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The Hidden Epidemic

Clarence Chant

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Even before the COVID-19 pandemic, the opioid overdose epidemic was causing significant loss of lives. Unfortunately, while the world's collective attention has been focused on various aspects of the pandemic, the opioid epidemic continues, and its impact is increasing. As just one example, a recent study reported an increase of 135% (and up to 320%) in deaths from opioid overdoses during the first months of the COVID-19 pandemic in a single Canadian province.[1]

Excessive and potentially inappropriate prescribing of opioids and their diversion from health care institutions have been cited as factors contributing to the opioid epidemic. Given the increased severity of the opioid crisis, more studies and innovative solutions are urgently needed. In this issue of the *Canadian Journal of Hospital Pharmacy* (*CJHP*), Ti and others[2] describe a unique pilot project for a hospital-wide opioid stewardship program. Similar to the more prevalent antimicrobial stewardship programs (which Accreditation Canada now designates as Required Organizational Practices), this opioid stewardship program targeted specific populations and medications, providing audit and feedback about the appropriateness of prescribing. In the first year, more than 1500 recommendations were made for several hundred patients. Unfortunately, no outcome data (in terms of reduced usage, in morphine equivalents) are provided in the article. Other innovative programs have previously been reported, such as a prescribing force function to reduce the quantity of postoperative pain medications administered.[3] Although each of these studies tackled only one aspect contributing to the multifactorial opioid epidemic, these types of research offer important insights.

As for the second contributor, that of diversion of opioids from hospitals by staff members, research and understanding are not advancing in the same manner. Until recently, diversion was not a welcome topic of conversation. One recent review of 5 years of Health Canada data showed a substantial number of reports of loss of controlled substances—142 420 in all—from across the country in all types of facilities, with hospitals accounting for 17% of these losses.[4] What is more concerning is that the reasons for the losses were largely unexplained, at 33.4%! To further compound the problem, disciplinary actions in general, including those related to diversion by hospital staff, are rarely reported to regulatory colleges, despite it being a mandatory requirement in many jurisdictions. Also in this issue of the *CJHP,* Fung and others[5] corroborate these general observations of under-reporting through a qualitative study, using semistructured interviews with pharmacy directors across the country. The authors found five themes for under-reporting to regulatory bodies, namely a robust organizational discipline process, union representation, preference for remediation, promotion of a practice environment that promotes competency, and unclear regulatory requirements. While these themes are logical and reasonable, they do not help in understanding the issue of opioid diversion by staff, because it is difficult or impossible to devise solutions to a problem that is largely hidden and unknown.

Despite the fact that the American Society of Health-System Pharmacists[6] and the Canadian Society of Hospital Pharmacists[7] have published guidelines to help detect and deal with diversion in hospitals, there remain numerous institutions, especially in Canada, that have not implemented a formal diversion committee or a fulsome program on this topic. Although opioid stewardship programs like the one described by Ti and others[2] borrow learnings from antimicrobial stewardship, many hospitals do not seem to have learned from the medication incident knowledge domain, whereby reporting of all medication incidents, even the near misses, is an essential pillar of system improvement to better patient care. Opioid diversion does lead to patient harm in many ways, not the least of which is that patients do not receive the pain management medications intended for them. A systematic review documented that opioid diversion and substitution of IV opioid with saline after self-injection of the opioid by a health care professional led to several outbreaks of gram-negative bacteremia and hepatitis C infections in patients who received the saline through contaminated needles.[8] In fact, ISMP Canada has called for a culture shift related to opioid diversion, from one of personal failing that requires punishment and termination to one of open communication whereby system gaps can be better addressed, similar to the improved culture of reporting medication errors that has contributed to greater medication safety.[9]

So, perhaps there are really two hidden epidemics here: the opioid crisis and a crisis of diversion and under-reporting. If pharmacists and pharmacy technicians are

indeed champions of medication safety, then diversion prevention should become an openly discussed topic that is part of their daily work and is included in their respective school curriculums and research publications.

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ON THE FRONT COVER

Wapta Mountain, Yoho National Park, British Columbia

June Chen captured this photograph of Wapta Mountain in Yoho National Park with a Canon PowerShot SD1100 IS digital camera while hiking the Emerald Triangle trail.

June is a clinical pharmacist at the University of Alberta Hospital in Edmonton. She practices on the cardiac intensive care and cardiovascular surgery units. During the summer months, she enjoys hiking in the mountains, and all year round, she likes to dance contemporary jazz.

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

L'autre épidémie

par Clarence Chant

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Même avant la pandémie de COVID-19, l'épidémie de surdoses d'opioïdes était à l'origine de nombreux décès. Malheureusement, tandis que l'attention du monde s'est braquée sur les divers aspects de la pandémie de COVID-19, l'épidémie d'opioïdes, quant à elle, continue à faire rage et ses conséquences augmentent. À titre d'exemple, une étude récente rapporte une augmentation de 135 % (et jusqu'à 320 %) des décès par surdose d'opioïdes au cours des premiers mois de la pandémie de COVID-19 dans une seule province canadienne[1].

La prescription excessive et potentiellement inappropriée d'opioïdes et leur détournement des établissements de soins de santé ont été cités comme des facteurs contribuant à cette épidémie. Compte tenu de sa gravité croissante, davantage d'études et de solutions innovantes sont nécessaires de toute urgence. Dans ce numéro du *Journal canadien de la pharmacie hospitalière* (JCPH), Ti *et al.*[2] décrivent un projet pilote unique relatif à un programme de gestion des opioïdes dans l'ensemble des hôpitaux. À l'instar des programmes plus répandus de gestion de l'utilisation des antimicrobiens (qu'Agrément Canada désigne désormais comme des « Pratiques organisationnelles requises »), ce programme de gestion des opioïdes ciblait des populations et des médicaments spécifiques; il permettait en outre de vérifier et de recueillir des commentaires sur la pertinence des prescriptions. La première année, plus de 1500 recommandations ont ainsi été émises pour plusieurs centaines de patients. Malheureusement, aucune donnée sur les résultats (en termes de réduction de l'utilisation, en équivalents morphine) n'est fournie dans l'article. D'autres programmes innovants ont déjà été signalés, comme une « fonction de contrainte » en matière de prescription pour réduire la quantité d'analgésiques postopératoires administrés[3]. Bien que chacune de ces études n'ait abordé qu'un seul aspect contribuant à l'épidémie multifactorielle d'opioïdes, elles offrent des informations importantes.

Quant au deuxième facteur, celui du détournement des opioïdes des hôpitaux par les membres de leur personnel, la recherche et la compréhension n'avancent pas au même rythme. Jusqu'à récemment, le détournement n'était pas un sujet de discussion facile. Un examen récent portant sur 5 ans de données de Santé Canada a montré un nombre important de rapports de perte de substances contrôlées partout au pays – 142 420 en tout – et dans tous les types d'établissements, les hôpitaux représentant 17 % de ces pertes[4]. Ce qui est plus inquiétant, c'est que les raisons des pertes étaient en grande partie inexpliquées, à 33,4 %! Pour aggraver le problème, les mesures disciplinaires en général, y compris celles liées au détournement par le personnel hospitalier, sont rarement signalées aux ordres professionnels, malgré l'obligation de le faire dans de nombreuses régions. Toujours dans ce numéro du *JCPH*, Fung *et al.*[5] corroborent ces observations générales de sous-déclaration au moyen d'une étude qualitative menée à l'aide d'entrevues semi-structurées avec des directeurs de pharmacie partout au pays. Les auteurs ont dégagé cinq thèmes favorisant la sous-déclaration aux organismes de réglementation, à savoir : un processus de discipline organisationnelle robuste; la représentation syndicale; la préférence pour la remédiation; la promotion d'un environnement de pratique qui encourage la compétence; et le manque de clarté en matière d'exigences réglementaires. Bien que ces thèmes soient logiques et raisonnables, ils n'aident pas à comprendre la question du détournement des opioïdes par le personnel, car il est difficile, voire impossible, de trouver des solutions à un problème qui est en grande partie caché et inconnu.

Malgré la publication des lignes directrices de l'American Society of Health-System Pharmacists[6] et de la Société canadienne des pharmaciens d'hôpitaux[7] pour aider à détecter et traiter les détournements au sein des hôpitaux, de nombreux établissements, particulièrement au Canada, n'ont pas encore mis en place de comité officiel ni de programme complet consacré à ce sujet. Bien que les programmes de gestion des opioïdes comme celui décrit par Ti *et al.*[2] empruntent les enseignements tirés de la gestion des antimicrobiens, de nombreux hôpitaux ne semblent pas avoir tiré les leçons des incidents liés aux médicaments, selon lesquelles la déclaration de tous les incidents, même ceux évités de justesse, est un pilier essentiel de l'amélioration du système et permet d'améliorer les soins aux patients. Le détournement des opioïdes entraîne des préjudices pour les patients de nombreuses manières, et non des moindres, les patients qui ne reçoivent pas les médicaments de gestion de la douleur qui leur sont destinés. Une revue systématique a permis de documenter que le détournement des opioïdes et la substitution d'opioïdes IV par une solution saline après

son auto-injection par un professionnel de la santé avaient entraîné plusieurs éclosions de bactériémie à Gram négatif et d'infections par l'hépatite C chez des patients ayant reçu la solution saline au moyen d'aiguilles contaminées[8]. En fait, ISMP Canada a appelé à un changement de culture lié au détournement des opioïdes : passer d'une culture où l'échec d'un membre du personnel doit entraîner une punition et un licenciement, à une culture où la communication ouverte permet de mieux combler les lacunes du système, semblable à la culture améliorée de signalement des erreurs de médication qui a contribué à une plus grande sécurité des médicaments[9].

Alors, peut-être que deux épidémies sont vraiment cachées ici : la crise des opioïdes et une crise du détournement et de la sous-déclaration. Si les pharmaciens et les techniciens en pharmacie sont effectivement les champions de la sécurité des médicaments, la prévention de ces détournements devrait alors être un sujet discuté ouvertement, faire partie de leur travail quotidien et être incluse dans les programmes scolaires et les publications de recherche.

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Ambulatory Heart Function and Transplant Patients' Perceptions of Drug–Drug Interactions: A Qualitative Study

David Poon, Michael Legal, Louise Lau, Harkaryn Bagri, and Karen Dahri

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ABSTRACT

Background: Drug–drug interactions (DDIs) can cause adverse drug events, leading to hospitalizations and an increase in the risk of morbidity and mortality. Until now, patients' perceptions of DDIs have represented an understudied area of research.

Objectives: To explore patients' perceptions of DDIs and identify factors important to patients' understanding of their medications.

Methods: Participants were recruited from 2 ambulatory clinics (heart function and transplant) in Vancouver, British Columbia. Participants engaged in key informant interviews and were asked to provide their demographic information, rate their understanding of their own medications, and define a DDI. Afterward, participants were interviewed to gather their perceptions of DDIs and factors important to their understanding of their medications.

Results: A total of 7 patients were recruited. Participants struggled to define a DDI and were unsure if they had ever experienced a DDI. There was a reliance on health care professionals to help manage DDIs. Participants did not identify barriers preventing them from accessing medication information from health care professionals; however, they independently sought medication information found on the internet.

Conclusions: Patients in this study had an incomplete understanding of DDIs and had difficulties differentiating DDIs from side effects of medications. As a result of their limited understanding of DDIs, patients relied on health care professionals to inform and manage their DDIs. Although patients did not identify barriers to accessing medication information, their pervasive use of the internet suggests that there are unidentified barriers preventing patients from speaking directly to their health care professionals regarding their medication therapy.

Keywords: drug interactions, patient perceptions, health care professionals

RÉSUMÉ

Contexte : Les interactions médicamenteuses (IM) peuvent provoquer des événements indésirables, entraînant des hospitalisations et une augmentation du risque de morbidité et de mortalité. Jusqu'à présent, les perceptions des patients concernant les IM représentaient un domaine de recherche sous-étudié.

Objectifs : Explorer les perceptions des patients à l'égard des IM et recenser les facteurs importants pour qu'ils comprennent leurs médicaments.

Méthodes : Les participants ont été recrutés dans deux cliniques ambulatoires (de la fonction cardiaque et de transplantation) à Vancouver, en Colombie-Britannique. Ils ont participé à des entretiens à titre d'informateurs clés et ont été invités à fournir leurs informations démographiques, à évaluer leur niveau de compréhension de leurs médicaments et à définir ce qu'on entend par « IM ». Par la suite, les participants ont été interrogés pour savoir comment ils percevaient les IM et pour recenser des facteurs importants leur permettant de comprendre leurs médicaments.

Résultats : Au total, 7 patients ont été recrutés. Les patients avaient du mal à définir une IM et ne savaient pas s'ils avaient déjà vécu une IM. Ils comptaient ainsi sur les professionnels de la santé pour les aider à les gérer. Les patients n'ont identifié aucun obstacle les empêchant d'accéder aux informations sur les médicaments fournis par les professionnels de la santé; cependant, ils ont, de manière indépendante, cherché des informations sur les médicaments sur Internet.

Conclusions : Les patients de cette étude avaient une compréhension limitée des IM et avaient des difficultés à faire la différence entre les IM et les effets secondaires des médicaments. En raison de cette compréhension limitée, les patients comptaient sur les professionnels de la santé pour les informer et gérer leurs IM. Bien que les patients n'aient pas signalé d'obstacles les empêchant d'accéder aux informations sur les médicaments, leur utilisation systématique d'Internet suggère que des obstacles non identifiés les empêchaient de parler directement à leurs professionnels de la santé au sujet de leur traitement médicamenteux.

Mots-clés : interactions médicamenteuses, perceptions des patients, professionnels de la santé

INTRODUCTION

Drug–drug interactions (DDIs) can alter the efficacy of patients' medication therapy, leading to adverse events, which can cause patient harm. There are 2 categories of DDIs, related to pharmacodynamics and pharmacokinetics. The concept of pharmacodynamics refers to the effect that a drug may have on the body.[1] Pharmacodynamic DDIs can result from one drug antagonizing another drug, thereby reducing the therapeutic effect of one or both of the drugs.[2] Alternatively, the interacting drugs can have an additive therapeutic effect when combined. In contrast, the concept of pharmacokinetics refers to the effect that the body may have on a drug. Pharmacokinetic DDIs change the absorption, distribution, metabolism, and excretion of one or both of the interacting drugs. DDIs may increase the severity of adverse events or increase the chance of treatment failure.[3] In certain applications, prescribers may take advantage of known DDIs by deliberately administering an interacting drug to increase the effects of another drug; for example, cobicistat may be used to boost the effect of protease and integrase inhibitors for the treatment of HIV.[4]

The overall prevalence of DDIs varies from study to study. In one review article, the authors found that the prevalence of DDIs in hospitals ranged between 15% and 45%.[5] Another study examining the prevalence of DDIs among hospitalized geriatric patients suggested that DDIs were responsible for 2% to 3% of hospital admissions, and up to 11% of patients were experiencing adverse drug effects that stemmed from DDIs.[6] The consequences of DDIs put patients at increased risk of hospitalization, morbidity, and mortality, in addition to increasing the costs of health care. For instance, the concurrent use of allopurinol and azathioprine may cause bone marrow suppression, thereby increasing a patient's susceptibility to infection. Another example could be the concurrent use of citalopram and sotalol, which may cause QTc prolongation and increase the risk of a fatal ventricular arrhythmia.[7]

The risk of DDIs increases with the number of medications that a patient is taking. Patients have access to numerous different prescription and nonprescription medications. Polypharmacy, the concurrent use of 5 or more different medications, was found to be common in the elderly population.[8] The number of drug classes involved in cases of polypharmacy can also be important in relation to DDIs. A drug class is a group of similar medications used to treat a particular medical condition. In 2016, 65.7% of Canadian seniors had medications prescribed from 5 or more different drug classes, 26.5% had medications prescribed from 10 or more drug classes, and 8.4% had medications prescribed from 15 or more drug classes.[9] The probability of DDIs increases with other risk factors, such as advanced age, comorbidities, narrow therapeutic range of drugs, drug dosage, multiple prescribers, and self-prescribing of medications.[10]

Previous research has focused on pharmacists' perceptions of DDIs and the thought processes they apply when assessing DDIs. It has been shown that flagging of DDIs by clinical decision software systems can be excessive and can lead to alert fatigue, which increases the risk of pharmacists missing an important DDI alert.[11] In addition, there were discrepancies between the severity ranking of DDIs in a decision software system and actions taken by pharmacists to manage DDIs based on their clinical judgment.[12] Despite the intention of using clinical decision software systems to prevent DDIs, the onus is on the clinician to determine an appropriate course of action.

Patients' perceptions of DDIs have represented an understudied area of research. Evaluating patients' attitudes, beliefs, and interpretations of DDIs can be used to identify possible knowledge gaps and determine ways to improve their understanding of DDIs. There is limited literature examining patients' knowledge of DDIs and their opinions of how health care professionals should help manage their DDIs, what important medication information they seek, and how medication information can be best communicated to them. The objectives of this study were to explore patients' perceptions of DDIs and to identify factors important to patients' understanding of medications.

METHODS

The consolidated criteria for reporting qualitative research (COREQ) were reviewed for transparent data reporting.[13] We utilized the COREQ checklist to ensure proper reporting of the data and have included detailed answers to each of the checklist items in Appendix 1 (available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/208).

Study Population and Recruitment

This qualitative study involved key informant interviews. Convenience sampling was used to recruit English-speaking participants. Recruitment occurred from November 2019 to March 2020; however, further recruitment was stopped because of the COVID-19 pandemic. Participants were primarily recruited from 2 outpatient clinics: an ambulatory renal transplant clinic at St Paul's Hospital and a heart function clinic at Vancouver General Hospital. These clinics were selected because the patients they serve are often taking more medications than the general population, which puts them at higher risk of experiencing DDIs. Patients from other ambulatory clinics could also have been recruited by either clinic's pharmacist through professional interactions. As a result, participants in the study may have shared a unique perspective of DDIs, based on their past experiences, thoughts, and opinions in the context of complex medication regimens.

The role of the pharmacist within each clinic was to identify drug-related problems, provide medication

recommendations, counsel patients about new medications, and answer medication-related questions from health care professionals and patients. For each patient, the physician and the pharmacist were the 2 primary health care professionals responsible for identifying, resolving, and communicating DDI information. Recruitment posters were placed within each clinic. The pharmacist in the heart function clinic did not recruit any participants through professional interactions, but patients coming to this clinic saw the recruitment poster and asked the clinic pharmacist for more information. The pharmacist in the renal transplant clinic recruited stable renal transplant recipients who had undergone transplant within the previous 3 months. In addition, professional interactions involving the renal transplant pharmacist led to recruitment of 1 participant from the ambulatory lung transplant clinic. Potential participants received study information from the clinic pharmacists. Although these clinic pharmacists were responsible for recruitment, they had no role in data collection or analysis of study results.

Research ethics board approval to conduct the study was obtained from the University of British Columbia's Behavioural Research Ethics Board, and informed consent was provided by all participants before their interviews.

Interviews

A focus group was initially planned; however, because of the impending COVID-19 pandemic, it was decided to conduct interviews instead. Study participants were given the option of having the interview conducted either in person or over the telephone; ultimately, because of the COVID-19 pandemic, all interviews were done over the phone for safety reasons.

The interviews followed a semi-structured format, and all interviews were audio-recorded. Each interview consisted of 3 parts, and all interviews were conducted by the same investigator (D.P.) (Appendix 2; available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/208). The first part of the interview consisted of gathering baseline demographic information. Participants were asked to provide their age, gender, education, number of medical conditions, and current number of medications. The second part of the interview consisted of assessing participants' understanding of their medications and DDIs. Participants were asked to rate their understanding of their medications using a Likert scale from 1 to 5, with 1 being a very poor understanding and 5 being a very good understanding. Participants were then asked to verbally define a DDI.

For the third part of the interview, participants were asked a series of open-ended questions. Because few similar studies are available in the literature, the questions for this part of the interview were developed by the study team based upon our research group's prior qualitative studies.[11,12] The questions were also reviewed by the ambulatory clinic pharmacists at St Paul's Hospital and Vancouver General Hospital. The questions first explored participants' perceptions of DDIs (Appendix 2). Next, participants were asked to describe the responsibilities of health care professionals in managing patients' DDIs. Participants were then asked to discuss factors important to the understanding of their own medications and barriers that prevented them from accessing medication information. Lastly, communication of medication information from health care professionals to patients was examined.

Analysis

Qualitative thematic analysis was used to develop major themes from the interviews. Our research philosophy follows an interpretivist approach.[14] The recorded interviews were transcribed verbatim into Word software (Microsoft Corporation). Transcripts were input into NVivo 12 Pro, version 12.6.0.959 (QSR International), a software program used to help with data management. Reflexive journaling was done during the data analysis. Our qualitative approach was suited to uncovering patients' perceptions of DDIs by exploring their understanding of medications. One investigator (D.P.) coded the data. The codes were discussed by the research group to discern emergent patterns. Thematic analysis was done using an inductive approach. Codes and themes that were unclear were discussed by the authors until consensus was reached.

RESULTS

A total of 7 participants were included in the qualitative analysis, 5 men and 2 women. Most of the participants had received postsecondary education. Participants had an average of 3.1 medical conditions and were taking an average of 9.3 medications (Table 1).

Using a Likert scale from 1 to 5, participants rated their understanding of their own medications as good (average 4 out of 5, where 5 was defined as "very good") (Table 2). For purposes of determining participants' understanding of DDIs, the authors pre-established the definition of a DDI as the situation that occurs when one drug increases or decreases the therapeutic effect of another drug. The authors then interpreted each participant's response to determine if it was correct or incorrect, according to the pre-established definition. When asked to define a DDI in their own words, 2 of the 7 participants provided an accurate response:

> Okay, so I would define a drug interaction as when the effects of one drug interferes with the effects of another drug. (Participant 3)

> A drug interaction … the effects of one medication might have on the other. Or the, how one medication might amplify the effects of another medication. (Participant 7)

TABLE 1. Characteristics of Study Participants

Interview No.	Clinic	Sex	Age (Years)	Education	No. of Medical Conditions[a]	No. of Medications[b]
1	Heart function	Male	72	Postsecondary	6	10
2	Renal transplant	Male	76	Apprenticeship	3	10
3	Heart function	Female	65	Postsecondary	1	8
4	Other[c]	Male	72	Postsecondary	2	9
5	Renal transplant	Male	66	Diploma	4	7
6	Renal transplant	Male	42	Postsecondary	3	12
7	Renal transplant	Female	49	Postsecondary	3	9

[a]Medical conditions were self-reported. The mean number of medical conditions was 3.1 per patient.
[b]Includes prescription and nonprescription medications. The mean number of medications was 9.3 per patient.
[c]Patient was recruited from an ambulatory lung transplant clinic.

TABLE 2. Patients' Self-Reported Understanding of Medications

Aspect of Knowledge	Result (n = 7)	
Understanding of medications[a]	Mean ± SD 4 ± 1	
Definition of a drug–drug interaction[b]	Correct 2	Incorrect 5

[a]Patients were asked to self-report their understanding of their own medications using a Likert scale (1 = very low, 3 = average, 5 = very good).
[b]Patients were asked to define a drug–drug interaction in their own words. The patient's definition was compared with the authors' predetermined definition and was designated as correct or incorrect.

In contrast, 5 of the 7 participants provided a vague definition, as in the following examples:

> My understanding of it is that where drugs that have conflicting properties are prescribed or taken at the same time. So that, one … the interaction between the two of them is detrimental to the patient. (Participant 5)

> Drug interaction is, could possibly fatal or harmful to patients. (Participant 6)

No new emerging themes were identified following the last interviews, so it was concluded that data saturation had been achieved. Three themes were identified from the patient interviews: an incomplete understanding of DDIs, a strong reliance on health care professionals to identify and manage DDIs, and a lack of inquiry by patients about their DDIs.

In terms of the first theme, the interviews showed that participants had an incomplete understanding of DDIs and often equated them with side effects (Appendix 3, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/208). Participants were unsure whether adverse events in their past had been caused by a DDI, had been a side effect from one or more medications, or had occurred because of their medical condition.

> Well I don't know what interaction if any is causing [my symptoms] or if it's something totally separate. (Participant 1)

> I think I had a drug … I'm not positive if drug interaction, but I was taking allopurinol and candesartan when my kidney function was declining, and I had quite a bit of rash, and some changes in my blood work. (Participant 7)

When asked to provide examples of concerning outcomes of minor and moderate DDIs, participants conveyed that central nervous system side effects, such as headache, and gastrointestinal side effects, such as nausea, abdominal pain, and diarrhea, were most important to them.

> … [a] minor [drug interaction] might be like an inconvenience where I don't know, like, that your quality of life reduced. Like it may, the drug may, the interaction of the drugs may affect some daily living activity, to a certain extent like maybe being more tired, little bit more dizzy or a little bit more abdominal cramping or something like that. (Participant 3)

> [a] moderate [drug interaction] would be pain that doesn't seem to wanna go away. (Participant 5)

The second overarching theme was that patients relied heavily on health care professionals to identify and manage DDIs. Participants believed these professionals should inform patients of DDIs and provide an action plan to mitigate associated risks.

> I would expect it be explained to me, what the interaction is … telling me what happened, the reason it's happened, and what they plan [to do] about it … (Participant 5)

> … they should find an alternative to one or both of the medication … contact me for sure and let me know if I should stop taking one or both of them. (Participant 7)

Both the pharmacist and the physician were thought to be integral to the management of DDIs, given their respective backgrounds.

> I think the physician who's prescribing, as well as the pharmacy who fills my prescription. Assuming that you go to the same pharmacy and they have a record of what you're taking. (Participant 7)

Pharmacists were thought to have the pharmacological knowledge to detect DDIs.

> But I still feel that the pharmacist would have more knowledge [than physicians] because [pharmacists are] more specialized in drugs… (Participant 1)

> The doctors and the pharmacists … They're the two professions that I recognize to be an expert in the field. As such they should be responsible. (Participant 2)

In comparison, physicians were thought to be responsible for the medications being prescribed to patients.

> I would expect the prescribing physician would know what [the drug interactions] are … (Participant 4)

> The doctor should be aware of the, all the medication the patient has been taking. So he won't be able or she won't be able to mix and match the medication that interact each other. (Participant 6)

The third main theme was that patients did not specifically seek information related to DDIs. In terms of medication counselling, patients were most concerned about and wanted to have additional information with respect to the side effects of medications.

> … potential or possible side effects that they should be letting the patient know that. (Participant 4)

> … well, number one thing is probably understanding the side effects of the drugs that I'm taking. (Participant 6)

DDI information was considered to be an important counselling point for only 2 participants.

> Just like for instance, as far as interactions. The likelihood, okay the likelihood of an interaction is like, you know 0.5% or 0.05% or common or you know. What's the prevalence of interactions with these medications, you know. (Participant 3)

> Yeah and what I should be, what I should not be taking to interact with my current prescriptions. Like for example with my anti-rejection, I should not be consuming any grapefruit at all or something like that. (Participant 6)

Overall, the participants did not believe there were any barriers preventing them from accessing medication information.

> I don't know if there any barriers to access the information. (Participant 2)

> I have no barriers when I go looking for information. (Participant 4)

In addition, they expressed that they could readily find medication information online.

> You know, in today's world of technology, as long as you're going to the right places on the internet, there's all kind of information out there … (Participant 4)

> There's, there's information readily available as long as you know where to look on the internet. (Participant 5)

DISCUSSION

The results of this study indicate that patients may have a limited understanding of DDIs and the impact that DDIs could have on their health. Although study participants perceived a greater-than-average understanding of their own medications (where "average" was defined as 3 on a 5-point Likert scale), testing of their knowledge of DDIs indicated only limited understanding. For example, participants associated DDIs with gastrointestinal and central nervous system side effects. In fact, participants were more aware of medication side effects than of DDIs. Their inability to distinguish a DDI from a medication side effect suggested that they do not understand the ramifications of DDIs. During the interviews, participants were uncertain whether they had experienced a DDI in the past because they did not know what to expect as an outcome of a DDI. Given participants' limited understanding of DDIs, they were therefore reliant on health care professionals to help manage their DDIs.

Health care professionals such as physicians and pharmacists have medication knowledge that can be used in managing a patient's DDIs. In complex cases involving patients with multiple comorbidities who are taking numerous medications, it becomes difficult, even for experienced clinicians, to ascertain if a patient's symptoms are due to deterioration of their medical condition, medication side effects, or DDIs. It would be unrealistic and potentially dangerous to expect patients to self-manage their DDIs, as many do not have a background in pharmacotherapeutics. However, similar to counselling patients to recognize key side effects of their medications, it may be important for

patients to be made aware of and told how to recognize key DDIs that could pose a risk to their health. When selecting an over-the-counter product, a patient who is cognizant of the risk of DDIs might check with their pharmacist to determine if the product can be safely taken with their current medications. For example, patients who are taking warfarin should be aware that their risk of bleeding will increase if they take nonsteroidal anti-inflammatory drugs. Pharmacists have been identified as having a major role in detecting and preventing adverse drug events, including DDIs.[15] During medication counselling involving DDIs, pharmacists may counsel patients to avoid certain medication combinations or modify doses of medications affected by DDIs, and they may provide education so that patients can self-monitor for adverse effects. Pharmacists can also help mitigate DDIs by adjusting the administration times of medications. For example, to improve absorption of doxycycline, pharmacists could counsel patients to separate the administration time of antacids, calcium, and iron products from the administration time of doxycycline. To enhance patients' understanding of DDIs, pharmacists could provide specific DDI handouts tailored to each patient's medication profile, reinforce important DDI information at subsequent visits, and check for patients' understanding of DDIs at each visit.

Medication counselling by a pharmacist or a physician may be instrumental in a patient's understanding of their medications.[16] Patients have different perspectives when it comes to the importance of DDIs affecting their health. In a focus group study involving patients, physicians, and pharmacists, the authors evaluated what patients wanted to know about their medications.[17] The results suggested that patient-important factors during medication counselling provided by health care professionals included wanting to know about medication side effects and risks, duration of therapy, cost, different treatment options, and whether the medication was indicated for the particular patient.[17] Patients also wanted to know about possible DDIs and contraindicated medications that could affect their medical therapy.[17] Similarly, in a mixed-methods qualitative study examining pharmacy quality assurance, most participants thought that DDI information constituted important safety counselling points.[18] In contrast to the unavoidable side effects of medications, DDIs are preventable. However, in this study, participants were primarily interested in understanding the side effect profile of their medications. Only 2 (29%) of the 7 participants wanted to know more about DDIs that could affect their medication therapy. Our results were comparable to those of another study based on interviews with 600 patients or caregivers at community pharmacies, which found that when starting new medications, "31.7% of participants wanted to know about drug interactions with prescription and non-prescription medications".[19] Furthermore, in a survey study of 5014 patients receiving statin therapy, 76% were "not at all concerned" or "not very concerned" about DDIs with other medications, suggesting that for the majority of patients, the desire to understand DDIs remains low.[20] Given the results from these studies and ours, it remains unclear whether patients were simply not interested in DDIs or if they were not concerned about the implications of DDIs because of their low baseline knowledge of DDIs. Patients' inability to recognize the importance of DDIs may be the result of incomplete understanding of DDIs arising from insufficient medication counselling by health care professionals. During counselling, patients may be told to avoid certain drugs or foods but may not be specifically told that the reason for the recommendation could be the risk of a DDI. In a South Korean questionnaire study, the authors found a gap between patients' expectations and perceptions during medication counselling at community pharmacies.[21] The largest gaps were related to counselling about adverse drug reactions, DDIs, and past drug allergies. Poor communication between health care professionals and patients may be contributing to patients' uncertainty of what exactly constitutes a DDI and if they have truly experienced a DDI in the past or not.

Medical and medication information is available through various sources. Numerous professionals, including physicians, pharmacists, nurses, and dietitians, are involved in the health care of ambulatory clinic patients. Participants in this study, all of whom were recruited from ambulatory clinics, felt confident when assessing their own understanding their medications, perhaps because of consistent follow-up and access to different health care professionals involved in their care. Their self-confidence in understanding their medications may also have been bolstered by the ready availability of medication information on the internet, a feature of the current digital age. Although it was an underexplored area in our study, most participants acknowledged using the internet to find supplemental medication information. Some online sources of health information are reliable, such as government and hospital websites, as well as websites with the Health on the Net certification.[22] However, concerns remain about websites with different levels of readability and reliability, which may lead to misinterpretation of information.[23,24] It is particularly concerning that patients may be interpreting medication information from online sources without speaking to a health care professional; this suggests that there were barriers preventing patients from speaking directly to their care providers about their medication therapy. Although not explored specifically in this study, possible barriers to speaking with health care professionals may include patients' negative experiences with such professionals in the past, as well as patients feeling embarrassed, neglected, or dismissed when they have asked questions. Health care professionals failing to sufficiently address patients' questions or concerns because of time constraints, patients forgetting to ask questions during their clinic

visits, and patients requiring more time to process and formulate questions may be other reasons why patients turn to the internet to find medication information.

