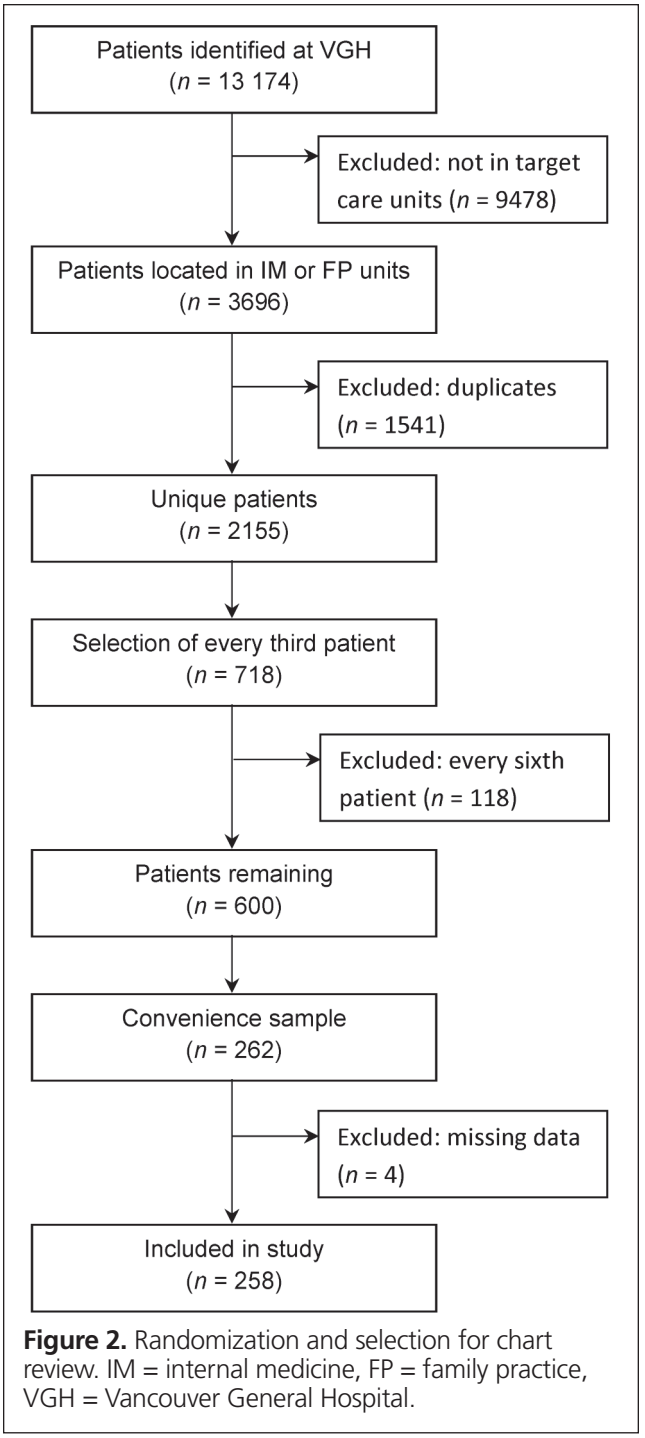

Figure 2. Randomization and selection for chart review. IM = internal medicine, FP = family practice, VGH = Vancouver General Hospital.

Phase 2

A total of 46 health care professionals participated in the qualitative survey (Table 4). Given the large number of health care professionals who had rotations in the internal medicine and family practice units, we could not determine the number of staff who were exposed to any aspect of the intervention and hence could not calculate the response rate. Of the 46 survey respondents, 17 (37%) reported that they had attended an in-service session or watched the online presentation, and 16 (94%) of these found it to be an educational and effective use of their time (Figure 4). Of the educational resources available during the 2 months of the intervention, respondents were most aware of the PPI infographic (shown in Figure 1), reporting it to be an effective method of communicating information about appropriate PPI prescribing. Only 7 (15%) and 6 (13%) of survey respondents

Table 1. Baseline Characteristics of Study Population

Characteristic	No. (%) of Patients* (*n* = 258)
Age (years), mean ± SD	74 ± 15
31–40	9 (3)
41–50	13 (5)
51–60	28 (11)
61–70	36 (14)
71–80	61 (24)
81–90	84 (33)
91–100	26 (10)
≥ 101	1 (< 1)
Sex	
Men	135 (52)
Women	123 (48)
Hospital unit	
Internal medicine	163 (63)
Family practice	95 (37)
Length of stay in hospital, median (IQR)	9 (3–19)
No. of comorbidities, mean ± SD (range)	5 ± 2 (1–10)
Type of comorbidity	
Cardiac	227 (88)
Gastrointestinal	188 (73)
Musculoskeletal	140 (54)
Endocrine/metabolic	128 (50)
Psychiatric	126 (49)
Respiratory	105 (41)
Renal	83 (32)
Cancer	71 (28)
Genitourinary	69 (27)
CNS/neurologic	61 (24)
Other	45 (17)
Dermatologic	39 (15)
No. of medications before admission, mean ± SD (range)	8 ± 4 (0–22)

CNS = central nervous system, IQR = interquartile range, SD = standard deviation.
*Except where indicated otherwise.

were aware of the PPI prescribing card and patient counselling sheet, respectively. Overall, 24 (52%) of the survey respondents felt that the resources provided had had an impact on their clinical practice.

Table 2. Assessment of PPI Orders at Vancouver General Hospital

Characteristic	No. (%) of Patients* (*n* = 258)
Timeframe of PPI use	
PPI initiated in hospital	83 (32)
PPI continued on admission	175 (68)
Duration of PPI use before admission (weeks), median (IQR)	18 (0–31)
≤ 8 weeks	63 (24)
9–52 weeks	71 (28)
> 52 weeks	41 (16)
PPI given during hospital stay	
Pantoprazole (oral)	235 (91)
20 mg once daily	5 (2)
30 mg once daily	1 (<1)
40 mg once daily	181 (77)
40 mg twice daily	48 (20)
Esomeprazole (oral)	23 (9)
40 mg once daily	1 (4)
40 mg twice daily	22 (96)

IQR = interquartile range, PPI = proton pump inhibitor.
*Except where indicated otherwise.

DISCUSSION

Overall, 36% of patients were taking PPIs that had been ordered without an appropriate indication. More specifically, for 34% of patients with PPIs initiated during the admission and 38% of those with continuing PPI therapy (i.e., started before admission), there was no appropriate indication for the PPI order. These findings are similar to the incidence of inappropriate PPI prescribing reported in the literature.[3,16,17,20] They also illustrate that PPI prescribing at Vancouver General Hospital is vulnerable to "prescribing inertia", a situation in which medications are automatically continued despite resolution of the original indication[18] and prescribers fail to de-escalate therapy when the therapy is no longer indicated. The observed incidence of inappropriate PPI prescribing may also be secondary to perceived negative consequences if the medication is discontinued, both for the prescriber (diminished credibility and therapeutic relationship with the patient, conflict with other prescribers and health care professionals) and for the patient (need to manage withdrawal

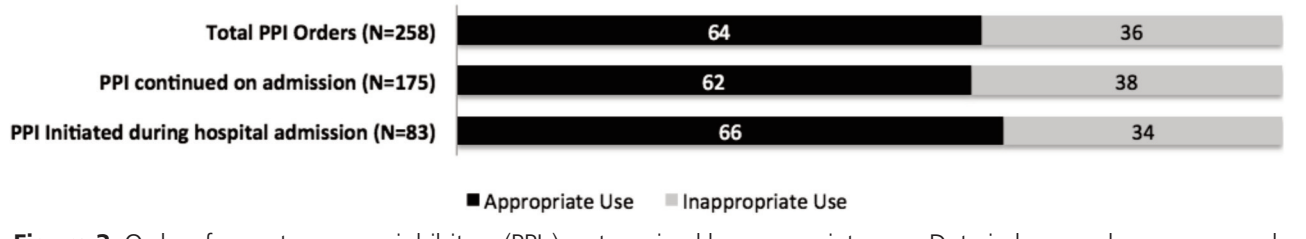

Figure 3. Orders for proton pump inhibitors (PPIs), categorized by appropriateness. Data in bar graph are expressed as percentages.

Table 3. Potential Adverse Events Associated with Long-Term PPI Use

Outcome	No. (%) of Patients (*n* = 49)*
Clostridium difficile infection	15 (31)
Community-acquired pneumonia	25 (51)
Fracture	6 (12)
Vitamin B_{12} deficiency	3 (6)
Other	3 (6)
Unknown	3 (6)

*Patients may have experienced multiple adverse effects

Table 4. Professions of Survey Respondents

Profession	No. (%) of Respondents (*n* = 46)
Nurse	22 (48)
Medical resident	10 (22)
Physician	8 (17)
Pharmacist	3 (7)
Medical student	3 (7)

symptoms, symptom relapse, complications, morbidity).[19] The finding that more than one-third of PPI prescriptions at Vancouver General Hospital were without an appropriate indication supports modification of current practice to favour a more thoughtful and proactive approach to weighing the therapeutic benefits and risks when prescribing PPIs (e.g., lowest effective dose for the minimally indicated duration).[14]

Another important finding of this study was the duration of PPI use for orders continued from before the admission: median 18 weeks, with an IQR of 0–31 weeks (Table 2). Considering that one-third of all PPI orders were prescribed inappropriately, this result quantifies the potential duration of unnecessary exposure to PPI therapy, especially if the original indication was an acute condition (requiring less than 8 weeks of treatment in total). Also, although a causative relationship between adverse events and long-term PPI use was not elucidated in this study, the association of community-acquired pneumonia and *C. difficile* infections with PPI use corroborates data reported in the literature.[3,27-29] The combination of these results with the observation that 44 of the 49 patients who experienced an adverse event had been taking a PPI for longer than 8 weeks further reinforces the need to regularly evaluate the appropriateness of continuing this type of medication beyond the recommended short-term duration.

Regarding the educational initiatives used to improve PPI prescribing, 94% of the 17 survey respondents who attended an in-service session or watched the online video found that this resource was educational and an effective use of their time. In addition, survey respondents were most aware of the PPI infographic as a tool to disseminate information on appropriate PPI prescribing. These findings suggest that accessibility of and exposure to educational resources may have the greatest impact on PPI prescribing practices in the future, and are echoed by the results of similar studies reported elsewhere. For example, the OPTI-SCRIPT study explored this concept in general practitioner practices.[30] The intervention in that study included having a pharmacist provide a 30-min academic detailing session with the physician to discuss potentially inappropriate prescribing practices, a medication review that detailed web-based pharmaceutical treatment algorithms on alternative pharmacologic and nonpharmacologic treatment options, and patient information leaflets describing the reasons why a medication might not be appropriate and outlining alternative therapies that the physician

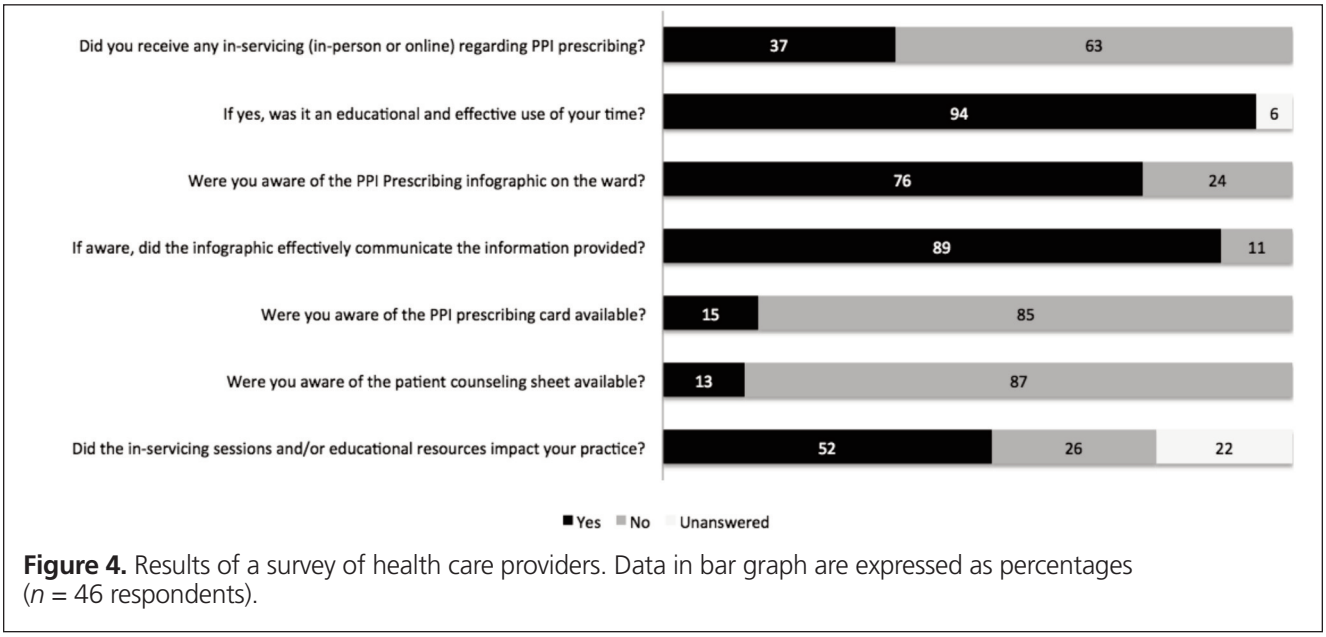

Figure 4. Results of a survey of health care providers. Data in bar graph are expressed as percentages (*n* = 46 respondents).

could offer. Over a 6-month period, 30% of inappropriate PPI therapy was stopped or changed to a histamine receptor antagonist, and among the patients who continued to receive treatment, 50% had a dose reduction. The authors concluded that these initiatives could effectively modify and reduce PPI prescribing.[30] The academic detailing session and patient information leaflet used in the OPTI-SCRIPT study were similar to our in-service session and educational materials. Given these similarities and the success of the OPTI-SCRIPT study, it can be theorized that had we raised more awareness of the resources available at our site, and continuously advocated for and implemented the algorithms for appropriate prescribing and deprescribing, we could have achieved similar improvements in PPI prescribing.

With more than half of survey respondents reporting that the educational intervention had an impact on their clinical practice, next steps may include continuing to educate the interdisciplinary team to (1) reassess the indication and need for a PPI at the time of admission, throughout the hospital stay, and upon discharge; and (2) specify the indication and stop date for discharge prescriptions (Figure 1). Moreover, early evaluation of PPI therapy may allow time for patient education (Appendix 3) and monitoring of symptom relapse if PPI discontinuation or step-down is initiated during hospital admission, and specifying the indication and stop date on discharge prescriptions may clarify the care plan as the patient transitions from the hospital to the community setting. Where possible, clinical pharmacists could also intervene and provide prescribers with tapering regimens specific to each PPI, as well as making recommendations for adjunctive therapy during the taper period (histamine receptor antagonists, nonpharmacologic management) (Figure 1). Future studies at our site to assess and quantify the effect of these initiatives on PPI prescribing would be beneficial.

Limitations

The limitations of this study include the small sample size and the descriptive, single-centre, retrospective design. Patient records that did not document the indication for PPI use were excluded, and the results presented may under- or over-estimate the rate of inappropriate PPI prescribing. The duration of PPI use was quantified using the patient's medication reconciliation record or PharmaNet profile (see Appendix 1 for definition), which displayed all medications dispensed to a patient within a 6- or 14-month period before the hospital admission, respectively. Because a majority of patients in the convenience sample had only 1 admission during the study period, and because there was a lack of documentation as to whether the medication reconciliation record or PharmNet profile had been used, delineation of the duration of PPI use beyond 6 months may be biased. Also, because this study endeavoured to detect adverse events with PPI use, we must clarify that the number of adverse events reported is likely an overestimate, given the small sample size, and the adverse events observed may not be secondary to PPI use alone, but rather may have been confounded by other factors (e.g., comorbidities [such as osteoporosis, which may result in bone fractures], disease severity, and medications [such as metformin, which reduces vitamin B_{12} absorption and may potentiate vitamin B_{12} deficiency]). We were unable to determine the number of staff exposed to any aspect of the intervention and therefore could not determine the survey response rate. This limitation may have introduced selection and participation bias, and the opinions of the 46 survey respondents may not be representative of all individuals exposed to the intervention. Changes in PPI prescribing after the intervention period (e.g., number of appropriate PPI orders, number of PPIs discontinued, dose reductions, change in therapy to a histamine receptor antagonist) were not quantified.

CONCLUSION

Overall, one-third of patients receiving PPI therapy did not have an appropriate indication. In an era in which patients taking PPIs are of advanced age, have multiple comorbidities, experience substantial pill burden associated with an increasing number of long-term medications, and are at risk of adverse drug reactions, it is important to continue to emphasize appropriate prescribing, documentation of indications for use, and ongoing re-evaluation of long-term PPI therapy. As shown in this study, one approach may be to implement multidisciplinary teaching and provide educational resources. Success in changing practice is well documented, and minimizing exposure to PPI therapy over the long term may positively affect patient outcomes.

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ORIGINAL RESEARCH

Characterization of Serious Adverse Drug Reactions in Hospital to Determine Potential Implications of Mandatory Reporting

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ABSTRACT

Background: The *Protecting Canadians from Unsafe Drugs Act* will eventually require institutions to report all serious adverse drug reactions (ADRs), although the proposed regulations do not yet define what will need to be reported and by whom. Knowledge about the occurrence of serious ADRs in the hospital setting is needed to optimize the effectiveness of reporting and to determine the potential implications of mandatory reporting.

Objectives: To quantify and characterize suspected serious ADRs in patients admitted to a general medicine service, to assess the likelihood of causality, and to determine inter-rater agreement for identification of ADRs and assessment of their likelihood.

Methods: This prospective observational study involved 60 consecutive patients admitted to a general medicine service at a tertiary care teaching centre starting on March 28, 2016. The primary outcome was the number of serious ADRs, defined by Health Canada as ADRs that result in hospital admission, congenital malformation, persistent or significant disability or incapacity, or death; that are life-threatening; or that require significant intervention to prevent one of these outcomes. Medical records were reviewed independently by pairs of pharmacists for serious ADRs, and the likelihood of causality was assessed using the World Health Organization–Uppsala Monitoring Centre system. Inter-rater agreement was calculated using the kappa score, and disagreements were resolved by discussion and consensus.

Results: Twenty-three serious ADRs occurred in the sample of 60 patients. The proportion of patients experiencing a serious ADR that contributed to the original hospital admission was 19/60 (32%, 95% confidence interval [CI] 20%–43%), and 4 patients (7%, 95% CI 0%–13%) experienced a serious ADR during their hospital stay. Inter-rater agreement for occurrence of serious ADRs was moderate (kappa 0.58, 95% CI 0.35–0.76).

Conclusion: Reportable serious ADRs were common among patients admitted to a general medicine service. Canadian hospitals would face difficulties reporting all serious ADRs because of the frequency of their occurrence and the subjectivity of their identification.

Keywords: adverse drug reactions, postmarket surveillance, adverse drug reaction reporting, hospital pharmacy

RÉSUMÉ

Contexte : La *Loi visant à protéger les Canadiens contre les drogues dangereuses* obligera éventuellement les établissements à déclarer tout cas de réactions indésirables graves aux médicaments (RIM), quoique les règlements proposés n'indiquent pas encore ce qui devra être déclaré et par qui. Des données sur la survenue de RIM graves en milieu hospitalier sont nécessaires pour optimiser l'efficacité de la déclaration et pour déterminer les implications potentielles d'une déclaration obligatoire.

Objectifs : Quantifier les RIM graves soupçonnées chez les patients admis à un service de médecine générale et en offrir un portrait, évaluer la probabilité d'une relation de causalité et déterminer l'accord interévaluateurs pour le repérage des RIM et l'évaluation de leur probabilité.

Méthodes : La présente étude observationnelle prospective comptait 60 patients admis consécutivement à partir du 28 mars 2016 à un service de médecine générale d'un centre hospitalier universitaire de soins tertiaires. Le principal paramètre d'évaluation était le nombre de RIM graves, définies par Santé Canada comme des RIM qui mènent à une hospitalisation, à une malformation congénitale, à une invalidité ou à une incapacité persistante ou importante; qui mettent la vie en danger ou entraînent la mort; ou qui nécessitent une intervention significative pour prévenir l'un de ces résultats. Les dossiers médicaux ont été examinés indépendamment par des paires de pharmaciens à la recherche de RIM graves et la probabilité d'une causalité a été évaluée à l'aide du système du Centre de pharmacovigilance d'Uppsala de l'Organisation mondiale de la Santé. L'accord interévaluateurs a été mesuré à l'aide du coefficient kappa et les désaccords ont été résolus par la discussion et l'atteinte d'un consensus.

Résultats : Vingt-trois RIM graves sont survenues dans l'échantillon composé de 60 patients. La proportion de patients ayant subi une RIM grave qui a contribué à l'hospitalisation initiale était 19/60 (32 %, intervalle de confiance [IC] de 95 % de 20 %–43 %); de plus, 4 patients (7 %, IC de 95 % de 0 %–13 %) avaient subi une RIM grave au cours de leur séjour à l'hôpital. L'accord interévaluateurs sur la survenue de RIM graves était modéré (kappa = 0,58, IC de 95 % de 0,35–0,76).

Conclusion : Les RIM graves à déclaration obligatoire étaient courantes chez les patients admis à un service de médecine générale. Les hôpitaux

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canadiens auraient de la difficulté à déclarer tous les cas de RIM graves à cause de leur fréquence et de la subjectivité de leur repérage.

Mots clés : réactions indésirables aux médicaments, pharmacovigilance, déclaration des réactions indésirables aux médicaments, pharmacie hospitalière

INTRODUCTION

Health Canada relies on spontaneous reporting of adverse drug reactions (ADRs) to optimize the postmarket safety of medications. Previously unknown ADRs are often identified in clinical practice, and pharmacovigilance centres rely primarily on voluntary reporting of ADRs by health professionals.[1] Reporting is particularly important for ADRs that are rare or that occur only after long-term use, as these types of ADR are not likely to be identified in premarket clinical trials.[1] Important safety signals arising from spontaneous ADR reports have led to regulatory actions, including withdrawal of drugs from the market, labelling changes, public alerts, and notices sent to health professionals.[2] For example, the prescription drug cisapride, indicated for the treatment of refractory gastroparesis, intestinal pseudo-obstruction, and gastroesophageal reflux disease, was approved for the Canadian market in 1991.[3,4] Health Canada subsequently received 44 spontaneous ADR reports of cardiac rhythm abnormalities in patients taking cisapride, including 10 reports of death associated with the use of this drug. Likewise, the US Food and Drug Administration received 341 ADR reports of cardiac rhythm abnormalities, including 80 reports of death associated with its use. These spontaneous ADR reports led to changes in the product monograph, safety warnings, and the eventual withdrawal of cisapride from the Canadian market (in the year 2000).[4]

Currently, the reporting of ADRs to Health Canada by health professionals is voluntary. Health Canada's ADR reporting guideline[5] states that "any suspected" ADR should be reported, especially those that are "unexpected" (not consistent with product information or labelling), regardless of their severity; those that are serious, whether expected or not; and those related to a health product that has been on the market for less than 5 years.

Adverse reactions are defined in the Health Canada guideline as "noxious and unintended effects to health products".[5] The guideline notes that adverse reaction reports are most typically "only *suspected associations*" and that a health professional does not have to be certain that the reaction was due to a drug (or other health product) in order to report the reaction.[5] A serious adverse reaction is defined as "one which requires hospitalization or prolongation of existing hospitalization, causes congenital malformation, results in persistent or significant disability or incapacity, is life-threatening, or results in death. Adverse reactions that require significant medical intervention to prevent one of these outcomes are also considered to be serious."[5]

The *Protecting Canadians from Unsafe Drugs Act*, which was enacted in November 2014, aims to improve Health Canada's ability to collect postmarket safety information. As part of this act, also known as Vanessa's Law, institutions will be required to report all serious ADRs.[6] However, this requirement is not yet being enforced, because supporting regulations are not yet available.[7]

Subjectivity in the identification of serious ADRs will make it difficult to enforce mandatory reporting by health professionals. Signs and symptoms of ADRs can be nonspecific, and it is therefore often difficult for clinicians to differentiate an ADR from a current illness.[8] Furthermore, many clinicians report lack of time as a barrier to ADR reporting.[9] Additionally, reporting reactions that are well established as being associated with a particular drug is likely not an optimal use of scarce resources. For example, there is a multitude of evidence that warfarin causes bleeding and that benzodiazepines cause sedation and delirium. Reporting of suspected serious ADRs like these, which are well-known side effects of medications that occur with high frequency, would require substantial resources and would be unlikely to improve knowledge of a medication's safety.

The foregoing considerations indicate that reporting all suspected serious ADRs has uncertain benefit and, furthermore, that institutions in Canada may face difficulties meeting the requirements of the *Protecting Canadians from Unsafe Drugs Act*. We therefore conducted a prospective observational study of patients admitted to a general medicine service at a tertiary care teaching hospital to determine the type and frequency of suspected serious ADRs, as well as inter-rater agreement in these determinations. We also characterized the ADRs to inform the operationalization of the *Protecting Canadians from Unsafe Drugs Act* for hospitals.

This study had the following objectives:

- to quantify the number of suspected serious ADRs in patients admitted to a general medicine service

- to characterize the suspected serious ADRs in patients admitted to this general medicine service
- to assess the likelihood of causality of the suspected serious ADRs in patients admitted to this general medicine service
- to determine inter-rater agreement for identification of suspected serious ADRs and assessment of their likelihood.

METHODS

Study Design, Setting, and Population

This prospective observational study was based on data from patients' health records. Ethics approval was obtained from the Ottawa Health Science Network Research Ethics Board, which waived the need for informed consent.

The study took place at a 1122-bed tertiary care teaching centre in Ontario, Canada. Consecutive patients admitted through the emergency department to the general medicine service at the largest campus of this institution (over a period of 8 consecutive days starting on March 28, 2016) were eligible for inclusion. Patients were excluded if the investigators could not access their paper charts. Patients' data were censored if the hospital stay extended beyond 28 days.

Consecutive patients were considered for inclusion until the prespecified sample size of 60 was reached. The sample size of 60 was chosen because chart review for this number of patients was feasible, given resources available at the time of the study. Also, it allowed for adequate precision for estimates of proportions: the 95% confidence interval (CI) would be precise to ±13% at maximum variance (i.e., a proportion of 50%).

Assessment of Causality

The World Health Organization–Uppsala Monitoring Centre system for standardized case causality assessment (referred to hereafter as the WHO-UMC system) was chosen as the method for determining the likelihood of causality of each ADR. The WHO-UMC system classifies ADRs into 6 broad categories: certain, probable/likely, possible, unlikely, conditional/unclassified, and unassessable/unclassifiable.[10] To classify the likelihood of causality, the assessor considers the event, the plausibility of the time relationship, the response to withdrawal (if applicable), and other possible contributing factors. Complete definitions for the WHO-UMC causality categories are presented in Appendix 1.

Data Collection

A single investigator, a pharmacy resident licensed as a pharmacist (S.G.), collected data from the paper and electronic health records of all included patients. For each patient, a second pharmacist (from a pool of 4 pharmacists with hospital residency training who were practising in a range of clinical areas, all with 7 or more years of experience in inpatient care [J.W., S.K., T.N., E.M.]) independently reviewed and assessed the health records for the occurrence of suspected serious ADRs, and assessed the likelihood of causality of any suspected serious ADRs according to the WHO-UMC system. Specifically, for each patient, the 2 pharmacists independently reviewed the admission diagnoses (primary and contributing) from the admission consult, the best possible medication history, the admitting team's daily progress notes, documentation from consulting services, medications ordered in hospital, and discharge summaries to identify suspected serious ADRs and to assess their likelihood. Laboratory measures, vital signs, and the medication administration record were reviewed when either of the pharmacists deemed this information to be relevant to the assessment of a suspected serious ADR. This chart review was intended to reflect how a pharmacist would review the chart during the course of usual patient care. The 2 pharmacists independently assessed whether a primary or contributing admission diagnosis should be considered to represent a suspected serious ADR. Additionally, the 2 pharmacists independently assessed whether a suspected serious ADR occurred during the hospital stay. For each suspected ADR, the 2 pharmacists used the WHO-UMC system to independently assess the likelihood that a particular drug caused the reaction. Disagreements were resolved by discussion and consensus. When deemed necessary by either of the 2 pharmacists, drug product monographs, accessed from Health Canada's Drug Product Database, were reviewed to help make the assessment of likelihood. Other references, such as Lexi-Drugs, Micromedex, and MedEffect Canada databases, were also accessed at the discretion of the pharmacists.