Our study had several limitations. First, it was a small study involving key informant interviews with 7 participants. Second, all of the participants in this study were ambulatory clinic patients who had many health care professionals actively involved in their care. Such patients are often routinely followed over the course of months to years by physicians, pharmacists, and nurses, who can support a patient's understanding of medications. As a result, this study may not be applicable to inpatients or patients in the community who are not attending an ambulatory clinic. Finally, because this was a qualitative study, the analysis and interpretations of results may be subjective. Nonetheless, we believe that our data are rich in content from the unique perspective that each participant provided. Future studies may assess the use of different educational interventions during medication counselling to promote patients' understanding of clinically important DDIs. A future project could also explore physicians' and pharmacists' attitudes and perceptions when communicating DDIs to patients, to gain insight and improve the communication of medication information.

CONCLUSION

In our study, patients did not fully understand the concept of DDIs, how DDIs might affect their medication therapy, and the potential negative health outcomes that DDIs may cause. Although some patients wanted to be informed of DDIs, they relied heavily on their physician and pharmacist to manage interactions. Participants reported that during medication counselling, they felt that DDI information was not as important as understanding the side effects caused by medications. Health care professionals play an important role in promoting the health literacy of patients. Rather than only counselling patients on what medications or foods to avoid because of DDIs, they could play a more active role in promoting why it is important for patients to understand DDIs. Patients could be counselled to monitor for the adverse effects of DDIs and report them to a health care professional. To increase overall DDI knowledge, patients could also be counselled to understand the difference between DDIs and side effects of medications, and how DDIs can affect their medication therapy and their health.

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A Point Prevalence Survey of Antimicrobial Usage in New Brunswick Hospitals

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ABSTRACT

Background: Prevalence surveys are useful tools for assessing the appropriateness of antimicrobial therapy.

Objectives: The primary objective was to assess patterns of antimicrobial utilization and appropriateness in New Brunswick hospitals. The secondary objective was to assess the impact of hospital size and the presence of a penicillin allergy label on antimicrobial appropriateness.

Methods: A point prevalence survey was conducted of inpatients taking 1 or more systemic antimicrobials during admission to hospitals in New Brunswick. A structured protocol and web-based data collection tool (National Antimicrobial Prescribing Survey) were used for this survey. Data regarding hospital size and presence of a penicillin allergy label were also collected. Antimicrobial utilization was assessed in terms of guideline compliance and appropriateness. Results were summarized descriptively. A χ^2 analysis was performed to describe secondary outcomes.

Results: Ten hospitals participated, and a total of 2200 patients were admitted at the time of the survey. The overall prevalence of antimicrobial use was 22.7% (500/2200). A total of 648 antimicrobials were ordered. The most frequently prescribed antimicrobials by class were first-generation cephalosporins (14.0%, 91/648), third-generation cephalosporins (11.3%, 73/648), and piperacillin–tazobactam (10.2%, 66/648). The most common indications for antimicrobial therapy were respiratory tract infections (27.3%, 177/648), urinary tract infections (12.2%, 79/648), and intra-abdominal infections (11.4%, 74/648). Compliance with local or regional treatment guidelines, where applicable, was 66.2% (188/284). Provincially, 68.1% (441/648) of the antimicrobial orders were deemed appropriate. Larger centres had substantially higher rates of appropriateness ($p < 0.001$). The presence of a penicillin allergy label had no impact on appropriateness ($p = 0.21$).

Conclusions: Several opportunities for targeted interventions were identified to improve antimicrobial prescribing, including decreasing the use of broad-spectrum antimicrobials, increasing guideline compliance, and ensuring documentation of antimicrobial duration by prescribers.

Keywords: antimicrobial, prevalence survey, stewardship, antimicrobial utilization, appropriateness

RÉSUMÉ

Contexte : Les enquêtes de prévalence sont des outils utiles permettant d'évaluer la pertinence de la thérapie antimicrobienne.

Objectifs : L'objectif principal consistait à évaluer les modèles d'utilisation des antimicrobiens et leur pertinence dans les hôpitaux du Nouveau-Brunswick. L'objectif secondaire consistait, quant à lui, à évaluer l'effet de la taille de l'hôpital et de la présence d'une étiquette indiquant une allergie à la pénicilline sur la pertinence des antimicrobiens.

Méthodes : Une enquête ponctuelle a été menée auprès de patients hospitalisés prenant un ou plusieurs antimicrobiens systémiques lors de leur admission dans des hôpitaux du Nouveau-Brunswick. Un protocole structuré et un outil de collecte de données en ligne (National Antimicrobial Prescribing Survey, ou *enquête nationale sur la prescription d'antimicrobiens*) ont été utilisés pour cette enquête. Des données concernant la taille de l'hôpital et la présence d'une étiquette indiquant une allergie à la pénicilline ont aussi été recueillies. L'utilisation des antimicrobiens a été évaluée sur le plan de la pertinence et de la conformité aux lignes directrices. Les résultats ont été résumés de manière descriptive. Une analyse χ^2 a été effectuée pour décrire les résultats secondaires.

Résultats : Dix hôpitaux ont participé, et un total de 2200 patients ont été admis au moment de l'enquête. La prévalence globale de l'utilisation d'antimicrobiens était de 22,7 % (500/2200). Au total, 648 antimicrobiens ont été prescrits. Les antimicrobiens les plus fréquemment prescrits (par classe) étaient les céphalosporines de première génération (14,0 %, 91/648); les céphalosporines de troisième génération (11,3 %, 73/648); et la pipéracilline-tazobactam (10,2 %, 66/648). Les indications les plus courantes de l'antibiothérapie étaient les infections des voies respiratoires (27,3 %, 177/648), les infections des voies urinaires (12,2 %, 79/648) et les infections intra-abdominales (11,4 %, 74/648). Le respect des directives de traitement locales ou régionales, le cas échéant, était de 66,2 % (188/284). À l'échelle provinciale, 68,1 % (441/648) des ordonnances d'antimicrobiens ont été jugées appropriées. Les grands centres avaient des taux de pertinence sensiblement plus élevés ($p < 0,001$). La présence d'une étiquette indiquant une allergie à la pénicilline n'a eu aucun effet sur la pertinence ($p = 0,21$).

Conclusions : Plusieurs occasions d'interventions ciblées ont été dégagées pour améliorer la prescription d'antimicrobiens, y compris la diminution de l'utilisation d'antimicrobiens à large spectre, une plus grande conformité aux lignes directrices et l'assurance que la durée de l'antimicrobien est consignée par les prescripteurs.

Mots-clés : antimicrobien, enquête de prévalence, gestion responsable, utilisation des antimicrobiens, pertinence

INTRODUCTION

According to the World Health Organization, antimicrobial resistance "threatens the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi".[1] Because of the increasing consumption and misuse of antimicrobials globally, the threat of antimicrobial resistance to public health is currently on the rise.[1] Infections associated with antimicrobial resistance are concerning because they lead to longer hospital stays, higher medical costs, and increased risk of death.[2] According to a 2014 report from the Public Health Agency of Canada, more than 18 000 patients in Canadian hospitals acquire antimicrobial-resistant infections every year.[3] Government and societal action are therefore required to combat this problem.[1] In 2015, the Government of Canada released a federal action plan to address this issue by increasing both the surveillance of antimicrobial use and the implementation of strong stewardship practices.[4] To inform antimicrobial stewardship practices locally, it becomes essential to comprehend patterns of antimicrobial utilization and the threats of antimicrobial resistance that exist.

Prevalence surveys have proven useful tools in determining the appropriateness of antimicrobial therapy.[5] Point prevalence surveys have been used to assess antibiotic utilization both internationally and within Canada.[6-17] Several such surveys assessing antimicrobial appropriateness have been conducted in New Brunswick to date, including the Global Point Prevalence Survey (from the Netherlands)[18] and a modified version of the European Surveillance of Antimicrobial Consumption point prevalence survey.[19] Unfortunately, these studies lacked a broad assessment of antimicrobial appropriateness, because they were limited to evaluations of compliance with provincial guidelines or predefined definitions (e.g., therapy duplication, inappropriate route or dose, no documented indication, bug–drug mismatch, opportunity to de-escalate, treatment of asymptomatic bacteriuria), leaving upwards of 50% of antimicrobial orders without an assessment of appropriateness, where neither provincial guidelines nor the predefined definitions were applicable.[18,19] As a result, current understanding of antimicrobial usage and appropriateness within New Brunswick is based on an incomplete picture.

Data from previous provincial point prevalence surveys were highly suggestive that antimicrobial guideline compliance varies by hospital size, with substantially higher rates of guideline compliance at referral centres than at nonreferral hospitals.[18,19] Several surveys found in the literature also demonstrated an association between the presence of an antimicrobial allergy label and a higher rate of inappropriate antimicrobial prescribing.[20,21] Although the effects of allergy labels in general have been investigated, the specific impact of a penicillin allergy label on antimicrobial appropriateness has yet to be established.

The recent introduction of the Australian National Antimicrobial Prescribing Survey (NAPS; https://www.naps.org.au), now available for use in Canada, facilitates a broad assessment of antimicrobial appropriateness, distinct from guideline concordance. In addition, this survey provides an estimate of antimicrobial use.[22] With the use of this tool, the present study aimed to assess patterns of antimicrobial utilization and appropriateness within NB hospitals. Furthermore, the study assessed the impact of a penicillin allergy label and hospital type (referral or nonreferral centre) on appropriateness. The results will be used to identify opportunities to improve patient outcomes and safety through the implementation of targeted antimicrobial stewardship initiatives.

METHODS

This study was a province-wide point prevalence survey of antimicrobial usage. It included inpatients admitted to 10 regional hospitals in New Brunswick, Canada, who were receiving 1 or more antimicrobials. The study was approved by the research ethics boards of Horizon Health Network, on October 2, 2019 (File 100513), and Vitalité Health Network, on October 23, 2019 (File CER-2019-21). This study met the criteria for the secondary use of information under TCPS2 (Tri-Council Policy Statement) article 5.5A, and informed consent was therefore not obtained.

Study Setting and Patient Population

At each participating hospital, a list of all inpatients admitted at 08h00 on each day of the audit was produced, and patients were screened for eligibility. Data were included in the NAPS database for all inpatients who had an active antimicrobial prescription on their medication chart at 08h00 on the audit day, as well as those who had received a stat dose of an antimicrobial within the previous 24 hours, including for surgical prophylaxis. Patients receiving ambulatory care (day stay and outpatients), hospital-in-the-home patients, residential aged care patients (i.e., in veterans' units and nursing homes), and emergency department patients not yet admitted to the hospital were excluded from the survey.

Data Collection

Survey data were collected between November 2019 and February 2020 and were submitted from participating hospitals to a central database through a web-based interface. A formal training session was provided to all surveyors before the survey began. Most data collection took place in the months of November and December 2019. Once the survey had been initiated within a given site, data collection was completed within a 4-week window. Because it was not feasible to sample all inpatients in the larger health care facilities on 1 calendar day, different wards were surveyed over separate days, with each ward being surveyed only

once. More than half of the sites (n = 6) needed more than 2 days to complete the survey. Patient flow within the hospital was considered, to prevent patients from being counted twice if they were likely to be moved (e.g., from critical care to a step-down unit). Additionally, the surgical wards were surveyed on days after the days when most elective procedures were scheduled (i.e., Tuesday to Friday) to facilitate an assessment of duration of prophylactic therapy in the preceding 24 hours.

Individual patient charts were reviewed. Data were collected using the NAPS standardized structured protocol and web-based data entry tool. The NAPS data set included the following: demographic characteristics, specifically date of survey, hospital, patient identification number, age, sex, and specialty of admission; antimicrobial use, specifically antimicrobial agent, route, dose, frequency, indication (documented or presumed), and documentation of stop date; guideline compliance and assessment of appropriateness; and, if applicable, allergies to antimicrobials, surgical procedure performed, microbiology test results, and clinical notes or comments. Appropriateness was assessed according to the structured algorithm (accessed through https://www.naps.org.au), which consists of 5 categories of appropriateness, defined as 1 = optimal, 2 = adequate, 3 = suboptimal, 4 = inadequate, and 5 = not assessable. The structured algorithm provides a methodical and combined assessment of appropriateness through compliance with guidelines (local), patient allergies, surgical prophylaxis duration (less than or greater than 24 hours), microbiology, route, dose or frequency, duration, antimicrobial spectrum (too broad or too narrow), indication, and any restrictions that applied. If patients' cases were too complex (due to multiple comorbidities, allergies, or microbiology results), if there was insufficient documentation, or if notes were not comprehensive enough, appropriateness was considered "not assessable" (score of 5). A score of 1 or 2 was considered to represent "appropriate" prescribing and a score of 3 or 4 was considered to represent "inappropriate" prescribing.[22]

In addition to the standard data set, information about a patient's penicillin allergy label, including the type of reaction (high-risk reaction, not a high-risk reaction, or unknown) and the presence or absence of appropriate documentation of the reaction, was collected. A predefined tool, with definitions, was provided to guide the investigators in answering these additional survey questions. The hospital from which a patient's data were collected was entered into the NAPS database, which then categorized the data according to the bed count of the particular hospital site. The hospital site was considered to be a referral centre if the bed count was 250 or more; nonreferral centres encompassed hospitals with fewer than 250 beds. Although the definitions based on bed count were arbitrary, this was considered a reasonable division based upon hospital sizes in the province of New Brunswick and their provision of clinical services.

Compliance with Guidelines and Assessment of Appropriateness

The data collection and assessments of antimicrobial appropriateness were undertaken by the auditing team in accordance with the definitions outlined by the NAPS (Appendix 1, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/208). The team consisted of 1 or more clinical pharmacists based at each of the 10 sites (including T.M., R.H., D.L.) and a pharmacy resident (R.C.). Two of the clinical pharmacist team members (T.M, D.L.) were part of the infectious disease service at their respective hospitals; they also served on the provincial antimicrobial stewardship team. Investigators at each site collected the data and assessed guideline compliance and appropriateness. All antimicrobial entries were then jointly validated by 2 infectious disease pharmacists (alternate investigators). If the alternate investigators had difficulty interpreting the assessment, they contacted the investigator who did the initial data collection or assessment, and a conclusion was reached by consensus. Additionally, if an investigator deemed an antimicrobial order as "not assessable", an alternate investigator was consulted for confirmation or further evaluation.

Data Analysis

Data acquired during the point prevalence survey were presented using descriptive statistics. Continuous variables (such as patient age, antimicrobial dose, and frequency) were described using means, standard deviations, and ranges, whereas categorical variables (such as guideline compliance, appropriateness, and indication) were described using frequencies and percentages. Assessments of antimicrobial appropriateness in relation to hospital type (referral versus nonreferral) and in relation to presence or absence of a penicillin allergy label were compared using a 2×2 χ^2 test. For the purposes of these χ^2 tests, the unit of analysis was the antimicrobial. All tests were assessed using an α level of 0.05. Cramer V effect sizes were reported for χ^2 tests (95% confidence intervals [CIs] for effect sizes are also reported). An a priori power analysis, performed using G*Power software (α = 0.05, power = 0.8, df = 1, effect size = 0.3, minimum sample size = 88), indicated sufficient power for these analyses, given the sample size of this study.

RESULTS

Ten hospitals within the province of New Brunswick participated in the survey. Included were regional and major sites from each zone: 5 from Horizon Health Network and 5 from Vitalité Health Network. Four of these sites were considered to be referral centres (≥ 250 beds), and 6 sites were considered to be nonreferral centres (< 250 beds). Three of the 4 referral sites employed infectious disease physicians certified by the Royal College of Physicians and Surgeons of Canada.

Overall Antimicrobial Usage

A total of 2220 patients were admitted at the time of the survey, of whom 500 (22.7%) were receiving systemic antimicrobial therapy. Approximately two-thirds of the patients included in the analysis (i.e., receiving an antimicrobial) were admitted within Horizon Health Network and one-third from Vitalité Health Network. Approximately 50% of these inpatients were male, and roughly 75% were receiving only 1 antimicrobial agent, as summarized in the baseline characteristics presented in Table 1. A total of 648 antimicrobial agents were prescribed for 76 types of indications. The most common types of indications were respiratory tract infections (27.3%, 177/648), urinary tract infections (UTIs) (12.2%, 79/648), and intra-abdominal infections (11.4%, 74/648), as illustrated in Figure 1.

TABLE 1. Baseline Characteristics of Patients Receiving Antimicrobial Agents at New Brunswick Hospitals

Variable	No. (%) of Patients[a] (*n* = 500)	
Age (years) (mean ± SD)	67.7 ± 17.0	
Sex		
Female	251	(50.2)
Male	249	(49.8)
Health authority		
Horizon Health Network	334	(66.8)
Vitalité Health Network	166	(33.2)
Admitted to ICU		
No	457	(91.4)
Yes	33	(6.6)
Not specified	10	(2.0)
Microbiology		
Sample collected	279	(55.8)
Allergies to antimicrobials		
Present	125	(25.0)
None known	373	(74.6)
Not documented	2	(0.4)
Renal replacement in previous 24 h		
No	479	(95.8)
Yes	11	(2.2)
Not specified	10	(2.0)
Specialty		
General medicine	358	(71.6)
Intensive or critical care	34	(6.8)
General surgery	108	(21.6)
No. of antimicrobials prescribed		
1	379	(75.8)
2	100	(20.0)
≥ 3	21	(4.2)

ICU = intensive care unit, SD = standard deviation.
[a]Except where indicated otherwise.

Overall, 52.3% (339/648) of the prescriptions were for parenteral antimicrobial agents, and 47.7% (309/648) were for oral antimicrobial agents. The most commonly prescribed antimicrobials were first-generation cephalosporins (14.0%, 91/648), third-generation cephalosporins (11.3%, 73/648), piperacillin–tazobactam (10.2%, 66/648), and fluoroquinolones (9.1%, 59/648), as shown in Figure 2.

Performance Indicators

Documentation of the indication for antimicrobial prescribing occurred for 90.3% (585/648) of the prescriptions. The intended duration of antimicrobial therapy (i.e., stop or review date) was documented for only 67.1% (435/648) of the antimicrobial orders.

A total of 54 (8.3%) antimicrobials were prescribed for surgical prophylaxis. Of these, 77.8% (42/54) were ordered for a duration up to 24 hours and 22.2% (12/54) for longer than 24 hours. Cefazolin was the most frequently prescribed antimicrobial (79.6%, 43/54) for this indication. Metronidazole (7.4%, 4/54) and ciprofloxacin (3.7%, 2/54) were the next mostly commonly used.

Of the 648 antimicrobial orders assessed, local, regional, or provincial guidelines were applicable in 284 (43.8%) cases. Of these 284 antimicrobial orders with an applicable guideline, 66.2% (188/284) were deemed compliant and 33.8% (96/284) were deemed noncompliant. No guidelines were available for 161 (24.8%) of the 648 antimicrobial orders assessed. Antimicrobial therapy was directed toward the causative pathogen (based on available microbiology results) in 192 (29.6%) of the 648 cases. The remaining 11 (1.7%) orders were deemed not assessable with regard to guideline applicability.

Overall Assessment of Appropriateness

Across the 10 hospitals surveyed, antimicrobial prescriptions were deemed optimal in 53.4% (346/648) of cases and adequate in 14.7% (95/648) of cases. Therefore, 68.1% (441/648) of antimicrobial orders provincially were deemed appropriate. Conversely, 17.4% (113/648) of prescriptions were considered suboptimal, and 13.6% (88/648) were considered inadequate. As such, 31.0% (201/648) of all antimicrobial orders were deemed inappropriate. A total of 6 (0.9%) antimicrobial entries were regarded as not assessable because of lack of documentation or notes or the heightened complexity of the case. Figure 3 shows the overall provincial assessment of appropriateness.

In terms of antimicrobial appropriateness according to specified indications, concerning trends were noted for antimicrobials prescribed for UTIs: more specifically, 54.4% (43/79) of these entries were deemed inappropriate. Ciprofloxacin was the most commonly prescribed antimicrobial for this indication (25.3%, 20/79).

Fluoroquinolones were the most inappropriately prescribed antimicrobial class, as illustrated by the

appropriateness ratings for the top 4 broad-spectrum antimicrobial agents (Figure 4). Fluoroquinolones were predominantly prescribed for UTIs (cystitis, pyelonephritis, asymptomatic bacteriuria, and catheter-associated UTI). UTIs accounted for more than half (55.2%, 16/29) of inappropriate fluoroquinolone prescriptions.

The distinct medical specialties appeared to have similar rates of inappropriate prescribing. In general medicine (e.g.,

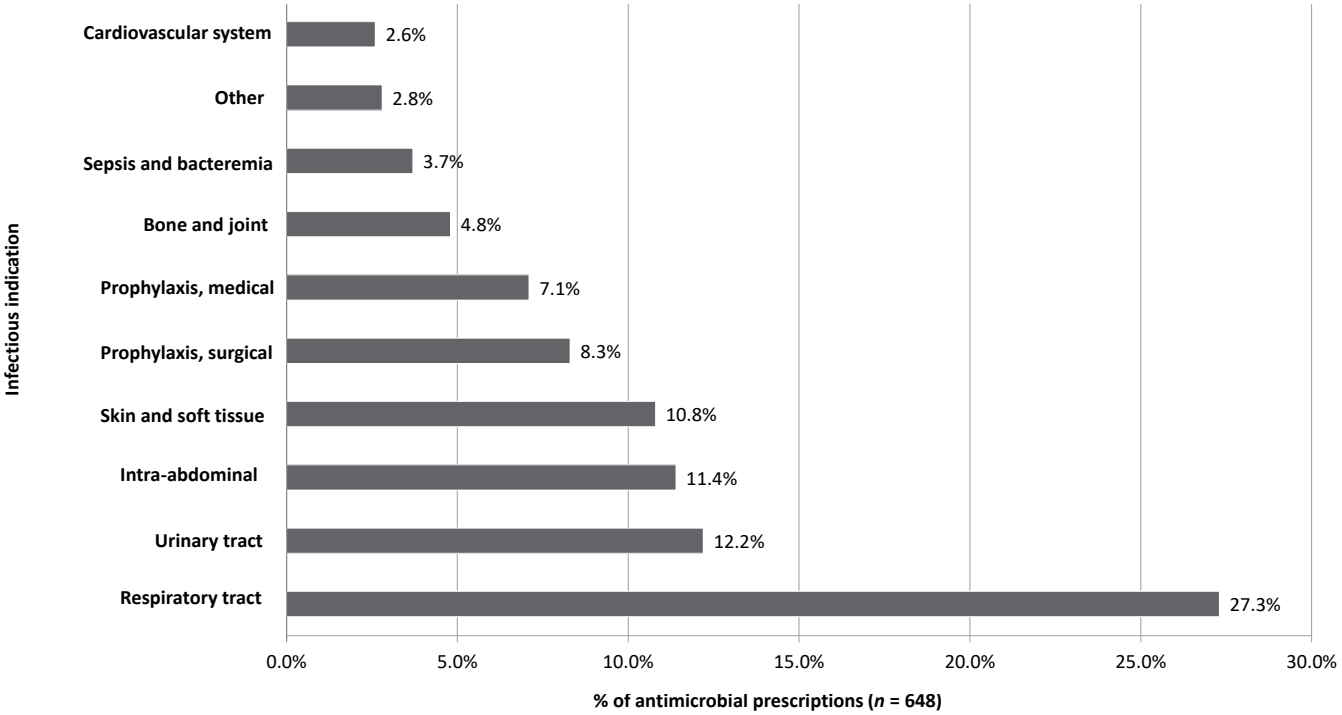

FIGURE 1. Top 10 indications for antimicrobial use in New Brunswick hospitals.

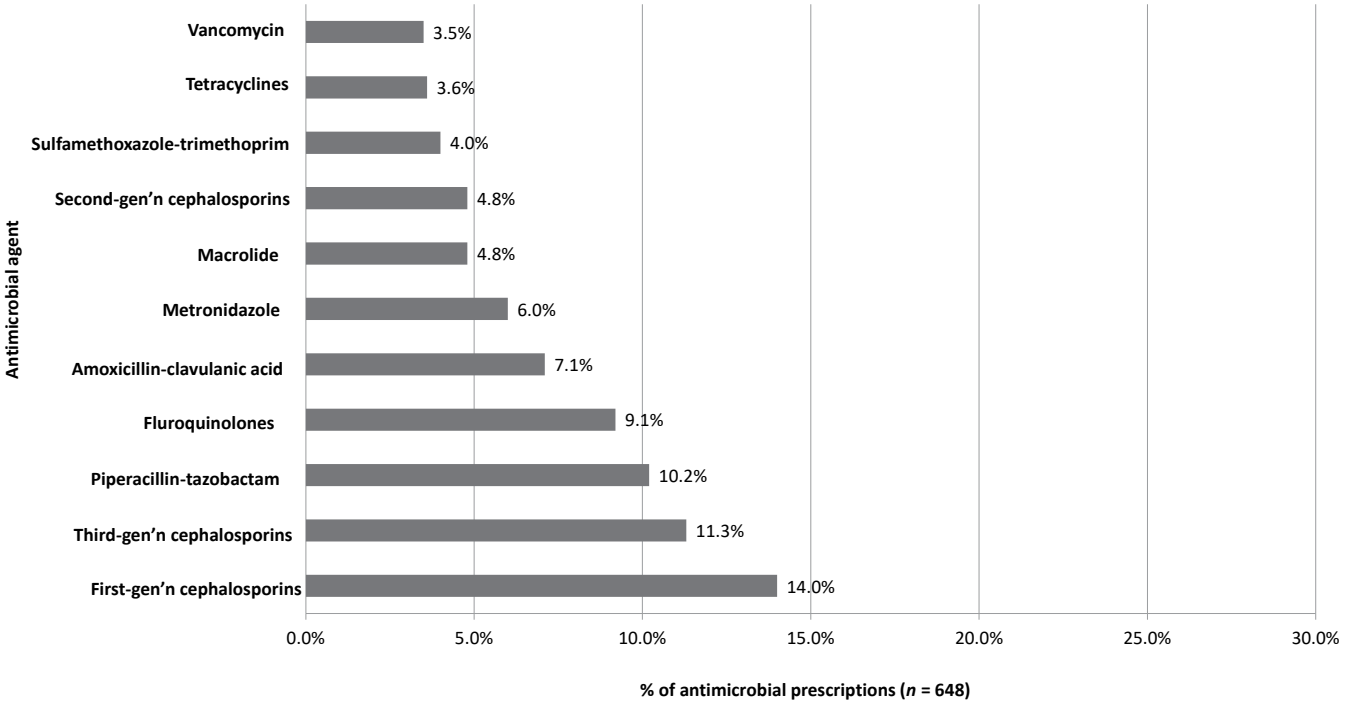

FIGURE 2. Antimicrobial agents most frequently prescribed in New Brunswick hospitals.

medical oncology and family medicine), 32.9% (151/459) of antimicrobial orders were deemed inappropriate; the proportions were 28.1% (38/135) in general surgery (e.g., vascular, gastroenterological) and 25.0% (12/48) in intensive or critical care.

Factors Driving Inappropriateness

Factors driving inappropriateness were collected to inform the NAPS appropriateness assessment, and more than 1 factor could be applied to each prescription. For the

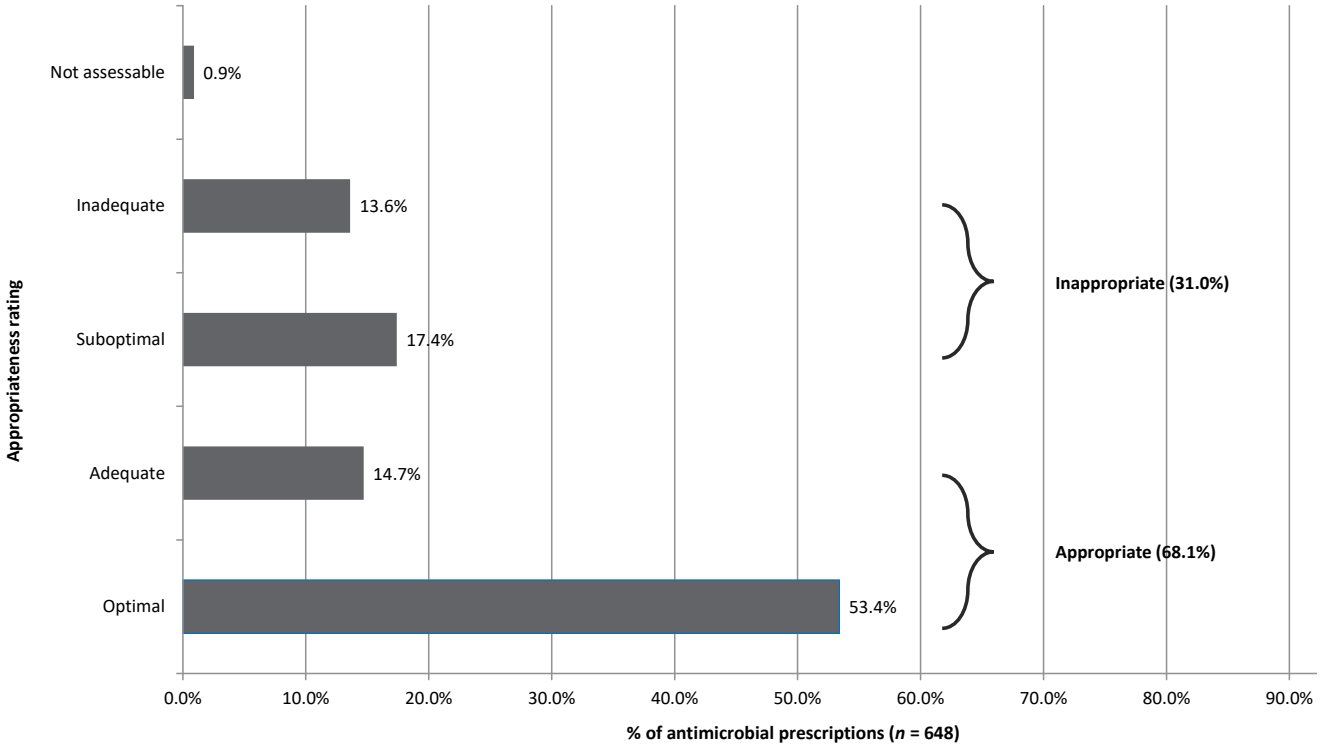

FIGURE 3. Summary of level of antimicrobial appropriateness in New Brunswick hospitals.

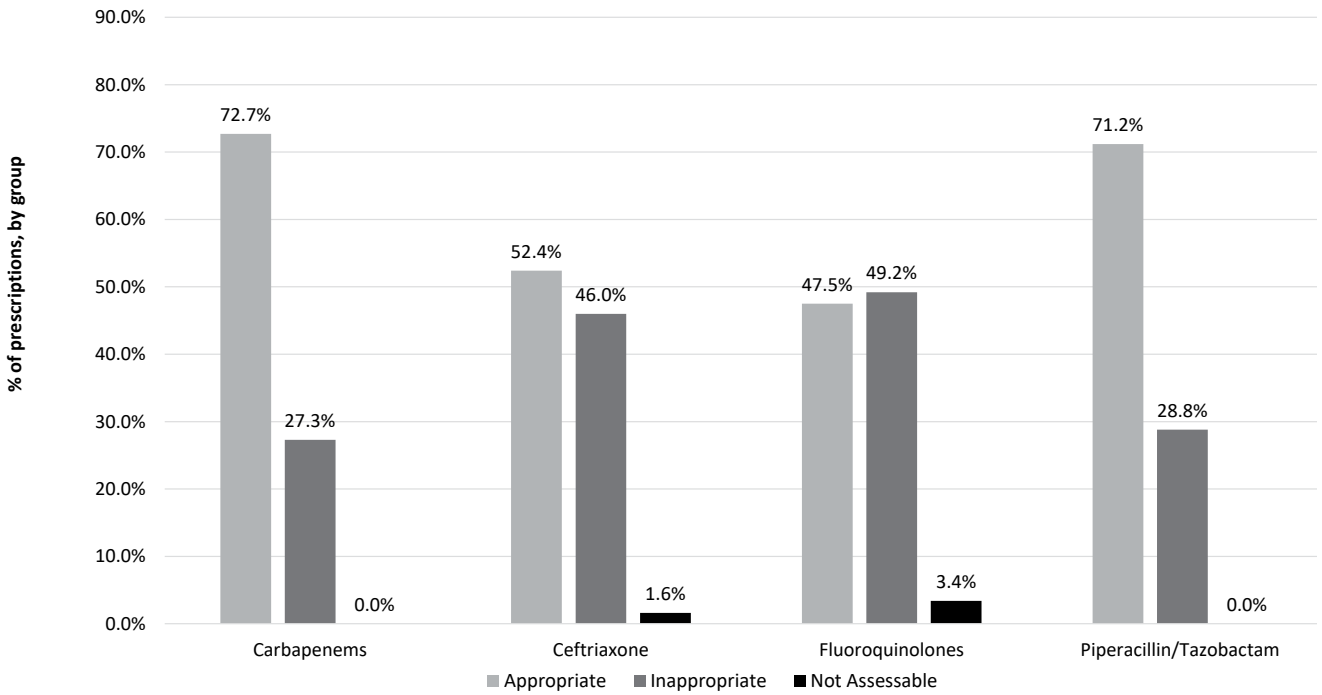

FIGURE 4. Assessment of appropriateness for the top 4 broad-spectrum antimicrobial agents. Numbers of antimicrobial orders: $n = 22$ for carbapenems, $n = 63$ for ceftriaxone, $n = 59$ for fluoroquinolones, and $n = 66$ for piperacillin–tazobactam.

201 antimicrobial orders deemed inappropriate, the top 3 factors driving inappropriateness were as follows: the spectrum of the antimicrobial was "too broad" for the given indication (34.8%, 70/201), the duration of therapy was incorrect (18.4%, 37/201), and an antimicrobial was "not indicated" (15.9%, 32/201) (Table 2).

The top 3 factors associated with inappropriate prescribing of fluoroquinolones were as follows: the spectrum of activity was unnecessarily broad (51.7%, 15/29), the dose or frequency was incorrect (20.7%, 6/29), and the route of administration was incorrect (17.2%, 5/29). The primary factor leading to inappropriateness of fluoroquinolone prescribing for UTIs was the spectrum of activity being deemed "too broad" for this indication (68.8%, 11/16).

For a given antimicrobial, factors driving inappropriateness at nonreferral centres (< 250 beds) included incorrect duration (26.7%, 24/90), spectrum too broad (25.6%, 23/90), and antimicrobial not indicated (22.2%, 20/90). In comparison, spectrum too broad (42.3%, 47/111) was the most common factor associated with an inappropriate rating for a given antimicrobial prescription at referral centres (≥ 250 beds).

Secondary Outcomes

There was a substantially higher rate of appropriate prescribing in referral centres than in nonreferral centres (75.0% versus 54.0%; χ^2 [df = 1, n = 642] = 28.0; $p < 0.001$; effect size 0.21 [95% CI 0.14–0.29]).

A penicillin allergy label was identified for 14.2% (71/500) of the patients surveyed. There was no significant difference in appropriateness rating of antimicrobial therapy for patients with and without a penicillin allergy label (69.9% versus 63.0%; χ^2 [df = 1, n = 642] = 1.60; p = 0.21; effect size 0.05 [95% CI 0.00–0.13]).

DISCUSSION

In this study, conducted in 2019–2020, approximately one-fourth (22.7%) of the hospital inpatient population in New Brunswick was receiving 1 or more systemic antimicrobial agents. These findings are in keeping with previous point prevalence surveys completed in New Brunswick in 2012 and 2018.[18,19] Slightly higher rates of antimicrobial usage have been reported in other provinces across Canada and internationally, with upwards of 30% of inpatients receiving antimicrobial therapy in those jurisdictions.[18,23-25]

First-generation cephalosporins were the most frequently prescribed antimicrobials in NB hospitals, with cefazolin being the most frequently ordered of this class. It is postulated this result was secondary to the implementation of provincial surgical prophylaxis and β-lactam allergy guidelines.[26,27] Cefazolin is recommended as first-line therapy for most surgical procedures, irrespective of penicillin allergy status.[26] The most frequently ordered antimicrobials provincially had broad spectra of activity. According to the NB guidelines, these antimicrobials are usually indicated for nosocomial infections or severe community-acquired infections. Given the results of this survey, overuse of broad-spectrum antimicrobials should be considered as an area of potential improvement in antimicrobial utilization. The results of the current survey are consistent with previous Canadian literature, where high use of piperacillin–tazobactam and ceftriaxone has also been reported.[18,23,24] Similarly, data from other Canadian surveys have indicated high usage of fluoroquinolones, specifically ciprofloxacin.[16,18,24]

Concerning utilization patterns and appropriateness for specific indications were identified during this study, in particular the frequent use of fluoroquinolones (specifically

TABLE 2. Factors Driving Inappropriateness in Nonreferral (< 250 Beds) and Referral (≥ 250 Beds) Centres

Factor	Type of Centre; No. (%) of Inappropriate Orders[a]		
	Nonreferral (n = 90)	Referral (n = 111)	Total (n = 201)
Surgical prophylaxis > 24 h	6 (6.7)	6 (5.4)	12 (6.0)
Allergy mismatch	1 (1.1)	0 (0.0)	1 (0.5)
Microbiology mismatch	7 (7.8)	8 (7.2)	15 (7.5)
Incorrect route	9 (10.0)	17 (15.3)	26 (12.9)
Incorrect dose or frequency	13 (14.4)	13 (11.7)	26 (12.9)
Incorrect duration	24 (26.7)	13 (11.7)	37 (18.4)
Spectrum too broad	23 (25.6)	47 (42.3)	70 (34.8)
Spectrum too narrow	3 (3.3)	7 (6.3)	10 (5.0)
Antimicrobial not indicated	20 (22.2)	12 (10.8)	32 (15.9)

[a]Percentages in each column do not sum to 100% because more than 1 factor could be applied to each prescription.

ciprofloxacin) for patients with UTIs. The appropriate use of fluoroquinolones represents an important target to optimize provincial prescribing patterns (especially in the context of UTIs). Prescribers may benefit from education about the risks associated with excessive and inappropriate use of fluoroquinolones, such as risk of resistance to this class and to other antimicrobial classes.[28] Fluoroquinolones are unnecessarily broad, in terms of their spectrum of activity, for empiric treatment of most community-acquired infections, and they are associated with several adverse drug reactions (such as *Clostridioides difficile* infection, tendinitis, tendon rupture, peripheral neuropathy, QTc prolongation, and dysglycemia), particularly among older adults.[29]

A need to improve documentation was observed in the participating hospitals. Patient charts in both paper and electronic form were reviewed, and approximately 1 in 3 charts had no documentation of planned duration of therapy or review date, and 1 in 10 charts had no documentation of the indication for antimicrobial therapy. Data from previous point prevalence surveys conducted in Nova Scotia and New Brunswick reported documentation of indication in approximately 80% of cases and documentation of duration in only half of all cases.[6,19] Higher rates (ideally 100%) of documentation should be targeted, as these indicators are considered essential components of antimicrobial prescribing. Documentation of the indication for and duration of antimicrobial therapy in the patient's medical record facilitates informed assessment and reassessment of therapy, supports seamless transfer of care between medical teams, enables institutional antimicrobial audits, and promotes accountability.[30]

Lack of compliance with local guidelines was observed in this study. Approximately 1 in 3 antimicrobial entries were deemed noncompliant with local guidelines, when an applicable guideline was present. The antimicrobial stewardship committee should conduct further investigations to determine the reasons for noncompliance with local guidelines. Potential reasons for physicians' noncompliance to guidelines identified in the literature include lack of awareness, lack of familiarity and disagreement with developed guidelines, inertia, contrasting patient and physician goals of care, and environmental constraints.[31,32]

Referral centres had substantially higher rates of appropriate antimicrobial prescribing than nonreferral centres. A similar trend was observed in previous provincial surveys.[18,19] Greater access to resources at referral centres, such as infectious disease physicians, microbiologists, and clinical pharmacists, may contribute to the observed significant findings, but further investigation is warranted.

Notably, this study revealed that the presence of a penicillin allergy label had no significant impact on the appropriateness of antimicrobial therapy. This result conflicts with one earlier study, which demonstrated that higher rates of inappropriate prescribing (odds ratio 1.68) and increased use of broad-spectrum antimicrobials were associated with antimicrobial allergy labels.[20] Advancement in prescribers' knowledge of β-lactam allergy and cross-reactivity due to implementation of β-lactam allergy guidelines[27] may have contributed to the current study's finding.

This study had several strengths. To the authors' knowledge, it is the first provincial point prevalence study based on the NAPS method. The data provide a baseline measurement of current antimicrobial utilization and appropriateness for the province of New Brunswick as a whole, in addition to data for individual hospital sites. The study grants insight as to where opportunities exist to improve patient outcomes and safety through targeted antimicrobial stewardship initiatives. The point prevalence survey can be repeated in the future to measure the impact of such interventions on antimicrobial utilization and appropriateness. Researchers considering this type of study in other parts of Canada will be able to replicate the current study using the standardized NAPS protocol in both referral and nonreferral centres. Because the NAPS method allows for a certain degree of subjectivity in ratings, we employed an independent second check by 2 infectious disease pharmacists to standardize assessment and reduce potential bias. In addition, to the authors' knowledge, this is the first point prevalence study in Canada to report the association between antimicrobial appropriateness and hospital size and presence of a penicillin allergy label.

Although the results of this survey provide valuable insights into antimicrobial utilization by NB hospitals, several limitations should be considered. Point prevalence surveys are limited to a moment in time (i.e., a single day) and may not reflect overall prescribing trends within provincial health networks. The data for this study were not collected on the same day for all sites; therefore, it is possible (though unlikely) that seasonal variation affected the results. The findings may reflect or may have been influenced by select individuals' case loads or practice sites, especially for smaller sites. Generalizability to other regions in Canada may be limited, given that prescribing trends and antimicrobial resistance rates vary across the country. Even though definitive conclusions cannot be drawn from a point prevalence survey such as this, the trends observed can help to indicate where future antimicrobial stewardship efforts should be focused.

CONCLUSION

This study contributes to knowledge about the prevalence of antimicrobial utilization, compliance with guidelines, level of appropriateness, and documentation in Canada and can be used locally as a benchmark to identify targets for future antimicrobial stewardship interventions. Key targets for quality improvement initiatives include decreasing the use of broad-spectrum antimicrobials, especially fluoroquinolone (ciprofloxacin) for UTIs; increasing guideline

compliance; and ensuring documentation of antimicrobial duration by prescribers. There is also a need to address higher rates of inappropriate antimicrobial prescribing among smaller rural hospitals in New Brunswick. Regular repetition of such surveys (every 2 or 3 years) would be an effective tool to evaluate the effectiveness of future planned interventions.

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Methods of Therapeutic Drug Monitoring to Guide Vancomycin Dosing Regimens: Trough Concentration versus Ratio of Area Under the Curve to Minimum Inhibitory Concentration

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ABSTRACT

Background: The most recent vancomycin monitoring guideline recommends targeting a value for area under the curve (AUC) of 400 to 600 mg*h/L, with an assumed minimum inhibitory concentration (MIC) of 1 mg/L. Few studies have investigated the effect of this method on vancomycin dosing regimens, relative to a target trough concentration of 15 to 20 mg/L.

Objective: To compare vancomycin dosing regimens generated with the 2 monitoring methods.

Methods: This retrospective chart review included hospitalized patients who received vancomycin between May 2019 and April 2020. The dosing regimens were compared, with the paired Student *t* test, in terms of unit dose, daily dose, and dosing interval. Variables of interest were collected from electronic medical charts. A pharmacy resident used first-order pharmacokinetic equations to determine dosing regimens based on AUC monitoring. Local pharmacists retrospectively determined dosing regimens for trough-based monitoring.

Results: Of 100 courses of treatment initially identified, 66 were included in the analysis. The unit dose was similar with the 2 methods (1086 mg with AUC-based monitoring versus 1100 mg with trough-based monitoring; $p = 0.62$). AUC monitoring was associated with a 12.8% lower daily dose (2294 mg versus 2630 mg; $p < 0.001$) and a 13.5% longer dosing interval (13.24 h versus 11.67 h; $p < 0.001$) relative to trough-based monitoring. AUC monitoring also generated a lower extrapolated trough concentration (12.90 mg/L versus 16.22 mg/L; $p < 0.001$).

Conclusions: A target trough concentration of 15 to 20 mg/L was confirmed as being unnecessarily high. AUC monitoring could allow a reduction in daily vancomycin dose and an extension of the dosing interval relative to trough-based monitoring.

Keywords: area under the curve, drug regimen, pharmacokinetics, pharmacodynamic, therapeutic drug monitoring, vancomycin

Note: This article contains supplementary material (Supplements 1 and 2), available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/208

RÉSUMÉ

Contexte : La plus récente directive en matière de surveillance de la vancomycine recommande de cibler une valeur de surface sous la courbe (*en anglais*, AUC) de 400 à 600 mg*h/L, avec une concentration minimale inhibitrice (CMI) supposée de 1 mg/L. Peu d'études ont étudié l'effet de cette méthode sur les schémas posologiques de la vancomycine, par rapport à une concentration minimale cible de 15 à 20 mg/L.

Objectif : Comparer les schémas posologiques de la vancomycine générés avec les 2 méthodes de surveillance.

Méthodes : Cette revue rétrospective des dossiers comprenait des patients hospitalisés ayant reçu de la vancomycine entre mai 2019 et avril 2020. Un test de Student pour données appariées a été réalisé afin de comparer les schémas posologiques sur le plan de la dose unitaire, de la dose quotidienne et de l'intervalle de dosage. Les variables d'intérêt ont été recueillies à partir de dossiers médicaux électroniques. Un résident en pharmacie a utilisé des équations pharmacocinétiques de premier ordre pour déterminer les schémas posologiques en fonction de la surveillance de l'AUC. Les pharmaciens locaux ont déterminé rétrospectivement les schémas posologiques pour la surveillance basée sur la concentration résiduelle.

Résultats : Sur 100 cours de traitement initialement identifiés, 66 ont été inclus dans l'analyse. La dose unitaire était similaire avec les 2 méthodes (1086 mg avec surveillance basée sur l'AUC contre 1100 mg avec surveillance basée sur la concentration résiduelle; $p = 0,62$). La surveillance de l'AUC était associée à une dose quotidienne inférieure de 12,8 % (2294 mg contre 2630 mg; $p < 0,001$) et à un intervalle de dosage plus long de 13,5 % (13,24 h contre 11,67 h; $p < 0,001$) par rapport à la surveillance basée sur la concentration résiduelle. La surveillance de l'AUC a également généré une concentration minimale extrapolée plus faible (12,90 mg/L contre 16,22 mg/L; $p < 0,001$).

Conclusions : Une concentration résiduelle cible de 15 à 20 mg/L a été confirmée comme étant inutilement élevée. La surveillance de l'AUC pourrait permettre une réduction de la dose quotidienne de vancomycine et un allongement de l'intervalle de dosage par rapport à la surveillance basée sur la concentration résiduelle.

Mots-clés : surface sous la courbe, schéma thérapeutique, pharmacocinétique, pharmacodynamique, suivi thérapeutique médicamenteux, vancomycine

INTRODUCTION

Vancomycin is an antibiotic widely used for severe gram-positive infections, especially in the treatment of infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA), which can lead to more than 20% mortality.[1] Therapeutic drug monitoring is essential for patients receiving vancomycin therapy to ensure that serum concentrations are sufficient to treat the infection.[2] However, high serum trough concentrations of vancomycin are associated with an increased risk of acute kidney injury (AKI).[2,3]

In 2020, the US consensus guideline for therapeutic monitoring of vancomycin was revised on the basis of the best current evidence.[4] According to the guideline, therapeutic drug monitoring of vancomycin should be based on the ratio of area under the curve over 24 hours to minimal inhibitory concentration (AUC_{24}/MIC).[4] An AUC_{24}/MIC ratio of 400 to 600 (assuming vancomycin broth microdilution MIC of 1 mg/L) should be advocated to achieve efficacy and patient safety for serious MRSA infections.[4]

Previously, the 2009 version of the guideline advised targeting a serum trough concentration of 15 to 20 mg/L for severe infections as a surrogate marker for AUC_{24}/MIC ratio above 400.[5] This method was easy to use and required only 1 blood sample. However, it was later shown that the trough concentration does not adequately predict AUC in at least 25% of cases, leading to an overestimation of the required dose and thereby increasing patients' exposure to vancomycin.[6,7] Several studies also showed an increased risk of AKI with this approach.[8,9] Some patients may not fully recover from vancomycin nephrotoxicity, and even patients with mild AKI have significantly increased morbidity, length of stay, and health care costs.[10]

Trough-based monitoring is still widely used by physicians and pharmacists in health care centres in Canada and the United States. A national survey of vancomycin monitoring was conducted in the United States in 2019, with responses from 78 representatives of hospital pharmacy departments.[11] The study showed that 77% of medical centres were still using trough-based monitoring and that the main barrier to the implementation of AUC monitoring was a lack of knowledge. Other barriers identified were a lack of time, the impression that the AUC method has not proven superior, and other logistical reasons, such as frequent errors in the timing of blood samples.[11]

Until recently, our Canadian centre was still determining vancomycin dosing regimens according to target trough concentration, with pharmacists monitoring serum trough concentrations of vancomycin for all patients treated with this antibiotic. A transition to monitoring based on AUC_{24}/MIC would be a significant change of practice and represented a great challenge.

Although software using Bayesian methods can estimate AUC from a single serum concentration, acquisition of such a software program is not currently being considered at our centre. Therefore, first-order pharmacokinetic equations are required to estimate the AUC. This approach relies on the determination of 2 serum concentrations from samples obtained at or near steady-state, which increases the need for nursing time and laboratory resources.[12]

Despite growing data on the subject, few studies have looked at the differences between dosing regimens generated with these 2 monitoring methods. Some data on cumulative exposure are available, but not information on the dosing intervals used.[13] We performed a local study to determine the impact of implementing routine AUC_{24}/MIC monitoring on dosing regimen adjustments made by pharmacists.

The primary objective of this study was to compare vancomycin dosing regimens generated with trough-based monitoring and AUC_{24}/MIC monitoring. The dosing regimens generated were compared in terms of unit dose, total daily dose, dosing interval, extrapolated trough concentration, and extrapolated AUC. The secondary objectives were to describe the relationship between the trough concentration and the AUC and to describe the prevalence of AKI associated with vancomycin therapy under current practice at our centre.

METHODS

This retrospective chart review was conducted at a 250-bed teaching hospital in Canada, which serves as the regional referral centre for patients with peripheral vascular disease. The study included hospitalized patients who received IV vancomycin between May 2019 and April 2020 and was approved by the hospital's research ethics board. Courses of therapy were systematically selected after application of specific inclusion and exclusion criteria, described below. To improve the sample size, a given patient was eligible for selection if they received multiple courses of vancomycin treatment (e.g., during different hospital stays).

Courses of therapy were eligible for inclusion if the patients were 18 years of age or older and had been treated with vancomycin for a suspected or confirmed pathogen that required this antibiotic. In addition, to allow performance of AUC calculations, eligibility required at least 2 measured values for serum vancomycin concentration: a postdistributional peak concentration (0.5–3 hours) and a trough concentration at the end of the dosing interval (0–0.5 hours). Samples for determination of serum concentration had to have been drawn near steady state, as defined by a peak obtained after the third (or a later) vancomycin dose. Patients with a preexisting need for renal replacement therapy,[14] those receiving vancomycin by a route other than IV, and those with central nervous system infection were excluded.[12,15] Bone cement loaded with vancomycin, which may be applied locally during surgery, also affects serum concentration of the drug; patients treated with this cement were also excluded.[16]

All data were collected by a single reviewer, a pharmacy resident (A.D.S.), using a standardized data collection tool. In May 2020, demographic data, weight, indication for antibiotic therapy, total duration of treatment, medication administration record, and laboratory values were collected from the patients' electronic medical charts. The indication for vancomycin therapy was obtained from the pharmacist's note or the final discharge summary (if not clearly mentioned in the note). The dates and times of administration of vancomycin, the infusion rate, and the dosing regimens were obtained from the medication administration record. Other potentially nephrotoxic medications were also identified. The following drugs were considered nephrotoxic: aminoglycosides, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, amphotericin B, IV contrast dyes, furosemide, nonsteroidal anti-inflammatory drugs, piperacillin–tazobactam, and vasopressors.[3]

For determination of AUC, first-order pharmacokinetic equations developed by Pai and others were used, which allow AUC to be reliably estimated from 2 blood samples[17,18] (detailed equations are available in Supplement 1, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/208). A local spreadsheet (Office 365 Excel, Microsoft Corporation) was used to generate the dosing regimens from 2 blood samples. The target AUC_{24}/MIC was 400 to 600.[4] For this study, the MIC was presumed to be 1 mg/L, rather than being measured, because vancomycin resistance is rare at our centre (less than 1% for the period 2016–2019). This assumption also corresponds to international MRSA surveillance data and current guideline recommendations for monitoring vancomycin.[4,19,20]

For trough-based monitoring, a panel of 3 pharmacists, including the pharmacy resident (A.D.S.), determined the dosing regimens for purposes of the study. Trough values, current dosing regimen, age, and estimated glomerular filtration rate, as collected from the medical charts, were provided to the pharmacists, with peak values blinded. The pharmacists were instructed to adjust the dose of vancomycin on the basis of their clinical experience, assuming that the sample for determination of trough concentration was drawn at steady state and the target trough concentration was 15 to 20 mg/L. The pharmacists independently determined each patient's adjusted dosing regimen. Any disagreements were resolved by discussion and consensus. No additional information was given to or considered by the panel. This approach closely approximates the method currently used for dosage adjustments in our centre.

The dosing regimens generated with both monitoring methods were then entered in a spreadsheet containing pharmacokinetic equations to determine the extrapolated trough concentration and extrapolated AUC based on the patient's medication half-life and volume of distribution previously calculated from the 2 blood samples. Given the retrospective design of this study, the patients did not actually receive the dosing regimens generated by either monitoring method.

For determination of AKI prevalence at our centre, we defined a nephrotoxic event as an increase in serum creatinine of 44 μmol/L or greater than 50% relative to pretreatment values for more than 2 consecutive days during vancomycin treatment.[5] Trough-based monitoring was routinely used at our centre during the study period.

Where appropriate, descriptive statistics, such as means with standard deviations and medians, were calculated for quantitative variables of the dosing regimens and to describe the study population. Mean unit doses, daily doses, weight-based daily doses, and dosing intervals were compared with the paired Student *t* test to meet the primary objective, namely the comparison of dosing regimens determined with the 2 monitoring methods. The extrapolated trough and AUC values obtained for the new dosing regimens determined with the 2 monitoring methods were also compared with the paired Student *t* test. A scatter plot of these 2 markers was prepared to describe the relationship between trough concentration and AUC. For calculating the prevalence of nephrotoxicity, each patient was included only once, regardless of the number of courses of vancomycin treatment. All statistical tests were 2-sided, and p values less than 0.05 were considered statistically significant. Statistical analyses were performed with SPSS software (version 25.0; IBM Corporation).

RESULTS

One hundred courses of vancomycin therapy administered during the study period (May 2019 to April 2020) were screened. Of these, 34 courses were excluded, mainly because they did not reach a steady state before blood sampling (n = 16) or because the sample for peak concentration was drawn at the wrong time, mostly during the infusion period (n = 13). Other courses of therapy were excluded because the charts were incomplete (n = 4 with no data for time of blood sampling) or because vancomycin cement was used during surgery (n = 1). After these exclusions, a total of 66 courses of treatment, received by 51 patients, met the inclusion criteria. Patients' ages ranged from 26 to 84 years. Baseline demographic and clinical characteristics of the study population are shown in Table 1.

Patients received 3 to 12 doses of vancomycin before sampling for the peak value used for this study (third dose for 38 courses of therapy, fourth dose for 17 courses of therapy, and fifth or subsequent dose for 11 courses of therapy). The mean daily vancomycin dose was 29.94 mg/kg at that time. The mean elimination half-life in the study population was 9.64 hours, and the mean volume of distribution was 0.74 L/kg. Detailed characteristics can be found in Supplement 2 (available at: https://www.cjhp-online.ca/index.php/cjhp/issue/view/208).

TABLE 1. Demographic and Clinical Characteristics[a]

Variable	No. (%) of Treatment Courses[b] (*n* = 66)
Age (years) (mean ± SD)	64.9 ± 11.9
Sex, male	43 (65)
Weight (kg) (mean ± SD)	76.56 ± 16.31
BMI (mean ± SD)[c]	26.85 ± 5.31
Baseline eGFR (mL/min/1.73 m^2)	
< 30	0 (0)
30–59	5 (8)
60–89	20 (30)
≥ 90	41 (62)
Length of hospital stay (days) (median and range)	12 (2–90)
Total length of treatment (days) (median and range)	6 (1–38)
ICU admission	34 (52)
Septic shock	7 (11)
Infection-related death	3 (5)
Bacteria	
Known MRSA carrier	2 (3)
Proven MRSA infection	7 (11)
Staphylococcus epidermidis	14 (21)
Enterococcus	10 (15)
Other	15 (23)
Culture unavailable	20 (30)
Indication for vancomycin	
Bacteremia	5 (8)
Abdominal infection	5 (8)
Skin and soft tissue infection	7 (11)
Pneumonia	4 (6)
Bone and joint infection	8 (12)
Urinary tract infection	2 (3)
Endocarditis	8 (12)
Endovascular prosthesis	10 (15)
Postoperative wound	6 (9)
Prosthetic joint	4 (6)
Unknown	7 (11)

BMI = body mass index, eGFR = estimated glomerular filtration rate, ICU = intensive care unit, MRSA = methicillin-resistant *Staphylococcus aureus*, SD = standard deviation.

[a]The data represent 51 individual patients, with some patients contributing data for more than 1 course of treatment.

[b]Except where indicated otherwise.

[c]*n* = 64 (data missing for 2 courses of therapy).

For the primary outcome, vancomycin dosing regimens generated with the 2 monitoring methods are shown in Table 2. A significantly lower daily dose was obtained with AUC monitoring than with trough-based monitoring, but the mean unit doses were similar with the 2 methods.

The dosing intervals were significantly longer with AUC monitoring than with trough-based monitoring. The distributions of dosing intervals with the 2 monitoring methods are shown in Figure 1.

First-order equations were used to calculate the extrapolated trough and AUC values for each dosing regimen obtained with each monitoring method. The results are also shown in Table 2. The mean extrapolated trough concentration with trough-based monitoring was 16.22 mg/L, which correlated with pharmacists' instructions to achieve a trough concentration between 15 and 20 mg/L.

The relationship between the trough concentration of vancomycin and AUC is shown in Figure 2. Of the 17 patients with a trough concentration between 15 and 20 mg/L, 10 (59%) had an AUC in the therapeutic target of 400 to 600 mg*h/L, whereas 6 (35%) had an AUC of more than 600 mg*h/L. Conversely, of the 28 patients with a trough concentration between 10 and 14 mg/L, 25 (89%) had an AUC of 400 to 600 mg*h/L, and only 2 (7%) had an AUC below 400 mg*h/L.

The prevalence of AKI during vancomycin treatment in the study population was another secondary outcome of this study, and results related to this outcome are displayed in Table 3. Most patients (*n* = 37/51, 73%) were receiving at least 1 concomitant nephrotoxic medication; in relation to the 66 courses of treatment, the most frequent nephrotoxic medications were contrast dye (*n* = 20/66, 30%) and furosemide (*n* = 16/66, 24%). At our centre, 6 of the 51 patients had AKI during their vancomycin treatment; as noted above, the monitoring method used at the time was mostly trough-based monitoring. Patients with AKI were treated with vancomycin for a median of 14 days (range 5–28 days). Subgroup analysis could not be performed because of the low number of events.

DISCUSSION

To our knowledge, this is the first study to compare vancomycin dosing regimens determined retrospectively by 2 different methods for the same patients, which ensured similarity of the comparator groups, with limited confounding. Our results show that use of AUC for therapeutic drug monitoring would allow a significant reduction in daily dose of vancomycin and a significant lengthening of the dosing interval, which would expose patients to a lower trough concentration and lower AUC.

We hope that our data, combined with those from other studies, will prove to physicians and pharmacists that the trough concentration is not a good surrogate marker for AUC and that its use may lead to overtreatment of patients. Indeed, in our study, more patients had the dosing regimen adjusted upward with trough-based monitoring (relative to AUC-based monitoring) to achieve the unnecessarily high target trough concentration of 15 to 20 mg/L, which is consistent with many observations reported in the literature.[17,21]

For example, in a Monte Carlo simulation of 5000 patients, Pai and others[17] showed that 60% of patients could reach a therapeutic AUC (> 400 mg*h/L) with a trough concentration of less than 15 mg/L. In our study, the proportion was even higher than that, with 89% of patients who had a trough concentration between 10 and 14 mg/L having an AUC of 400 to 600 mg*h/L.

Our results are also useful to help health care professionals better understand the difference between the 2 monitoring methods, through provision of specific clinical variables, such as the unit dose and the dosing interval. Few other studies have examined actual differences between dosing regimens. In a retrospective, quasi-experimental study of 1280 hospitalized patients, Finch and others[13] compared

TABLE 2. Vancomycin Dosing Regimens with Therapeutic Drug Monitoring Based on Trough Concentration and AUC (*n* = 66 Treatment Courses)[a]

Variable	TDM Method; Mean ± SD		Mean Difference (95% CI)		Relative Difference (%)	*p* Value
	Trough	AUC				
Unit dose (mg)	1100 ± 191	1086 ± 197	–14	(–70 to –42)	–1.27	0.62
Daily dose (mg)	2630 ± 907	2294 ± 901	–336	(–460 to –212)	–12.76	< 0.001
Daily dose, weight-based (mg/kg)[b]	35.05 ± 12.34	30.24 ± 10.60	–4.81	(6.48 to –3.15)	–13.72	< 0.001
Interval (h)	11.67 ± 6.28	13.24 ± 6.76	+1.58	(–0.77 to 2.38)	+13.45	<0.001
Extrapolated trough (mg/L)	16.22 ± 3.28	12.90 ± 2.49	–3.32	(–4.25 to –2.38)	–20.47	<0.001
Extrapolated AUC (mg*h/L)	594.77 ± 104.36	509.48 ± 58.64	–85.29	(–111.61 to –58.98)	–14.34	<0.001

AUC = area under the curve, CI = confidence interval, SD = standard deviation, TDM = therapeutic drug monitoring.
[a]Comparison analyzed by paired *t* test.
[b]Divided by total body weight in kilograms.

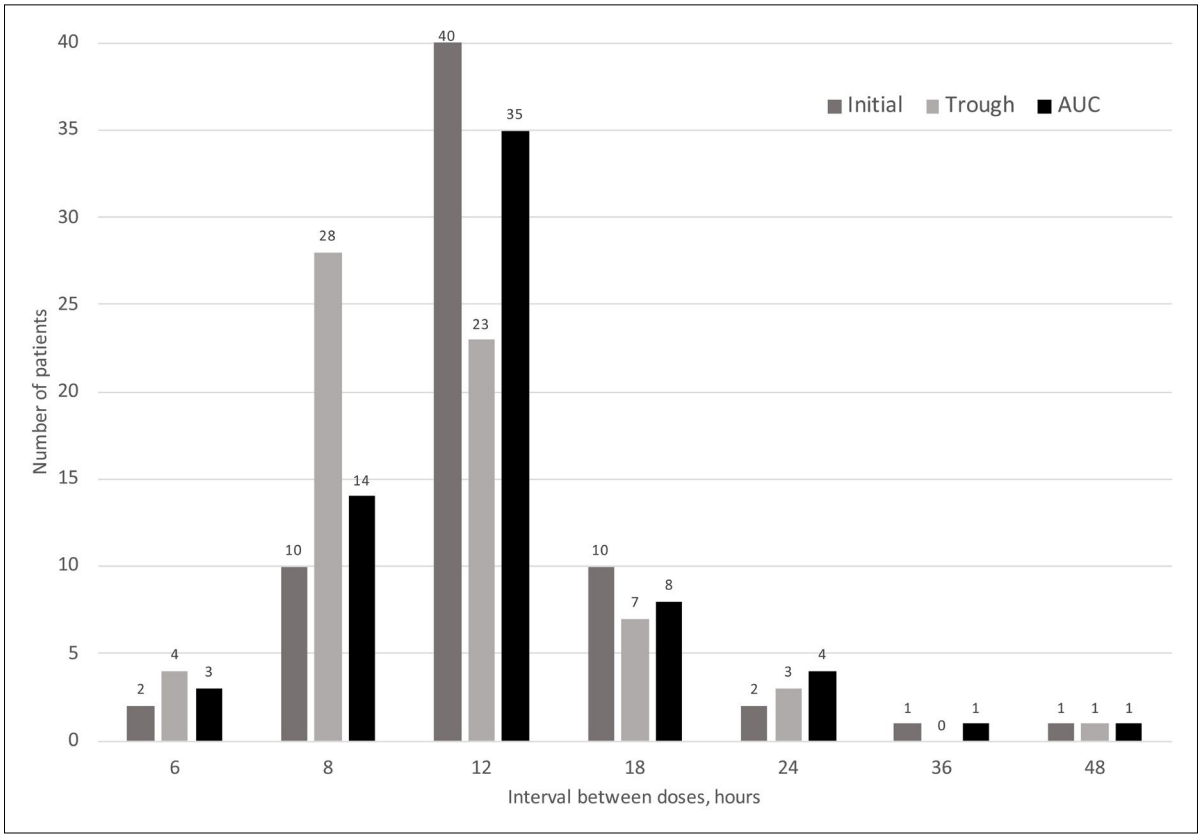

FIGURE 1. Vancomycin dosing interval with the initial dose and the 2 monitoring methods after dosing adjustment (*n* = 66 treatment courses). Trough = monitoring on the basis of trough concentration of medication, AUC = monitoring on the basis of area under the curve.