The pharmacists did not communicate with a patient's health care team unless they felt that they had identified a serious ADR of which the team was unaware and that warranted intervention. ADRs identified during the course of the study were reported to Health Canada at the discretion of the team pharmacist (not the study investigators), in accordance with Health Canada's current guidance and current practice at the study institution.

Outcomes

The primary outcome was the number of suspected serious ADRs contributing to the reason for hospital admission or occurring during the hospital stay.

Secondary outcomes were the number of suspected serious ADRs contributing to the reason for hospital admission; the number of suspected serious ADRs occurring during the hospital stay; the proportions of patients experiencing suspected serious ADRs (overall, upon admission, and during the hospital stay); the mean number of suspected serious ADRs per patient; the proportion of suspected serious ADRs that were unexpected (where, for the purposes of this study, an "unexpected" reaction was one not listed in the product monograph), the proportion that were caused by a "new" drug (one that had been on the market for less than 5 years), and the proportion that met both of these criteria;

the proportion of suspected serious ADRs that were considered to be possible, likely, or certain according to the WHO-UMC system; and inter-rater reliability for the identification of a suspected serious ADR and for the classification of likelihood of a suspected serious ADR.

Statistical Analysis

Data are reported as frequencies and proportions, with 95% CIs as appropriate. A kappa score was calculated to quantify inter-rater agreement for the identification of suspected serious ADRs and their likelihood. Excel (Microsoft Corporation, Redmond, Washington) and SAS version 9.4 statistical software (SAS Institute Inc, Cary, North Carolina) were used for all statistical analyses.

RESULTS

A total of 67 consecutive, potentially eligible patients were admitted to the general medicine service between March 28 and April 4, 2016, but 7 patients were excluded from analysis because their paper charts were inaccessible. The mean age of the 60 patients included in the analysis was 67 (range 19–95) years, and the mean number of medications at the time of admission, as recorded in the patients' admission medication history was 11 (range 0–25). Thirty-two (53%) of the patients were men.

Primary Outcome

A total of 23 serious ADRs were identified in 21 of the 60 patients. For each ADR, the drug (or drugs) implicated and the associated reactions, outcomes, and actions taken with regard to the implicated drugs are described in Table 1.

Secondary Outcomes

Nineteen of the 23 serious ADRs contributed to hospital admission for a total of 19 of the 60 patients (32%, 95% CI 20%–43%). Four of the 23 serious ADRs occurred during the hospital stay for a total of 4 patients (7%, 95% CI 0%–13%). Two of the patients each experienced 2 serious ADRs; as such, a total of 21 of the 60 patients (35%, 95% CI 23%–47%) experienced a suspected serious ADR contributing to the reason for hospital admission and/or during the hospital stay. The mean number of suspected serious ADRs per patient was 0.4.

The proportion of suspected serious ADRs caused by a new drug (marketed for less than 5 years) was 2/23 (9%). Only one (4%) of the 23 suspected serious ADRs was considered unexpected (not described in the product monograph). None of the suspected ADRs met both of these criteria. Figure 1 depicts the expected frequency of occurrence of an ADR, as stated in the product monographs for the 31 drug–ADR pairs identified in this study (as listed in Table 1). According to the WHO-UMC system, 15 (65%) of the 23 serious ADRs were considered possible, 8 (35%) were considered probable, and none were considered certain.

In 12 instances, one of the pharmacists identified a serious ADR that the other pharmacist did not identify. After discussion and consensus, 9 of these events were included as ADRs for the purposes of the analysis, and 3 were excluded. The kappa score for inter-rater agreement on identification of ADRs was 0.58 (95% CI 0.35–0.76), indicating a moderate level of inter-rater agreement. There was disagreement in the assessment of likelihood for 4 of the 23 ADRs. In each of these 4 instances, one of the pharmacists considered the reaction to be "probable" and the other pharmacist considered it to be "possible" (i.e., for these 4 ADRs, neither of the pharmacists assessed the likelihood as "certain"). The kappa score for inter-rater agreement for likelihood of a suspected serious ADR was also moderate, at 0.62 (95% CI 0.28–0.96).

DISCUSSION

One-third of general medicine patients admitted to a Canadian tertiary care teaching centre experienced a suspected serious ADR contributing to the reason for hospital admission or occurring during their hospital stay. Only a small proportion of these ADRs were unexpected (4%) or caused by drugs that were newly marketed (9%), with none of the ADRs meeting both of these criteria. None of the suspected serious ADRs were classified by the assessing pharmacists as "certain" according to the WHO-UMC causality classification system, and only 35% were classified as "probable", whereas the majority (65%) were classified only as "possible". By definition, a possible reaction is one that "could also be explained by disease or other drugs".[10] Classification of the majority of suspected serious ADRs as possible (rather than probable or certain) reinforces the inherent ambiguity of the identification of ADRs. In many instances, no changes were made to the patient's regimen for the drugs implicated in the adverse reactions (see Table 1). This outcome is not surprising, given that "possible reactions" will, by definition, often have other potential explanations.

Although only one of the ADRs in this study was classified as unexpected, the definition of "unexpected" is another point of ambiguity. We elected to classify a reaction as unexpected only if it was not listed as a possible adverse effect in the product monograph. In other words, for the purposes of our study, any reaction mentioned in the product monograph would not have been classified as unexpected, regardless of rarity and regardless of whether the reaction was detected only in postmarketing case reports. If regulations for the mandatory reporting of serious ADRs were to require the reporting of unexpected reactions only (as opposed to all serious ADRs), Health Canada would need to carefully consider the definition of "unexpected". For example, the definition could include reactions that are listed in the project monograph but that occur only rarely or for which causality has not been established.

Table 1. Characteristics of Suspected Serious Adverse Drug Reactions

Drug(s) Implicated	Serious ADR*	Likelihood†	Harm Code‡ (Outcome)	Action by Team with Respect to Drug(s) Implicated
ADRs contributing to reason for admission (*n* = 19)				
Hydromorphone	Nausea	Probable	3	Dose reduced
Fentanyl + morphine	Syncope	Possible	3	Dose reduced
Rivastigmine	Syncope	Possible	1	Medication held for 10 days
Oxazepam	Decreased level of consciousness	Probable	3	Dose reduced
Lorazepam	Delirium	Probable	3	Discontinued
Pregabalin + mirtazapine	Decreased level of consciousness	Possible	3	Both drugs discontinued
Tocilizumab	Abdominal abscess	Probable	5	Medication held during hospital admission
Citalopram	UGIB	Possible	5	No action taken
Desvenlafaxine	UGIB	Possible	5	No action taken
Apixaban + prednisone	UGIB	Possible	5	Apixaban discontinued
Apixaban +/– ibuprofen	UGIB	Probable	5	Apixaban held during hospital admission and restarted at a lower dose
Methylprednisolone	Hyperglycemia	Possible	5	No action taken
Fluticasone	Pneumonia	Possible	5	No action taken
Denosumab	Infection (cellulitis)	Possible	5	No action taken
Azathioprine	Infection (cholangitis)	Possible	5	Medication held during admission
Antibiotics	*Clostridium difficile*–associated diarrhea	Probable	5	No action taken
Clozapine + valproic acid	Severe constipation	Possible	5	No action taken
Spironolactone + ramipril + furosemide	Hyperkalemia / acute kidney injury	Probable	5	Spironolactone and ramipril discontinued
Nitrofurantoin	Worsening interstitial lung disease	Possible	5	Discontinued
ADRs occurring during hospital stay (*n* = 4)				
Ibuprofen	Rash	Probable	5	Discontinued
Prednisone	Hyperglycemia	Possible	5	No action taken
Tamoxifen	NSTEMI (unexpected)	Possible	5	No action taken
Warfarin + fluconazole	INR 9.3	Possible	5	Warfarin held

ADR = adverse drug reaction, INR = international normalized ratio, NSTEMI = non-ST segment elevation myocardial infarction, UGIB = upper gastrointestinal bleeding.
*ADRs that were unexpected are indicated.
†Likelihood according to World Health Organization–Uppsala Monitoring Centre causality category (see Appendix 1).
‡Harm codes: 1 = monitoring required to confirm that no harm resulted and/or intervention required to preclude harm, 2 = temporary harm that may have required intervention, 3 = temporary harm that prolonged hospital stay, 4 = permanent harm, 5 = intervention required to sustain life, 6 = contributed to death.

The frequency of occurrence of serious ADRs as reported in other studies varies substantially, likely because of differences in the populations studied, differences in methodology, a lack of standard definitions for "ADR" and "adverse drug event", and subjectivity in outcome assessment. Several previous studies have reported on the occurrence of adverse drug events and/or ADRs in Canadian hospitals. Samoy and others[11] conducted a prospective observational study of 565 adult patients admitted to the internal medicine service of a Canadian hospital in which the frequency of drug-related hospital admissions was 24.1%. However, ADRs were just 1 of 8 categories of adverse drug events potentially leading to admission, and only adverse drug events relating to the chief complaint on admission were considered. Forster and others[12] examined the occurrence of adverse events in a random sample of 502 patients admitted with nonpsychiatric illness to a single institution. The incidence of any adverse event was 12.7%, and 50% of these adverse events were deemed to be due to a drug (i.e., adverse drug events). The results of the current study are not consistent with these previous results, for several possible reasons. For example, the study methodologies were different. In addition, in the earlier studies, occurrence of an ADR had to have been documented in the chart at the time of patient care in order for the event to be counted as an outcome, whereas in our study a pharmacist critically reviewed the patient health record in an attempt to identify suspected ADRs.

Sikdar and others[13] found a prevalence of adverse drug events of only 2.4% in a sample of 1458 patients presenting to the emergency departments at 2 tertiary care hospitals in St John's,

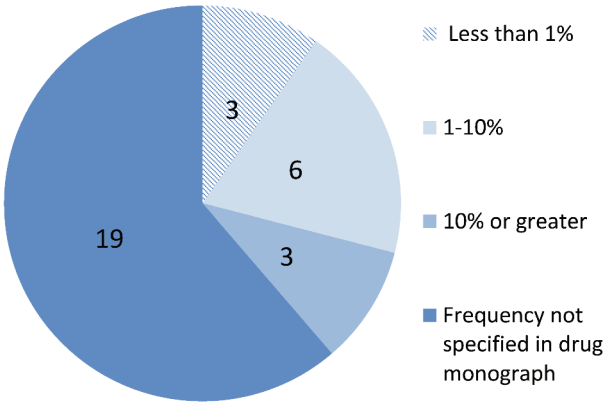

Figure 1. Frequency of occurrence of adverse drug reactions (ADRs) as reported in monographs for the 31 drug–ADR pairs listed in Table 1. For the purpose of this figure, an ADR for which 2 drugs were implicated (e.g., syncope in a patient taking fentanyl + morphine) generated 2 drug–ADR pairs.

Newfoundland and Labrador. This estimate was much lower than what is reported here for ADRs, especially considering that the definition of "adverse drug event" is broader than (and indeed encompasses) the definition of "ADR". The difference in outcome estimates may be due to population differences, as the St John's study was not restricted to internal medicine and included patients who were not admitted to hospital from the emergency department. Additionally, the chart reviews in the St John's study were conducted retrospectively,[13] whereas our study was prospective.

The frequency of occurrence of ADRs has also been reported in meta-analyses. A 1998 meta-analysis of 39 prospective studies conducted in hospitals in the United States reported an incidence of serious ADRs causing hospital admission or occurring in hospital of 6.7% (95% CI 5.2%–8.2%).[14] The lower frequency in that study, as compared to the study reported here, may be explained by the exclusion of serious ADRs that were classified as "possible", defined as those that followed a "reasonable temporal sequence and for which the ADR is a known response to the drug, although the response may also be explained by the patient's clinical state."[14] In our study, 8 (13%) of the 60 patients experienced an ADR that was considered probable (i.e., when those with ADRs considered as "possible" were excluded). A more recent meta-analysis of 22 prospective studies, published in 2012, found that 16.9% (95% CI 13.6%–20.2%) of patients experienced an ADR during their hospitalization.[15] All suspected ADRs were included in this analysis, not only those that were serious. The validity of this pooled estimate is questionable, however, because significant statistical heterogeneity was observed (I^2 = 99%). The authors stated that differing methodologies represented the most important contributor to heterogeneity across the included studies.[15]

The results of the current study suggest that indiscriminate reporting of all suspected serious ADRs would unnecessarily burden clinicians. Assuming that preparation of an ADR form for submission to Health Canada takes 10–20 min per ADR, it would take 5–10 h/week to submit reports for all suspected serious ADRs occurring on the general medicine service at a single campus of our institution. This time estimate is anecdotal, based on our own and our colleagues' experience reporting ADRs. The majority of ADRs identified in this sample of 60 patients were well-known side effects, and the reporting of these established ADRs would be unlikely to improve knowledge about the safety of these medications, despite the substantial investment of time required.

As described in a public consultation on the mandatory reporting of serious ADRs held in summer 2017, proposed changes to the regulations have not yet been finalized.[16] Which health care institutions should report ADRs, what types of serious ADRs will be reported, what information should be included in an ADR report, and the expected timelines for reporting have not yet been defined. Clear guidance for health professionals that prioritizes reporting of those ADRs most likely to increase medication safety knowledge could increase the effectiveness and feasibility of mandatory reporting.

Subjectivity in ADR identification will make it difficult to execute and enforce mandatory reporting by health professionals. In our study, pairs of pharmacists identified and assessed the likelihood of causality for all suspected serious ADRs that were identified, with moderate inter-rater agreement. The signs and symptoms of ADRs can be nonspecific and indistinguishable from symptoms of the underlying disease; therefore, it is often difficult for clinicians to differentiate an ADR from a current illness.[8]

Our study had several limitations. The results may not reflect the incidence of suspected serious ADRs outside of the general medicine service at the study institution or at other institutions. The study was conducted over a single 8-day period and involved a relatively small number of patients at a single institution. Identification of ADRs was limited by the information available in the patients' health records. Discussions with patients, caregivers, and the medical team might have led to identification of additional suspected ADRs or a different classification of likelihood, but such discussions were not feasible. The definition of "ADR" used in this study was the one provided in Health Canada's guideline on adverse reaction reporting for health professionals.[5] Definitions of "ADR" and "adverse drug event" are not consistently reported in the available literature, which makes it challenging to compare and synthesize the results of different studies. Furthermore, there is currently no universally accepted method for assessing the causality of suspected ADRs.[8] The WHO-UMC system was chosen as the method of causality assessment for this study because it is a practical tool for determining the likelihood of causality of an ADR that is based

on spontaneous ADR data from around the world, as received and analyzed by the WHO's Uppsala Monitoring Centre. Although the Naranjo algorithm is often used in research, it was not selected as a method of causality assessment in this study because it is less practical for application in practice, for several reasons; for example, it asks whether the reaction reappeared with the administration of a placebo, and it considers blood concentrations of the drug in question, information that is often not available when likelihood is assessed in practice.[17]

CONCLUSION

Suspected serious ADRs were identified in about one-third of patients admitted to a general medicine service at a tertiary care teaching centre. Institutions in Canada would likely face difficulties in reporting all suspected serious ADRs because of the frequency of their occurrence, subjectivity in the assessment of occurrence of ADRs and their likelihood, and the implications for health professionals' workload. The majority of ADRs identified were well-known side effects, and reporting them would be unlikely to improve overall knowledge relating to medication safety.

The provision of clear guidance for health professionals with respect to the identification of reportable suspected serious ADRs and assessment of the likelihood of causality could minimize false safety signals and improve medication safety.

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Appendix 1: Causality categories in the World Health Organization–Uppsala Monitoring Centre system for standardized case causality assessment. Reproduced, with permission of the publisher, from: *The Use of the WHO-UMC System for Standardised Case Causality Assessment.* Uppsala (Sweden): Uppsala Monitoring Centre; 2018. Available from: https://www.who-umc.org/ media/164200/who-umc-causality-assessment_new-logo.pdf

Causality Term	Assessment Criteria
Certain	• Event or laboratory test abnormality, with plausible time relationship to drug intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically, pathologically) • Event definitive pharmacologically or phenomenologically (i.e. an objective and specific medical disorder or a recognised pharmacological phenomenon) • Rechallenge satisfactory, if necessary
Probable/Likely	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Unlikely to be attributed to disease or other drugs • Response to withdrawal clinically reasonable • Rechallenge not required
Possible	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Could also be explained by disease or other drugs • Information on drug withdrawal may be lacking or unclear
Unlikely	• Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible) • Disease or other drugs provide plausible explanations
Conditional/Unclassified	• Event or laboratory test abnormality • More data for proper assessment needed, or • Additional data under examination
Unassessable/Unclassifiable	• Report suggesting an adverse reaction • Cannot be judged because information is insufficient or contradictory • Data cannot be supplemented or verified

REVIEW

Roles and Impacts of the Transplant Pharmacist: A Systematic Review

Sébastien Sam, Aurélie Guérin, André Rieutord, Stéphanie Belaiche, and Jean-François Bussières

ABSTRACT

Background: Pharmacists have been involved in the care of transplant recipients for several decades, and a growing body of literature shows the beneficial effects of clinical pharmacist care on important outcomes for these patients.

Objectives: The primary objective was to describe the roles and impacts of pharmacists in a solid organ transplant setting. The secondary objective was to describe and rate the pharmacists' interventions.

Data Sources: Three databases —PubMed, Embase, and Evidence-Based Medicine Reviews —were searched from January 1, 1990, to June 16, 2015.

Study Selection and Data Extraction: All studies addressing the roles of pharmacists and the impacts of clinical pharmacy services on the care of solid organ transplant recipients were considered. Only studies providing a statistical analysis were included. Design, setting, sample size, patient characteristics, pharmacists' interventions, study bias, and outcomes were extracted for analysis.

Data Synthesis: Four randomized controlled trials, 4 cohort studies, 3 pre–post studies, and 1 quasi-randomized controlled trial were included in the review, representing a total of 1837 patients. Of the 12 studies included, 8 specifically focused on renal transplant, and 1 each focused on liver, lung, abdominal organ, and general solid organ transplant. The pivotal pharmacist activities leading to the main patient outcomes were medication counselling (n = 8 studies), medication reconciliation (n = 5), and reviewing and optimizing drug therapy (n = 3). Improvements to medication adherence (n = 6 studies), morbidity (n = 4), costs (n = 2), and medication errors (n = 2) were reported.

Conclusion: Currently available evidence suggests that pharmacists can improve patient outcomes in the solid organ transplant setting. Adherence, morbidity, costs, and medication errors were identified as the main outcomes that were improved by pharmaceutical interventions. Transplant programs need to invest more in this resource.

Keywords: pharmacist, organ transplantation, impact, clinical pharmacy, outcome-based research

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RÉSUMÉ

Contexte : Les pharmaciens participent aux soins des greffés depuis plusieurs décennies et un nombre croissant de publications révèlent les effets bénéfiques des soins prodigués par les pharmaciens cliniciens quant aux résultats thérapeutiques importants pour ces patients.

Objectifs : L'objectif principal était de décrire les rôles des pharmaciens et leurs influences par rapport aux greffes d'organes solides. L'objectif secondaire était de décrire et d'évaluer les interventions des pharmaciens.

Sources des données : Les bases de données PubMed, Embase et Evidence-Based Medicine Reviews ont été interrogées pour la période allant du 1er janvier 1990 au 16 juin 2015.

Sélection des études et extraction des données : Toutes les études abordant les rôles des pharmaciens et l'influence des services de pharmacie clinique sur les soins des receveurs d'organes solides ont été prises en considération. Seules les études présentant des analyses statistiques ont été retenues. Le plan d'étude, le contexte, la taille de l'échantillon, les caractéristiques des patients, les interventions des pharmaciens, les biais et les résultats thérapeutiques ont servi à l'analyse.

Synthèse des données : Quatre études contrôlées à répartition aléatoire, 4 études de cohorte, 3 études avant-après et 1 essai comparatif à répartition quasi-aléatoire ont été retenus pour l'analyse, ce qui représentait au total 1837 patients. Parmi les 12 études retenues, 8 abordaient spécifiquement la greffe rénale et chacune des 4 autres concernait respectivement une greffe hépatique, une greffe pulmonaire, une greffe d'organe abdominal et une greffe d'organe solide. Les activités clés des pharmaciens menant aux principaux résultats thérapeutiques étaient les conseils sur les médicaments (n = 8 études), l'établissement du bilan comparatif des médicaments (n = 5) ainsi que l'examen et l'optimisation de la pharmacothérapie (n = 3). On a constaté des améliorations des taux d'observance pharmacothérapeutique (n = 6 études), des taux de morbidité (n = 4), des coûts (n = 2) et des taux d'erreurs de médicaments (n = 2).

Conclusion : Les données probantes disponibles laissent croire que les pharmaciens peuvent améliorer les résultats thérapeutiques en ce qui concerne les greffes d'organes solides. Les taux d'observance pharmacothérapeutique, les taux de morbidité, les coûts et les taux d'erreurs de médicaments ont été désignés comme les résultats principaux qui ont été améliorés par les interventions pharmaceutiques. Les programmes de greffe doivent investir davantage dans cette ressource.

Mots clés : pharmacien, greffe d'organe, effet, pharmacie clinique, recherche axée sur les résultats

INTRODUCTION

Solid organ transplant has been one of the most important therapeutic advances in medicine over the past 60 years. Since the first transplants were performed, it has become the recommended therapeutic approach for many end-stage chronic diseases. In Canada, 2835 transplant procedures were done in 2016.[1]

Patients who have received a solid organ transplant require lifelong immunosuppressive treatments. Nonadherence to post-transplant drug therapy and recommendations is a major issue that can lead to misdiagnosis of subsequent health problems, poor health affecting quality of life, graft rejection, or death.[2,3]

Pharmacists have been involved in direct patient care since the early 1970s. The first report outlining specific activities of a dedicated transplant pharmacist was published in 1976.[4] This article introduced the transplant pharmacist as an individual with specific expertise in transplantation pharmacology who actively participated in the medical management of organ transplant recipients and provided direct patient medication counselling. Since that time, the overall pharmacy practice model has evolved from a product-oriented to a patient-oriented model, and there have been advances in the field of transplant pharmacy as well. In the United States, for example, a "pharmacology expert" is now mandatory in transplant centres.[5]

A growing body of literature has shown the beneficial effects of clinical pharmacist care on important outcomes for both hospitalized and ambulatory patients; however, in the context of solid organ transplant, the majority of published studies have focused on renal transplant recipients.

There is high heterogeneity among the interventions described in studies evaluating the impact of clinical pharmacy services. Several authors have characterized the descriptions of interventions in pharmacy practice studies as inconsistent or even poor.[6,7] Authors have therefore recommended that interventions be clearly reported, with a detailed explanation of the intervention, a description of the pharmacist–patient and pharmacist–provider relationships, and details about the setting where the study took place.[8] A more comprehensive understanding of clinical pharmacy interventions for transplant patients would help in achieving better outcomes.

The primary objective of this systematic review was to describe the roles and impacts of pharmacists in a solid organ transplant setting. The secondary objectives were to describe and rate pharmacists' interventions.

METHODS

All specifications of the PRISMA 2009 checklist[9] were followed for reporting this systematic review.

Data Sources

Four systematic searches were carried out in 3 databases (PubMed, Embase, and Evidence-Based Medicine Reviews) for articles published between January 1, 1990, and June 16, 2015. Manual reference checks were performed to search for potentially missing studies. Search strategies are presented in Appendix 1 (available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/186/showToc).

Study Selection and Data Extraction

All studies addressing the impact of clinical pharmacy services on the care of patients with solid organ transplant were considered. Studies providing a statistical analysis on the impact of pharmaceutical activities were included. Studies that presented only descriptive results, studies addressing only the economic impact of transplant services, descriptive reviews, case reports, journal letters, journal notes, commentaries, and editorials were all excluded. Also excluded were secondary sources such as literature reviews, systematic reviews, and meta-analyses. Articles in either English or French were included.

All references were screened by 2 independents reviewers (A.G., J.F.B.). If there were any discrepancies in the decision to include or exclude studies, a third researcher was consulted (S.B.). Study selection was accomplished through 3 phases of screening. During the first phase, titles were reviewed for relevance. During the second phase, abstracts from articles retained in the first phase were reviewed for relevance. In the third and final phase, the full texts of articles retained in the second phase were reviewed.

Data extraction was performed by 2 authors (A.G., S.S.), under the supervision of 1 reviewer (J.F.B.). Data from the included studies were synthesized into summary tables.

Rating of Descriptions of Pharmaceutical Interventions

The DEPICT tool[10] was used to evaluate the description of pharmaceutical interventions. Rating was performed by 2 authors (A.G., S.S.), under the supervision of 1 reviewer (J.F.B.), and a DEPICT score was assigned to each study. The DEPICT score evaluates studies according to 12 sections, with multiple items per section. For each section, a score of 1 is assigned if the reviewers answer "yes" for at least 1 item within the section; otherwise, a score of 0 is assigned for that section. The DEPICT score is determined by summing the number of sections with a score of 1 (maximum score = 12).

Risk of Bias in Individual Studies

Individual study limitations, including risk of bias, were reported as described by the authors of each included article. The risk of bias across studies was assessed informally by the authors of the current systematic review.

RESULTS

Literature Search, Study Selection, and Data Extraction

The search yielded 1603 articles. Of these, 1518 were excluded after review of titles and abstracts. Of the 85 potentially eligible studies, 73 were excluded after review of the full-text articles. Twelve studies involving a total of 1837 patients were included in the analysis (Figure 1).[11-22] Manual searching of the reference lists of these included articles yielded no additional eligible articles.

Synthesis of Results

Eight studies focused on kidney transplant, one on liver transplant, one on lung transplant, one on abdominal transplant, and one on general solid organ transplant. The studies were conducted in the United States (*n* = 8 studies), Canada (*n* = 2), and Germany (*n* = 2). No differences were observed in terms of pharmacist roles or patient outcomes in relation to the geographic location of the studies.

The study characteristics are presented in Table 1 and the outcomes of individual studies in Table 2.

The pivotal pharmacist activities in the setting of solid organ transplant included patient education and counselling (*n* = 9 studies), reviewing and optimizing drug therapy (*n* = 7), and medication reconciliation or medical history (*n* = 5). Improvements were reported in the following areas: medication adherence (*n* = 6 studies), morbidity (*n* = 4), cost (*n* = 2), and medication errors (*n* = 2).

Pharmaceutical interventions were sufficiently described to understand the role of pharmacists. The average DEPICT score was 8.4 (standard deviation 1.4, minimum 6, maximum 11) (Table 3). The pharmaceutical interventions that were less frequently reported included the timing of the intervention, the support resources provided by pharmacists, and the pharmacist's autonomy to perform some specific tasks.

Risk of Bias

Risk of bias is reported here as described by the authors of each article (Table 1). Many studies lacked a control group and had a small sample size. Three of the included studies were carried out by the same multidisciplinary renal transplant team at the Medical College of Georgia Hospital and Clinics.[15,19,21] A fourth study had the same first author as these 3 studies (Marie A Chisholm-Burns, formerly Marie A Chisholm), but was conducted within a different organization.[17]

DISCUSSION

Our detailed literature search identified few studies describing the inclusion of clinical pharmacists as members of multidisciplinary teams in the organ transplant setting. In these studies, transplant pharmacists were involved in medication reconciliation, drug therapy evaluation and monitoring, patient education, and problem-solving. All of the studies included in our review suggested that transplant pharmacists could improve the management and medication adherence of patients and consequently could have a positive impact on patients' morbidity, medication errors, and costs. However, each of the studies was conducted in a single centre, and it might be difficult to show significant evidence of a pharmacist's impact in small, focused patient populations like these.