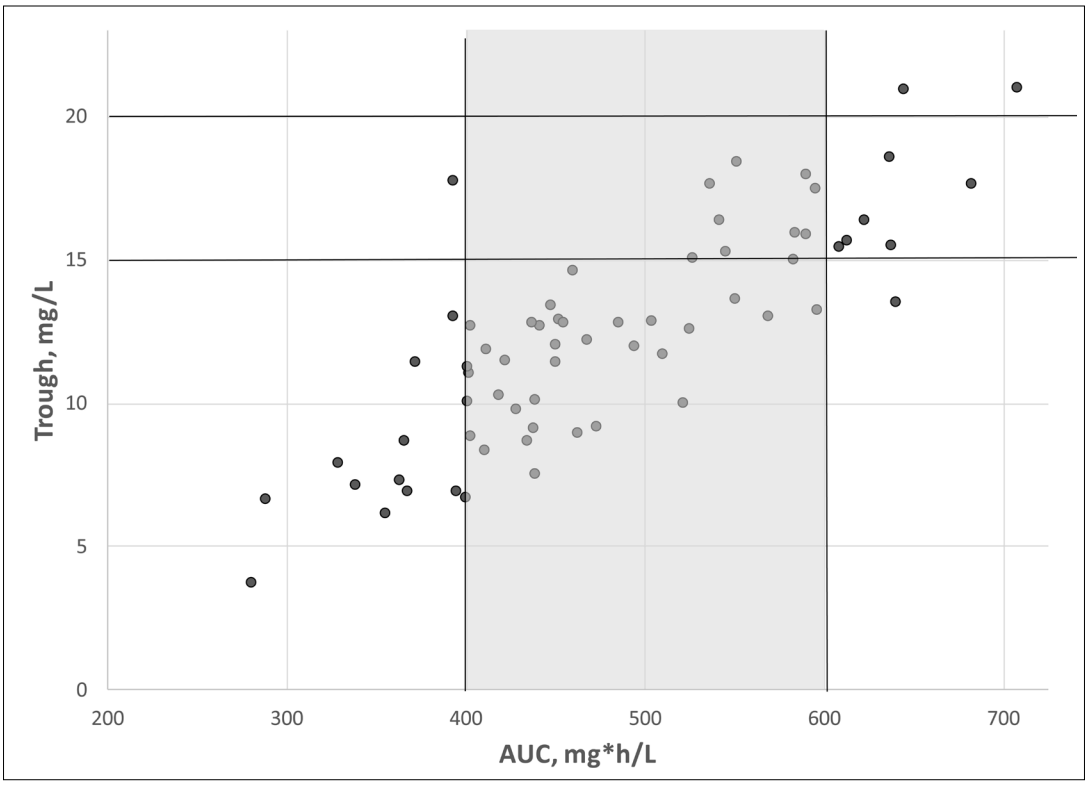

FIGURE 2. Relationship between trough concentration of medication and area under the curve (AUC) in patients receiving vancomycin (n = 66 treatment courses).

TABLE 3. Acute Kidney Injury during Vancomycin Treatment

Variable	No. (%) of Patients[a] (n = 51)
Total length of treatment (days) (median and range)	6.00 (1–38)
Nephrotoxic event	6 (12)
Concomitant nephrotoxic drugs	n = 6 events
0 or 1	0 (0)
2	4 (67)
≥3	2 (33)
Concomitant drug therapy	n = 6 events
Furosemide	4 (67)
ACE inhibitor or ARB	3 (50)
Piperacillin–tazobactam	2 (33)
Contrast dye	2 (33)
Vasopressors	2 (33)

ACE = angiotensin-converting enzyme, ARB = angiotensin receptor blocker.
[a]Except where indicated otherwise.

cumulative doses of vancomycin determined with AUC- and trough-based monitoring. AUC-based monitoring allowed 4% to 7% lower cumulative vancomycin doses at 24, 48, and 72 hours than trough-based monitoring. This difference was statistically significant but appears small relative to our results, which would have allowed a significant reduction in vancomycin dose of about 13%. However, the previous authors did not directly compare the dosing regimens generated by the 2 methods. Also, the 2 cohorts in the study by Finch and others[13] were not similar: the AUC-based monitoring group had a higher infection severity score and comorbidity index, which limited the interpretation of results for cumulative doses.

Of note, the pharmacists involved in determining dosing regimens with trough-based monitoring in our study mentioned that, in clinical practice, they would tend to tolerate trough concentrations slightly below 15 mg/L, as they would expect the accumulation of vancomycin and rising trough concentrations with monitoring early in therapy. During our study, pharmacists were instructed to design a dosing regimen that would necessarily generate a trough concentration between 15 and 20 mg/L without consideration of other variables; this might have increased the difference in daily doses determined by the 2 methods.

In our study, we found that the dosing regimens with AUC- and trough-based monitoring differed more in terms of the dosing intervals than in terms of the unit dose. Nix and others[22] studied the impact of dosing interval in limiting vancomycin AUC with trough-based monitoring. Their data suggested that maintaining a longer dosing interval and escalating unit doses to achieve a target trough concentration results in excessive vancomycin exposure (as reflected in the AUC), with potentially high peak

concentrations. They recommended shortening the dosing interval with the trough-based method to maintain a therapeutic AUC. This recommendation contrasts with our data: even if our pharmacists tended to shorten dosing intervals when the target trough concentration of 15 to 20 mg/L was not reached (rather than increasing the unit dose), the mean predicted AUC was still high, just below the nephrotoxicity threshold of 600 mg*h/L.

The prevalence of nephrotoxic events in this study was 12%, greater than other recent data showing that AKI occurs in about 5% of patients exposed to vancomycin.[23,24] The prevalence of AKI observed in our study occurred in the context of trough-based monitoring, the method used at our centre at the time of data collection. This finding concurred with several recent studies showing that higher vancomycin exposure and trough-based monitoring are linked with nephrotoxicity.[3,8,13,23] The risk of AKI is potentiated by the concomitant use of nephrotoxic drugs, which was high in our study, with 73% of patients taking at least 1 concomitant nephrotoxic drug. It would be relevant to compare the prevalence of nephrotoxicity at our centre before and after large-scale implementation of the AUC-based monitoring method.

This study had some limitations. It was a single-centre, retrospective study; however, there were very few missing data for the selected patients. Some blood sampling times may have been incorrect, because nurses in our centre often enter timing data into the electronic records before actually taking the sample. However, given that the same data were used to compare the 2 methods, we do not expect that differences in sampling time would lead to significant differences in our results. Patients with unstable renal function or presenting with AKI before or during treatment were not excluded from the study; this might have affected the data obtained, given that steady state is usually not achieved in these cases.[25] Also, critical care patients frequently have unstable vancomycin clearance, which prevents achievement of a steady state.[26] In 52% of the courses of therapy in our study, the patients were admitted to the intensive care unit during their vancomycin treatment, but few had septic shock, and creatinine levels were stable in most patients. In addition, the mean volume of distribution for vancomycin in the study population was 0.74 L/kg, which is similar to what has been described in the literature.[27,28]

Our institution-specific practice (with a high rate of endovascular infections) and the study's exclusion criteria (with exclusion of patients undergoing renal replacement therapy, those with central nervous system infection, and pediatric patients) limit extrapolation of data to these populations. In addition, our study did not aim to compare Bayesian-determined dosing regimens.

Our study compared dosing regimens in terms of pharmacokinetic parameters; it was not designed to evaluate clinical efficacy. Only 11% of the treatment courses included in the analysis were for proven MRSA infection, which may bring the relevance of our results into question; according to the monitoring guideline, there is insufficient evidence to provide recommendations on vancomycin monitoring for patients with infections other than MRSA.[4] However, our study data compared well with the most extensive prospective study of AUC-guided vancomycin dosing in adults, in which, similarly, only 10% of the study population had microbiologically proven MRSA infections.[29] In that study, there was no difference in clinical efficacy between AUC- and trough-based monitoring.[29] Further research is warranted in this area, as prospective data for vancomycin monitoring in infections other than MRSA are still rare.

CONCLUSION

AUC-based monitoring could allow a significant reduction in daily vancomycin doses and a significant lengthening of dosing intervals relative to trough-based therapeutic drug monitoring. Extrapolated trough concentrations and AUC values were also considerably lower with AUC-based monitoring, and we confirmed that a target trough concentration of 15 to 20 mg/L is unnecessarily high. These benefits have the potential to reduce nephrotoxicity at our centre, and AUC-guided dosing for vancomycin should therefore replace trough-based monitoring.

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Reasons for Low Regulatory Body Discipline Rates for Canadian Hospital Pharmacists

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ABSTRACT

Background: Past research on disciplinary action by pharmacist regulatory bodies has shown that most cases concern community pharmacists, with few occurring in a hospital setting.

Objective: To investigate how discipline-related issues involving pharmacists are dealt with by hospital pharmacy departments in Canada.

Methods: Hospital pharmacy directors and managers from small, medium, and large hospitals across Canada were invited to participate in semi-structured telephone interviews. The interview questions focused on the discipline process in participants' organizations, the situations when reporting to the regulatory body is deemed to be warranted, possible penalties, and recommendations for improving the regulatory body or organizational discipline process.

Results: Ten participants, from British Columbia, Saskatchewan, Ontario, New Brunswick, Prince Edward Island, and Newfoundland and Labrador, agreed to be interviewed. Five key themes emerged as contributing to lower rates of hospital pharmacist discipline cases being escalated to the regulatory college level: robust organizational discipline processes independent from the regulatory college, a practice environment promoting competence, union representation, preference for a remedial approach to discipline, and lack of clarity about when to report to the regulatory authority.

Conclusions: This study identified a number of reasons why discipline of hospital pharmacists by a regulatory body may be less prevalent than discipline relating to community pharmacists. The main reasons may be lack of clarity about when to report a case to the regulator and a lack of transparency, given that many cases are handled internally within hospitals. Environmental supports for competence and employee protections (e.g., through a union) may also reduce discipline cases.

Keywords: hospital pharmacy, disciplinary action, organizational discipline, pharmacy

RÉSUMÉ

Contexte : Des recherches antérieures sur les mesures disciplinaires prises par les organismes de réglementation des pharmaciens ont montré que la plupart des cas concernaient des pharmaciens communautaires, et que peu se produisaient en milieu hospitalier.

Objectif : Examiner comment les questions disciplinaires impliquant des pharmaciens sont traitées par les départements de pharmacie hospitalière au Canada.

Méthodes : Les directeurs et gestionnaires de pharmacies de petits, moyens et grands hôpitaux au Canada ont été invités à participer à des entrevues téléphoniques semi-structurées. Les questions portaient sur le processus disciplinaire en place dans les organismes des participants; les situations où le signalement à l'organisme de réglementation était jugé justifié; les sanctions possibles; et les recommandations pour améliorer le processus disciplinaire de l'organisme de réglementation ou de l'organisme.

Résultats : Dix participants de la Colombie-Britannique, de la Saskatchewan, de l'Ontario, du Nouveau-Brunswick, de l'Île-du-Prince-Édouard et de Terre-Neuve-et-Labrador ont accepté d'être interrogés. Cinq thèmes clés ont été identifiés comme contribuant au taux plus faible de cas de discipline des pharmaciens hospitaliers remontés au niveau de l'organisme de réglementation : des processus disciplinaires organisationnels solides indépendants de l'organisme de réglementation; un environnement de pratique favorisant la compétence; la représentation syndicale; la préférence pour une approche corrective de la discipline; et le manque de clarté quant au moment où il faut signaler à l'autorité de réglementation.

Conclusions : Cette étude a identifié un certain nombre de raisons pour lesquelles les mesures disciplinaires relatives des pharmaciens hospitaliers par un organisme de réglementation peuvent être moins répandues que celles liées aux pharmaciens communautaires. Les principales raisons pourraient être le manque de clarté quant au moment de signaler un cas à l'autorité réglementaire et un manque de transparence, étant donné que de nombreux cas sont traités en interne dans les hôpitaux. Les soutiens environnementaux pour la compétence et la protection des employés (par exemple, par l'entremise d'un syndicat) peuvent également réduire les cas de discipline.

Mots-clés : pharmacie hospitalière, mesure disciplinaire, discipline organisationnelle, pharmacie

INTRODUCTION

Hospital pharmacists are much less likely than community pharmacists to be disciplined by a regulatory body. Although 15% of licensed Canadian pharmacists work in hospitals,[1] a Canadian review of regulatory body disciplinary cases from 2010 to 2017 showed that only 1% (6/558) of cases occurred in a hospital setting.[2] Of the 558 cases, 503 (90%) occurred in a community setting, 2 in long-term care, 1 in a family

health team, and 46 in an unspecified place of practice.[2] Studies from the United Kingdom have also found that most pharmacist disciplinary cases concern community pharmacists. One UK study found only 1 case (0.3%) involving a hospital pharmacist within the 12-year study period, whereas 86.3% involved community pharmacists, and the remainder involved students or an undetermined place of practice.[3] A second UK study found that 8 cases (6.8%) involved hospital pharmacists, 89 cases (76.1%) involved community pharmacists, and the rest involved pharmacists in primary care, industry, academia, or an undetermined place of practice.[4]

Given the lack of data on this topic, the objective of this study was to investigate how discipline-related issues involving pharmacists are dealt with by hospital pharmacy departments in Canada.

METHODS

Study Design and Participant Recruitment

This study received ethics clearance through the University of Waterloo Research Ethics Committee. Our reporting follows the consolidated criteria for reporting qualitative research (COREQ) checklist.[5] We identified a purposive sample of select hospital pharmacy directors to ensure representation from various Canadian provinces and from large (> 500 beds), medium (201–500 beds), and small (< 200 beds) hospitals.[6] A purposive sample "purposefully" or intentionally selects information-rich cases so as to include a certain range of cases.[7]

Seventeen participants were contacted by email using contact information retrieved from professional connections or publicly available sources. A follow-up email was sent 1 week after the initial invitation, for those who had not responded. Written or verbal informed consent was obtained from all those who agreed to participate. Open-ended, semi-structured interviews were conducted from October to December 2020 by telephone or video call; the interviews were audio-recorded, with participants' consent. The lead authors (A.F. and A.F.-R.) conducted all interviews. Audio recordings were transcribed by a professional transcribing company, and the transcriptions were reviewed for accuracy by the lead authors. The duration of each interview was determined from the audio recording.

We initially arranged for a minimum of 10 interviews, with the option to pursue more interviews if needed to reach saturation. Although thematic analysis was not performed concurrently with data collection, saturation was determined according to the opinion of the 2 interviewers, who kept interview notes and discussed key points after each interview and identified that after 8 interviews, no new major points were being discovered.

The data were analyzed systematically using thematic analysis, in accordance with the Framework Method.[8] These steps consist of transcription, familiarization with the content of each interview, coding, development of a working analytical framework, application of the framework, charting of data into the framework matrix, and interpretation of the data. Codes were created after 3 interviews had been conducted and were then applied to the transcripts of 2 of these 3 interviews. The codes were refined and applied to the third transcript, at which point they were found to be sufficient to encompass the data for all 10 interviews. Each transcript was coded in Word software (version 16.43, Microsoft Corporation), with coding performed independently by the lead authors. Themes were continually refined through consensus discussion to ensure consistency. Quotations used in the final manuscript and their context were returned to participants to verify transcription and interpretation and to allow participants to add comments or corrections. Study results were made available to participants upon request.

Interview Guide

The interview guide (Appendix 1) was developed with pre-existing knowledge about themes of disciplinary action involving community pharmacists.[2-4] We used an iterative approach to modify the interview guide throughout the data collection process to incorporate new themes that emerged. Not all interview questions were intended to yield a reported result or contribute to a theme, as some questions were general and intended to help familiarize the interviewers with processes at participants' hospitals.

Each interview was divided into 4 sections. The first section sought to generate an understanding of current discipline processes for pharmacists within each organization and insight as to why hospital pharmacists are subject to regulatory body discipline less frequently than community pharmacists. The second section focused on reasons why pharmacists are disciplined. In the third section, hypothetical case-based scenarios were presented to the participants, with the aim of gathering data on whether and how a pharmacist would be penalized and whether the scenario would be reported to the regulatory body. The last section discussed ways to improve the disciplinary process. The interview guide was pilot-tested by 2 hospital pharmacists who otherwise were not involved in the study, to ensure clarity of the questions.

RESULTS

Of the 17 participants we contacted, 10 agreed to participate in an interview (Table 1). Two regional hospital directors were working at the provincial level, 2 were regional pharmacy directors of a large health authority, and the others were pharmacy directors of their respective hospitals. Interviews ranged in duration from 24 to 43 minutes (mean 33 minutes).

The data analysis highlighted 5 themes describing why discipline of hospital pharmacists is less prevalent than

TABLE 1. Characteristics of Hospitals Represented by Participants

Participant	Province	Level of Management	Hospital Size[a,b]	Unionization
1	Ontario	Hospital	Small	Yes
2	Newfoundland and Labrador	Health authority	Large	Yes
3	British Columbia	Hospital	Medium	Yes
4	Ontario	Hospital	Medium	No
5	New Brunswick	Health authority	Medium	Yes
6	Ontario	Hospital system	Large	Yes
7	Ontario	Hospital system	Medium	Yes
8	Prince Edward Island	Health authority	Medium	Yes
9	Saskatchewan	Health authority	Large	Yes
10	Saskatchewan	Health authority	Small	Yes

[a]Small hospitals had fewer than 200 beds, medium-sized hospitals had 201–500 beds, and large hospitals had more than 500 beds.[6]
[b]For participants from health authorities where the size of the health authority was not described in the *Hospital Pharmacy in Canada Report*,[6] the size of the largest hospital in the health authority was used.

discipline of community pharmacists, as discussed in the sections below.

Organizational Discipline Processes

Organizational discipline encompasses the processes used to correct employee behaviour when there is a justifiable reason for such correction. It involves confirming that the employee committed an offence, that the offence warrants correction, and that the penalty is appropriate.[9-11] Progressive discipline is typically used, whereby disciplinary measures are gradual and appropriate to the offence.[11,12] All participants described an organizational discipline process independent of the regulator that was used to handle most cases of pharmacist misconduct or incompetence.

> Participant 9: I'm unaware of any instances in my 30-year history that ever went to the college. And the reason for that is we would have nipped that in the bud far before it's gone to the college.

Participants described various penalties imposed by the hospital, including a reprimand or discussion with the employee, restrictions or conditions on practice (e.g., restricting the employee's access to narcotics, relocating the employee to a different clinical setting), remediation, suspension, and termination.

Another organizational attribute of hospitals is that they have formal processes to receive and address patient complaints, which likely diverts complaints from a pharmacy regulatory body.

> Participant 2: The fact that there is an opportunity for a client or a client family member who has concerns about the appropriateness or quality of the service that they received [decreases reports to the college], because I think that can be very de-escalating.

Union Representation

Participants described organizational discipline processes involving all or some of the following parties: the employee in question; a pharmacy director or manager; and representatives of human resources, quality and risk management, professional practice, labour relations, and the union. All but one participant reported that pharmacists in their organization were unionized. Participants stated that terms negotiated through the union directed the discipline process, including whether or not cases were reported to the regulator.

> Participant 9: There are very clear pathways to move into progressive discipline. And within those pathways, it is all within the contract, the next steps that will be taken.

> Participant 1: I think one of the potential differences is the fact that all pharmacists in my site are part of the union. So, there's obviously that human resources and union component [that] has to be established first before the college would be approached.

Participants also described how the union can influence and limit the penalties that can be applied in a disciplinary case.

> Participant 9: And within a unionized environment, there is a defined process that is utilized prior to separation. It takes a significant series of actions and it takes a significant demonstration of attempts to remediate.

Practice Environment

This theme focused on how the hospital environment reinforces competence and minimizes reliance on a traditional regulatory discipline process.

First, lower discipline rates for hospital pharmacists were credited to a probationary period during which newly hired pharmacists could be terminated if they did not meet required competence standards. Additionally, participants cited the hiring of residency-trained pharmacists as a reason for lower discipline rates.

> Participant 4: We also have probationary periods when they first start, and we're very careful to monitor those probationary periods to ensure that they're performing at the levels we need. And if not, then we just terminate their employment before they actually reach that level.

> Participant 7: I think residency-trained pharmacists come in with a much better clinical skill set and knowing the boundaries of that skill set.

The collaborative nature of clinical decision-making in hospitals may also support safer or more competent practice.

> Participant 1: In community, you frequently just practise by yourself. You just kind of have to make a decision in the moment and you don't have access to other people, but in hospital there are so many people around all the time.

The highly collaborative nature of hospital practice leads to a shared liability, both among health care providers, but also with the organization itself. This leads to a shared sense of responsibility for medication errors or clinical incidents, as there are many clinicians involved in the care of a patient.

> Participant 6: What I do know is that going to the college level of discipline for a hospital pharmacist is a really rare event, because most of the time they're working within a team or a collaborative practice environment ... they have readily available backups to help support them through that situation.

That said, the organizational safeguards that are in place in hospital environments can lead to different reasons for discipline than in community practice, with a few participants specifying privacy and confidentiality violations as a common reason for discipline.

> Participant 6: We tend to have a different role in the community, so there's not a lot of dispensing errors as the main driver of a patient complaint. Where we will wind up having more potential challenges are if somebody goes sifting for personal health information on an individual who's been admitted to our hospital.

These same safeguards may ensure there is less opportunity for intentional misconduct, such as narcotic theft and diversion in hospital. Although it is a common reason for discipline among community pharmacists, participants attributed the lower rate of this violation in hospitals to increased controls and policies.

> Participant 2: And part of that I think is because of the rigorous control that exists within this institution around controlled substances. It's highly automated, very highly documented with a lot of oversight.

However, the size of the hospital is key. Participants mentioned that a smaller hospital might not have the same resources to support professionalism and competence.

> Participant 7: We would like to do a lot more education on … professional responsibilities, rights, scope, all of that. That's where we don't have the resources that a larger hospital that has dedicated resources for education, teaching.

Preference for Remedial Approach to Discipline

Participants described hospitals having a nonpunitive atmosphere that tends to emphasize remediation and rehabilitation. Most reported that cases are typically handled within the organization and are not reported to the regulatory authority, unless termination of employment is involved.

> Participant 9: If a lack of competence was demonstrated, we would put that person into a further training perspective and then take it from there.

The focus on remediation and rehabilitation stems from hospitals working toward a culture of safety and away from one of placing blame on a specific health professional for a particular negative outcome.

> Participant 2: The culture within our practice is, very much so, learning from clinical type[s] of errors and process errors and improving the system and putting supports in place to prevent them, rather than punitive because a disciplinary response would certainly discourage reporting of such occurrences, which doesn't help anybody.

Although it was not a universal opinion, one participant viewed reporting to the regulator as punitive, and thus a deterrent to reporting. A less punitive approach could support hospitals in reporting concerns to a college.

> Participant 7: I believe there is still quite a bit of bias in the pharmacist and technician community that the college reporting system is for bad members.

> If the college tried to shift that perception a little bit by offering help to individual members that an employer [reports] or self-referral … then I might change my answer.

Lack of Clarity about When to Report to Regulatory Body

None of the participants had dealt with a case where an inpatient pharmacist was reported to the regulator (although two had dealt with cases in which an outpatient hospital pharmacist was reported). In addition, a few participants expressed uncertainty about when to report a case to the regulator and noted that this study had prompted reviews of their organizational procedures.

> Participant 7: It's just our thinking on, "Why have we never [reported to the college]?" ... It's like, "Well, should that be a last resort or should it be built into the process earlier on if our performance development reveals professional practice issues or deficiencies?" Again, we're right in the middle of this right now because your email sort of started the conversation.

Participants agreed that an isolated clinical error would not be reported to the regulatory body, but would be discussed with the health professional, investigated as a medication incident, and addressed with remediation. Participants also agreed that cases of gross or repeated incompetence that did not improve with remediation could be reported to the regulator. However, when asked whether they would report a pharmacist with a history of incompetence who changed employment of their own accord, not through termination, participants disagreed on whether this would be reported to the regulator. Nine of the 10 participants agreed that a substance use disorder would be reported, and participants agreed that cases involving theft of a narcotic (e.g., diversion or trafficking) could also be reported to the regulator.

Some participants explained that their organizations had clearly defined processes for reporting to the regulator.

> Participant 4: We actually have a professional practice framework in the hospital so that there is clear guidance as to when we have to report to the college.

Others identified that increased clarity on this process within their organization, developed in conjunction with the regulator, could improve the discipline process.

> Participant 10: Development of an algorithm that if A happens, this is the road it takes, if B happens, this is the road it takes would be useful. It feels that it would be really hard to apply because every situation offers its own nuances but it would provide some guidance and a starting point.

However, the main confusion was about issues that fall outside clear violations.

DISCUSSION

This study identified possible reasons why pharmacists in Canadian hospitals are less likely than community pharmacists to be disciplined through the relevant regulatory body. This difference may be due to organizational discipline processes, union representation, the nature of the practice environment, a nonpunitive approach to discipline, and lack of clarity about when reporting to the regulator is warranted. This study highlights how hospitals often assume the disciplinary role of the regulator in all but the most serious cases. By comparison, community pharmacies are, anecdotally, less widely unionized and would therefore lack the organizational structure to handle complaints or discipline, leading to a higher proportion of regulatory involvement. In their review of pharmacist discipline, Phipps and others[4] also speculated that this was the reason for fewer hospital discipline cases in the United Kingdom.

Hospital pharmacy directors in our study emphasized the value of collaborative practice for promoting competence and safety. Austin and Gregory,[13] in their work on competence drift, noted that professional isolation or working alone increases a pharmacist's risk of becoming disengaged from the profession, resulting in a higher risk of not meeting competence standards. They attributed this higher risk to fewer opportunities for peers to observe their practice, fewer opportunities to compare themselves with peers, and fewer role models in practice.[13] Phipps and others[4] also highlighted that the higher discipline rate in the community setting could reflect a higher risk when working alone compared with working in a collaborative hospital environment. Outside pharmacy, the same can be said for physicians; for example, Alam and others[14,15] found that the medical specialists most likely to be disciplined in Canada were family doctors and psychiatrists, who often work alone, have more frequent patient interactions, and develop long-term relationships with their patients. Furthermore, physicians in ambulatory care settings have higher discipline rates than those working in inpatient settings, where a multidisciplinary, multispecialty team reduces risk by aiding in clinical decision-making or detecting mistakes, or where the patient may be unable to determine which clinician was responsible for an incident.[16] These considerations further support the integration of hospital pharmacists into collaborative teams.

Participants' agreement that isolated clinical incidents would not be reported to the regulator supports a previous review of pharmacist discipline, which found that most cases involved multiple or repeated violations.[2] However, there was a lack of clarity among participants in our study about what would actually be reported to a regulator. For

example, provinces typically require health professionals to report other health professionals if there is a concern about incompetence or incapacity, or any concern about their ability to provide care, as outlined by provincial laws, regulations, codes of ethics, and standards of practice. However, few participants in the study were able to describe the specific reporting requirements in their respective provinces.

While the organizational structure of hospitals may support competence and reduce the need for discipline, hospital processes lack transparency. Despite significant efforts to make cases of complaints and discipline involving health care professionals public, handling of cases by hospitals means that fewer hospital pharmacists have a public discipline record.

Interprovincial differences in oversight of hospitals by regulatory bodies could influence reporting to those bodies. In some provinces, hospital pharmacists are regulated by the regulatory body, but hospitals are not; it is possible that in such provinces fewer incidents involving hospital pharmacists would be reported to the regulator. In contrast, the Ontario College of Pharmacists regulates both hospitals and hospital pharmacies.[17] Even so, the regulation of hospitals by this college only began in 2016, and it is possible that fewer hospital cases might be reported to the regulator in the years after such a change, as a sort of "legacy" effect as institutions adjust to the new regulatory regime.[4,17]

While disciplinary action by regulatory bodies aims to protect the public, other factors influence organizational discipline. For example, workplaces with a higher union presence have fewer dismissals and disciplinary sanctions.[18] Also, studies of nurse discipline found that organizational discipline issues were often dealt with informally by managers and were deliberately not escalated to formal organizational discipline, to decrease costs and keep the number of disciplinary actions low.[19,20] A conflict-of-interest issue arises when organizations attempt to protect both public and organizational interests.

A few limitations of our study should be considered. First, we interviewed a broad sample of hospital pharmacy directors to explore this topic across Canada, and thus could not identify granular processes within a single region. Second, the generalizability of these results may be limited, given that participants generally spoke from their experience in large hospitals. This limitation was mitigated somewhat by the inclusion of pharmacy directors who worked solely in small hospitals, but only 3 participants had this background. Third, we were unable to identify participants in all provinces, although this limitation was mitigated by the inclusion of a sample of managers from different hospital and provincial structures. Finally, our methodology was subject to certain biases, such as choosing participants on the basis of availability and the use of semi-structured interviews, whereby not every participant was asked the same set of questions.

CONCLUSION

The results of this qualitative study indicated that hospitals have clear organizational discipline processes that can support employees in maintaining competence and protect against discipline imposed by regulatory bodies. However, the study also suggests that there is both a lack of clarity about when hospitals should report pharmacists to their regulator and a lack of transparency about the reasons why hospital pharmacists are disciplined within their institutions. Specific characteristics such as collaborative practice and unionization appear to protect against disciplinary action. Future research could expand upon this study to include a larger sample, with small, medium, and large hospitals from all provinces, to gain a better understanding of hospital discipline processes in Canada and to clarify the relationship between organizational discipline and regulatory body discipline.

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APPENDIX 1: Interview guide.

Topic	Question
General	Describe a case where the pharmacist would be reported to the college.
	Are you aware of any hospital pharmacists disciplined through the college? If none or very few, why do you think it is this way?
	Are pharmacists disciplined using a different process from pharmacy technicians?
	Do hospitals administer their own penalties, like suspensions or restrictions? Who consists of the panel that decides on a fair penalty for the pharmacist in the hospital?
	For cases that would require disciplinary action, describe the process that hospital pharmacies use to discipline employees or provide remediation.
Reasons	What concerns are hospital pharmacists most commonly disciplined or provided remediation for?
Case-based scenarios	A pharmacist is caught taking fentanyl ampoules from the vault without logging / signing them out in an attempt to divert them. How will the pharmacist be disciplined? How would this change if the pharmacist was successful in stealing them, and then caught after? What if the pharmacist was stealing dextromethorphan tablets instead? Will this be reported to the college?
	A patient's labs come back with increasing WBC counts and symptoms of cellulitis, and the physician asks the pharmacist on duty to recommend an antibiotic. Failing to catch the patient's low CrCl, the pharmacist recommends vancomycin at a dose that is too high. The physician catches this mistake and orders another antibiotic. Will the pharmacist be disciplined, and if so, how? What if the mistake wasn't caught but no consequences were suffered by the patient? What if the patient developed AKI as a result? Will this be reported to the college?
Improvements	If you had the ability to change this disciplinary process, how would you improve it?

AKI = acute kidney injury, CrCl = creatinine clearance, WBC = white blood cells.

BRIEF RESEARCH REPORT

Nationwide Trends in Dispensing of Sodium Glucose Cotransporter 2 Inhibitors

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ABSTRACT

Background: Three large cardiovascular outcome trials have investigated the safety of sodium glucose cotransporter 2 (SGLT2) inhibitors.

Objective: To analyze the nationwide dispensing of SGLT2 inhibitors before and after the publication of these trials.

Methods: A cross-sectional study was conducted of monthly prescription dispensing of SGLT2 inhibitors from May 23, 2014, to April 30, 2019, using nationwide data for Canada. An autoregressive integrated moving average (ARIMA) model was fitted to the monthly number of tablets dispensed for each SGLT2 inhibitor; the model included a ramp intervention function at the publication dates of interest to estimate the impact on SGLT2 inhibitor dispensing patterns.

Results: The rate of canagliflozin and dapagliflozin dispensing declined after publication of results of the empagliflozin cardiovascular trial in September 2015. After publication of results of the canagliflozin trial in June 2017, which indicated a reduction in cardiovascular events and an increase in the risk of lower-limb amputation, canagliflozin remained the most commonly dispensed SGLT2 inhibitor, but its rate of dispensing declined further. In contrast, the rate of empagliflozin dispensing increased, while the rate of dapagliflozin dispensing was unchanged. After publication of the dapagliflozin trial in November 2018, which indicated no clear reduction in cardiovascular events, short-term trends in dispensing of canagliflozin, empagliflozin, and dapagliflozin were largely unaffected.

Conclusions: The cardiovascular outcome trials appeared to have an important impact on the dispensing of SGLT2 inhibitors in Canada.

Keywords: diabetes, sodium glucose cotransporter 2 (SGLT2) inhibitors, health policy, epidemiology

RÉSUMÉ

Contexte : Trois grands essais portant sur les résultats cardiovasculaires avaient pour objet l'étude de l'innocuité des inhibiteurs du cotransporteur sodium-glucose de type 2 (SGLT2).

Objectif : Analyser la délivrance nationale des inhibiteurs du SGLT2 avant et après la publication de ces essais.

Méthodes : Une étude transversale a été menée sur la délivrance d'ordonnances mensuelles d'inhibiteurs du SGLT2 du 23 mai 2014 au 30 avril 2019, à l'aide de données nationales pour le Canada. Un modèle de moyenne mobile intégrée autorégressive (ARIMA) a été adapté au nombre mensuel de comprimés distribués pour chaque inhibiteur du SGLT2; le modèle comprenait une fonction d'intervention progressive aux dates de publication d'intérêt pour estimer l'effet sur les schémas de délivrance d'inhibiteurs du SGLT2.