The number of studies that met our inclusion criteria (*n* = 12) was low compared with studies examining the roles of pharmacists in other settings (e.g., cancer, hypertension, and asthma).[23] In fact, the involvement of clinical pharmacists in transplant medicine is recent. The American Society of Health-System Pharmacists now offers a pharmacy residency in solid organ transplant,[24] but no European recommendations have been formulated regarding the role of the clinical pharmacist in transplantation. Lack of knowledge and/or experience in designing and administering such services, as well as difficulty in procuring funding and reimbursement for services, can limit

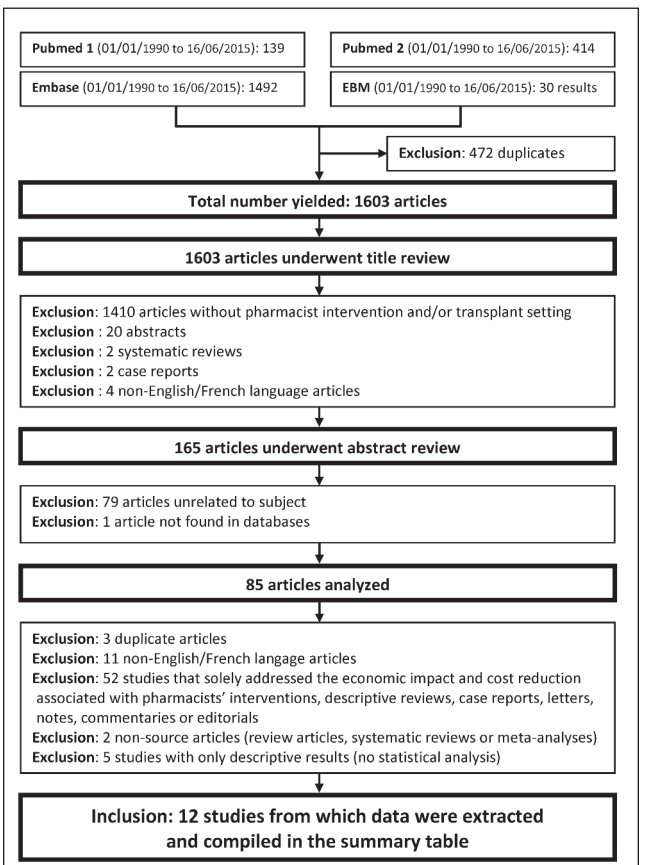

Figure 1. Selection of studies for a systematic review of the roles and impacts of transplant pharmacists.

Table 1 (part 1 of 4). Study Characteristics

Reference	Study Design and Timeframe	Setting	Sample Size and Patient Characteristics	Pharmacists' Interventions	Bias
Randomized controlled trials					
Chisholm et al. 2001[15]	RCT, prospective February 1997 to January 1999	United States: Medical College of Georgia—Hospital and Clinics Renal transplant clinic	Control (C): *n* = 12 Intervention (I): *n* = 12 Mean age ± SD: 49.2 ± 10.2 years Sex, male: 75% (18/24) Kidney transplant recipients	At least monthly direct patient care clinical services in person or by phone: - Obtaining medication histories - Reviewing and optimizing medication therapy - Making recommendations to the nephrologists - Providing oral and/or written medication counselling for patients	- To strengthen compliance assessment, serum drug concentrations were measured, but patients may have increased compliance before the blood samples and may have been inaccurate due to incorrect sampling times in relation to medication administration - Small sample size (*n* = 24)
Chisholm et al. 2002[21]	RCT, prospective Inclusion from November 1996 to March 1998	United States: Medical College of Georgia Renal transplant clinic	Control (C): *n* = 10 Intervention (I): *n* = 13 Mean age ± SD C: 47±12.7 years I: 51±16.8 years Sex, male: C: 70% I: 61.5% African-American kidney recipients	Direct care clinical pharmacy services: - Meeting with patient at least twice monthly during the first 3 months after transplant, at least monthly during months 4–8, and at least once during months 8–12 - Giving information about the medication - Obtaining medication histories - Reviewing medication therapy, with emphasis on controlling blood pressure - Preventing or resolving medication problems - Sending recommendations to the nephrologists	- Contamination bias: members of health care team may have progressively been influenced by the pharmacist's recommendations, affecting the care provided to the control group - Performance bias: study did not prevent patients from seeing additional health care providers - Small sample size (*n* = 23) - No objective measurement of compliance with antihypertensive medication regimen - Exclusively African-American study population may affect external validity
Klein et al. 2009[18]	RCT, prospective Inclusion from September 2003 to January 2005	Germany: University Hospital Mainz Transplant surgery unit	Control (C): n = 24 Intervention (I): *n* = 26 Mean age: C: 50.1 years I: 52.8 years Sex, male: C: 54% I: 54% Liver recipients	Pharmaceutical care services: - 3 or 4 meetings with patients in the week before discharge, for education about immunosuppressive therapy - On discharge, provision of a discharge medication plan, written information about the medication, and a diary for laboratory data and vital signs - 4 to 12 meetings in the first year after transplant to discuss changes in medication, laboratory values, and other problems - Drug therapy review	- Contamination bias: patients in the intervention and control groups visited the outpatient clinic at the same time and were able to exchange written and oral information - Performance bias: control and intervention groups received their immunosuppressant from the same pharmacist, who had to respond to questions and problems from both groups (for ethical reasons) - Minimum threshold of compliance rate to classify a patient as "noncompliant" was set arbitrarily, because it is mostly unknown in literature the point at which noncompliance becomes clinically relevant

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the implementation of clinical pharmacy services in particular settings and locations.[25]

Pharmacists' Activities

The included studies reported a large range of pharmacist activities in solid organ transplant for both hospitalized and ambulatory patients, as described in Table 1.

Alloway and others[5] highlighted the following basic activities of the transplant pharmacist: dedicating time for the care of transplant recipient; attending daily rounds to evaluate pharmacotherapy; coordinating development and implementation of drug therapy protocols; providing medication

Table 1 (part 2 of 4). Study Characteristics

Reference	Study Design and Timeframe	Setting	Sample Size and Patient Characteristics	Pharmacists' Interventions	Bias
Chisholm-Burns et al. 2013[17]	RCT, prospective January 2010 to November 2012	United States: Avella Specialty Pharmacy (specialty pharmacy network), multicentre	Control (C): *n* = 74 Intervention (I): *n* = 76 Mean age ± SD: C: 51.32±13.69 years I: 52.78±13.55 years Sex, male: C: 55.4% I: 56.6% Kidney recipients	Semistructured 20- to 30-min meetings with patients at 0, 3, 6, 9, and 12 months to sign or renew an adherence-promoting behavioural contract and discuss its 6 components: - Goal-setting - Motivation - Social support - Memory techniques - Problem-solving - Consequences of nonadherence	- No "attention" control group receiving interactions with a study pharmacist without the behavioural contract - A single pharmacist performed the intervention, limiting generalizability - No direct collection of utilization and cost data, although the methods used (self-report and Medicare Expenditure Panel Survey) have been validated - No measurement of self-efficacy - White, Hispanic, and female patients were over-represented in the study compared with the general United States population
Quasi-randomized controlled trial					
Joost et al. 2014[11]	Quasi-randomized controlled trial, prospective August 2008 to July 2010	Germany: Erlangen University Hospital Outpatient clinic of Department of Nephrology and Hypertension	Control (C): *n* = 39 Intervention (I): *n* = 35 Mean age ± SD: C: 54±11.9 years I: 51±13.3 years Sex, male: C: 62% I: 77% Kidney recipients	- 3 standardized counselling sessions of 30 min each within first 2 weeks after transplant - 1 to 3 quarterly follow-up counselling sessions over 12 months - Additional pharmaceutical care over phone or by email when necessary	- Selection bias: only 40% of eligible transplant patients agreed to participate in the study (nonadherence could be a cause of refusal) - One-year time horizon: the results cannot be extrapolated beyond 1 year - Contamination bias: patients in the intervention group may have shared their new-found knowledge with patients in control group
Cohort studies					
Harrison et al. 2012[14]	Cohort study, prospective Control: November 2007 to June 2008 Intervention: July 2008 to January 2009	Canada: Toronto General Hospital Outpatient lung transplant clinic	Control (C): *n* = 43 Intervention (I): *n* = 43 Age (years): 18–39: 30% (C) vs 12% (I) 40–59: 47% (C) vs 51% (I) ≥60: 23% (C) vs 37% (I) Sex, male: C: 56% I: 56% Lung recipients	- Primary pharmaceutical care intervention (drug therapy review, therapeutic recommendations) - Patient teaching - Medication reconciliation - Referral of issue for team follow-up - Optimization of medication adherence - Medication information and advice for patients and the team - Assistance with drug coverage issues - Collaboration with community pharmacists	- Performance bias: clinicians may have not performed a comprehensive drug therapy assessment, knowing that patients would be subject to subsequent pharmacist reviews - Inconsistencies of intervention: pharmacists in the study received no formalized training in outpatient practice - Most patients met with pharmacist only once during the timeframe of the study (additional visits over a longer period might lead to greater impact on patient care outcomes)

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reconciliation, medication therapy management, and discharge counselling; providing education to members of the transplant team; facilitating cost and pharmacotherapy optimization to maximize patient outcomes; providing transplant medication education to patients; leading and assisting with clinical and pharmacoeconomic research; and providing 24/7 pharmacotherapeutic support. This list strongly concurs with the interventions summarized in Table 1 of this review, except for research. Indeed, the most frequently reported activities in studies included in our review were patient education and counselling, reviewing and optimizing drug therapy, and medication reconciliation or medical history.

Table 1 (part 3 of 4). Study Characteristics

Reference	Study Design and Timeframe	Setting	Sample Size and Patient Characteristics	Pharmacists' Interventions	Bias
Maldonado et al. 2013[12]	Cohort study, retrospective Control cohort: 2007 Intervention cohort: 2011	United States: Providence Sacred Heart Medical Center & Children's Hospital Inpatient and outpatient transplantation clinic	Control (C): *n* = 60 Intervention (I): *n* = 54 Mean age at transplant: C: 51.4 years I: 55.0 years Sex, male: C: 65% I: 63% Kidney recipients	- Daily rounds with the interdisciplinary team - Pharmacotherapy recommendations to physicians, surgeons, and midlevel practitioners - Active drug monitoring - Medication reconciliation and discharge planning - Patient education	- Performance bias: changes in usage of anti-thymocyte globulin induction therapy, a new program director, and addition of a transplant nurse practitioner may have influenced the results - No assessment of patient health literacy or medication compliance, which are viewed as the primary contribution of transplant pharmacists
Musgrave et al. 2013[13]	Cohort study, prospective Retrospective cohort: 2006 to 2008 Prospective cohort: 2011	United States: Medical University of South Carolina Department of Transplant Surgery	Retrospective cohort (C): *n* = 128 Prospective cohort (I): *n* = 64 Median age: C: 51.5 years I: 54 years Sex, male: C: 65.6% I: 68.8% Abdominal transplant patients	- At discharge, 5–30 min (median 15 min) spent per patient to verify medication reconciliation - At the first follow-up appointment (next business day following discharge), 0–90 min (median 20 min) spent per patient to review medications - Prevention and/or correction of the identified drug-related problems	- Chart review to identify errors was done with retrospective records, which do not always provide explanations for changes that might seem like errors but could have been intentional - Analysis bias: chart review was conducted by a single reviewer - Analysis bias: classification of errors by severity was performed by a single reviewer (but this was controlled by use of a validated rating tool) - In the retrospective period, no correlation of the errors to detrimental clinical outcomes
Tschida et al. 2013[20]	Cohort study, retrospective Inclusion from August 2007 to December 2007	United States: United Healthcare Pharmacy (specialty pharmacy network), multicentre	Retail pharmacy group (C): *n* = 519 Specialty pharmacy group (I): *n* = 519 Mean age (years): C: 49.78 years I: 49.78 years Sex, male: C: 62% I: 61% Renal transplant patients	Transplant medication specialty pharmacy program: - Monthly face-to-face consultations for the first 3 months after transplant, then about every 3 months - Additional clinical counselling sessions by phone - Provision of clinical expertise and patient education in transplant medications and comorbid conditions - Monthly refill reminders, adherence screening (intervention with physician if necessary) - 24/7 pharmacist support available to patient	- Selection bias: patients may have self-selected into either the specialty or retail pharmacy benefit programs (sicker patients may have differentially chosen one type of pharmacy over the other) - Adherence estimations using retrospective data do not always give an accurate representation of whether the medication was taken exactly as prescribed - No measurement of how consistently and how many patients participated in the pharmacy consultations on an ongoing basis of monthly and every 3 months meetings

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Patient education and teaching sessions aimed to educate patients about all aspects of their medications and the risks of nonadherence, and to answer questions. Handing out information sheets and providing support by phone or e-mail were activities performed by pharmacists in many of the studies.