Résultats : Le taux de délivrance de canagliflozine et de dapagliflozine a diminué après la publication des résultats de l'essai cardiovasculaire empagliflozine en septembre 2015. Après la publication des résultats de l'essai cardiovasculaire canagliflozine en juin 2017, qui indiquaient une réduction des événements cardiovasculaires et une augmentation du risque d'amputation des membres inférieurs, la canagliflozine est restée l'inhibiteur du SGLT2 le plus couramment délivré, mais son taux de délivrance a encore diminué. En revanche, le taux d'empagliflozine délivré a augmenté, tandis que le taux de délivrance de dapagliflozine est resté identique. Après la publication de l'essai sur la dapagliflozine en novembre 2018, qui n'indiquait aucune réduction nette des événements cardiovasculaires, les tendances à court terme de la délivrance de la canagliflozine, de l'empagliflozine et de la dapagliflozine n'ont pratiquement pas changé.

Conclusions : Les essais portant sur les résultats cardiovasculaires semblaient avoir un effet important sur la délivrance des inhibiteurs du SGLT2 au Canada.

Mots-clés : diabète, inhibiteurs du cotransporteur sodium-glucose de type 2 (SGLT2), politique de santé, épidémiologie

INTRODUCTION

Sodium glucose cotransporter 2 (SGLT2) inhibitors are an effective class of medications for adults with type 2 diabetes mellitus.[1–3] Canagliflozin was the first SGLT2 inhibitor to be approved in Canada (in May 2014), followed by dapagliflozin (December 2014) and then empagliflozin (July 2015). Although their initial listing on the drug formulary varied by province, canagliflozin was listed on most formularies by October 2015, dapagliflozin was listed on most formularies by January 2017, and empagliflozin was listed on most formularies by May 2016. Cardiovascular outcome trials have demonstrated that, compared with placebo, empagliflozin reduced cardiovascular events and

all-cause mortality (trial published on September 17, 2015),[1] canagliflozin reduced cardiovascular events but not all-cause mortality and increased the risk of lower-limb amputation and bone fracture (trial published on June 12, 2017),[2] and dapagliflozin did not reduce the risk of cardiovascular events or increase the risk of lower-limb amputation or bone fracture (trial published on November 10, 2018).[3] Our objective was to analyze nationwide dispensing of SGLT2 inhibitors before and after these 3 trials were published.

METHODS

We conducted a cross-sectional study of monthly dispensing of prescriptions for SGLT2 inhibitors in Canada from May 23, 2014 (the date of Health Canada approval for the first SGLT2 inhibitor), to April 30, 2019 (date of last available data), using nationwide IQVIA Geographic Prescription Monitor data.[4] The IQVIA database contains prescription transactions from Canadian pharmacies for all dispensed products. At the national level, more than 79% of total prescriptions dispensed are captured by a panel composed of approximately 6600 pharmacies. The monthly estimates are created using IQVIA's patented geospatial projection methodology to report on total prescriptions dispensed across Canada at various levels of geography.[4] Although health care in Canada is publicly funded for all residents, drug coverage is not publicly funded and therefore varies by province[5] (for additional details about coverage, see Appendix 1, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/208).

We fit an autoregressive integrated moving average (ARIMA) model to the monthly number of tablets dispensed for each SGLT2 inhibitor. We used an ARIMA model because it is a common method for interrupted time series analysis. We added a ramp intervention function to the models, which allowed us to estimate gradual slope changes in the trends for dispensing of SGLT2 inhibitors. For additional details about the modelling, see Appendix 1.

RESULTS

Before September 2015, the most commonly dispensed SGLT2 inhibitor was canagliflozin (14 865 886 tablets; 82.9% of all SGLT2 tablets), followed by dapagliflozin (3 065 436 tablets; 17.1%) (Figure 1). During that period, most dispensing of SGLT2 inhibitors was paid for with

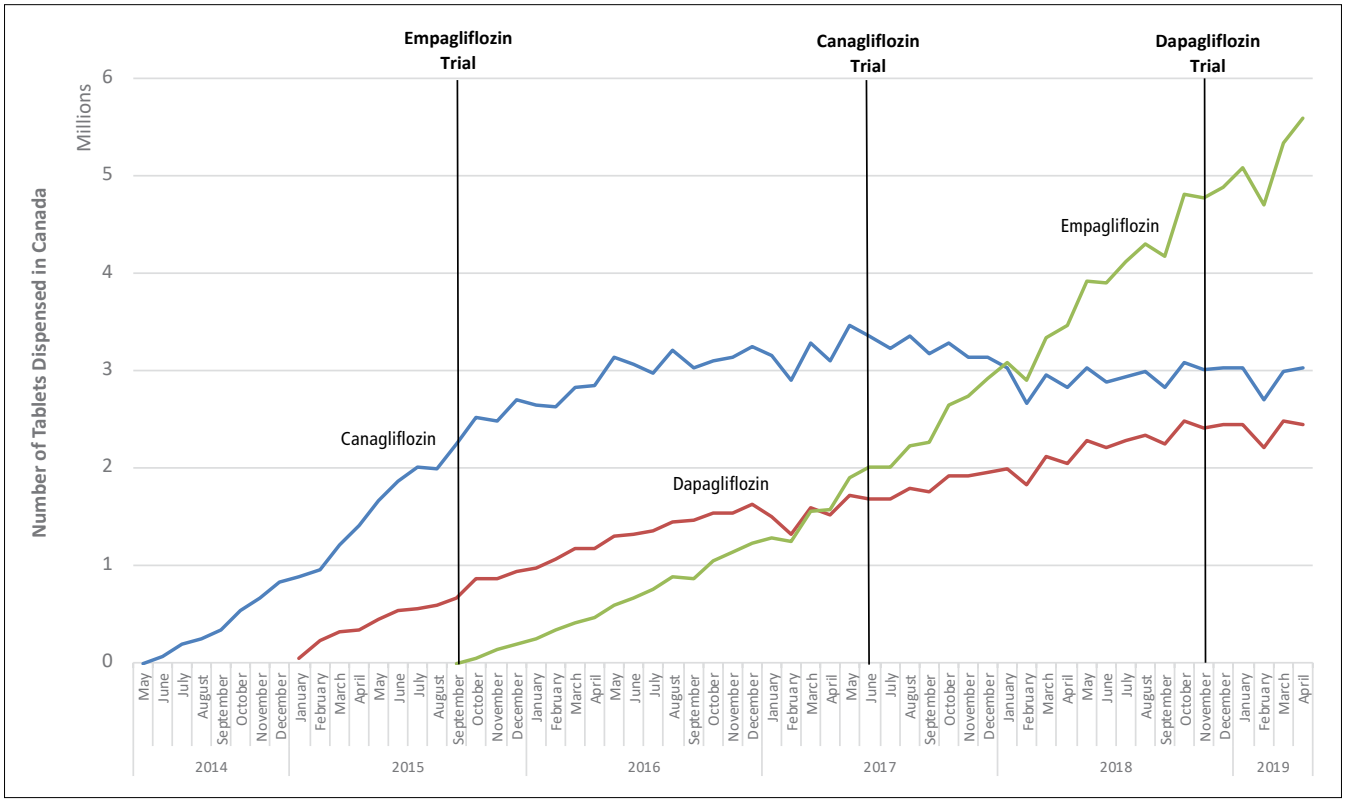

FIGURE 1. Nationwide dispensing of sodium glucose cotransporter 2 (SGLT2) inhibitors in Canada between 2014 and 2019. All of the trials were placebo-controlled and showed the following: empagliflozin reduced cardiovascular events and all-cause mortality (study published September 17, 2015); canagliflozin reduced cardiovascular events (but not all-cause mortality) and increased the risk of lower-limb amputation and bone fracture (study published June 12, 2017); and dapagliflozin did not reduce the risk of cardiovascular events or increase the risk of lower-limb amputation or bone fracture (study published November 10, 2018). Canagliflozin (blue line) was the first SGLT2 inhibitor approved in Canada (May 2014), followed by dapagliflozin (red line; December 2014) and then empagliflozin (green line; July 2015).

cash or by private insurance (for canagliflozin, 78.2%; for dapagliflozin, 89.9%). The results of the empagliflozin cardiovascular trial, published in September 2015, showed a reduction in cardiovascular events and all-cause mortality, which coincided with empagliflozin availability and uptake in Canada. Because empagliflozin was not available before this period, we were unable to quantify the impact of trial results on empagliflozin dispensing. However, we were able to quantify the impact on the other two SGLT2 inhibitors, which were already available in Canada. There was a reduction in the rate of dispensing of both canagliflozin ($p < 0.001$) and dapagliflozin ($p = 0.033$).

The results of the canagliflozin trial, published in June 2017, indicated a reduction in cardiovascular events but not all-cause mortality and an increase in the risk of lower-limb amputation. After publication of this study, canagliflozin remained the most commonly dispensed SGLT2 inhibitor, but its rate of dispensing decreased further ($p < 0.001$). In contrast, the rate of dispensing of empagliflozin increased ($p < 0.001$), and the rate of dispensing was unchanged for dapagliflozin (Table A1 in Appendix 1). In January 2018, empagliflozin (3 079 165 tablets; 38.1%) became the most commonly dispensed SGLT2 inhibitor (canagliflozin, 37.4%; dapagliflozin, 24.5%).

The results of the dapagliflozin trial, published in November 2018, indicated no clear reduction in cardiovascular events or all-cause mortality, and short-term dispensing trends were largely unaffected for canagliflozin ($p = 0.28$), empagliflozin ($p = 0.41$), and dapagliflozin ($p = 0.52$) (see Table A1 in Appendix 1). By the end of our study period, in April 2019, empagliflozin remained the most commonly dispensed SGLT2 inhibitor (5 591 477 tablets, 50.5%; canagliflozin, 3 018 130, 27.3%; dapagliflozin, 2 452 022, 22.2%), and approximately half (51.2%) of all dispensing of SGLT2 inhibitors was paid for with cash or by private insurance.

DISCUSSION

In this nationwide study of dispensing of SGLT2 inhibitors over a 5-year period, the cardiovascular outcome trials appeared to have an important impact on the dispensing of SGLT2 inhibitors in Canada. For example, there was a reduction in the rate of dispensing of canagliflozin following publication of the empagliflozin cardiovascular outcome trial. However, the publication date coincided with when empagliflozin became available in Canada, and it is therefore difficult to determine the relative contribution of each event.

Following publication of results from the cardiovascular outcome trial for canagliflozin, there was a significant reduction in the rate of canagliflozin dispensing, although it remained the most commonly dispensed SGLT2 inhibitor for the next 7 months (until January 2018). This finding was surprising, because canagliflozin was the only SGLT2 inhibitor with an increased risk of amputation and bone fracture, and 2 alternative SGLT2 inhibitors were approved for use in Canada.[1] However, canagliflozin was the first SGLT2 inhibitor to become available in Canada. Similar findings have been observed for other classes of medications (e.g., direct oral anticoagulants, antiplatelet agents), whereby the first medication approved within a class is often the most commonly prescribed, even after alternative options become available.[6] This pattern may reflect prescribing inertia or simply familiarity with the first available medication.[7]

One limitation of this study was the lack of patient-level and provider-level data, which meant we were unable to estimate how often patients were directly switched from one SGLT2 inhibitor to another. Furthermore, we had data only up to April 2019; as such, we were able to assess only the short-term impacts of the dapagliflozin trial (5 months of data) and were unable to analyze the impact of the positive renal outcomes trial for canagliflozin.[8] Similarly, the results of trials evaluating heart failure outcomes with dapagliflozin or empagliflozin were published after April 2019.[9,10]

CONCLUSION

Our study provides a contemporary example of the lasting impact of being the first medication approved within a class and also shows how dispensing patterns change in response to updated clinical evidence.

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Assessment of Intravenous versus Oral Antimicrobials in a Large Regional Health Authority

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ABSTRACT

Background: Many antimicrobials given by the intravenous (IV) route have oral (PO) formulations with high oral bioavailability. The advantages of using the PO rather than the IV formulation include lower risk of adverse reactions, shorter length of hospital stay, and lower health care costs.

Objectives: The primary objective was to determine the proportions of patients who received the IV and PO formulations of antimicrobials with high oral bioavailability. The secondary objectives were to determine the proportion of patients who were eligible to receive PO antimicrobials from the start of treatment, the proportion who qualified for IV-to-PO step-down, and areas of improvement to increase use of PO antimicrobials.

Methods: A retrospective chart review was conducted in hospitals in the Fraser Health Authority, British Columbia, between October 18, 2019, and March 5, 2020. Two hundred charts were randomly selected for patients who had received either azithromycin, ciprofloxacin, clindamycin, fluconazole, levofloxacin, linezolid, moxifloxacin, metronidazole, sulfamethoxazole–trimethoprim, or voriconazole.

Results: Of the 200 patients, 124 (62.0%) received the PO formulations, while 76 (38.0%) received the IV formulations. Of the 76 patients receiving IV antimicrobials, 39 (51.3%; 95% confidence interval 44.7%–57.9%) were eligible to receive PO antimicrobials from the start of treatment or could have been stepped down from IV to PO administration.

Conclusions: More than half of patients who received IV therapy were eligible to receive the PO formulation of antimicrobials known to have high oral bioavailability; relative to earlier studies, this proportion has not improved over time. This finding highlights the need for continued vigilance in encouraging the use of PO rather than IV formulations for hospitalized patients.

Keywords: antimicrobials, intravenous therapy, oral therapy, intravenous-to-oral step-down

RÉSUMÉ

Contexte : De nombreux antimicrobiens administrés par voie intraveineuse (IV) ont des formulations orales (PO) avec une biodisponibilité orale élevée. Les avantages de l'utilisation de cette formulation plutôt que de la formulation IV comprennent un risque moins élevé d'effets indésirables, une durée d'hospitalisation plus courte et des coûts de soins de santé inférieurs.

Objectifs : L'objectif principal visait à déterminer les proportions de patients ayant reçu les formulations IV et PO d'antimicrobiens à haute biodisponibilité orale. Les objectifs secondaires consistaient, quant à eux, à déterminer la proportion de patients pouvant recevoir des antimicrobiens par voie orale dès le début du traitement, la proportion de patients qualifiés pour passer de l'administration IV à l'administration par voie orale et les domaines d'amélioration pour augmenter l'utilisation des antimicrobiens par voie orale.

Méthodes : Un examen rétrospectif des dossiers a été effectué dans les hôpitaux de la Fraser Health Authority, en Colombie-Britannique, entre le 18 octobre 2019 et le 5 mars 2020. Deux cents dossiers ont été sélectionnés au hasard pour les patients qui avaient reçu soit de l'azithromycine, de la ciprofloxacine, de la clindamycine, du fluconazole, de la lévofloxacine, du linézolide, de la moxifloxacine, du métronidazole, de la sulfaméthoxazole-triméthoprime ou du voriconazole.

Résultats : Sur les 200 patients, 124 (62,0 %) ont reçu les formulations PO, tandis que 76 (38,0 %) ont reçu les formulations IV. Sur les 76 patients recevant des antimicrobiens par voie intraveineuse, 39 (51,3 %; intervalle de confiance à 95 % 44,7 % à 57,9 %) étaient admissibles pour recevoir des antimicrobiens par voie orale dès le début du traitement ou auraient pu passer de l'administration IV à l'administration par voie orale.

Conclusions : Plus de la moitié des patients ayant reçu une thérapie IV étaient admissibles pour recevoir la formulation PO d'antimicrobiens connus pour avoir une biodisponibilité orale élevée; par rapport aux études antérieures, cette proportion ne s'est pas améliorée avec le temps. Cette découverte souligne la nécessité d'une vigilance continue pour encourager l'utilisation de formulations PO plutôt que IV pour les patients hospitalisés.

Mots-clés : antimicrobiens, thérapie intraveineuse, thérapie orale, passage voie intraveineuse voie orale

INTRODUCTION

Hospitalized patients are often given intravenous (IV) formulations of antimicrobials that also have oral (PO) formulations with excellent bioavailability.[1] Use of PO rather than IV antimicrobials offers advantages such as lower costs, shorter length of hospital stay, and lower risk of adverse events.[2] A previous evaluation in the Fraser Health Authority found suboptimal use of PO antimicrobials.[3] This evaluation was undertaken to investigate the current state of antimicrobial prescribing in the same health authority to determine if the rate of prescribing of PO antimicrobials had increased relative to prescribing of IV formulations.

The primary objective was to determine the proportion of patients who received IV or PO formulations from a prespecified list of antimicrobials known to have high oral bioavailability. The secondary objectives were to determine the proportion of patients who could have received PO antimicrobials upon treatment initiation and the proportion of patients eligible for step-down from IV to PO administration, and to identify areas of improvement to increase PO antimicrobial usage.

METHODS

Data collection for this retrospective chart review did not include patient identifiers. The information collected was available only to the investigators and remained confidential. The Fraser Health Research and Ethics Board provided an exemption from ethics approval for this study.

Antimicrobial Selection

Fraser Health formulary antimicrobials with high oral bioavailability were selected for analysis. The institution's existing IV-to-PO step-down protocols, as well as those of Northern Health, Vancouver Coastal Health, Alberta Health Services, and the Nebraska Medical Center, were examined to determine whether they listed the selected antimicrobials.[1,4-6] Ciprofloxacin, clindamycin, fluconazole, linezolid, moxifloxacin, metronidazole, sulfamethoxazole–trimethoprim, and voriconazole were common to all lists.[1,4-6] Some lists also included azithromycin or levofloxacin, and both of these medications were included in the review.

Setting and Participants

An evaluation of electronic medical records was conducted in Fraser Health hospitals between October 18, 2019, and March 5, 2020; this period was chosen because of the historically higher rates of respiratory infections and antimicrobial use during winter. Fraser Health is a large health authority with a spectrum of facilities, ranging from small rural community hospitals to large urban tertiary teaching centres. The following hospitals were included in the study: Abbotsford Regional Hospital and Cancer Centre, Burnaby Hospital, Chilliwack General Hospital, Delta Hospital, Eagle Ridge Hospital, Fraser Canyon Hospital, Langley Memorial Hospital, Mission Memorial Hospital, Peace Arch Hospital, Queen's Park Care Centre, Ridge Meadows Hospital, Royal Columbian Hospital, and Surrey Memorial Hospital.

Patients older than 17 years of age who were admitted to any of these facilities and received 1 of the 10 prespecified antimicrobials during the study period were eligible for inclusion.

Sample Size

A MEDITECH report for any of the prespecified antimicrobials (IV or PO formulation) yielded a total of 19 343 orders. From this list, 200 charts were selected using systematic, random sampling with proportional representation from sites. This sample achieved a confidence interval of 95% and 6.6% margin of error for the primary outcome (proportions of patients who received IV and PO antimicrobials). The sample size was based on the assumption that 37% of all orders for IV antimicrobials could have been for PO formulations, based on an unpublished scoping review of previously published IV-to-PO evaluations identified through searches in Google Scholar, PubMed, and Ovid MEDLINE.[2,3,7,8]

Data Extraction

A student investigator (M.D.) used a pilot-tested data extraction form to collect data from the health region's pharmacy information software system (MEDITECH, Medical Information Technology Inc). Data extraction from the first 5% of charts was also conducted by the 2 other investigators (T.S., A.M.T.) to confirm accuracy. Another audit was done midway through the data collection process to confirm continued accuracy.

According to a draft document entitled *Sequential Antimicrobial Therapy in Adults – Best Practice Recommendations,* prepared in 2020 by the BC Health Authorities Pharmacy & Therapeutics Committee, the criteria for initiating or converting to PO administration are defined as the absence of nausea, vomiting, dysphagia, gastrointestinal (GI) bleeding, loss of consciousness without a nasogastric or orogastric tube present, poorly functioning GI tract (ileus, GI obstruction, short GI transit time, malabsorption, gastrectomy, short bowel syndrome), or any significant drug interactions between a fluoroquinolone and enteral formula. Additionally, patients had to be able to tolerate other oral medications and a solid or liquid diet. Those in shock and receiving vasopressors, as well as those with conditions that could only be treated with IV antimicrobials (e.g., meningitis), were considered ineligible for PO therapy. Only descriptive statistics were used.

Consultation with the antimicrobial stewardship (AMS) group concluded that IV antimicrobials were appropriate for patients with blood culture results pending. For those with positive results on blood culture, IV therapy was deemed appropriate, whereas negative results meant that step-down to PO therapy should occur.

Concurrent antimicrobials were noted but were not assessed for appropriateness of route of therapy, given that for each patient included in the study, the sole focus was the antimicrobial identified in the MEDITECH report.

RESULTS

Of the 200 charts initially selected for review, using site-based, proportional, systematic random sampling, 13 documented an order for an antimicrobial that was not administered; data were not collected for those patients, and in each case the next randomized chart from the same hospital was selected. Of the final sample of 200 patients, 124 (62.0%) received PO antimicrobials, while the remaining 76 (38.0%) received IV medications (Table 1, Figure 1).

Of the 76 patients receiving IV therapy, 5 were considered eligible to receive IV antimicrobials because they had positive results on blood culture. Thirty-nine patients (51.3%, 95% confidence interval 44.7%–57.9%) could have been initiated on or stepped down to PO therapy. More specifically, 18 (23.7%) of the 76 patients should have been initiated on PO therapy, and 21 (27.6%) should have been converted to PO therapy (Figure 1). The remaining 32 patients (42.1%) had a legitimate reason to receive IV antimicrobials (i.e., ineligible to receive PO antimicrobials; see Table 1).

The following areas were identified as possible targets for future interventions: therapy for respiratory infections; use of azithromycin, ciprofloxacin, or moxifloxacin; and therapy for patients whose blood culture results are negative. IV antimicrobials were most commonly used to treat respiratory infections (Table 1); further investigation is required to determine why this was the case. Furthermore, it is unknown why azithromycin, ciprofloxacin, and moxifloxacin were disproportionately administered by the IV route (Table 1). Finally, patients may require IV antimicrobials while waiting for the results of blood culture; however, once a negative result is determined, patients should be assessed and switched to PO therapy as soon as possible.

For the 76 patients who received IV antimicrobial therapy, the total number of days of IV therapy was 218. The number of days of IV therapy that could have been saved with appropriate use of PO therapy was calculated post hoc. For the 18 patients who could have been initiated on PO therapy, 44 days of IV therapy might have been saved. For the 21 patients with negative blood culture results, 26 days of IV therapy could have been saved. Therefore, in total, 70 (32.1%) of the 218 days of IV therapy could have been saved with use of PO antimicrobials.

DISCUSSION

More than half of the patients in this study were eligible to receive PO antimicrobials either from initiation of therapy or through IV-to-PO conversion during treatment. This

TABLE 1. Patient Characteristics

Characteristic	No. (%) of Patients[a] (*n* = 200)	
All patients		
Age (years) (median and range)	68.4	(21–103)
Sex, male	101	(50.5)
Hospital site		
Abbotsford Regional Hospital and Cancer Centre	34	(17.0)
Burnaby Hospital	9	(4.5)
Chilliwack General Hospital	21	(10.5)
Delta Hospital	4	(2.0)
Eagle Ridge Hospital	7	(3.5)
Fraser Canyon Hospital	5	(2.5)
Langley Memorial Hospital	9	(4.5)
Mission Memorial Hospital	8	(4.0)
Peace Arch Hospital	9	(4.5)
Queen's Park Care Centre	1	(0.5)
Ridge Meadows Hospital	7	(3.5)
Royal Columbian Hospital	28	(14.0)
Surrey Memorial Hospital	58	(29.0)
Duration of stay (days) (mean and range)	4.4	(1–102)
Indication for antimicrobials		
Respiratory infection	85	(42.5)
Urinary tract infection	13	(6.5)
Gastrointestinal infection	13	(6.5)
Sepsis or bacteremia	11	(5.5)
Fungal infection	8	(4.0)
Abscess	6	(3.0)
Cellulitis	6	(3.0)
Colitis	3	(1.5)
Other	55	(27.5)
Patients receiving IV antimicrobials	***n* = 76**	
Indication		
Respiratory infection	49	(64.5)
Sepsis or bacteremia	7	(9.2)
Gastrointestinal infection	3	(3.9)
Cellulitis	2	(2.6)
Pancreatitis	2	(2.6)
Shock	2	(2.6)
Other	11	(14.5)
IV antimicrobial received		
Azithromycin	41	(53.9)
Ciprofloxacin	15	(19.7)
Moxifloxacin	12	(15.8)
Fluconazole	3	(3.9)
Linezolid	3	(3.9)
Metronidazole	2	(2.6)
Patients ineligible for PO antimicrobials	***n* = 32**	
Nausea or vomiting	13	(40.6)
Dysphagia	7	(21.9)
NPO order	5	(15.6)
Loss of consciousness without NG/OG tube	3	(9.4)
Shock	2	(6.3)
Interaction or non-adherence	2	(6.3)

IV = intravenous, NG = nasogastric, NPO = nothing by mouth, OG = orogastric, PO = oral.
[a]Except where indicated otherwise.

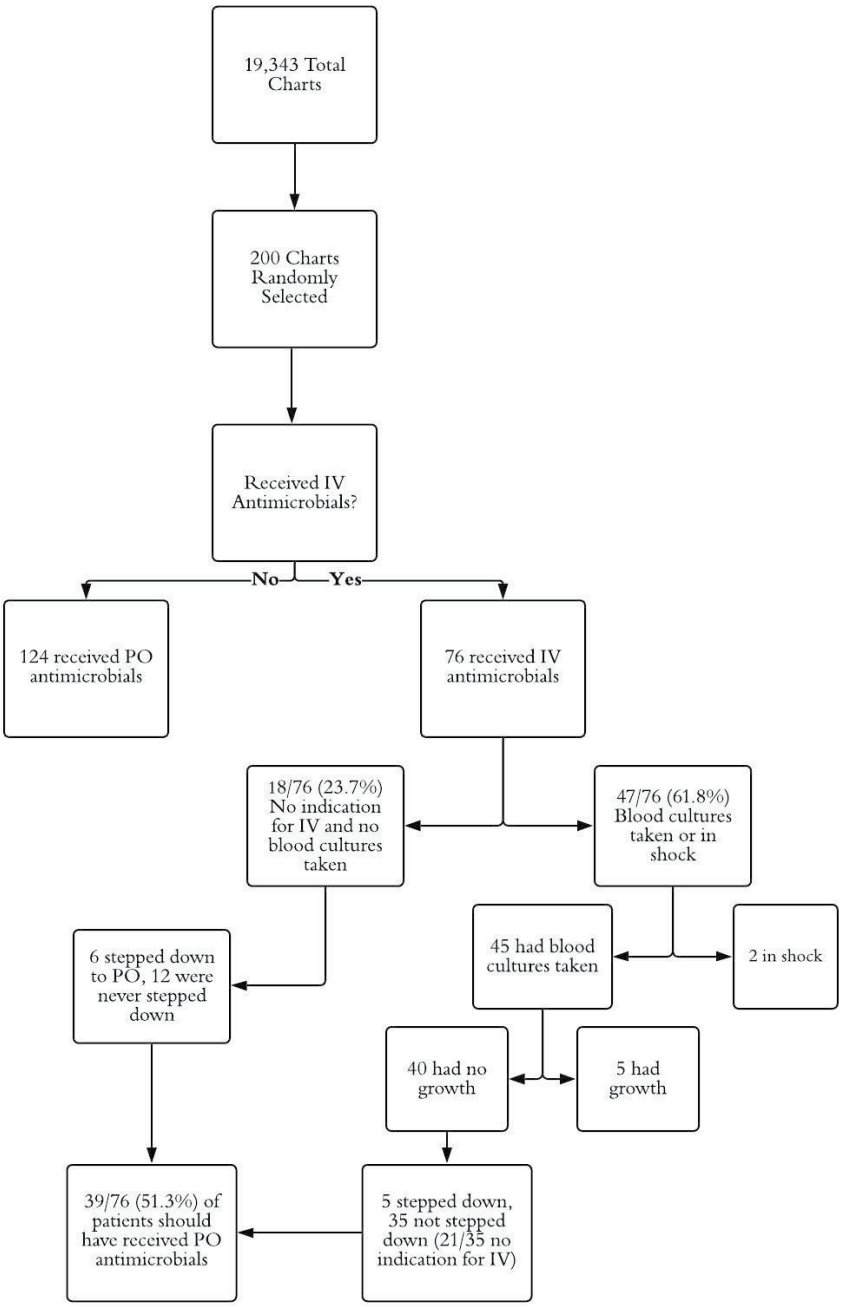

FIGURE 1. Flow chart for analysis of therapy for patients receiving intravenous (IV) or oral (PO) antimicrobials. Those receiving IV antimicrobials were further categorized according to whether IV administration was or was not warranted. Among the 76 patients who received IV antimicrobials, the figure shows 18 patients with no indication and no blood culture and 47 patients with blood culture or shock; in addition, there were 11 patients without blood culture for whom IV therapy was warranted because they were ineligible for PO therapy (e.g., because of dysphagia, shock, nausea and vomiting).

proportion is likely an underestimate, as we did not assess concurrent antimicrobials for appropriateness for IV-to-PO step-down. For example, if the MEDITECH system identified a patient receiving metronidazole PO for whom ceftriaxone IV was also prescribed, only the metronidazole therapy was evaluated for this study; the potential for use of oral ceftriaxone was not assessed.

An additional evaluation showed that 70 days of IV therapy could have been saved if patients had been started on PO therapy or stepped down to PO therapy once appropriate. This result represents an additional area of potential improvement and cost savings in the future.

A previous Fraser Health study investigated patients eligible for conversion to PO therapy and determined that

34.7% (95% confidence interval 29.7%–39.7%) were eligible for IV-to-PO conversion.[3] The current evaluation suggests continued suboptimal use of oral antimicrobials in Fraser Health hospitals (with 27.6% of patients being eligible for step-down), despite focused AMS efforts (e.g., clinical pharmacy assessment of most antimicrobial orders, standardized order sets suggesting PO antibiotics, and recent development of internal clinical practice guidelines for sequential antimicrobial therapy). This situation highlights the need for continued vigilance and periodic re-evaluation. Our results may not directly apply to other jurisdictions, but they serve as a call to action. Whether or not particular organizations have done similar evaluations in the past, and even for those organizations that have had success in reducing unnecessary IV antimicrobial use, we suggest performing or repeating evaluations to determine current status and to identify areas for improvement. In our case, areas for potential improvement include increasing the use of PO therapy for respiratory infections and as the initial route of administration, as well as determining why IV is more frequently prescribed than PO therapy for azithromycin, ciprofloxacin, and moxifloxacin.

One limitation of our study relates to blood culture: we assumed that a negative blood culture result made sepsis or bacteremia unlikely and IV antibiotics unnecessary (according to the appropriateness criteria of our local AMS group). However, it is possible that, despite a negative blood culture result, there may have been valid reasons for a patient to remain on IV antibiotics (e.g., abscess, joint sepsis, intermittent bacteremia). A post hoc assessment suggested that 9 patients may have been in this situation; for these patients, the indications were abscess, gangrene, or "other". If it is assumed that all of these patients received IV antibiotics appropriately, then our original estimate of the proportion who should have received PO therapy upon initiation would be reduced from 27.6% (21/76) to 15.8% (12/76). In our opinion, this more conservative estimate still represents an important problem.

Another limitation was lack of consideration of the impact of clinical practice guidelines on prescribing behaviour. Most notably, some guidelines recommend initial IV antibiotic therapy for patients admitted to hospital for respiratory infections, with switching to PO therapy when the fever abates.[9] Although we may not agree with all aspects of these guidelines, these points could be considered in future analyses.

CONCLUSION

In a randomly selected sample of hospitalized patients receiving antimicrobial therapy, approximately 50% could have been started on or stepped down to PO versions of their medication. This proportion is larger than reported from previous evaluations and supports continued efforts to evaluate and optimize PO antimicrobial use.

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Implementation of an Opioid Stewardship Program to Promote Safer Opioid Prescribing

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INTRODUCTION

Prescription opioid misuse and illicit use have become an increasing public health challenge, with deaths from illicit drug toxicity now exceeding deaths from suicide and motor vehicle incidents combined.[1-4] Though often overlooked, hospitals can be a major contributor to the overdose epidemic and related adverse events.[5-8] Given that acute pain is common among hospital inpatients, initial exposure to opioids and their continued use, sometimes at unnecessarily high doses, is frequent in the hospital setting.[7,9] Previous studies have shown a high prevalence of inappropriate prescribing practices in these settings, including prescription of high-dose opioids, at levels above those recommended in Canadian guidelines (i.e., greater than 90 morphine milligram equivalents), prescription of multiple as-needed opioids, and concurrent prescription of opioids with benzodiazepines.[10-12] Concerningly, in at least one study, hospitals that used opioids were those most frequently associated with increased risk of severe opioid-related adverse events.[7] Past research has also documented inappropriate opioid prescribing practices in hospitals leading to continued use after discharge, which in turn can result in increased risk of various harms in the community, such as development of an opioid use disorder, overdose, or opioid-induced hyperalgesia.[10,13,14] Despite these associations, hospitals are typically not considered as a prime setting for harm production and an area for fruitful intervention.