Nonadherence to the immunosuppressive regimen after transplant is a major issue than can lead to serious outcomes, such as transplant rejection or even death. Clinical pharmacists can improve patient adherence to medications.[15] In a unique approach, Chisholm-Burns and others[17] used a behavioural

Table 1 (part 4 of 4). Study Characteristics

Reference	Study Design and Timeframe	Setting	Sample Size and Patient Characteristics	Pharmacists' Interventions	Bias
Pre–post studies					
Partovi et al. 1995[22]	Pre–post study, prospective March to June 1993	Canada: Vancouver Hospital and Health Sciences Centre Solid organ transplant clinic	Group: *n* = 28 Mean age: 47.2 years Sex, male: 43% Solid organ recipients	Medication counselling program: - Oral counselling by a pharmacist and provision of medication teaching sheets (step 1) - Patient participation in self-medication program (step 2) Four identical tests given to patients throughout the program to evaluate knowledge retention: - Pre-test (just before step 1) - Post-test 1 (2–3 days after step 1) - Post-test 2 (3–5 days after step 2) - Post-test 3 (5–7 days after post-test 2)	- Only short-term knowledge retention was assessed - Inconsistency of the quality of teaching provided by each of the 4 pharmacists involved in the counselling and testing - Confounding factors: patients who had health-related jobs scored higher; central nervous system depressive drugs lowered test performance - No control group
Chisholm et al. 2007[19]	Pre–post study, retrospective Inclusion from November 1999 to September 2005	United States: Medical College of Georgia Renal transplant clinic	Group: *n* = 36 Mean age ± SD: 52.78±13.37 years Sex, male: 61.1% Kidney recipients	Medication therapy management services (provided at least once a month): - Review of medication profile to ensure therapeutic outcomes and minimize adverse drug events - Identify, resolve, and prevent medication-related problems - Interview patients - Answer drug information questions - Make therapeutic recommendations	- No control group - Small sample size (*n* = 36)
Pinelli et al. 2014[16]	Pre–post study, prospective 2014	United States: Henry Ford Hospital Transplant institute	Group: *n* = 22 Mean age ± SD: 59.3 ± 9.5 years Sex, male: 79% Kidney recipients	Establishment of a pharmacist-managed diabetes and cardiovascular risk reduction clinic (PMDC): - 60-min appointment within 7 days of discharge by inpatient transplant team - 30-min follow-up appointments at least monthly over 3 months - Disease state management for diabetes, hypertension, and dyslipidemia - Standardized diabetes self-management education curriculum - Referral to transplant nutrition support services as needed - Medication reconciliation at each visit - Standardized discharge process from PMDC at 3 months to endocrinologist or primary care provider	- Small sample size (*n* = 22) - No control group

RCT = randomized controlled trial, SD = standard deviation.

Table 2 (part 1 of 3). Outcomes of Individual Studies

Reference	Type of Outcome	Main Study Outcomes	Main Results
Randomized controlled trials			
Chisholm et al. 2001[15]	Compliance	1. Compliance rate (mean ± SD)	1. At 1 year post-transplant: control 81.6% ± 11.5% vs intervention 96.1% ± 4.7%; $p < 0.001$
		2. Duration of compliance (as proportion of compliant patients at 12 months after transplant)	2. Control $n = 4/12$ vs intervention $n = 9/12$; $p < 0.05$
		3. Rate of patients achieving target serum cyclosporine and tacrolimus concentrations	3. Control 48% vs intervention 64%; $p < 0.05$
Chisholm et al. 2002[21]	Morbidity	Mean systolic and diastolic blood pressure change:	
		1. From baseline for 1st quarter	1. Control –8/–4 mm Hg vs intervention –7/–1 mm Hg; $p > 0.05$
		2. From baseline for 2nd quarter	2. Control +17/+5 mm Hg vs intervention –12/–7 mm Hg; $p < 0.01$
		3. From baseline for 3rd quarter	3. Control +13/–1 mm Hg vs intervention –14/–12 mm Hg; $p < 0.01$
		4. From baseline for 4th quarter	4. Control +18/+8 mm Hg vs intervention = –5/–6 mm Hg; $p < 0.01$
Klein et al. 2009[18]	Compliance	1. Dosing compliance, as % of days (mean ± SD) with correct number of MEMS bottle openings (compliance threshold is 80%)	1. Control 80.8% ± 12.4% vs intervention 90.2% ± 6.2%; $p = 0.015$. *Noncompliant patients*: control 43% vs intervention 10%; $p = 0.032$
		2. Timing compliance: % of days (mean ± SD) on which bottle was opened within 3 h of target time	2. Control 81.1% ± 13.8% vs intervention 87.9% ± 8.0%; $p = 0.088$
		3. Compliance according to pill counts (tablets or capsules remaining in MEMS bottles during each patient visit) (mean ± SD)	3. Control 97.2% ± 13.6% vs intervention 101.1% ± 2.6%; $p = 0.030$
		4. Rate of immunosuppressant serum concentrations achieving "target"	4. Control 51% vs intervention 78%; $p < 0.001$
		5. Compliance according to Morisky score	5. 62% of control group vs 87% of intervention group answered "no" to all questions (good compliance); $p = 0.083$
		6. No. of rejection episodes	6. Control 5 vs intervention 3; $p = 0.456$
Chis holm-Burns et al. 2013[17]	Compliance	**Adherence**	**Adherence**
		1. At baseline	1. No significant difference
		2. At 3 months	2. No significant difference
		3. At 6 months	3. Intervention group had significantly greater adherence than control group; $p = 0.0099$
		4. At 9 months	4. Intervention group had significantly greater adherence than control group; $p = 0.0065$
		5. At 12 months	5. Intervention group had significantly greater adherence than control group; $p = 0.0076$
		6. Over 1-year study period	6. Intervention group had significantly greater adherence than control group; $p = 0.0071$
		7. At 3 months post-intervention	7. Intervention group had significantly greater adherence than control group; $p = 0.044$
	Cost	**Health care utilization**	**Health care utilization**
		8. Proportion of patients with at least 1 day in hospital among patients who reported any hospitalization during 1-year study	8. Control 57.3% vs intervention 23.9%; $p < 0.001$
		9. Probability of not being hospitalized	9. Intervention increased the probability of not being hospitalized by ~78% (RR 1.785, 95% CI 1.314–2.425)

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contract and trimestral meetings to maximize patient adherence.

Reviewing and optimizing drug therapy helps in identifying, resolving and preventing drug-related problems. Musgrave and others[13] reported a "significant" decrease of medication errors per patient at discharge because of pharmacist interventions. Chisholm and others[15,19,21] also reported that pharmacist recommendations helped nephrologists to optimize prescriptions for transplant recipients.

Few of the included studies reported medication reconciliation. Nevertheless, this has been shown to be an essential component in optimizing the quality of prescriptions, prevent-

Table 2 (part 2 of 3). Outcomes of Individual Studies

Reference	Type of Outcome	Main Study Outcomes	Main Results
Quasi-randomized controlled trial			
Joost et al. 2014[11]	Compliance	1. Daily adherence (as % of days with correct dosing of MMF/MPA) during 1-year monitoring period	1. Control 57% (20/35) vs intervention 84% (27/32); $p = 0.015$
		2. Taking adherence (as % of doses taken [bottle opening] compared with overall doses prescribed)	2. Control 57% (20/35) vs intervention 84% (27/32); $p = 0.015$
		3. Timing adherence (as % of doses taken within a 6-h interval [±3 h] of standard intake time)	3. Control 86% (30/35) vs intervention 97% (31/32); $p = 0.110$
		4. Adherence rate (as measured by pill count)	4. Control 63% (22/35) vs intervention 84% (27/32); $p = 0.047$
		5. No. of drug holidays (defined as no MMF/MPA intake for > 48 h)	5. Control 43% (15/35) vs intervention 81% (26/32); $p = 0.001$
		6. Adherence, as measured with Morisky questionnaire	6. Control 63% (22/35) vs intervention 63% (20/32); $p = 0.695$
		7. Self-reported adherence	7. Control 77% (27/35) vs intervention 72% (23/32); $p = 0.193$
Cohort studies			
Harrison et al. 2012[14]	Medication errors	1. No. of DTPs identified per visit (control group, clinic visits; intervention group, clinic visits and pharmacist visits) (mean ± SD)	1. DTPs identified per: - Intervention pharmacist visit: 1.05 ± 1.34 - Intervention clinic visit 0.51 ± 0.64; $p = 0.018$ relative to intervention pharmacist visit - Control clinic visit 0.74 ± 0.81; $p = 0.19$ relative to intervention pharmacist visit
Maldonado et al. 2013[12]	Morbidity	1. Mean hospital length of stay	1. Control (2007) 7.8 days vs intervention (2011) 3.4 days; $p < 0.001$
		2. All cause 30-, 90-, and >90-day readmission rates	2. No significant differences; $p > 0.09$ for all comparisons
Musgrave et al. 2013[13]	Medication errors	1. No. of medication errors per patient at discharge avoided through pharmacist intervention (mean ± SD)	1. Retrospective 0 vs prospective 1.9 ± 1.7; $p < 0.0001$
		2. No. of medication errors per patient at discharge persisting until first follow-up appointment (mean ± SD)	2. Retrospective 3.4 ± 1.9 vs prospective 1.1 ± 1.4; $p < 0.0001$
		3. % of discharges with no medication errors	3. Retrospective 3.9% vs prospective 25%; $p < 0.0001$
Tschida et al. 2013[20]	Cost	1. Mean total cost per patient in the first follow-up year	1. 13% lower in the specialty pharmacy group ($24 315 vs $27 891); $p = 0.03$
	Compliance	2. Mean no. of oral transplant prescriptions dispensed per patient	2. Retail pharmacy group 17.90 vs specialty pharmacy group 18.67; $p < 0.05$
		3. Weighted medication possession ratio	3. Retail pharmacy group 0.83 vs specialty pharmacy group 0.87; $p < 0.0001$
		4. No. of patients with medication gap (at least 60 days without immunosuppressive drugs but followed by re-initiation within study period)	4. Retail pharmacy group 53 vs specialty pharmacy group 29; $p = 0.006$
		5. No. of patients with discontinuation (at least 60 days without immunosuppressive drugs, never followed by re-initiation within the study period)	5. Retail pharmacy group 104 vs specialty pharmacy group 39; $p < 0.0001$
		6. Mean no. of dialysis-related inpatient hospital stays per patient	6. Retail pharmacy group 0.04 vs specialty pharmacy group 0.02; $p < 0.03$
Pre–post studies			
Partovi et al. 1995[22]	Other	% change in knowledge score (mean ± SD)	
		1. Pre-test to post-test 1	1. 24.8% ± 10.6%; $p < 0.05$
		2. Pre-test to post-test 2	2. 36.7% ± 11.8%; $p < 0.05$
		3. Pre-test to post-test 3	3. 40.9% ± 12.7%; $p < 0.05$
		4. Post-test 1 to post-test 2	4. 11.9% ± 9.7%; $p < 0.05$
		5. Post-test 2 to post-test 3	5. 4.21% ± 8.9%; $p < 0.05$

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Table 2 (part 3 of 3). Outcomes of Individual Studies

Reference	Type of Outcome	Main Study Outcomes	Main Results
Chisholm et al. 2007[19]	Morbidity	1. Clinical indicators for diabetes mellitus (fasting blood glucose and HbA1c) (mean ± SD)	1. Fasting blood glucose: 129.22 ± 18.25 mg/dL (pre) vs 112.22 ± 17.43 mg/dL (post); $p = 0.001$ HbA1c: 8.07% ± 0.81% (pre) vs 7.42% ± 0.61% (post); $p = 0.002$
		2. Clinical indicators for hyperlipidemia (LDL and total cholesterol) (mean ± SD)	2. LDL: 305.48 ± 66.20 mg/dL (pre) vs 191.78 ± 27.39 mg/dL (post); $p < 0.001$ Total cholesterol: 345.83 ± 108.33 mg/dL (pre) vs 239.91 ± 47.24 mg/dL (post);$p < 0.001$
		3. Clinical indicators for hypertension (systolic and diastolic blood pressure) (mean ± SD)	3. Systolic: 140.52 ± 7.81 mm Hg (pre) vs 134.30 ± 7.54 mm Hg (post); $p < 0.001$ Diastolic: 79.19 ± 3.97 mm Hg (pre) vs 77.04 ± 4.24 mm Hg (post); $p < 0.001$
		4. Serum tacrolimus concentration (mean ± SD)	4. 8.67 ± 3.5 ng/mL (pre) vs 10.17 ± 1.17 ng/mL (post); $p = 0.343$ No significant difference in no. of patients achieving target concentrations
		5. Serum cyclosporine concentration (mean ± SD)	5. 178.77 ± 61.4 ng/mL (pre) vs 214.7 ± 44.14 ng/mL (post), $p = 0.007$ Significant improvement in no. of patients achieving target concentrations; $p = 0.008$
		6. No. of graft rejections (mean ± SD)	6. 0.50 ± 0.51 (pre) vs 0.22 ± 0.42 (post); $p = 0.008$
		7. Health-related quality-of-life scores	7. Significantly increased scores for General Health, Social Functioning, Role Emotional, Mental Health, Physical Component Summary, and Mental Component Summary scales; $p < 0.01$
Pinelli et al. 2014[16]	Morbidity	**HbA1c (mean ± SD)** **Intention-to-treat analysis**	**HbA1c (mean ± SD)** **Intention-to-treat**
		1. At 3 months in patients with baseline HbA1c < 7.0%	1. Baseline 6.0% ± 0.5% vs 3 months 6.6% ± 0.9%; $p = 0.20$
		2. At 6 months in patients with baseline HbA1c < 7.0%	2. Baseline 6.0% ± 0.5% vs 6 months 6.2% ± 0.6%; $p = 0.48$
		3. At 3 months in patients with baseline HbA1c ≥ 7.0%	3. Baseline 8.1% ± 1.0% vs 3 months 7.3% ± 1.2%; $p = 0.07$
		4. At 6 months in patients with baseline HbA1c ≥ 7.0%	4. Baseline 8.1% ± 1.0% vs 6 months 7.5% ± 0.8%; $p = 0.16$
		Per protocol analysis	**Per protocol analysis**
		1. At 3 months in patients with baseline HbA1c < 7.0%	1. Baseline 6.0% ± 0.5% vs 3 months 6.3% ± 0.8%; $p = 0.55$
		2. At 6 months in patients with baseline HbA1c < 7.0%	2. Baseline 6.0% ± 0.5% vs 6 months 6.1% ± 0.6%; $p = 0.48$
		3. At 3 months in patients with baseline HbA1c ≥ 7.0%	3. Baseline 8.3% ± 1.0% vs 3 months 6.8% ± 1.2%; $p = 0.0041$
		4. At 6 months in patients with baseline HbA1c ≥ 7.0%	4. Baseline 8.3% ± 1.0% vs 6 months 7.5% ± 1.0%; $p = 0.15$

CI = confidence interval, DTP = drug therapy problem, HbA1c = glycated hemoglobin, LDL = low-density lipoprotein, MEMS = medication event monitoring system, MMF = mycophenolate mofetil, MPA = mycophenolic acid, RR = rate ratio, SD = standard deviation.

ing drug-related problems, and significantly reducing readmission rates in the emergency department.[26] In the study by Maldonado and others,[12] pharmacists proposed a discharge plan to the patients, in addition to performing medication reconciliation. Harrison and others[14] described collaboration with community pharmacists; such collaborations reflect the importance of continuity of care between the transplant team and community practitioners to ensure an optimal prognosis. The development of telepharmacy tools may help with post-transplant home care.