There is a dearth of research to rigorously explore systems-level interventions to improve the safety and appropriateness of opioid prescribing in these settings. On the basis of experiences from other clinical areas (e.g., hospital-based antimicrobial stewardship programs),[15,16] opioid stewardship is one emerging model that hospitals can use to promote safer opioid prescribing and reduce adverse health outcomes.[17,18] Although a range of models have been implemented globally, the concept of opioid stewardship is loosely described as a set of coordinated interventions designed to monitor and improve the prescribing of opioids in clinical settings.[19] Despite these potential benefits, a recent global review of opioid stewardship programs (based mainly on data from US hospitals) indicated that just 23% of the 133 hospitals included in the study reported having an opioid stewardship program, and only 14% reported having a prospective audit-and-feedback screening process.[19]

In an effort to optimize opioid prescribing in hospital settings, the British Columbia Centre on Substance Use, in collaboration with St Paul's Hospital, implemented a hospital-based opioid stewardship program focused on improving the prescribing, utilization, and monitoring of opioids, with the ultimate aim of improving or maintaining pain control and preventing adverse events.

METHODS

Setting

The opioid stewardship program was implemented at St Paul's Hospital, an acute care teaching hospital located in downtown Vancouver, British Columbia, in January 2020. Given the hospital's close proximity to the city's Downtown Eastside neighbourhood (an area rife with homelessness, poverty, addiction, and mental illness), the hospital provides care to a significant number of individuals with structural vulnerabilities. With more than 400 beds, the hospital is also the provincial referral centre for specialty surgical services, including general surgery, cardiac surgery, and orthopedic surgery. Several consult services operate within the hospital to address issues related to pain and addiction, including an interdisciplinary addiction medicine consult team, as well as acute and complex pain services.

Multidisciplinary Expertise

The opioid stewardship team comprises a diverse group, including physicians, pharmacists, and researchers with formal training and expertise in hospital and addiction medicine, as well as pain management. The opioid stewardship program's clinical team comprises a clinical pharmacy specialist and an addiction medicine physician, who conduct the audit-and-feedback, consultation, and education components of the program. Operational oversight of the opioid stewardship program is provided through the pharmacy department, which helps to ensure that day-to-day

operations of the program run smoothly and effectively (e.g., staff recruitment, integration into hospital operations, and workflow). Involvement of researchers with expertise in health services and clinical evaluation during the planning and implementation phase has also been valuable for conducting rigorous scientific evaluation of the program and assessing its effectiveness.

An opioid stewardship advisory committee was also formed, bringing together representatives from major stakeholder groups to provide advisory support and direction, as well as to disseminate information from the program. Committee members include individuals representing a range of practice and community areas, such as addiction medicine, nursing, internal medicine, pharmacy, patient and family engagement, obstetrics and gynecology, acute pain, and surgery. Importantly, patients are essential stakeholders and decision-makers within the program: because pain is often multifactorial and subjective, in-depth assessment in collaboration with the patient is required to determine the most appropriate areas for adjustment and improvement.

Audit and Feedback

As an initial screening approach, the opioid stewardship program's clinical pharmacy specialist extracts data and reviews daily reports of patients who have been admitted to hospital and exposed to prescription opioids, to identify those who would most benefit from reassessment and intervention. All patients who are admitted to an inpatient unit at St Paul's Hospital and for whom an opioid is prescribed are included in the program. Those admitted under the hospital's critical care units or emergency department are excluded, given their unique requirements for opioids and differing risks compared with the general population. Patients followed by the addiction medicine, palliative care, and acute and complex pain services are also excluded, given that these patients are already being followed by an opioid prescribing specialist.

An automated screening algorithm was developed to assist the opioid stewardship program's clinical team in identifying specific indicators that can be used to guide further assessment and recommendations for changes to treatment. We adapted 13 outcome indicators from national and international clinical guidelines, research articles,[10,19,20] and those developed by health care providers with pain-related expertise to create a comprehensive a priori definition of inappropriate opioid prescribing that could increase the likelihood of an opioid-related adverse event and long-term dependence (Box 1).

Patients with the highest number of indicators (Box 1) are prioritized for review by the opioid stewardship program's clinical team. Although there may be variability among the patients who are assessed daily (in terms of their characteristics and diagnoses), there is little evidence as to whether there would be any benefit to weighting these indicators; as such, the 13 indicators are treated as having equal weight. Once identified, these selected patients receive a full clinical assessment by the opioid stewardship program's clinical team (i.e., the clinical pharmacy specialist and the addiction medicine physician) to determine how analgesic therapy can be optimized to improve or maintain pain management while also improving opioid safety. The team's recommendations are conveyed to the patient and the patient's primary care team in the following ways: documenting a note in the patient's electronic medical record, speaking to the patient and family members, and/or speaking to the attending physician or ward pharmacist. A follow-up assessment is conducted by the opioid stewardship program's clinical pharmacy specialist within 24–72 hours to determine whether the provider has accepted the recommendations proposed by the opioid stewardship program's clinical team.

At hospital discharge, the opioid stewardship program's clinical team connects with the patient's outpatient provider to ensure that any interventions performed during the hospital stay are transitioned to community care and that any plans that require ongoing management are communicated appropriately.

BOX 1. Indicators for Opioid Stewardship Program

Use of parenteral opioids when orders suggest the patient is receiving a normal diet and taking nutrition orally
High-frequency opioid prescribing (< 4 hours between doses)
Multiple different concomitant opioids prescribed for regular and PRN use
Regular use of an opioid that is prescribed for PRN use
Prescription of long-acting opioids within the first 5 days of a patient's hospital stay
High daily dose of an opioid, defined as a prescribed daily dose of 90 MME or greater
Long duration of opioid prescribing, defined as a patient receiving opioids on or beyond hospital day 5
Concurrent prescription of an opioid and a sedative (e.g., benzodiazepine)
No adjunctive order for non-opioid analgesics, such as acetaminophen, NSAIDs, and/or medication for neuropathic pain (where appropriate)
Use of opioid medication in a patient who is opioid naïve
Use of opioid medication in a patient with history of depressive disorder, anxiety disorder, and/or post-traumatic stress disorder
Use of opioid medication in a patient older than 60 years of age
Use of opioid medication in a patient for whom naloxone administration was required in the past 24 hours

MME = morphine milligram equivalent, NSAID = nonsteroidal anti-inflammatory drug, PRN = as needed.

Consultation Service

In addition to conducting audit and feedback for identified cases, the opioid stewardship program's clinical team responds to spontaneous requests for consultation throughout the hospital. These consultations mostly involve complex cases in which patients have greater need for time-sensitive assessment and opioid prescribing recommendations. The consultation service allows clinical teams to request care for patients who may require substantial support but who may not be reached through the automated screening algorithm; these may include patients followed by services that were originally excluded from the audit-and-feedback system.

Education and Development/Review of Guidelines and Order Sets

The opioid stewardship program is involved in a number of educational initiatives, including presentations to various departments and health care professionals, development of new guidelines, and review of new order sets within the electronic records system to increase safe and effective opioid prescribing. For example, new evidence-based guidelines were developed in collaboration with the obstetrics and gynecology department, and multiple electronic order sets were revised to include opioid stewardship principles. Moreover, guidelines and education sessions relating to safer opioid prescribing were developed in consultation with the internal medicine department.

RESULTS

Within the first year of the opioid stewardship program (excluding a 1.5-month interruption in service provision due to the COVID-19 pandemic), a total of 3059 patient encounters, involving 1605 unique patients, were screened (i.e., an active opioid had been prescribed during the encounter; Figure 1). Of those screened, 1084 encounters involving 696 unique patients met the criteria for inclusion (i.e., an active opioid had been prescribed, and the patient had been admitted to a non–critical care unit and was not being followed by the addiction medicine, acute or complex pain, or palliative care service). Among those included, intervention was deemed necessary and recommendations were provided for 576 encounters involving 402 unique patients.

As shown in Figure 2, a total of 1599 interventions were recommended for the 576 patient encounters. The 4 most common interventions were stopping as-needed opioids (28%), adding or increasing a non-opioid analgesic (18%), educating patients about opioid use and providing educational materials (15%), and adjusting (by either decreasing or increasing) the dosage of the prescribed opioid (11%). Other interventions included ordering inpatient naloxone or a naloxone kit upon discharge; referring the patient to the acute or complex pain, addiction medicine, or palliative care service; and changing the quantity and/or formulation of opioid on the discharge prescription. The overall intervention acceptance rate among providers was 93%. While almost all recommendations were fully accepted, a few were partially accepted (e.g., the provider reduced the dose of opioid but not to the specific dose recommended by the opioid stewardship program's clinical team).

In total, the opioid stewardship program received 49 requests for consultations during the 1-year period. The number of consultations steadily increased over time, from a low of 1 in January 2020 to a high of 9 in June 2020, averaging approximately 4 consultations per month. Within the year, a total of 2 guidelines and 4 order sets were developed, and these are in process of being implemented in clinical practice.

DISCUSSION

A systems-level opioid stewardship program at St Paul's Hospital was established in January 2020, with the overall aim of optimizing opioid prescribing practices by monitoring opioid prescribing and utilization within this acute care

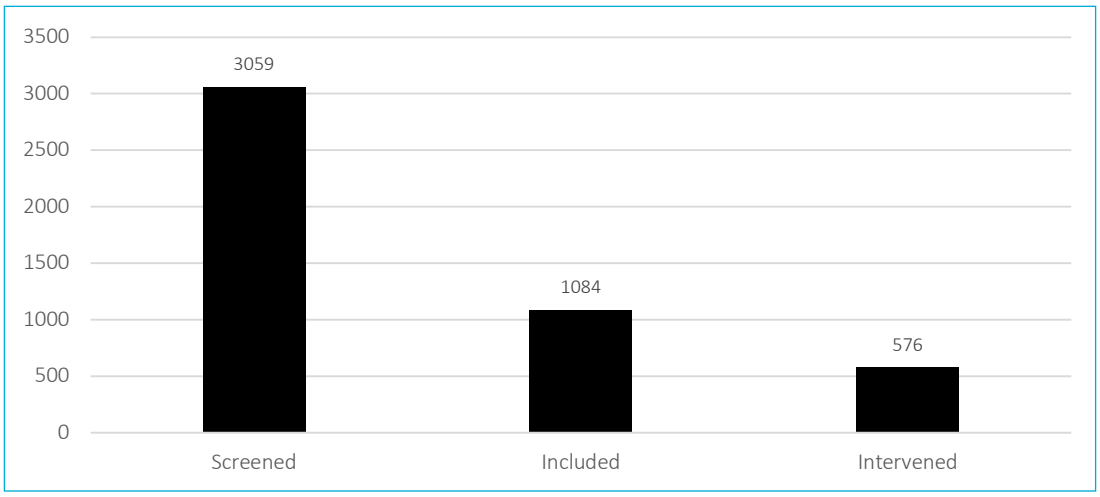

FIGURE 1. Patient encounters screened and included in the opioid stewardship program, and interventions offered.

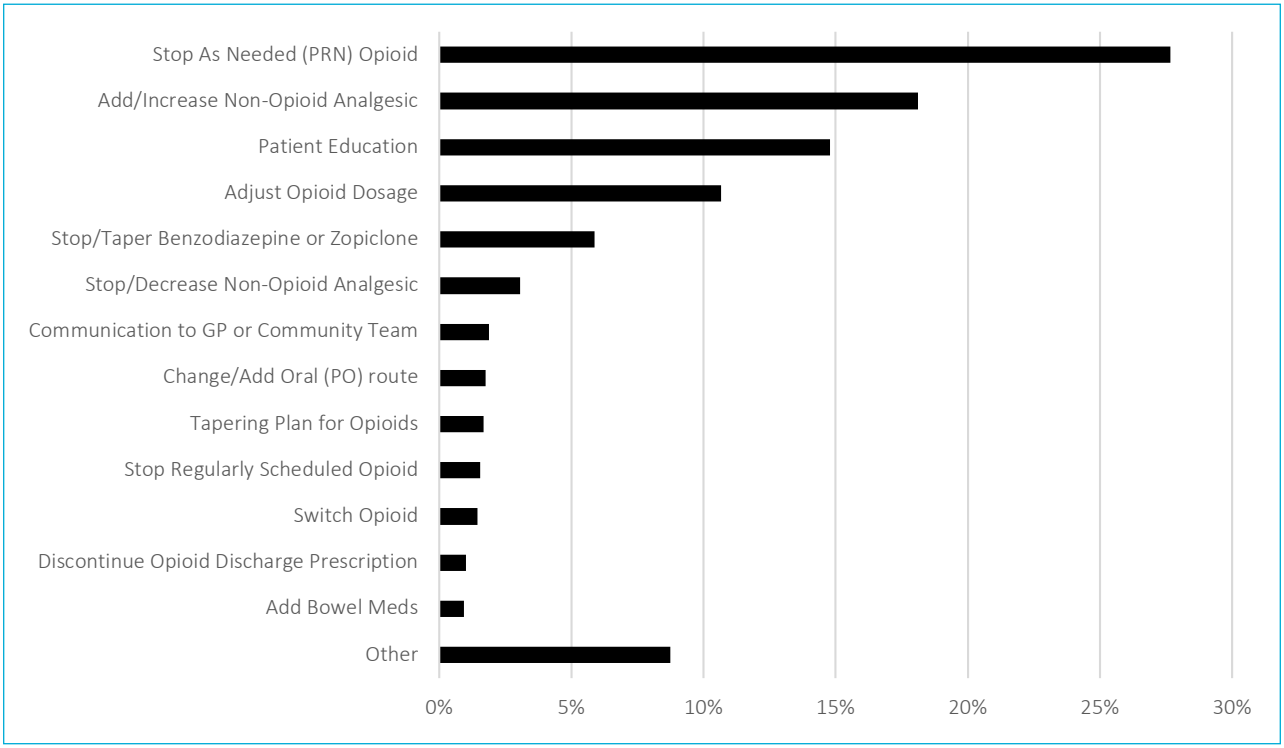

FIGURE 2. Types of interventions provided by the opioid stewardship program (n = 1599 interventions). Each patient could receive multiple interventions. GP = general practitioner.

setting. During the first year of the program, we provided recommendations for more than 400 unique patients with prescriptions for opioids that could increase their risk of harm, and we observed a high rate of acceptance of the recommended interventions among providers. We were also able to show an increasing awareness of the opioid stewardship program through the number of consultations provided and the education presentations given. Our findings shed light on the potential for an innovative systems-level opioid stewardship program to promote safe and effective use of opioid medications in hospital settings.

One key implementation challenge was establishing the role of the opioid stewardship program within other clinical units and consultation services (i.e., addiction medicine and acute and complex pain services), given the overlapping scope of opioid prescribing. We sought to streamline this process by including department heads and key representatives from each of the units as members on the opioid stewardship advisory committee. Doing so yielded buy-in from many of the stakeholders, which helped to ensure that the program would achieve sustainability.

An evaluation plan to assess the impact of the opioid stewardship program is currently underway, with the primary outcome being the change in the proportion of patients with an indicator of inappropriate opioid prescribing (before versus during implementation of the opioid stewardship program). Key secondary outcomes will include the impact on high-dose opioid prescribing, opioid-related adverse drug events, and hospital length of stay. In parallel, we are conducting patient and provider satisfaction surveys as a quality improvement initiative to support the opioid stewardship program. Evaluation of this novel multidisciplinary opioid stewardship program will provide crucial data to inform evidence-based health system changes related to opioid prescribing practices in hospital settings.

Several limitations to this program should be noted. First, St Paul's Hospital provides care to a unique population, including a disproportionate number of patients who have substance use and psychiatric comorbidities; therefore, the generalizability of these findings to other hospitals may be limited. Similarly, the extent to which an opioid stewardship program could be implemented in remote, rural, and/or resource-limited settings has not been explored.

CONCLUSION

We found that the opioid stewardship program provided an innovative way to improve opioid prescribing in our acute care setting and that it was well received by health care providers. A collaborative approach involving a multidisciplinary group of providers, researchers, and other key stakeholders was essential for the program's success. Findings from an in-depth evaluation of the program will give health care providers and policy-makers evidence that will position them to improve health systems and policies in hospital settings.

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Chronic Digoxin Toxicity Leading to Institutionalization of an Elderly Woman

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INTRODUCTION

Cardiac glycosides were discovered by Sir William Withering more than 200 years ago and remain in use for pharmacologic treatment of atrial fibrillation and heart failure.[1] With the availability of alternative treatments and the lack of mortality benefit, prescribing of digoxin has decreased significantly over the past 20 years; however, toxicity-related mortality rates have not decreased to the same degree.[2] Nonetheless, digoxin remains widely used despite its narrow therapeutic window,[1-3] particularly as second-line therapy for patients with atrial fibrillation (with or without heart failure) for whom β-blockers are not an option because of intolerance or insufficient therapeutic effect.[4] In a recent study comparing digoxin and bisoprolol in patients with permanent atrial fibrillation and symptoms of heart failure, digoxin was associated with greater improvements in New York Heart Association functional class and fewer adverse events.[4] The recognition of patients who are at greater baseline risk for digoxin toxicity, as well as careful monitoring during therapy, is therefore important to ensure clinicians continue to prescribe digoxin only for patients who would safely benefit from it.

In clinical practice, serum concentration of digoxin is a surrogate marker for toxicity and adverse outcomes.[3] Independent post hoc analyses of the DIG (Digitalis Investigation Group) and ARISTOTLE (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation) trials demonstrated a significant relationship between digoxin serum concentration and mortality.[3,5] Both analyses showed that concentration of 1.2 ng/mL or above was associated with increased risk of death.[3,5]

Digoxin serum concentrations and overall pharmacokinetics can be affected by patient-specific factors, such as renal function, muscle mass, and age, or by external factors, such as drug–drug interactions.[6,7] Although strong P-glycoprotein inhibitors and inducers affect the bioavailability of digoxin,[6] diuretics have also been shown to increase the risk of digoxin toxicity because of their associated risk of renal and electrolyte disturbances.[8] Loop diuretics are associated with the highest risk of digoxin toxicity, followed by thiazides and potassium-sparing diuretics.[8]

The incidence of digoxin toxicity is also markedly more prevalent among elderly patients than among younger people. The increased prevalence of toxicity is thought to be secondary to a decline in renal function and volume of distribution and an increase in the number of comorbidities.[7] Chronic toxicity in elderly patients consists of a well-documented syndrome of cardiac (lengthening of the PR interval, shortening of the QT interval, depression of the ST segment and t-wave, arrhythmias, bradycardia), gastrointestinal (anorexia, nausea, vomiting, diarrhea, abdominal pain), neurologic (hallucinations, paranoia, trigeminal neuralgia, depression, headaches, dizziness, malaise, fatigue), and visual manifestations, along with electrolyte disturbances.[1,7] Here, we report a case of chronic digoxin toxicity leading to institutionalization and later hospitalization of an elderly woman.

CASE REPORT

A 79-year-old woman with a variety of comorbidities, including chronic obstructive pulmonary disease (COPD), type 2 diabetes mellitus, stable coronary artery disease, stage G3bA1 chronic kidney disease (CKD; baseline serum creatinine 100–110 μmol/L), gout, atrial fibrillation, and heart failure with mildly reduced ejection fraction (40%–45%), presented to the emergency department of a large tertiary care centre.* In the emergency department, her family reported 4 days of confusion and generalized weakness, 1 to 2 months of progressive nausea and vomiting, weight loss of 15 kg, and low mood. Upon review of her provincial drug record and pharmacy medication list, her home medications were identified as acetylsalicylic acid 81 mg daily, metoprolol 12.5 mg twice daily, digoxin 0.125 mg daily, rosuvastatin 20 mg daily, rivaroxaban 20 mg daily, allopurinol 300 mg daily, nitroglycerin patch 0.2 μg/h daily, furosemide 60 mg daily, metformin

*The patient and her family provided informed consent for publication of this case report.

1000 mg twice daily, mirtazapine 15 mg at bedtime, tiotropium bromide 2 puffs inhaled daily, fluticasone–salmeterol 2 puffs inhaled daily, salbutamol 100 µg inhaled every 4 hours as needed, and pantoprazole 40 mg daily.

The patient had previously lived independently on her own, but 8 months before the current presentation, she moved to her son and daughter-in-law's home, where she lived for the next 4 months. Although she had several short admissions to hospital over this 4-month period, she had been coping at home until she was admitted to a rural hospital for urinary tract infection, COPD exacerbation, heart failure, and atrial fibrillation, about 4 months before the current presentation. Upon discharge from this 19-day admission, she was started on digoxin 0.125 mg for rate control. The specific reasons for the decision to initiate digoxin were not available. Unfortunately, 8 days after discharge, she was readmitted, with a similar presentation, for another 3 weeks. Because of ongoing low blood pressure during this admission, medication changes at discharge included discontinuation of ramipril 1.25 mg daily (which she had been taking for only 3 weeks) and initiation of furosemide 20 mg daily. Her heart rate was 101/min on admission for the 3-week stay, and her renal function at that time was stable, with serum creatinine of 103 µmol/L. One month after discharge from this hospital stay, the patient's furosemide was increased from 20 mg to 60 mg daily, with no further monitoring of her renal function.

Within 1 month, the patient demonstrated rapid decline in memory and mobility at home and was moved by her family to a supportive living facility. Over the 3-month period since moving to supportive living, the patient was noted to have reduced appetite, with limited oral intake, which did not improve with a trial of ondansetron. She also experienced low mood, and an adjustment disorder was diagnosed, secondary to her increasing functional limitation. Worsening of her mobility and memory led to transfer to a long-term care facility approximately 3 weeks before the current presentation. Mirtazapine had been prescribed 1 week before the current admission, with no demonstrated benefit, as reported by her family. In the last few days before admission, the family had noted rapid worsening of dehydration, weakness, and confusion, which culminated in altered level of consciousness.

When she presented to the emergency department, the patient weighed 70 kg and was found to be bradycardic (heart rate 55/min), hypotensive (blood pressure 96/48 mm Hg), and afebrile. Telemetry monitoring in the emergency department revealed further bradycardic events, with her heart rate intermittently dropping to 30–40/minute, as well as bigeminy alternating with sinus bradycardia interrupted by frequent premature ventricular complexes. Her score on the Glasgow Coma Scale was calculated as 10 (E3V3M4), and results of the examination were otherwise significant for findings of clinical hypovolemia and anuria.

Initial laboratory investigations were significant for leukocytosis, with white blood cell count of 11.5×10^9/L and neutrophil count of 9×10^9/L; acute kidney injury, with serum creatinine of 841 µmol/L, from a baseline of 110 µmol/L; hyperkalemia, with presenting potassium of 6.2 mmol/L; anion gap metabolic acidosis, with pH of 7.14, urea of 26.5 mmol/L, bicarbonate of 14 mmol/L, and anion gap of 19 mmol/L; lactate level of 6.2 mmol/L; and hypoglycemia, with glucose level of 2.1 mmol/L. Urinalysis showed isolated pyuria, and chest radiography demonstrated a new right lower lobe consolidation. Electrocardiography showed accelerated junctional rhythm with occasional premature ventricular complexes, a previous inferior infarct, poor R wave progression, and low voltages. The digoxin serum concentration was markedly elevated, at 4.8 nmol/L; no previous digoxin concentration had been recorded in the electronic medical record since initiation of this medication. Her most recent laboratory testing had been approximately 3 months before this presentation.

Aggressive medical management was pursued consistent with goals of care ("do not resuscitate"), including volume resuscitation, shifting of potassium, empiric antimicrobials for infection (pneumonia versus urinary tract infection), and initiation of telemetric cardiac monitoring, with the family's consent. Poison control was activated, and 3 vials (120 mg) of digoxin immune fab were administered. Hemodialysis was deemed not to be consistent with the patient's goals of care. Home rate-modifying, antihypertensive, and nephrotoxic medications (metoprolol, nitroglycerin patch, and furosemide, respectively) were held, in addition to her anticoagulant, rivaroxaban.

During the 9-day admission at our facility, she received supportive care and made a dramatic recovery. Within days, the bradycardia and hypotension resolved, with subsequent resolution of her acute kidney injury, acidosis, and hyperkalemia. Her appetite, mood, and weakness improved with the resolution of her nausea and vomiting, and her family noted that her overall condition and cognition recovered to levels not seen before her move to supportive living 4 months prior. She worked with physiotherapy and occupational therapy and returned to baseline mobility with a gait aid. Her polypharmacy was addressed, and she left the hospital with discontinuation of digoxin, metformin, furosemide, nitroglycerin patch, and mirtazapine. The dosages of her other home medications were adjusted to take into account her baseline CKD. She was discharged home to her previous supportive living environment, instead of long-term care.

For several reasons, we attributed this patient's overall clinical presentation and institutionalization to chronic digoxin accumulation. Her calculated score on the Naranjo Adverse Drug Reaction Probability Scale[9] was 8, and the temporal sequence of events fit with the characteristics of chronic digoxin toxicity. Dose escalation of furosemide 2 months after initiation of digoxin, compounded by her

baseline CKD, likely triggered the cycle of toxicity that was further exacerbated by digoxin-induced nausea and vomiting, resulting in dehydration, worsening of renal function, and impairment of function and cognition necessitating placement in long-term care. The lack of renal function and therapeutic drug monitoring after therapy initiation also contributed to significant toxicity in this particular case. It does not appear that digoxin toxicity was ever considered as contributing to the patient's decline: in the 5 months since initiation of this drug, the patient did not undergo any measurement of digoxin serum levels.

DISCUSSION

This case of institutionalization and severe morbidity of a 79-year-old woman with symptoms of chronic digoxin toxicity highlights not only the clinical signs and symptoms of this type of toxicity but also the critical nature of drug monitoring in elderly patients for whom digoxin is initiated. Serum concentration monitoring can help to prevent toxicity associated with concomitant use of digoxin and diuretics and to reduce the risk of chronic accumulation. When digoxin is initiated in elderly patients, careful consideration should be given to the patient's weight, age, and renal function.[10]

Adequate drug monitoring to identify patients who stand to benefit most from digoxin withdrawal is even more crucial in light of the fact that stopping digoxin can be associated with adverse outcomes. Data from the PROVED (Prospective Randomized Study of Ventricular Failure and the Efficacy of Digoxin)[11] and RADIANCE (Randomized Assessment of the Effect of Digoxin on Inhibitors of the Angiotensin-Converting Enzyme)[12] studies, as well as an analysis of the OPTIMIZE-HF registry,[13] suggest that discontinuing digoxin in ambulatory patients with established heart failure with reduced ejection fraction is associated with worsening of heart failure symptoms and functional capacity and increases in rates of hospital admission for heart failure. However, 2 of these studies[11,12] excluded patients with severe CKD, which was a significant risk factor for digoxin toxicity in our patient and should be considered in the risk–benefit calculus when deciding to discontinue digoxin therapy.

To our knowledge, this is the first published report of chronic digoxin toxicity leading to institutionalization. Altered level of consciousness or drug-induced confusion may be the only symptom of digoxin toxicity in some elderly patients, and central nervous system effects can occur even when digoxin levels are within normal range.[14] There is limited evidence to support withdrawal of maintenance digoxin in elderly patients entering institutional living.[15] However, in a small study, 12 of 14 patients living in a long-term care facility tolerated discontinuation of digoxin, which suggested a high prevalence of polypharmacy.[15]

CONCLUSION

In elderly patients with atrial fibrillation or heart failure, we suggest consideration of an alternate agent instead of digoxin and deprescribing if possible. Alternatively, careful drug monitoring is essential, with an emphasis on clinical assessment in addition to measurement of drug levels, given that the latter can help to rule in digoxin toxicity but may be an unreliable rule-out test. We suggest that clinicians maintain a high index of suspicion for digoxin toxicity in elderly patients with renal impairment who are taking this drug and who present with confusion or altered level of consciousness, and that they consider ordering routine digoxin levels in this scenario.

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Rhabdomyolysis Possibly Triggered by Clozapine, Paliperidone, Hyponatremia, and Rapid Correction of Hyponatremia: A Case Report

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INTRODUCTION

This case report describes a patient with refractory schizophrenia admitted to the intensive care unit for symptomatic hyponatremia. This electrolyte imbalance was attributable to psychogenic polydipsia (PPD), a medical condition associated with psychiatric disorders and characterized by abnormal thirst and excessive fluid intake.[1] Rhabdomyolysis was also diagnosed and worsened during the correction of serum sodium, with the potential contribution of clozapine, paliperidone palmitate, and psychotic agitation.

Rhabdomyolysis is a clinical and biochemical syndrome resulting from the breakdown of muscle cells. This syndrome ultimately leads to leakage of intracellular content—specifically creatinine kinase (CK), myoglobin, and electrolytes—from the muscle cells into the circulation. The occurrence of rhabdomyolysis is rare, but the complications can be severe (e.g., acute kidney injury, electrolyte disturbance leading to cardiac arrhythmias).[2] Biological markers such as CK can help to confirm the diagnosis.[3] Common etiological risk factors for rhabdomyolysis include trauma, illicit drugs (e.g., cocaine, heroin, amphetamines), alcohol abuse, immobilization (e.g., coma, sedation, prolonged surgery), and medications (e.g., statins, antipsychotics, lithium, valproic acid, quinolones, colchicine).[4,5] Case reports in the literature have also suggested hyponatremia secondary to PPD as a precipitating factor for rhabdomyolysis.[6-21] Therefore, psychiatric patients can be considered at higher risk of rhabdomyolysis because of their prescribed psychiatric medications (e.g., neuroleptics and antipsychotics, such as haloperidol and atypical antipsychotics; selective serotonin reuptake inhibitors; lithium; valproic acid) and comorbidities (e.g., substance use disorder, involving illicit drugs and alcohol).[5]

Of particular interest in this case was the rapid increase in CK level to over 100 000 IU/L (normal range 0–150 IU/L), in a period of 4 days, in the presence of multiple contributing factors. This article highlights the numerous potential factors contributing to rhabdomyolysis and aims to increase health care providers' awareness of the importance of closely monitoring serum CK in patients with such a clinical presentation.

CASE REPORT

A 35-year-old white man with a history of schizophrenia, borderline personality disorder, attention deficit hyperactivity disorder, PPD, and substance use disorder was brought to the emergency department for confusion, vomiting, and umbilical pain.* A social worker had been making daily home visits to verify treatment adherence and had reported no issues of concern before this episode. His current medications included clozapine 400 mg at bedtime, sublingual atropine 1% drops at bedtime, and olanzapine 5 mg as needed. The clozapine had been gradually introduced to his therapy a month before his presentation to the emergency department. His smoking status had remained stable since then. Before clozapine, the patient had been receiving injections of paliperidone palmitate 350 mg every 3 months. His last dose was 3 months before presentation to the emergency department.

In the emergency department, physical examination revealed tachycardia, diaphoresis, tremor, and apyrexia. Initial laboratory investigations revealed severe hyponatremia (defined as serum sodium less than 120 mmol/L), with serum sodium of 113 mmol/L, urine osmolarity of 133 mmol/kg of water (reference range 50–1200 mmol/kg of water), and elevated serum CK level, at 1925 IU/L (reference range 0–185 IU/L). In addition, the serum clozapine level was at the upper limit of the normal range, at 1533 nmol/L (reference range 306–1836 nmol/L). The toxicology screen was negative for alcohol or other drugs of abuse (e.g., cocaine, cannabis, amphetamines, barbiturates, phencyclidine).

*The curateur public du Québec provided written consent for publication of this case report.

The patient was rapidly transferred to the intensive care unit. Initial treatment consisted of 150 mL of 3% sodium chloride administered over 20 minutes, followed by an infusion of 0.9% sodium chloride at a rate of 100 mL/h for 3 hours to compensate for the sodium deficit. Five hours after administration of the bolus, the patient experienced a serum sodium increase of 13 mmol/L, reaching a serum sodium level of 126 mmol/L (reference range 135–145 mmol/L). Administration of IV fluid was stopped, and he received 2 µg of IV desmopressin acetate to decelerate the sodium correction rate. Four hours later, an infusion of 0.45% sodium chloride was started, at a rate varying between 80 and 250 mL/h, and was continued for approximately 36 hours to maintain the sodium repletion and prevent rhabdomyolysis-induced renal failure. Natremia normalization was achieved between 35 and 42 hours after admission, with the serum sodium level reaching 136 mmol/L.

At the same time, progressive worsening of the rhabdomyolysis was observed. The serum CK level abruptly increased, reaching a maximum value of 102 816 IU/L on the fourth day of the hospital stay (116 hours after admission). It started to decrease on the fifth day after admission (see Figure 1). CK normalization was achieved 19 days after admission, with a level of 150 IU/L (reference range 0–185 IU/L). To prevent acute renal failure, a high volume of fluids (i.e., 200–300 mL/h for about 120 hours) was administered until the serum CK level fell below 10 000 IU/L at day 8, with close monitoring of natremia. The patient's renal function remained stable during the admission, with an estimated glomerular filtration rate above 120 mL/min.

With regard to his medication, clozapine was gradually reduced starting on day 1 of the admission and was stopped on day 6. Olanzapine 10 mg daily was introduced 36 hours after clozapine discontinuation (on day 7) and was titrated over a week up to 20 mg daily. During this therapeutic substitution, the patient had psychotic agitation. He fully recovered after the introduction of olanzapine. He was discharged on day 20 with olanzapine 5 mg in the morning and 15 mg at bedtime. The serum CK level was maintained in the normal range for at least a month after discharge.

According to the Naranjo probability scale, there was a probable causal relationship (score 5) between the use of clozapine and the clinical event.[22]

DISCUSSION

Usually, practitioners consider the possibility of rhabdomyolysis when the serum CK level is 5 times the upper limit of normal.[23] This patient had a mild case of rhabdomyolysis on admission (CK 1925 IU/L), which worsened during the hospital stay. It is essential to point out the pharmacokinetics of CK to establish the timeline of possible causes of the rhabdomyolysis. This biological marker usually increases approximately 2 to 12 hours following the breakdown of muscle cells. The peak occurs within 3 to 5 days after the injury. CK level diminishes over the subsequent 6 to 10 days, when multifactorial causes are corrected.[24] The potential factors contributing to the pathological state of rhabdomyolysis in this patient, discussed below, were medications, hyponatremia, and rapid correction of the hyponatremia.

Medications

Certain medications (e.g., statins, antipsychotics, lithium, valproic acid, quinolones, colchicine), alcohol, and convulsions can precipitate rhabdomyolysis.[4,5] This patient did

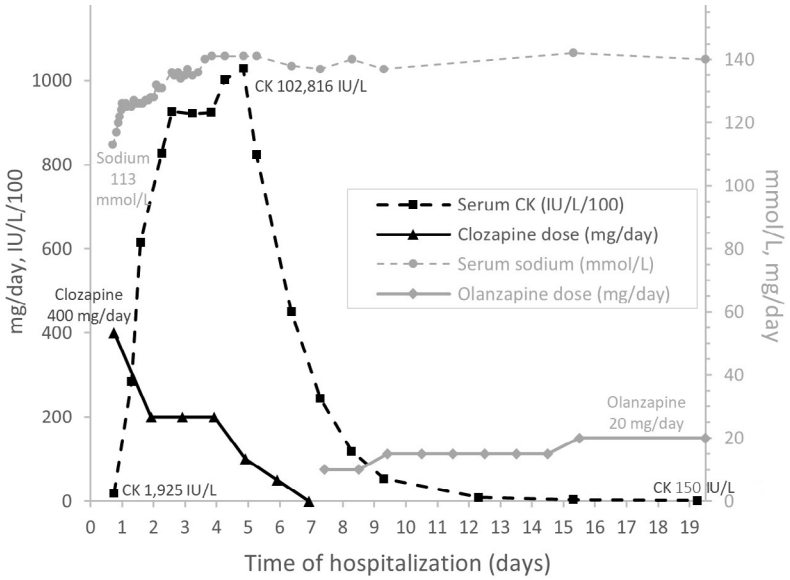

FIGURE 1. Time course of changes in the patient's doses of clozapine and olanzapine, as well as serum sodium and creatine kinase (CK) levels during the hospital stay.

not manifest any sign of seizures and had negative results on toxicology screening for alcohol and drugs. Therefore, we excluded these as potential contributing factors to the rhabdomyolysis, keeping in mind that drug testing has its limitations.

On the basis of the literature, we found a plausible relationship between the patient's medication regimen and his rhabdomyolysis. In a descriptive retrospective study, Packard and others[25] tried to establish a relationship between antipsychotics and rhabdomyolysis in patients admitted to a medical centre in Nebraska. Of the 673 cases of rhabdomyolysis, 71 (10.5%) involved patients who were taking at least 1 antipsychotic agent.[25] The exact mechanism of antipsychotic-induced rhabdomyolysis is still unclear. Two hypotheses have been proposed: serotonin antagonism increasing permeability to CK and dopaminergic blockade resulting in excessive movements and rigidity.[25] In the case reported here, recent exposure to olanzapine, paliperidone palmitate, and clozapine may have contributed to the patient's rhabdomyolysis. Because the olanzapine had been prescribed on an as-needed basis and the patient was not actually taking it, this antipsychotic will not be considered in our analysis. His last deltoid injection of 3-month paliperidone palmitate had been administered 3 months before the admission. Considering its long half-life (84 to 95 days) and the fact that only 1 half-life had passed, the significant amount of residual systemic paliperidone palmitate could have contributed to the rhabdomyolysis, as reported in the literature.[25-27] The recent introduction of clozapine might also have caused CK elevation. In the study by Packard and others,[25] clozapine was involved in 4% of the reported cases. To our knowledge, at least 7 cases specifically involving clozapine-associated rhabdomyolysis have been published.[7,16,19,28-31] In these cases, the following concomitant risk factors for rhabdomyolysis were identified: PPD, hyponatremia, seizure, lithium use, and electroconvulsive therapy.[25] Rhabdomyolysis occurred at various times after the introduction of clozapine, ranging from weeks to years. The serum CK level fluctuated between approximately 10 000 IU/L and 98 000 IU/L.[7,16,19,28-31] Discontinuation of clozapine and initiation of fluid therapy appear to have been the treatment adopted in the majority of cases.[7,16,19,28-31] All episodes of rhabdomyolysis resolved after the treatment. In 2 cases, a second episode of rhabdomyolysis occurred after a rechallenge.[29,30] Thus, it is plausible that clozapine could have contributed to rhabdomyolysis in the case reported here, even though the clozapine serum level was within the therapeutic range. There was no clozapine rechallenge in this case. Only 3 other case reports in the literature describe the combination of the same 3 contributing factors as we observed (clozapine, PPD, rapid serum sodium correction).[7,16,19] Of these, the case reported by Wicki and others[19] is the only one in which clozapine was rechallenged, and no recurrence of rhabdomyolysis was reported.

Moreover, the patient's psychiatric disorder was unstable during the gradual dose reduction of clozapine and the introduction of olanzapine, leading to psychotic agitation. Substantial psychomotor activation is also known as a potential contributor to rhabdomyolysis.[4,5]

Hyponatremia

Hyponatremia and hypo-osmolarity can cause rhabdomyolysis, which is attributable to a change in the transmembrane potential, leading to myolysis.[18]

A week before presentation to the emergency department, the patient's serum sodium was 140 mmol/L, subsequently decreasing to 113 mmol/L. PPD can lead to severe and symptomatic hyponatremia (< 120 mmol/L) in the following situations: excessive and rapid hydration (> 100 mL/kg daily), maximal urine dilution (< 100 mmol/kg of water), or additional contributing factors (e.g., syndrome of inappropriate antidiuretic hormone secretion, certain medications, malnutrition, alcohol, intrinsic renal disease).[1,32] According to Ali and Bazzano,[32] second-generation antipsychotics may also cause hyponatremia. The current medical history (i.e., development of symptoms consistent with severe hyponatremia in less than 24 hours in combination with PPD) and the laboratory results (i.e., low urine sodium, 21.0 mmol/L; dilute serum potassium, 3.1 mmol/L, and serum chlorine, 73 mmol/L; low urine osmolality, 133 mmol/kg of water; low serum osmolality, 235 mmol/kg of water) were consistent with excessive fluid intake over a short period secondary to PPD as the cause of severe hyponatremia.

The incidence of rhabdomyolysis in patients with PPD and severe hyponatremia is approximately 30% to 60%.[33,34] The first report of rhabdomyolysis associated with hyponatremia secondary to PPD was published in 1979.[6] We searched PubMed, MEDLINE, Embase (up to February 25, 2021), and the grey literature for case reports describing rhabdomyolysis with severe hyponatremia secondary to PPD. More than 20 cases, including ours, have now been reported (Table 1).[6-21,35,36] However, the underlying mechanism remains controversial. All patients in the reported cases had severe hyponatremia and serum sodium level on admission between 104 and 120 mmol/L. Among these cases, most patients were male and had a diagnosis of schizophrenia. Other contributing factors included seizures and medications (e.g., antipsychotics, lithium, valproic acid). Clozapine was used to treat schizophrenia in 4 cases, including the current case. The peak level of CK ranged from 10 642 to 102 816 IU/L between 24 and 144 hours after the diagnosis of hyponatremia. Hyponatremia was quickly managed in less than 48 hours. In rhabdomyolysis due to hyponatremia, the serum CK peak is often reached at 48 to 96 hours with a level less than 100 000 IU/L. Therefore, the high and delayed serum CK peak in the case reported here (102 816 IU/L at 116 hours) could be explained by another contributing factor: the serum sodium correction rate.[7,37]

TABLE 1. Reported Cases of PPD-Related Rhabdomyolysis and Their Contributing Factors[a]

Reference	Age (yr)	Sex	Underlying Disease(s)	Other Confounding Variables	Initial Serum Na (mmol/L)	Serum Na Correction Rate (mmol/L/h)	Na Correction Rate Considered as Contributing Factor?	Maximal Serum CK (IU/L)	Time to Reach Peak Serum CK (h)
Browne[6]	62	Male	PPD	Not described	116	0.27 (first 15 h)	Not discussed	98 000	36
Aguiar et al.[7 b]	49	Male	PPD, schizophrenia	Clozapine, risperidone	110	1.25 (first 12 h)	Yes	44 065	60
Akkaya et al.[8]	32	Male	PPD, schizophrenia	Ziprasidone, seizures	122 (at 24 h)	0.46 (first 48 h)	Yes	10 737	133
Chen et al.[9]	40	Male	PPD, schizophrenia	Paliperidone	113	0.4 (first 48 h)	Yes	30 505	NA
Dubin et al.[10]	58	Male	Schizophrenia, dyslipidemia	Zuclopenthixol, olanzapine	110	0.75 (first 24 h)	Not considered as contributing factor	26 750	24–48
Fernando et al.[11]	42	Male	PPD (possible), ureteric calculus	Convulsion	119	0.71 (first 24 h)	Not considered as contributing factor	54 841	96–120
Katsarou and Singh[12]	39	Male	PPD, bipolar disorder	Sodium valproate, risperidone, seizure	104	1.04 (first 24 h)	Yes	16 339	48–72
Korzets et al.[13]	28	Female	PPD, schizophrenia	Perphenazine, coma	109	0.67 (first 24 h)	Not discussed	72 000	72–96
Rizzieri[14]	34	Male	PPD, schizophrenia	Fluphenazine decanoate	110	0.85 (first 20 h)	Yes	> 40 000	48
Strachan et al.[15]	63	Male	PPD, bipolar disorder	Risperidone, lithium	110	0.38 (first 24 h)	Yes	10 642	NA
Tényi and Vörös[16 b]	46	NA	PPD, schizophrenia	Clozapine 400 mg/day, convulsion	113	1.125 (first 24 h)	Yes	52 090	120–144
Ting[17]	41	Male	PPD, schizophrenia	Thioridazine	113	NA	Not discussed	49 300	48
Ulstrup et al.[18]	30	Male	PPD, schizophrenia	Aripiprazole	115	0.78 (first 18 h)	Yes	29 900	48–72
Wicki et al.[19 b]	42	Male	PPD, schizophrenia	Clozapine 300 mg/day, seizures	120	1.54 (first 13 h)	Yes	62 730	68
Zaidi[20]	50	Male	PPD, schizophrenia	Ziprasidone, seizures	112	0.83 (first 12 h), 0.67 (first 24 h)	Yes	90 080	58
Ito[21]	44	Male	PPD, schizophrenia	Convulsion	110	1.6 (first 10 h), 0.67 (first 24 h)	Yes	88 400	48–72
Current report[b]	35	Male	PPD, schizophrenia	Clozapine	113	1.0 (first 12 h), 0.58 (first 24 h)	Yes	102 816	96–120

CK = creatinine kinase, Na = sodium, NA = not available, PPD = psychogenic polydipsia.
[a]Cases reported by Cronin[35] and by Sidi and others[36] are not included in this table because data were not provided by the authors.
[b]Cases involving clozapine.

Rapid Correction of Hyponatremia

A rapid rate of serum sodium correction can cause rhabdomyolysis.[16,33,34] More specifically, it can lead to the failure of cell volume regulation, which in turn results in membrane fragility and enzyme leakage.[16,33,34] Correction of hyponatremia, along with the rate of sodium correction, was considered a contributing factor to rhabdomyolysis in 70% of the cases reported in Table 1. Between 2012 and 2016, in a single-centre retrospective cohort study, Kashiura and others[34] showed that rapid correction of serum sodium was independently associated with rhabdomyolysis (defined as CK ≥ 1500 IU/L) in 56 cases of water intoxication. The median serum sodium correction was 1.15 mmol/L/h (interquartile range [IQR] 0.74–1.31 mmol/L/h) and 1.02 mmol/L/h (IQR 0.63–1.20 mmol/L/h) in the first 12 and 24 hours following admission, respectively. Among the 56 patients, 35 patients (62.5%) had rhabdomyolysis. The serum sodium level on admission was similar between patients with and without rhabdomyolysis (about 110 mmol/L). Patients with rhabdomyolysis had a higher median serum sodium correction rate in the first 12 and 24 hours than those without rhabdomyolysis (1.22 versus 0.71 mmol/L/h at 12 hours and 1.11 versus 0.60 mmol/L/h at 24 hours; $p < 0.001$). The serum CK level on admission was higher in patients with rhabdomyolysis (661 versus 215 IU/L, $p < 0.001$), which suggests that rhabdomyolysis might have occurred before admission. However, as an independent risk factor for rhabdomyolysis, the serum sodium correction rate may have contributed to the median serum CK peak of 10 323 IU/L (IQR 5775 to 35 695 IU/L) in patients with rhabdomyolysis.[34]

According to the literature, to prevent rhabdomyolysis, a serum sodium correction rate of less than 0.50 to 0.80 mmol/L/h and an increase in serum sodium of 10 to 12 mmol/L/24 h are recommended, and this approach to sodium correction should be undertaken within the first 24 hours of hyponatremia.[33,34] In the case reported here, the serum sodium increased from 113 to 126 mmol/L (a difference of 13 mmol/L) over 5 hours, and the serum sodium correction rate was 1.0 mmol/L/h for the first 12 hours after admission to hospital and 0.58 mmol/L/h for the first 24 hours after admission. These correction rates are faster than what is recommended. Consequently, rapid correction of hyponatremia could have enhanced rhabdomyolysis in this patient. Furthermore, rhabdomyolysis due to the correction of hyponatremia is often associated with a CK peak delayed over 96 hours, which was the case for this patient (CK peak 102 816 IU/L after 116 hours).

CONCLUSION

In the case reported here, the underlying cause of rhabdomyolysis could not be determined with certainty, given the multifactorial etiology of this condition. We considered several contributing factors, such as clozapine, paliperidone palmitate, psychotic agitation, severe hyponatremia secondary to PPD, and rapid correction of serum sodium. In assessing the risk of rhabdomyolysis, clinicians should be aware of the interplay of multiple factors, and serum CK level should be closely monitored when one or more of these contributing factors are identified. In addition, clinicians should be vigilant in setting the rate of correction of hyponatremia and should extend close monitoring of serum CK levels, given that the CK peak may be delayed.

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Correction to "Effectiveness and Safety of Palbociclib plus Endocrine Therapy in Hormone Receptor–Positive, HER2-Negative Metastatic Breast Cancer: Real-World Results"

Can J Hosp Pharm. 2022;75(2):128 DOI: 10.4212/cjhp.v75i2.3285

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In each of the three figures for this article, the horizontal axis showed incorrect units of time. The unit of measure for these data was months, not weeks. Data reported within the text use the correct unit of measure.

The three figures are reproduced here with the correct unit of measure. The article itself has been corrected (see DOI: 10.4212/cjhp.v75i1.3252).

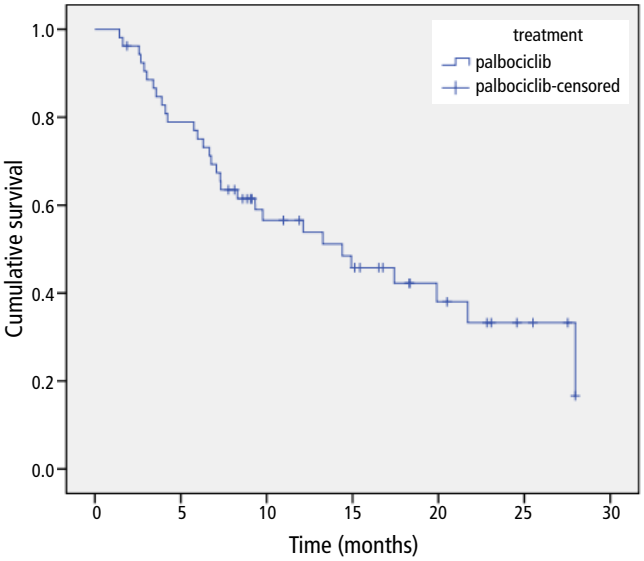

FIGURE 1. Progression-free survival of all patients treated with palbociclib.

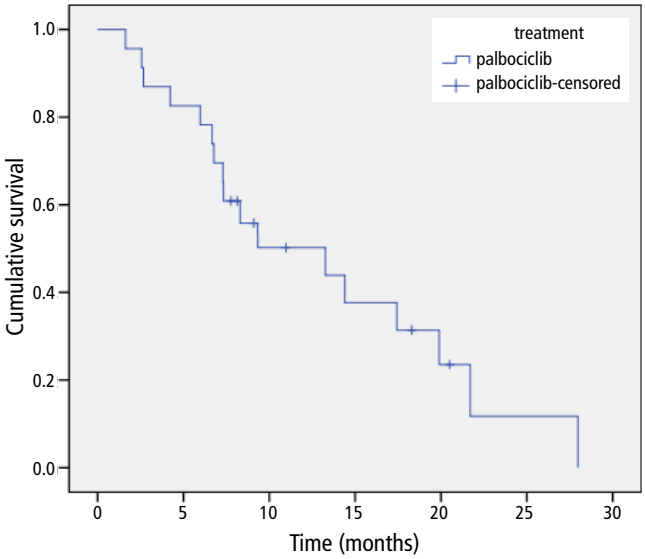

FIGURE 2. Progression-free survival of patients treated with palbociclib as second-line therapy.

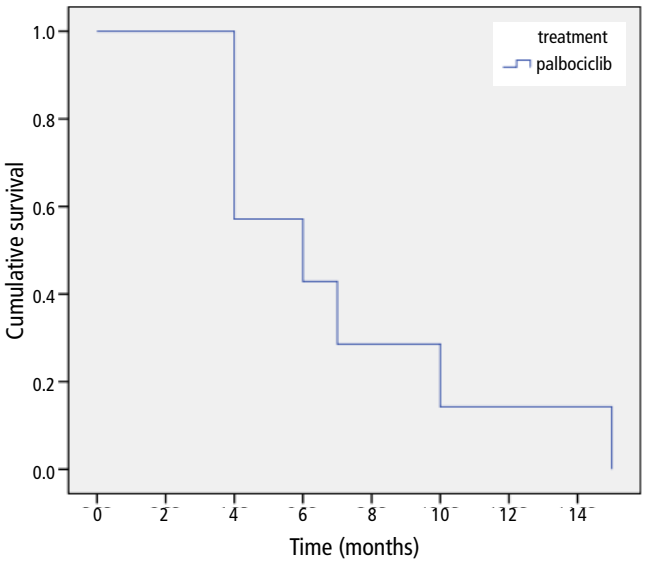

FIGURE 3. Progression-free survival of patients treated with palbociclib as third-line therapy.

2021–2022 Research, Education, and Sabbatical Grant Recipients

DOI: 10.4212/cjhp.v75i2.3298

CONGRATULATIONS TO THE 2021–2022 RECIPIENTS OF CSHP FOUNDATION RESEARCH GRANTS

Elizabeth Leung

Clinical Pharmacy Specialist Leader, St. Michael's Hospital, Unity Health Toronto

Real-world use of IL-6 inhibitors for treatment of COVID-19 during the Pandemic

Research Grant: $10,000

Facility: St. Michael's Hospital, Unity Health Toronto, Toronto, Ontario

Kerry Wilbur

Associate Professor and Executive Director, Entry-to-Practice Education, Faculty of Pharmaceutical Sciences, University of British Columbia

Social Network Analysis of Patient-Centered Pharmacist-Led Primary Care

Research Grant: $9,900

Facility: The University of British Columbia, Vancouver, British Columbia

CONGRATULATIONS TO THE 2021–2022 RECIPIENTS OF CSHP FOUNDATION EDUCATION GRANTS

Christine Peragine

Ambulatory Oncology Pharmacist, Odette Cancer Centre Pharmacy, Sunnybrook Health Sciences Centre

Complementary/Alternative Medicine and Anti-Cancer Therapy Interactions for Oncology Professionals and Patients – A Mobile Web Application

Education Grant: $4,970

Facility: Sunnybrook Health Sciences Centre, Toronto, Ontario

Theresa Schindel

Clinical Professor, College of Health Sciences, Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta

Development of a practice tool for pharmacists' experience with Medical Assistance in Dying

Education Grant: $5,000

Facility: University of Alberta, Edmonton, Alberta

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CONGRATULATIONS TO THE 2021 RECIPIENT OF THE CSHP FOUNDATION EDUCATION SABBATICAL GRANT

Certina Ho

Advisor, Medication Safety, ISMP Canada

Assistant Professor, Department of Psychiatry, Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, Ontario

Data Science Certificate Courses in the Application of Machine Learning and Artificial Intelligence to Medication Safety

Education Sabbatical Grant: $3,587

Facility: University of Toronto School of Continuing Studies

2022 CSHP NATIONAL AWARDS PROGRAM WINNERS / PROGRAMME NATIONAL DES PRIX 2022 DE LA SCPH : LAURÉATS ET LAURÉATES

The winner of the **Distinguished Service Award** (sponsored by Pharmascience Inc.) is **Glen J Pearson** (Edmonton, AB).

The winner of the **Hospital Pharmacy Student Award** (co-sponsored by the Canadian Society of Hospital Pharmacists [CSHP] and the Canadian Association of Pharmacy Students and Interns [CAPSI]) is **Christine S Vaccaro** (Winnipeg, MB).

DOI: 10.4212/cjhp.v75i2.3297

Excellence in Pharmacy Practice — Interprofessional Collaboration Award
Sponsored by **Teva Canada Limited**
Outcomes of Administering Cefazolin vs. Other Antibiotics in Penicillin-Allergic Patients for Surgical Prophylaxis at a Major Canadian Teaching Hospital (completed at Vancouver General Hospital, Vancouver, BC)
Nilufar Partovi, Tim TY Lau

Excellence in Pharmacy Practice — Leadership Award
Sponsored by **HealthPRO Procurement Services Inc.**
The Pharmacist's Role in the Hemophilia Clinic (completed at Children's Hospital of Eastern Ontario and Canadian Blood Services, Ottawa, ON)
Nisha Varughese, Sylvain Grenier, Sarah Jennings, Régis Vaillancourt

Excellence in Pharmacy Practice — Patient Care Award
Sponsored by **SteriMax Inc.**
Medication Assessment Centre Interprofessional Opioid Pain Service (MAC iOPS): A Novel Approach to Chronic Pain Management (completed at the University of Saskatchewan, Saskatoon, SK)
Katelyn Halpape, Derek Jorgenson, Eric Landry, Taylor Raiche, Amy Wiebe

The award-winning abstracts are published exactly as submitted by the authors and have not undergone any copyediting by the Canadian Journal of Hospital Pharmacy. *Le* Journal canadien de la pharmacie hospitalière *n'a pas soumis les résumés primés à une révision linguistique et les publie ici tels que remis par les auteurs.*

Outcomes of Administering Cefazolin vs Other Antibiotics in Penicillin-Allergic Patients for Surgical Prophylaxis at a Major Canadian Teaching Hospital

Excellence in Pharmacy Practice — Interprofessional Collaboration Award
Sponsored by Teva Canada Limited

Grant JM[1,2,3,4], Song W[5], Shajari S[1], Mak R[6], Meikle AT[7,8], Partovi N[9,10], Masri BA[11], Lau TTY[1,3,9,10]

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Background: Cefazolin surgical prophylaxis is associated with better patient outcomes, however, its use in penicillin-allergic patients is controversial. We evaluated safety and efficacy of cefazolin as surgical prophylaxis in penicillin-allergic patients, including those with anaphylaxis histories.

Patients and Methods: We conducted a pre-and post-intervention quality improvement evaluation of an institution-wide policy change at a tertiary-care hospital, before (October 2017–January 2018), during (February 2018–September 2018) and after (October 2018–October 2019) transition to routine cefazolin prophylaxis for penicillin-allergic patients, including those with anaphylaxis histories but excluding severe delayed reactions (e.g., Stevens-Johnson syndrome). Retrospective data was collected on all surgical prophylaxis patients with penicillin-anaphylactic histories between October 2017–September 2018. From October 2018, we prospectively reviewed adverse events with cefazolin. Primary outcome was adverse events in penicillin-allergic patients receiving cefazolin peri-operatively.

Results: From October 2017–October 2019, 27,467 surgeries were performed. Of 220 patients with penicillin-anaphylactic histories reviewed prior to full-policy change, no statistically significant differences were reported in allergic reactions (P=0.70), surgical site infections (P=1.00), or adverse events (P=0.32) with cefazolin compared to other antibiotics. Post-policy implementation, cefazolin usage increased 18.2%, while vancomycin and clindamycin decreased by 11.4% and 62.0%, respectively. No anaphylaxis was documented in penicillin-allergic patients receiving cefazolin in either the review or quality assurance follow-up after the change. Of 3 patients developing reactions to cefazolin, none had histories of penicillin allergy. Surgical site infection rates were similar between pre- and post-policy time-periods (P=0.842).

Conclusions: Administration of cefazolin in penicillin-anaphylactic patients for surgical prophylaxis appears to be safe and effective.

The Pharmacist's Role in the Hemophilia Clinic

Excellence in Pharmacy Practice — Leadership Award
Sponsored by HealthPRO Procurement Services Inc.

Varughese N[1], Grenier S[2], Wong A[1], Klassen R[3], Jennings S[2], Vaillancourt R[1]*
[1]Department of Pharmacy, Children's Hospital of Eastern Ontario, Ottawa, ON
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[3]Comprehensive Hemophilia Care Clinic, Children's Hospital of Eastern Ontario, Ottawa, ON
** At time of writing*

Background: Hospital pharmacists have traditionally not been involved with hospital blood banks or hemophilia clinics. However, coagulation factors used in the treatment of hemophilia follow complicated pharmacokinetic (pK) trajectories with tremendous inter-individual variation, and the optimal use of these products involves systematically assessing and interpreting the pK profiles of all patients. This makes hemophilia care an ideal therapeutic area for pharmacist involvement. Canadian Blood Services manages a national formulary of about 50 plasma protein and related products (PPRP) on behalf of provincial and territorial governments (excluding Quebec).

Objective: As formulary manager, Canadian Blood Services recognized an opportunity for substantial savings without compromising patient care. A pharmacist could individualize doses and regimens and switching to lower cost products when clinically appropriate.

Methods: Canadian Blood Services partnered with the Children's Hospital of Eastern Ontario (CHEO) on an innovative project integrating a pharmacist into the Hemophilia Treatment Centre (HTC). The pharmacist attended clinics, educated staff and patients, developed policies, and conducted pK evaluations.

Results: In less than one year, pharmacist interventions reduced annual treatment costs for 15 patients by $355,000. In a preliminary analysis, 1 patient had no change in bleeding events and 14 patients had fewer bleeds.

Conclusions: The results of this innovative project show promise for a new practice area for pharmacists.

Keywords: hemophilia, pharmacokinetics, pharmacists, pharmaceutical services, drug cost, formulary management

Medication Assessment Centre Interprofessional Opioid Pain Service (MAC iOPS): A Novel Approach to Chronic Pain Management

Excellence in Pharmacy Practice — Patient Care Award
Sponsored by SteriMax Inc.

Halpape K[1], Jorgenson D[1], Ahmed A[1], Johnston I[1], King J[1], Kizlyk K[1], Landry E[1], Marwah R[1,2], Raiche T[1], Walmsley T[1], Wiebe A[1]
[1]College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon, SK
[2]Family Medicine, University of Saskatchewan, Saskatoon, SK

Background: One in five Canadians experience chronic pain. Saskatchewan residents have limited access to interdisciplinary chronic pain management. The Medication Assessment Centre Interprofessional Opioid Pain Service (MAC iOPS) was created to fill this gap.

Objectives: To develop, implement, and evaluate an interdisciplinary, pharmacist-led, chronic pain clinic.

Methods: The program development and implementation included securing funding, hiring health professionals, creating a care model, and patient recruitment. Initial program evaluation includes:

1) retrospective chart audit

2) survey of patients and their healthcare professionals.

Results: The MAC iOPS was established, with federal funding, as an interdisciplinary chronic pain service in March 2020. The team includes four pharmacists, one chronic pain physician, one physical therapist, and two social workers. MAC iOPS is available to all Saskatchewan residents and services are delivered virtually or in-person. The MAC iOPS differs from traditional interdisciplinary teams in that pharmacists lead the team. The MAC iOPS does not prescribe but works with the patient's existing prescriber to implement treatment plans. Chart audit results (n=79) found reductions in mean daily morphine equivalents of 37 mg and improved Brief Pain Inventory scores of 1.3 points. Eleven patients were provided take home naloxone kits. Patient surveys (n=17) indicated that 65% of patients had improved overall health status and 94% were satisfied with their care. The health professional surveys (n=16) revealed that 100% would recommend MAC iOPS to colleagues and 69% were more confident managing chronic pain after working with MAC iOPS.

Conclusions: The MAC iOPS has improved access to interdisciplinary chronic pain management in Saskatchewan, resulting in improved overall self-reported health status of chronic pain patients, reduced opioid intake, and expanded access to take home naloxone. The service has been well received by patients and health professionals.

Keywords: interprofessional team, chronic pain, opioids

Declarations: Katelyn Halpape and Derek Jorgenson received funding from Health Canada Substance Use and Addictions Program, Indigenous Services Canada, Saskatchewan Health, and for the MAC iOPS.

Encore Presentation

TOGETHER: CANADA'S HOSPITAL PHARMACY CONFERENCE 2022 / ENSEMBLE : CONGRÈS DES PHARMACIENS D'HÔPITAUX DU CANADA 2022

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Facilitated Poster Sessions: Discussions of original research, pharmacy practice projects, and case reports.

Séance animée de présentations par affiches : Discussions sur des projets de recherche originale des projets dans le domaine de la pratique pharmaceutique et les observations cliniques.

ORIGINAL RESEARCH / RECHERCHE ORIGINALE

1. An Environmental Scan of Patient Safety Reporting and Learning Systems in Community Healthcare for Multi-Disciplinary Teams
2. A National Survey of Antimicrobial Stewardship Content in Canadian Undergraduate Pharmacy Programs
3. Characterization of Antithrombotic Regimens for Patients with Non-Valvular Atrial Fibrillation Undergoing Percutaneous Coronary Intervention
4. Characterization of Secondary Prevention Strategies after Coronary Artery Bypass Graft Surgery
5. Developing a Patient Safety Culture Training Curriculum for Healthcare Professionals
6. Defining Optimal Pharmacist Activities in Ambulatory Heart Failure Clinics Using a Modified Delphi Approach
7. Evaluating the Impact of a Clinical Pharmacist on an Acute Mental Health Unit
8. Evaluation of Rasburicase Use at Vancouver General Hospital: A Retrospective Review
9. Evaluation of Voriconazole Therapeutic Drug Monitoring in Malignant Hematology Patients
10. Exploring the Facilitators and Barriers toward the Use of Clinical Decision Support Tools by Healthcare Providers
11. Expression of Burnout Symptoms in Pharmacists Who Provide Telepharmacy Services in Canada
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13. Impact of Heparin for Umbilical Arterial Catheter on Patency and Electrolytes
14. Impact of Local Clinical Practice Guidelines for Urinary Tract Infections Treatment in a University Hospital Centre
15. Impact of Pharmacist-Led Post-Discharge Medication Reconciliation on Hospital Readmission Rates
16. Implementation of Pharmacist Competency Assessments
17. Insights into British Columbian Hospital Pharmacists' Perspectives on the Discharge Process
18. Intrapartum *Group B Streptococcus* Prophylaxis in Beta-Lactam Allergic Patients: An Interrupted Time Series Analysis
19. Meds to Beds: The Neonatal Intensive Care Unit Parent Perspective
20. Monitoring Program of Surface Contamination with 11 Antineoplastic Drugs in 122 Canadian Hospitals
21. Pharmacogenetic Testing in Pediatric Neurology: A Pragmatic Study Evaluating Clinician and Patient Perceptions
22. Portrayal of Autism Spectrum Disorder and Related Treatments in Printed Media
23. Probing Physicians' Perspectives on Pharmacist Prescribing Authority: 5P Study
24. Preliminary Results of an Intra-Hospital Study on the Reporting of Drug-Associated Adverse Events
25. Professional Identity of Hospital Pharmacists
26. Profil des décisions du conseil de discipline de l'Ordre des Pharmaciens du Québec de 1970 à 2021 : une étude descriptive
27. Physician and Nurse Practitioner Perceptions of the Routine Opioid Outcome Monitoring (ROOM) Tool
28. Revue d'utilisation des opioïdes au CHU Sainte-Justine : prescriptions émises au congé à la suite d'une chirurgie
29. Stability of Voriconazole 10 mg/mL in Isopto® Tears 0.5% Stored in Glass Vials and Low-Density Polyethylene Droppers at 4°C and 25°C for 28 Days
30. Status of Validation for Accuracy of Blood Pressure Devices Sold in Community Pharmacies in Qatar
31. The Drug Interactions between Tacrolimus and Fluconazole or Voriconazole in Heart Transplant Patients
32. The Emotional Impact of Medication-Related Patient Safety Incidents on Canadian Hospital Pharmacists: A Mixed Methods Study

TOGETHER CONFERENCE 2022 POSTER ABSTRACTS / RÉSUMÉS DES AFFICHES DU CONGRÈS ENSEMBLE 2022

PHARMACY PRACTICE / PRATIQUE PHARMACEUTIQUE

1. Customization of Order Alerts through Filters: Impact on Pharmacists' Override Rate and Perceptions of Alert Fatigue
2. Comprehensive Medication Reviews for Children with Medical Complexity
3. Decreasing Antibiotic Use in the Neonatal Intensive Care Unit by Limiting Time to Blood Culture Results to 36 Hours
4. Development and Validation of a Clinical Guide for the CannabisCareRx Program
5. Implementation of a Pharmacist-Led Proton Pump Inhibitor Deprescribing Assessment (PDA) Initiative in Complex Continuing Care Patients
6. Medication Safety Training: An Opportunity for Virtual Interactive Case System Innovation
7. Redevelopment of Clinical Orientation to Encourage Self-Reflection and Assessment
8. Working from Home for Clinical Pharmacists during the COVID-19 Pandemic

CASE REPORTS / OBSERVATIONS CLINIQUES

1. Ceftaroline Induced Neutropenia in the Setting of Methicillin Resistant *Staphylococcus aureus* Bacteremia Salvage Therapy: A Case Report
2. Dapsone-Associated Methemoglobinemia Treated with Cimetidine: A Case Report
3. Erroneous Computerized Interpretation of Corrected QT Interval and Influence on a Patient's Drug Therapy
4. Metronidazole and Mebendazole Combination Therapy for Treatment of Chronic Giardia in a Pediatric Patient with Immunodeficiency
5. Severe Pancytopenia Secondary to Azathioprine
6. Successful Use of Edoxaban for Resolution of Left Ventricular Thrombus

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ORIGINAL RESEARCH / RECHERCHE ORIGINALE

An Environmental Scan of Patient Safety Reporting and Learning Systems in Community Healthcare for Multi-Disciplinary Teams

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[2]Temerty Faculty of Medicine, University of Toronto, Toronto, ON

Background: Patient safety reporting and learning systems (RLS) have been increasingly employed globally as a tool for continuous quality improvement in healthcare via collecting, analyzing, and sharing patient safety incidents. Although multi-disciplinary RLSs are widely used in hospital practice, little is known about the current state of adoption and use of similar systems in community and primary care.