Outcomes

Improvements in medication adherence, morbidity, costs, and medication errors were reported in the selected studies, but these outcomes were not linked to specific pharmacist activities.

There were clear benefits in terms of patient adherence to immunosuppressive treatments.[11,15,17-20] Chisholm and others[19] reported a significant reduction in transplant rejections from 1 year pre-enrollment to 1 year post-enrollment ($p = 0.008$). Klein and others[18] found fewer rejection episodes in the intervention group, although the difference was not significant (small sample size). Three studies showed an increase in achievement of target serum concentrations of oral immunosuppressants.[15,18,19]

Significant positive outcomes were found in terms of comorbidities such as diabetes mellitus, hyperlipidemia, and hypertension, but the results were inconsistent for morbidity outcomes.[16,19,21]

In the study by Tschida and others,[20] implementation of a transplant pharmacy program resulted in a significantly lower

Table 3 (part 1 of 2). Rating of Pharmaceutical Interventions with DEPICT Tool[10]

	Study (by Reference Number)											
Element of Tool	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**
A. Contact with the patient												
1A. Face-to-face contact	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2A. Remote contact	Y	N	N	N	Y	N	Y	N	N	Y	Y	N
B. Timing of the intervention												
3B. At patient admission to a hospital, nursing home, or emergency department	N	Y	N	N	N	N	N	N	N	N	N	N
4B. During hospital or nursing home stay	Y	Y	N	N	N	N	N	Y	N	N	N	N
5B. At patient discharge or interfacility transfer	N	Y	Y	N	N	N	N	Y	N	N	N	N
6B. When a new or changed prescription is provided	N	N	N	N	N	N	N	N	N	N	N	N
7B. At the time of drug dispensing	N	N	N	N	N	N	N	N	N	N	N	N
C. Setting of the intervention												
8C. Participant's home	N	N	N	N	N	N	N	N	N	Y	N	N
9C. Community pharmacy	N	N	N	N	N	N	Y	N	N	Y	N	N
10C. Ambulatory or primary care setting co-located with medical services	Y	Y	N	N	N	Y	N	N	N	N	N	N
11C. Independent ambulatory or primary care setting	N	N	N	N	N	N	N	N	N	N	N	N
12C. Hospital	Y	Y	Y	Y	Y	N	N	Y	N	N	Y	Y
13C. Long-term care facility	N	N	N	N	N	N	N	N	N	N	N	N
D. Target population												
14D. Condition-specific intervention	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
15D. Population-specific intervention	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
E. Clinical data sources												
16E. All current medications in use by the patient	N	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	N
17E. Pharmacy or dispensing records	N	N	Y	N	Y	N	Y	N	N	N	Y	N
18E. Laboratory tests or drug monitoring data	N	Y	N	N	Y	N	N	N	N	N	Y	N
19E. Disease self-monitoring data	N	N	N	N	N	N	N	N	N	N	N	N
20E. Patient's physical or functional assessment	N	N	N	Y	N	N	N	N	N	N	N	N
21E. Medical records	N	Y	N	N	Y	N	N	N	N	N	Y	N
22E. Patient interview (anamnesis)	N	N	N	N	N	N	N	N	N	N	N	N
F. What is assessed												
23F. Medication-use process (errors)	N	N	Y	Y	N	N	N	N	N	N	N	N
24F. Legal or administrative aspects of drug prescriptions	N	N	N	N	N	N	N	N	N	N	N	N
25F. Patient's knowledge, health literacy, or communication skills	N	N	N	N	N	N	N	N	N	N	N	Y
26F. Patient's adherence to treatment	Y	N	N	N	Y	N	Y	Y	Y	Y	N	N
27F. Health outcomes	N	Y	N	N	N	Y	N	N	Y	N	Y	N
28F. Patient's quality of life	N	N	N	N	N	N	N	N	Y	N	N	N
29F. Patient's satisfaction	N	N	N	Y	N	N	N	N	N	N	N	N
30F. Costs of treatment	N	N	N	N	N	N	N	N	Y	Y	N	N
G. Pharmacist's autonomy to perform an action												
31G. Change dosage regimen	N	N	N	N	N	N	N	N	N	N	N	N
32G. Suspend medication	N	N	N	N	N	N	N	N	N	N	N	N
33G. Start a new medication	N	N	N	N	N	N	N	N	N	N	N	N
34G. Order laboratory tests or perform drug monitoring	N	Y	N	N	N	N	N	N	N	N	N	N
H. Pharmacist communication												
35H. Directly with the patient	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
36H. With the physician or health care team	N	Y	N	Y	Y	Y	N	N	Y	N	Y	N
37H. Written recommendations to the physician or health care team	N	N	N	Y	N	N	N	N	N	N	N	N
38H. Face-to-face or telephone recommendations to the physician of health care team	N	N	N	Y	N	N	N	N	N	N	N	N

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Table 3 (part 2 of 2). Rating of Pharmaceutical Interventions with DEPICT Tool[10]

	Study (by Reference Number)											
Element of Tool	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**	**21**	**22**
I. Support resources provided by the pharmacist												
39I. A patient's medication list to the physician	N	Y	N	N	N	N	N	N	N	N	N	N
40I. A medication list or summary to the patient	N	Y	N	Y	N	N	N	Y	N	N	N	N
41I. Written, video, or audio educational material to the patient	Y	N	N	N	Y	N	N	N	N	N	Y	Y
42I. Medication adherence or administration aid	Y	Y	N	Y	N	N	N	N	N	N	N	N
43I. Disease self-management diary	N	N	N	N	N	N	N	Y	N	N	N	N
J. Education and counselling												
44J. Disease-specific or medication counselling to the patient	Y	Y	N	Y	Y	Y	N	Y	N	Y	Y	Y
45J. Lifestyle or self-management education to the patient	N	N	N	N	N	N	Y	Y	N	N	N	N
46J. Education program to a group of patients	N	N	N	N	N	N	N	N	N	N	N	N
L. Follow-up												
47L. Focus on medication-use process	N	N	Y	N	N	N	N	N	N	N	N	N
48L. Focus on health or therapeutic outcomes	Y	Y	N	N	N	Y	N	Y	Y	N	N	N
49L. Follow-up is performed through face-to-face encounters	Y	Y	Y	N	Y	Y	N	Y	Y	N	Y	N
50L. Follow-up is performed through remote contacts	Y	N	N	N	Y	Y	Y	N	N	Y	Y	N
51L. Duration of the follow-up (write the number of months)	Y	N	N	N	Y	Y	Y	Y	N	Y	Y	N
M. Other actions												
52M. Screening for disease risk factors	N	N	N	N	N	Y	N	N	N	N	N	N
53M. Development of a drug formulary, guideline, or clinical protocol	N	N	N	N	N	N	N	N	N	N	N	N
54M. Provider or prescriber education	N	N	N	N	N	N	N	N	N	N	N	N
DEPICT score*	9	11	7	8	9	9	8	10	6	8	9	7

N = no (item not reported in study), Y = yes (item reported in study).
*For each of the 12 sections, a score of 1 was assigned if the reviewers answered "yes" to at least one element of the section. The number of sections with a score of 1 was summed to generate the overall DEPICT score (maximum 12).

mean total cost per patient ($24 315 versus $27 891, 13% decrease; $p = 0.03$), which the authors attributed mainly to a significantly lower mean transplant-related medical cost ($5960 versus $8486, 30% decrease; $p = 0.04$).

Musgrave and others[13] described the avoidance of discharge medication errors through pharmacist intervention, a decrease in discharge medication errors per patient persisting until the first follow-up appointment, and a greatly improved percentage of discharges with no medication errors. Harrison and others[14] reported a decrease in the mean number of drug therapy problems identified per visit.

Patients' knowledge of medications was appraised in only one study.[22] The benefits for short-term information retention were significant, but the study did not examine long-term retention. Given that patient motivation and care intensity often diminish with time, long-term persistence of pharmacist-induced outcomes needs to be evaluated.

Description of Pharmaceutical Interventions

In studies designed to evaluate the roles and impacts of health care professionals, it is very important to have a clear and complete description of the intervention. Associating an intervention with specific outcomes is especially difficult where multidisciplinary teams are involved. According to the DEPICT tool,[10] the descriptions of the interventions in the included studies were generally of good quality. Nonetheless, more complete descriptions should be provided in future studies, especially regarding the timing of the intervention and pharmacists' autonomy.

As for most pharmacy practice research studies, the studies included in this review had small sample sizes, some had no control group ($n = 3$), and the interventions were insufficiently described to be fully reproducible. Usual sources of bias were reported, including performance bias and contamination bias. In clinical practice within a hospital, it is usually difficult to eliminate these 2 types of bias.

Transplant Pharmacy Training

Transplant recipients are treated with multiple drugs, including medications with a narrow therapeutic index. It was therefore surprising to find only a limited number of articles describing pharmacists' roles and outcomes in this area. This systematic review highlights the need to structure teaching and internships in this discipline and to further document the practice of pharmacists in transplant medicine. Professional specialty networks may certainly contribute to better training,

organization, and documentation. For instance, the American Society for Transplantation has a transplant pharmacy community of practice.[27] In addition, the American College of Clinical Pharmacy has an immunology/transplantation practice and research network.[28] The Board of Pharmacy Specialties received a petition to recognize solid organ transplantation pharmacy as a new specialty; the Board's public comment period on this petition closed on May 15, 2018.[29]

In Canada, the Canadian Society of Transplantation has a pharmacist group whose mission is to "provide leadership and a collaborative forum for the advancement of pharmacist clinical practice in transplantation and pharmacist-led research and education".[30] The Canadian Society of Hospital Pharmacists has a transplant Pharmacy Specialty Network that promotes "practice excellence and the enhancement of patient-centred pharmacy practice through information sharing, educational events, and the facilitation of research for pharmacists who are interested in the area of transplant pharmacy practice (solid organ and hematopoietic stem cell transplant)".[31]

There is currently no published literature about transplant-specific training offered in pharmacy, in Canada or elsewhere. Such training may vary substantially among regions and programs, which may explain the paucity of data as well as the wide variety of roles described in the literature.

Limitations

The systematic literature search was conducted in only 4 databases, and all articles published in a language other than English or French were excluded. As a result, some eligible studies may have gone undetected. Although descriptive results lack statistical proof of significance, they may carry compelling information that could prove useful in establishing a more accurate image of the roles and impacts of the pharmacist. However, for practical reasons (notably the difficulty of screening for quality), they were omitted from this review. Eight studies involved kidney transplant recipients exclusively, and the 4 remaining studies were spread among recipients of abdominal, liver, lung, and unspecified transplants. Most anti-rejection medications are lifelong treatments, yet the temporal horizon was limited to a year or less in virtually all of the studies. It is unknown whether pharmacist interventions have lasting effects, especially in the case of temporary activities. It would be interesting to explore which interventions were the most time-effective.

CONCLUSION

Currently available evidence suggests that pharmacists can improve patient outcomes in solid organ transplant settings. Adherence, morbidity, costs, and medication errors were identified as the main outcomes that were improved by pharmaceutical interventions. Transplant programs need to invest more in this resource.

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ON THE FRONT COVER

Near the North Branch of the Thames River London, Ontario

The cover photograph was taken by pharmacist Linda Hooper along the bike path that parallels the north branch of the Thames River in London, Ontario, near her workplace (University Hospital, London Health Sciences Centre). The camera was a Canon EOS 40D.

Linda commented that the scene brought to mind a poem by Canadian poet William Wilfred Campbell. "When I was a kid, this Canadian poem was our memory work at school."

The *CJHP* would be pleased to consider photographs featuring Canadian scenery taken by CSHP members for use on the front cover of the Journal. If you would like to submit a photograph, please send an electronic copy (minimum resolution 300 dpi) to publications@cshp.ca.

Indian Summer

Along the line of smoky hills
The crimson forest stands,
And all the day the blue-jay calls
Throughout the autumn lands.

Now by the brook the maple leans
With all his glory spread,
And all the sumachs on the hills
Have turned their green to red.

Now by great marshes wrapt in mist,
Or past some river's mouth,
Throughout the long, still autumn day
Wild birds are flying south.

~ William Wilfred Campbell (1858?-1918)

Is It Necessary for Pharmacists to Evaluate Other Health Professionals' Satisfaction with Pharmacist Services?

THE "PRO" SIDE

Many institutions focus on evaluating patients' opinions about their health care experience, and rightly so. Patients and their caregivers are the primary users of health care, and their input about their own experiences is invaluable to administrators and health care providers. However, the multiple users or consumers of pharmacy services within the health care system include other health professionals, whose valuable feedback could also be sought through satisfaction surveys.

The quality of health care is typically assessed along a continuum, whereby institutions that demonstrate continuing improvement activities are considered to exemplify more mature organizations in terms of their quality practices. [1] Therefore, it can be argued that seeking feedback to understand customers' satisfaction with a service and then using this information to continually improve that service are signs of a more mature health care organization. As the roles of pharmacists have expanded over the past few decades, so too have the ways in which they work and interact with other health professionals. How will we pharmacists know we're getting it right if we don't ask them?

For the following reasons, it is essential for pharmacists to evaluate the satisfaction of all recipients of their services, including other health professionals. Feedback can facilitate pharmacists' professional development and can help in identifying areas for improvements in pharmacists' services. This type of interaction with health professionals also provides opportunities to further develop effective interprofessional collaborative practices. The most compelling reason to evaluate health professionals' satisfaction is that improvements to pharmacy services may lead to better patient care and better outcomes.

Measuring other health professionals' opinions about and satisfaction with pharmacists' performance provides important information that can enhance pharmacists' professional learning and development. Published reports of health professionals' views of and satisfaction with pharmacy tend to focus on the introduction of a new or changed service[2-4] or to report the results of one-time surveys.[5-8] Unfortunately, most pharmacy departments do not routinely continue measuring the health care team's satisfaction with pharmacy services at regular intervals after an initial evaluation. This represents a missed opportunity to gauge how well the pharmacy department and pharmacists working in health care teams meet the needs of their customers. Although many pharmacy departments incorporate feedback from other members of the health care team in the performance appraisals of individual pharmacists, these results should be interpreted cautiously as indicators of pharmacy services provided. That is because of potential biases in the process.[9] Feedback sought for the purposes of performance appraisal may be perceived to affect coworkers' careers, resulting in overly positive and less constructive responses. Instead, health professionals should be asked to complete satisfaction surveys about the services provided by the pharmacy team as a whole or pharmacy personnel working in their respective clinical areas, and to provide constructive recommendations intended to improve the services. Results of these surveys could be used to facilitate discussion within the pharmacy team about the survey outcomes and ways in which identified gaps could be addressed.

Surveying other health professionals allows pharmacy departments and decision-makers to better understand coworkers' satisfaction with pharmacy services and also highlights opportunities for improved interprofessional communication and collaboration. For any customer or client using a service, the level of satisfaction often reflects the difference between what the person expected to receive and what was actually received.[10,11] Therefore, health professionals' satisfaction can be viewed as their perception of the pharmacy services they received relative to what they expected to receive. High levels of satisfaction with pharmacy services imply that health professionals' expectations have been met. Conversely, low satisfaction with pharmacy services indicates that health professionals' expectations have not been met and pinpoints areas in which pharmacy services can be improved.

As well, these mismatches may highlight gaps in health professionals' knowledge about pharmacists' training and scope of practice. Several studies have provided evidence supporting these possibilities.[3,4,12,13] For example, in surveys distributed before and after the introduction of clinical pharmacy services to a surgery ward,[3] my own research team found marked differences among pharmacists, nurses, and physicians in terms of their views of certain pharmacist roles. In particular, pharmacists felt much more strongly than nurses or physicians (96% agreement versus 46% and 40%, respectively) that "ensuring patients receive

optimal drug therapy" was a key role for pharmacists.[3] These perceived differences in expectations of pharmacists indicate a need for all health professionals to learn more about each other's roles. Other researchers, who followed up with practising health professionals 5 years after participation in interprofessional education during their training, reported that participants' understanding of other health professionals' roles increased with time in practice.[14] Unfortunately, this same group of participants indicated declines in teamwork, collaboration, and respect after a period of time in practice as compared with the perspectives they held while engaged in the interprofessional education program.[14]

Role clarification, teamwork, and communication are among the 6 competency domains of the framework described by the Canadian Interprofessional Health Collaborative as necessary for effective interprofessional collaboration.[15] Surveys requesting feedback from health professionals about pharmacy services could help in uncovering confusion about roles and could provide a platform to discuss how interprofessional collaboration can be improved.

In summary, as the profession of pharmacy continues to evolve, it is essential that the pharmacist services provided are of high quality. To ensure this level of quality, all aspects of pharmacist services, including health professionals' satisfaction, need to be evaluated on an ongoing basis for continuous improvement. The evaluation of health professionals' feedback may lead to changes that improve pharmacist services and ultimately lead to higher quality of care for patients.

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THE "CON" SIDE

As pharmacists, our scope of practice is defined by our licensing and regulatory bodies, as well as by provincial legislation. Our purview for patient care is determined by these organizations, with the central tenet of optimizing patient care within our knowledge, skills, and abilities. Nowhere do our standards of practice indicate that we should satisfy the expectations of other health care professionals. For example, Standard 1 of the Alberta standards of practice indicates that pharmacists should act professionally, which includes working collaboratively with others, but the standard does not mention satisfying the needs of other health care professionals.[1] If we define satisfaction in terms of the level to which pharmacists are meeting the needs and/or expectations of others, the question of measuring health care professionals' satisfaction is really "Are we meeting the needs and expectations of other health care professionals?" I would argue that our goal in patient care is not to meet the expectations of other health care professionals but rather to meet the needs of our patients.

The care decisions that we make for, and in conjunction with, our patients should not be reliant on the satisfaction of other health care professionals. Instead, these decisions should be about the patient and for the patient. We have all had practice experiences where we have made a care decision with a patient that has definitely not been in alignment with the views and approaches of other health care professionals, but their dissatisfaction has not negated that decision nor made it incorrect.

We teach students and new pharmacists to apply the patient care process to patient interactions and, through this process, to determine a care plan.[2] This care plan is based on the patient's goals, our assessment of the patient's medications (in terms of indication, effectiveness, safety, and adherence), and other contributing data. The patient

care is then documented, and this information is shared with other members of the care team. Within this process, we, as pharmacists, must determine how best to collaborate with these other health care partners. However, in determining that collaboration, we should not be bound or limited by the level of satisfaction that other health care professionals have in our work. Our goal is to provide care and optimize patient outcomes through appropriate medication management. Clearly, the attitudes and level of satisfaction of other health care professionals can influence us, and previous research has shown that these contextual factors affect our work and even our care decisions.[3] These influences are practice- and context-specific, and need to be managed on an individual basis. However, research about general satisfaction with a pharmacist service does not inform how we deal with these difficult situations.

I think a prime example of a situation where the opinions of other health care professionals have been over-studied, with no benefit to care, is the case of immunization by pharmacists. As provinces in Canada and other countries move to increase patients' access to vaccinations, a lot of time, energy, and money has been spent on asking physicians and nurses for their opinions, attitudes, and satisfaction with administration of vaccines by pharmacists. The initiation of pharmacist immunization has been driven primarily by the need to increase vaccination rates and accessibility to vaccines.[4-8] In addition to increasing uptake, pharmacist vaccination has been shown to have economic benefits.[6] Furthermore, seeing a pharmacist for a vaccination offers patients an entry point into the health care system. Through their assessment of a patient's appropriateness of vaccination, pharmacists may identify other issues that the patient is experiencing, but has not yet sought care for.

The decision to expand pharmacists' scope of practice to include immunization is really about increasing patients' access to care. Given that the rationale for this decision is based on patient care, is it important at all to ask what other health care professionals think? Opinions, including level of satisfaction, are value-laden and biased, and do not necessarily relate to optimal patient care; rather, they may include factors such as loss of income and territoriality.[4] In one Canadian study, nurses and physicians were asked whether they supported the expansion of pharmacists' scope of practice to include vaccination; 32% of nurses and 46% of physicians strongly disagreed with the expansion of scope of practice.[9] Nonetheless, as of late 2018, all but one of Canada's 10 provinces have expanded pharmacists' scope to include vaccine administration.[10] Therefore, how has this research added value to our knowledge and understanding of pharmacist immunization programs?

Even with evidence supporting the role and legislation that allows us to include vaccination as part of our scope of practice, research continues on the satisfaction of other health care professionals in relation to pharmacist administration of vaccines.[8,11] Recently, Australia has gone through legislative and practice changes to allow for pharmacist immunizers, with both nurses and doctors voicing concern over the expansion of pharmacists' scope.[6] Many of the concerns are proffered under the guise of patient safety; however, loss of income has come up in some research as well.[4] So, if there is bias related to a loss of income, how can we consider these opinions as being important in improving patient care?

Finally, we need to consider why we include the concept of "satisfaction" in pharmacy practice research at all. Is the reason we do this research to affirm our role in patient care? Do we really lack that much confidence in our abilities that we must look to others to tell us that we are doing our job well?[12] As researchers, and as consumers of research, we need to think about our primary objectives in measuring satisfaction, and whether there is really an ongoing need for this type of work. Shouldn't our already limited research resources be spent on something more directly valuable to our patients?

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Évaluer les priorités et les ressources : un exercice d'équilibre

par Tania Mysak

Se serrer la ceinture. Travailler plus intelligemment, pas plus fort. Vivre selon ses moyens. Il y a de bonnes chances que vous ayez déjà entendu ces phrases ou des versions de celles-ci. Qu'il s'agisse des budgets fédéraux, des finances familiales ou de l'efficacité en milieu de travail, l'on s'attend à ce que nous réévaluions nos pratiques actuelles et que nous cherchions des façons de les rendre plus viables.

Ce processus est très semblable aux choix d'interactions que les pharmaciens font tous les jours dans leur prestation de soins aux patients. Nous établissons un ordre de priorité et planifions les heures limitées dont nous disposons chaque jour pour être aussi efficaces que possible et pour faire en sorte que ceux qui ont le plus besoin de nos soins les reçoivent. Nous fouillons les ressources disponibles aux patients pour nous assurer qu'ils reçoivent la pharmacothérapie la plus avantageuse qu'ils puissent se permettre. Une gestion adéquate des médicaments permet de s'assurer que les médicaments ajoutés à la pharmacothérapie ont une valeur réelle pour les patients et leurs objectifs de santé. S'il y a un médicament inutile dans la pharmacothérapie, il faut déprescrire : garder l'utile, éliminer le gaspillage.

Du point de vue de la gestion de pharmacie, nous appliquons également ces principes. Les gestionnaires et les directeurs de pharmacie doivent prendre en compte, pour ce qui touche à leur service, quelles unités recevront des soins proactifs, notamment par l'intégration de pharmaciens dans les équipes de soins, et quelles unités auront droit à une approche plus réactive, peut-être à partir de la pharmacie ou à distance. Ils doivent déterminer le niveau d'allocation de service qui peut être offert compte tenu des ressources disponibles et ils doivent établir comment prioriser les exigences toujours changeantes concernant la distribution de médicaments sûrs.

Ultimement ces principes servent à prendre des décisions judicieuses pour ce qui est de répartir des ressources limitées.

À titre d'association professionnelle ayant comme mandat de servir ses membres, la Société canadienne des pharmaciens d'hôpitaux (SCPH) n'est pas à l'abri des exigences de révision des programmes compte tenu de ses ressources limitées. Nos principales sources de revenus en tant que société proviennent des cotisations et de la Conférence sur la pratique professionnelle, qui est lucrative grâce au généreux soutien de l'industrie. Nous faisons toujours face à des défis sur ces deux fronts et travaillons activement de concert avec nos sections et nos partenaires de l'industrie pour maintenir et augmenter ces sources de revenus. Tout en cherchant des occasions dans ces sphères, nous devons aussi tenir compte de notre programmation et nous occuper des passifs du bilan. Cet été, le conseil de la SCPH a commencé à évaluer nos nombreux programmes, les soumettant à une série de questions standards conçues pour juger la valeur que chaque programme offre à la Société. À mesure que cette évaluation avance, nous vous consulterons, vous les membres, pour connaître votre opinion. Ce sont des conversations délicates. Nous savons que, comme dans les exemples fournis ci-dessus, il est très difficile de dire « non » à quelque chose que l'on perçoit personnellement comme important ou que l'on fait depuis longtemps.

Le conseil de la SCPH adhère à la vision de la Société, soit d'être une « société dynamique, en constante évolution », et à notre objectif stratégique d'équilibre entre les priorités et les ressources. Nous nous ferons un plaisir de vous informer de nos progrès tout au long de cet important travail.

[Traduction par l'éditeur]

Tania Mysak, BSP, Pharm. D., est devenue présidente désignée et agente de liaison de la Société canadienne des pharmaciens d'hôpitaux lors de la réunion du conseil qui a suivi son élection à l'Assemblée générale annuelle en octobre 2018.

Evaluating Priorities and Resources: A Balancing Act

Tania Mysak

Tighten our belts. Work smarter, not harder. Live within our means. Chances are you have heard these phrases or versions of them at some point. Whether talking about federal budgets, home finances, or workplace efficiencies, there is an expectation that we review our current practices and look for ways of making them more sustainable.

This process is quite similar to the choices that pharmacists make every day in patient care interactions. We triage and plan our finite daily hours to be as efficient as possible and to ensure that those most in need of our care receive it. We navigate the resources available to patients to ensure they receive the drug therapy from which they are most likely to benefit and that they can afford. Proper medication management ensures that medications added to therapy are of real value to patients and their health goals. If there is an unnecessary drug in the mix, we deprescribe: keep the value, eliminate the waste.

From a pharmacy management perspective, we further apply these principles. Pharmacy managers and directors must consider, at the department level, which patient areas will receive proactive care, with integration of pharmacists into care teams, and which will receive a more reactive approach, perhaps from a dispensary or remote location. They must determine what level of service allocation can be provided with the resources available, and how to prioritize ever-changing requirements for the provision of safe medication.

Ultimately, these principles are about making judicious decisions as to how limited resources will be used.

As a professional association with a mandate to serve its membership, the Canadian Society of Hospital Pharmacists (CSHP) is not immune to the requirement to review programming in the context of finite resources. Our main sources of revenue as a society are membership dues and the Professional Practice Conference, which is profitable thanks to the generous support of industry. We continue to face challenges on both of those fronts and are actively working with our Branches and industry partners to maintain and increase these revenue streams. While looking for opportunities in these areas, we must also consider our programming and address the expense side of the balance sheet. This past summer, the CSHP Board began the work of evaluating our many programs, putting them through a standardized series of questions designed to examine the value that each program offers to the Society. As this evaluation proceeds, we will be reaching out to you, the members, for input and guidance. These are tough conversations; as we know from any of the examples provided above, it is really hard to say "no" to something you personally believe is important or have done for ages.

The CSHP Board is committed to the Society's Vision of being a "thriving, progressive society" and our strategic goal of alignment between priorities and resources. We look forward to updating you on our progress as we continue this important work.

Tania Mysak, BSP, PharmD, became President Elect and Vision Liaison for the Canadian Society of Hospital Pharmacists at the Board meeting following her election during the Annual General Meeting in October 2018.

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