Objective(s): We collaborated with the Manitoba Alliance of Regulatory Health Colleges (MARHC) and aimed to identify multi-disciplinary, community based RLSs that have been implemented in other jurisdictions.

Methods: With assistance from a faculty liaison librarian, an environmental scan was conducted via formal and grey literature searches. The formal literature search was performed on OVID MEDLINE and EMBASE databases. Titles and abstracts of journal articles were screened for relevance according to inclusion criteria. The grey literature search involved identifying websites and publications from regulatory authorities and policy institutes with a mission on patient safety, and personal communications with subject matter experts from the Canadian Patient Safety Institute and the International Medication Safety Network.

Results: A total of 629 articles were found between 2005 and 2020, from which RLSs in British Columbia (BC, Canada) and Spain were identified. Based on expert reviews and findings of a previous New Zealand environmental scan, the United Kingdom (UK) National Reporting and Learning System satisfied most of our search criteria. A summary of lessons learned from these multi-disciplinary, community based RLSs was also prepared.

Conclusion(s): Our environmental scan returned promising results of multi-disciplinary, community based RLSs in BC, Spain, and the UK. The MARHC will benefit from further analysis and lessons learned from these RLSs as it explores a central repository for Manitoba healthcare professionals to collect and share learning from patient safety events.

Encore Presentation

A National Survey of Antimicrobial Stewardship Content in Canadian Undergraduate Pharmacy Programs

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Background: Antimicrobial stewardship (AMS) interventions to address antimicrobial resistance (AMR) require knowledgeable and empowered healthcare workers, including pharmacists. However, the degree to which AMS content is covered in Canadian undergraduate pharmacy curricula is unknown.

Objectives: To describe the current landscape of AMS instruction in Canadian undergraduate pharmacy programs, and the perceived barriers and facilitators to enhancing AMS instruction.

Methods: A cross-sectional, electronic survey was distributed to faculty representatives from Canadian undergraduate pharmacy programs. Potential participants were identified through the Association of Faculties of Pharmacy of Canada (AFPC) and included content experts and faculty leaders with intimate knowledge of the curriculum. Curriculum content questions were created using AMS learning objectives developed in the United States and AFPC role statements for pharmacy graduates.

Results: Responses were received from all 10 faculties. All programs reported teaching AMS principles in their core curricula. Content coverage was variable, with programs covering on average 68% of previously published learning objectives, and only one program covering all objectives. Learning objectives within the role statements of "communicator" and "collaborator" were least consistently taught. Three programs also offered AMS content in their elective curricula. Didactic lectures and large group discussions were the most frequently used teaching methods. Multiple choice and written answer questions were the most common student assessment methods. Experiential rotations in AMS were offered by most programs. One program reported that students learned AMS content in an interprofessional setting. Time constraints were identified by all programs as a barrier to enhancing AMS instruction, while a course dedicated to AMS, a curriculum framework, and prioritization by each faculty's curriculum committee were perceived facilitators.

Conclusion: This study highlighted opportunities to advance Canadian AMS pharmacy education. A curriculum with standardized learning objectives and educational outcomes will be essential in preparing new pharmacists to address the challenge of AMR.

Characterization of Antithrombotic Regimens for Patients with Non-Valvular Atrial Fibrillation Undergoing Percutaneous Coronary Intervention

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Background: Antithrombotic medication management in patients with non-valvular atrial fibrillation (NVAF) undergoing percutaneous coronary intervention (PCI) is challenging. While a combination of oral anticoagulant (OAC) and dual antiplatelet therapy (DAPT) is technically indicated, this significantly increases bleed risk. The optimal combination and duration of antithrombotics is an area of ongoing research, and local prescribing patterns are unknown.

Objectives: To characterize antithrombotic regimens prescribed locally for patients with NVAF after a PCI with stent placement.

Methods: A retrospective chart review was completed on patients with NVAF indicated for OAC according to CHADS65 algorithm, who received PCI with stent. Primary outcome was description of OAC and antiplatelet therapies prescribed at discharge. Secondary outcomes included duration of antiplatelet therapy.

Results: A total of 131 patients discharged between December 2015 and November 2020 were included. At discharge, 50 (38.2%) patients received dual therapy, 40 (30.5%) received triple therapy, and 36 (27.5%) received DAPT. Rivaroxaban + Clopidogrel and Warfarin + Clopidogrel + ASA were the most common regimens used for dual therapy and triple therapy respectively, accounting for 42% and 53% each. OAC was not prescribed in 39 (29.8%) patients. The median durations for P2Y12 inhibitors and ASA were 1 year and 1 month respectively for triple therapy. For patients discharged on dual therapy, ASA was used in 68% post-PCI in hospital for a median duration of 2 days.

Conclusion: Local prescribing patterns closely aligned with the Canadian Cardiovascular Society guidelines. Adoption of new literature was evidenced by increasing favor of dual therapy over triple therapy or DAPT, and warfarin over DOACs from 2015 to 2020.

Encore Presentation

Characterization of Secondary Prevention Strategies after Coronary Artery Bypass Graft Surgery

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Background: Coronary artery bypass grafting (CABG) is a durable treatment for ischemic heart disease however, patients remain at risk of cardiovascular events due to progression of underlying coronary artery disease (CAD) and graft occlusion. Fortunately, evidence-based therapies exist to improve graft patency and reduce adverse cardiovascular events following surgery.

Objective: The aim of this study is to characterize the management of patients undergoing CABG surgery at Sunnybrook Health Sciences Centre (SHSC), both at discharge, and upon follow-up with a cardiologist and cardiac surgeon.

Methods: In this retrospective chart review, the charts of 74 patients admitted to SHSC for CABG between January 2017 and August 2020 were analyzed to characterize discharge recommendations and post-discharge follow-up. Descriptive statistics were used to analyze the data.

Results: Discharge summaries followed a standardized format and were complete with most pertinent information, including required follow-up appointments (>95%) and lab work (>70%) with respective timeframes. Prescribing rates of evidence-based therapies were high, with the exception of RAAS blockers and dual antiplatelet therapy, however there was high alignment with SHSC-specific antiplatelet guidelines for type of CABG (on- vs. off-pump). Follow-up data revealed that patients were seen by cardiologists and cardiac surgeons later than anticipated. Cardiologists made medications changes in 63% of patients, with RAAS blockers accounting for most changes. Surgeons made relatively fewer changes (26%) which focused on adjustment of antiplatelet agents.

Conclusion: Overall, discharge summaries for patients undergoing CABG at SHSC are highly standardized. Although prescribing rates of evidence-based therapies were generally high, there is opportunity to reassess the SHSC antiplatelet policy to delineate management of patients undergoing CABG electively or for acute coronary syndromes. Patients were seen by specialists later than the intended timeframe specified on discharge, highlighting a potential role for pharmacist-led virtual medication reconciliations to bridge the gap in care.

Developing a Patient Safety Culture Training Curriculum for Healthcare Professionals

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Background: As part of the World Health Organization (WHO)'s Global Patient Safety Action Plan for 2021–2030, establishing and maintaining a good safety culture is an indispensable prerequisite for the adoption of any safety initiatives. However, there is currently a paucity of ready-to-use, easy-to-translate patient safety culture training materials or guidelines for regulatory or health professional bodies to apply across a diversity of healthcare settings.

Objective(s): Our project is aimed to develop a translatable patient safety culture curriculum to support a multi-disciplinary provincial regulatory authority in Manitoba in advocating patient safety culture and leading province-wide patient safety initiatives.

Methods: A structured grey literature search, with support from a faculty liaison librarian, was performed to find relevant guiding documents from patient safety organizations, including those in the United Kingdom (UK), Canada, United States (U.S.), Australia, and New Zealand. We identified websites of regulatory authorities and policy institutes with a mission on patient safety, then located relevant documents on these sites via targeted Google search. Materials were synthesized through extracting overlapping competencies relevant to patient safety culture.

Results: Four patient safety guiding documents were identified from: UK (National Health Service), Canada (Canadian Patient Safety Institute), U.S. (International Health Institute), and WHO, from which a course syllabus was synthesized with a total of 5 competencies and 21 learning objectives, ranging from Organization Culture to Safety Leadership. We adopted Bloom's taxonomy and segregated the learning outcome domains into knowledge, skills, and attitude in the resulting Patient Safety Culture Training Curriculum for Healthcare Professionals.

Conclusion(s): Our syllabus, which was presented to key stakeholders of patient safety in Manitoba, serves as a primer for subsequent application and evaluation of educational content. The area of patient safety culture education is one that calls for further concerted efforts and innovations from all health professions and global jurisdictions.

Defining Optimal Pharmacist Activities in Ambulatory Heart Failure Clinics Using a Modified Delphi Approach

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Background: Heart failure (HF) is a major cause of morbidity and mortality. Pharmacist involvement in ambulatory HF management reduces morbidity, however strategies described in the literature vary widely. As such, attention must be given to defining optimal activities for pharmacists in this setting in order to optimize outpatient HF care.

Objective: To define optimal activities of pharmacists in ambulatory HF clinics.

Methods: Twenty-nine Canadian ambulatory HF clinic pharmacists participated in a modified Delphi approach, consisting of 3 iterative surveys. Participants were asked to rank a list of 44 candidate activities on 2 selection criteria, each on a 9-point Likert scale. Between survey rounds, participants were provided with aggregate group results alongside their respective individual responses. Consensus was defined as ≥75% of participants ranking both selection criteria ≥7 on the 9-point Likert scale. Descriptive statistics, including frequencies and percentages, were used to describe the Likert scale data.

Results: Of the 29 participants, 27 and 23 were retained on rounds 2 and 3 of the Delphi surveys, respectively. Of the 44 candidate activities for pharmacists in ambulatory HF clinics, 33 were included based on consensus. Consensus activities spanned a range of domains including patient assessment, medication management, patient education, and operations and administration.

Conclusion: A consensus list of 33 optimal activities for pharmacists in ambulatory HF clinics was defined. These results should be used to direct future involvement of pharmacists in ambulatory HF clinics as well as expand pharmacist scope of practice.

For the figure that goes with this abstract, please see Abstract Appendix, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/208

Evaluating the Impact of a Clinical Pharmacist on an Acute Mental Health Unit

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Background: Clinical pharmacists have a significant role in optimizing pharmacotherapy for patients admitted to acute care settings. Patients with mental health disorders are especially vulnerable to polypharmacy, adverse drug effects, medication non-adherence, and misconceptions about medication use. The Royal University Hospital currently lacks resources to provide optimal clinical pharmacy coverage for mental health inpatients.

Objectives: To evaluate the impact of a clinical pharmacist providing specialized care to patients on the Mental Health Short Stay Unit (MHSSU) at the Royal University Hospital in Saskatoon, SK.

Methods: A pharmacist with five years of mental health related pharmacy practice experience was temporarily assigned to MHSSU as a practical component of a pharmacy Master's program. Clinical activities to be completed by the pharmacist were defined based on available evidence, existing performance and quality assurance indicators, and prior experience. The pharmacist's activities and recommendations were tracked during each shift and the results are reported.

Results: Ninety-four patients were seen in 88 hours. There were a total of 61 recommendations made with a 90% psychiatrist acceptance rate and 42 medication changes initiated by the pharmacist. Forty-one patients (44%) received a thorough medication assessment, and 41% of patients were provided with individualized, and often specialized, education. The pharmacist was consulted by the psychiatrist 19 times.

Conclusion: Pharmacists have an important role in medication management and patient education for psychiatric inpatients, and the health care team relies on pharmacists' unique expertise. Additional resources dedicated to expanding and defining clinical pharmacy services on inpatient psychiatry units could further optimize patient care.

Encore Presentation

Evaluation of Rasburicase Use at Vancouver General Hospital: A Retrospective Review

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Background: Rasburicase is used to prevent and treat acute tumor lysis syndrome (TLS), a onco-metabolic emergency syndrome. Due to previous non-formulary status at Vancouver General Hospital (VGH), use criteria for rasburicase was implemented in 2010 by the Leukemia/Bone Marrow Transplant program (L/BMT). Rasburicase was since added to the provincial hospital formulary as unrestricted and the change in resulted in inconsistencies in prescribing practice and dispensing by pharmacy. A standardized evidence-based approach for rasburicase prescribing is needed.

Objective: The primary objective of this study was to determine the adherence of rasburicase utilization in relation to the pre-established use criteria. The secondary objectives included characterization of patient factors associated with non-adherence.

Methods: This was a retrospective chart review at VGH, using a convenience sample of 100 patients. Inclusion criteria included patients 17 year of age or older who received one or more doses of rasburicase at VGH from June 1, 2018 to November 30, 2020. Descriptive statistics and statistical analysis were conducted using Chi-squared and Student's t-test, where appropriate to compare patient factors.

Results: Overall, 13 of the 100 patients met the rasburicase use criteria. Majority of the non-adherence prescribing were for prevention (53%), TLS (22%), and non-criteria-based use (12%). Patients who met criteria were more like to be from L/BMT service, while preventative use was likely related to high tumor burden and ability to start chemotherapy within 72 hours. There were no differences in outcomes of renal replacement therapy within 7 days, seizures, arrhythmia, or ICU admissions across any of the subgroups. Patients with TLS were associated with a higher mortality rate.

Conclusion: The majority of the rasburicase used at VGH did not meet pre-established L/BMT use criteria. Most prescribers used rasburicase for preventative purposes. An updated use criteria has been proposed to promote optimal drug use and prescribing.

Evaluation of Voriconazole Therapeutic Drug Monitoring in Malignant Hematology Patients

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Background: Malignant hematology (MH) patients are susceptible to invasive fungal infections due to prolonged neutropenia and may require voriconazole therapy. Although voriconazole therapeutic drug monitoring (TDM) is common, evidence describing this practice is limited.

Objective: To describe the current practice of voriconazole TDM in MH patients at Princess Margaret Cancer Centre (PM).

Methods: A retrospective chart review was conducted for MH inpatients started on voriconazole at PM between November 1st, 2019 and November 13th, 2020. Voriconazole doses, levels, dose changes, and adverse effects were collected. The primary endpoint was the proportion of patients with initial voriconazole levels within therapeutic range (1-5 mg/L).

Results: Fifty-six patients were included in the study. The most common reason for starting voriconazole was possible invasive fungal infection, which included 44 (78.6%) patients. Fifty-one patients (91.1%) received a loading dose of voriconazole, averaging 386.5 ± 78.5 mg. The average maintenance dose was 242.1 ± 45.7 mg. An average of 2.6 ± 2.9 levels were drawn per patient with an average level of 3.2 ± 2.4 mg/L. Forty-one patients (73.2%) had an initial voriconazole level within therapeutic range. Fifty-five of 145 total levels (37.9%) were outside therapeutic range and 51 (92.7%) of them resulted in an intervention. Of these, 31 (60.8%) had a dose adjustment, 12 (23.5%) were held, and 8 (15.7%) were discontinued. For the 31 dose adjustments, 26 (83.9%) had a level redrawn and 17 (65.4%) of those levels were within therapeutic range. Twenty-three (41.1%) patients developed adverse effects, 8 (34.8%) of which had supratherapeutic levels. Nineteen (33.9%) patients experienced transaminitis, 3 (5.4%) experienced transaminitis and neurotoxicity, and 1 (1.8%) experienced photopsia.

Conclusion: Overall, 73.2% of patients achieved an initial voriconazole level within therapeutic range and 62.1% of total levels drawn were within therapeutic range, suggesting opportunities to optimize current approaches to voriconazole TDM.

Declarations: Jacqueline Flank received speaker/consulting fees from Jazz Pharmaceuticals. Samantha Polito received speaker fees from Novartis for a prior presentation. Karen Yee received research funding from Astex Pharmaceuticals, Forma Therapeutics, F. Hoffmann La-Roche, Genentech, Geron, Janssen Pharmaceuticals, Jazz Pharmaceuticals, MedImmune, Novartis, Onconova Therapeutics, and Tolero Pharmaceuticals. She is a consultant for Astex Pharmaceuticals, Bristol-Myers Squibb/Celgene, F. Hoffmann La-Roche, Novartis, Otsuka, Paladin, Pfizer, Shattuck Labs, Taiho Pharmaceutical and Takeda. She also received an honorarium from AbbVie and Novartis.

Exploring the Facilitators and Barriers toward the Use of Clinical Decision Support Tools by Healthcare Providers

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Background: Clinical decision-support (CDS) tools are systems that provide healthcare professionals (HCPs) with recommendations based on knowledge and patient-specific factors to facilitate informed judgments.

Objectives: To identify the key components of a CDS tool that are most important to HCPs in caring for older adults with a renal diagnosis, and to understand the facilitators and barriers toward using CDS tools in daily clinical practice.

Methods: An anonymous, online, cross-sectional survey of Canadian HCPs who were affiliated with a provincial college, nephrology organization, or advocacy body was conducted in September 2021. A 12-question (59-items) questionnaire was composed of a mix of question types to cover the main themes of the study.

Results: Sixty-three participants completed the questionnaire. Physicians (60%) and pharmacists (22%) composed the majority of the participants, most of them were specialized in nephrology (65%), family medicine (16%) and geriatrics (11%). The most important components in a CDS tool were the safety and efficacy of the medication (89%), the goal of therapy (89%), and patient's quality of life (87%). Forty percent agreed that time was not a barrier to use CDS tools in daily practice, as 90% were willing to use them and 57% are already using some CDS tools for prescribing. The majority of participants agreed that the value of CDS tools is their ability to assist in making decisions based on evidence-based medicine (91%) and agreed that they help in discussing decisions with patients (81%). The majority of the participants agreed that the validation of CDS tools (95%), accompanying the recommendations by the supporting evidence (84%), and the affiliation of the tools with known organizations (84%), were factors that facilitate the use of CDS tools.

Conclusion: CDS tools are being used and accepted by HCPs and are valued for their assistance in engaging patients in making well-informed decisions.

Declaration: Sherilyn Houle is on the advisory board/speaker bureau for AstraZeneca, Seqirus, and GlaxoSmithKline.

Expression of Burnout Symptoms in Pharmacists Who Provide Telepharmacy Services in Canada

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Background: Burnout is a syndrome based on the concept that chronic stress experienced by a person in their workplace remains unmanaged. The high prevalence of burnout reported in health care professionals can have negative consequences that affect individuals, patients, health teams, and institutions.

Objectives: The primary objective was to describe burnout symptom expression in Canadian pharmacists who work from home to provide Telepharmacy services using the Maslach Burnout Inventory-Human Services (MBI-HSS) tool encompassing 3 domains: emotional exhaustion (EE), depersonalization (DP) and personal accomplishment (PA). The secondary objective was to compare each domain's total score between work-related pharmacy practice and sociodemographic characteristic groups.

Methods: A cross-sectional study was conducted using a convenience sample of responses from pharmacists who had provided Telepharmacy services in Canada for at least 4 weeks prior to study initiation. We invited 120 pharmacists to take an anonymous electronically deployed survey comprised of the MBI-HSS and questions on work-related pharmacy practice and sociodemographic characteristics. Descriptive and inferential analyses were performed.

Results: The survey achieved a 63% (75/120) participation rate, representing full-time, part-time and casual tele-pharmacy employment from their home offices. Overall, EE (range 0-60, 60 the highest expression of burnout) had a median total score of 17 (IQR 7.5-26), DP (range 0-16, 16 the highest expression of burnout), median total score of 2 (IQR 1-4.5), and PA (range 0-50, with 0 being the highest expression of burnout), median total score of 39 (IQR 32.5-43.5). Significant associations with burnout symptom expression, positive and negative, in each of the 3 domains were found with work-related pharmacy practice and sociodemographic characteristics.

Conclusions: Compared to reported literature across various areas of pharmacy practice, burnout symptoms in Tele-pharmacists who work from home are lower. Both professional work-related and sociodemographic factors may have a positive or negative impact on burnout in Tele-pharmacists.

Declaration: Paula Newman is employed by Northwest Telepharmacy Solutions.

Hospital Pharmacists' Experience with Medical Assistance in Dying

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Background: Pharmacists have been involved in medical assistance in dying (MAiD) practice in Canada since 2016 and in various international jurisdictions for over two decades. Despite their involvement, little is known about pharmacists' actual experiences with MAiD. The experiences of pharmacists whose practice already encompasses MAiD will contribute to understanding pharmacists' roles and supporting others in adopting this practice in other countries.

Objective: To investigate pharmacists' experiences with MAiD practice in the hospital setting.

Methods: Semi-structured interviews were conducted with pharmacists that had cared for patients seeking MAiD. The interviews were digitally recorded and transcribed verbatim. A framework analysis approach was used to analyze data. Analysis included coding of data and identification of themes through an iterative process involving constant comparison. Data were managed and stored using Quirkos and Microsoft Excel software.

Results: A total of 19 hospital pharmacists representing a range of practice experience and settings in Alberta participated in the study between June 2019 and October 2020. Three themes illuminated participants' experiences with MAiD: 1) finding a place, 2) serving in a patient-centred role, and 3) bearing emotional burdens. Several considerations influenced pharmacists' decisions to participate in MAiD. The role focused on medication supply and documentation, yet it was experienced as a caring, patient-centred role. Opportunities to expand involvement beyond the medication-related responsibilities were welcomed by some participants. The experiences were associated with a range of emotions, both positive and negative. Participants described supports and actions taken to ease emotional burdens.

Conclusions: The results of this study will inform pharmacists, including those who are contemplating participation in MAiD practice, about the range of experiences associated with assisted dying practice. Pharmacy leaders may apply these results to further support pharmacists and expand pharmacists' roles in MAiD.

Declaration: Theresa J Schindel received funding from the CSHP Foundation.

Impact of Heparin for Umbilical Arterial Catheter on Patency and Electrolytes

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Background: In the Neonatal Intensive Care unit, umbilical arterial catheters (UACs) with heparin infusion are commonly used. Heparin infused through these lines reduces the risk of occlusion and thrombosis, though can cause electrolyte abnormalities, nutritional compromise and death. Heparin infusion concentrations and diluents currently vary between centers.

Objectives: To determine if the local heparin dosing guidelines provided heparin doses within the target of 10 to 50 units/kg/day, if the dose affected patency duration and if a relationship existed between heparin dose, serum electrolytes, and time to 100 mL/kg of feeds.

Methods: Chart review from January 1, 2015 to December 31, 2020 for neonates that received heparin in 0.45% sodium chloride via UAC, with catheter insertion and removal at the site. Descriptive and correlation statistics were used to summarize the data.

Results: Chart review occurred for 302 neonates and 222 were included. The average rate of heparin was 12.9 units/kg/day (range 3.4 to 30.8 units/kg/day). UACs were electively removed for 91%. Average patency duration was 113.5 hours. There was a moderate positive correlation between heparin dose and patency duration (r=0.44). There was a weak correlation between heparin dose and serum sodium levels (r=0.225), with moderate negative correlation between serum sodium levels and gestational age (r=-0.582) or birthweight (r=-0.557). The heparin dose did not correlate with the serum chloride or bicarbonate levels. There was a weak positive correlation between heparin dose and time to 100 mL/kg of feeds (r=0.305).

Conclusion: The dose of heparin given via UAC impacts the duration of patency and the time to reach 100 mL/kg of enteral feeds. The dose of heparin in 0.45% sodium chloride does not appear to impact the serum chloride or bicarbonate levels. Further research is needed to find the minimum heparin dose for UAC patency while allowing nutrition to be optimized.

Impact of Local Clinical Practice Guidelines for Urinary Tract Infections Treatment in a University Hospital Centre

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Background: Treatment of urinary tract infections (UTI) often leads to use of broad-spectrum antibiotics such as fluoroquinolones (FQ). Many antimicrobial stewardship initiatives aim at reducing prescription rate of this class of antimicrobials.

Objective(s): The primary objective was to assess the impact of local clinical practice guidelines publication on empirical treatments of UTI in adults admitted at the CHU de Québec-Université Laval.

Methods: Pre- and post-intervention evaluative study was conducted. Medical records of patients 18 years old or more admitted for cystitis or acute pyelonephritis (APN) between Jan 1st and Dec 31st, 2016 (pre-intervention) and between Jan 1st and Dec 31st, 2019 (post-intervention) were reviewed. Patients who received less than 24h of antibiotics and those with complex infections (e.g., nephrostomy) were excluded. Wilcoxon Mann-Whitney and Pearson Chi Square tests were used for quantitative and qualitative variables respectively.

Results: Conformity with local recommendations for UTI treatment increased in post-intervention period with 38,6% (64/166) appropriate empirical treatments according to guidelines versus 25,8% (46/178) in pre-intervention period (p = 0,012). FQ prescription rate did not differ between periods: 26,4% (49/178) pre- vs 22.3% (37/166) post-intervention (p = 0,26). However, we observed a reduction in total median treatment duration: 7 days (IQR 5-10) post-intervention versus 8 days (IQR 7-12) pre-intervention (p = 0,019). The reduction in median treatment duration was more significant in patients with APN: 13 (IQR 10-14) vs 10 (IQR 9-13.5) days (p = 0,006). Hospital length of stay remained unchanged between periods.

Conclusion(s): Although the publication of a local guide for the treatment of UTI resulted in improved conformity of empirical treatments and shorter treatment duration, significant reduction in the prescription of FQ was not observed.

Impact of Pharmacist-Led Post-Discharge Medication Reconciliation on Hospital Readmission Rates

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Background: Hospital readmissions in high-risk patient populations are common, costly, and often preventable. Pharmacists play an invaluable role in identifying drug-related problems and may have a significant impact in reducing preventable readmissions.

Objective(s): The aim of this study was to evaluate the impact of pharmacist-led post-discharge medication reconciliation on hospital readmission rates.

Methods: A retrospective chart review was conducted in Sunnybrook Academic Family Health Team patients who were admitted to Sunnybrook Health Sciences Centre from January 1, 2016 to December 31, 2019 with an index diagnosis of high-risk conditions including acute myocardial infarction, chronic obstructive pulmonary disease, or heart failure exacerbation; or any index diagnosis with existing co-morbid diabetes mellitus or chronic kidney disease. Patients who received medication reconciliation by a pharmacist within 14 days of discharge were compared to patients who did not receive this service. The main outcomes included 30- and 180-day readmissions, emergency department (ED) visits within 180 days, time to first readmission, and the number and type of discrepancies identified by the pharmacist through medication reconciliation.

Results: A total of 100 patients were included in this study; 38 in the medication reconciliation group compared to 62 in the control group. Among patients who received post-discharge medication reconciliation, there was a nonsignificant reduction in 30-day readmission rates (8% vs. 15%; p=0.53) and 180-day readmission rates (26% vs. 37%; p=0.28). There was no significant difference in ED visits or the time to first readmission between groups. The median number of discrepancies identified per medication reconciliation was 2, and the most common types of discrepancies identified were needs additional therapy and medication adverse event.

Conclusion(s): In conclusion, in this small retrospective study, pharmacist-led post-discharge medication reconciliation did not significantly reduce hospital readmission rates in the studied population.

Implementation of Pharmacist Competency Assessments

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Background: The pharmacist's role in optimizing medication use and patient outcomes requires specific knowledge and skills. Best practices for assessing this competence are uncertain.

Objectives: To determine if a pharmacist competency assessment program is feasible and acceptable.

Methods: The Pharmacist Skill Development Work-With is a competency assessment program within the pharmacy department, where pharmacists present a patient case or complete patient care activities, which a leadership team member evaluates using a competency rubric and provides feedback. Pharmacists could complete up to two assessments – one each of centralized and decentralized clinical services), and evaluators could evaluate multiple assessments. A within-site post-evaluation electronic survey adapted from a validated tool regarding perceptions of program feasibility and acceptability was emailed to the pharmacist following each competency assessment and to evaluators at study conclusion. Feasibility was also measured through reviewing rubrics for completion in the 2-hour assessment timeframe. Descriptive statistical analyses were calculated utilizing Microsoft Excel.

Results: Seventeen pharmacists completed a total of 20 competency assessments and seven evaluators provided feedback. Of the 26 post-evaluation surveys completed (18 [69%] by pharmacists, eight [31%] by assessors), respondents agreed or completely agreed that the competency assessments seem possible (89%), implementable (77%), doable (77%), easy to use (77%), they meet respondents' approval (85%), are welcomed (81%), liked (62%), and were appealing (58%). The time required and resources available were acceptable (69% and 84% agreed or completely agreed, respectively). Ten (50%) assessments were not completed in the allotted timeframe; five rubrics and seven feedback sessions were completed after this timeframe. Participants noted the assessments provided professional development and unique learning opportunities, but challenges included time and rubric convenience (e.g., not electronic).

Conclusion: The competency assessment program was acceptable and feasible; however, barriers regarding time and convenience persist, requiring modification and further study for sustainability.

Encore Presentation

Insights into British Columbian Hospital Pharmacists' Perspectives on the Discharge Process

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Background: Transitions of care represent a vulnerable time for patients. Unintended therapeutic changes are common and inadequate communication of information frequently results in medication errors. Further, more than half of hospital readmissions that occur within 30 days of discharge are avoidable. Pharmacists have a large impact on the success of patients during these care transitions; however, their role and experiences are largely absent from the literature.

Objectives: The purpose of this study was to gain a greater understanding of British Columbian hospital pharmacists' perceptions of the hospital discharge process and their role in it.

Methods: A qualitative study utilizing focus groups and key informant interviews of British Columbian hospital pharmacists was conducted from April to May 2021. Questions asked during interviews were developed following a detailed literature search and includes questions regarding the use of frequently studied interventions. Interview sessions were transcribed and then thematically analyzed using both NVivo software and manual coding.

Results: Three focus groups with a total of 20 participants and 1 key informant interview were conducted. Six themes were identified from the analysis: (1) overall perspectives; (2) important roles of pharmacists in discharges; (3) patient education; (4) barriers to optimal discharges; (5) solutions to current barriers; and (6) prioritization. Patient medication education, communication with other healthcare providers, post-discharge phone calls, and pharmacist led completion of discharge prescriptions and medication reconciliation were felt to be fundamental discharge interventions. Overall, time and resources were seen as the greatest barrier to optimal patient discharges.

Conclusions: Pharmacists play a vital role in patient discharges but due to limited resources and inadequate staffing models they are often unable to be optimally involved. Increased participation of pharmacists in transitions of care has the potential to improve quality of patient care and safety by reducing medication errors and adverse drug event related readmissions.

Intrapartum *Group B Streptococcus* Prophylaxis in Beta-Lactam Allergic Patients: An Interrupted Time Series Analysis

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Background: Pregnant women colonized with *Group B streptococcus* (GBS) are treated with penicillin G during delivery to reduce the risk of early-onset GBS disease in newborns. Growing evidence suggests that cefazolin can be safely given in those with IgE-mediated hypersensitivity reaction to penicillin due to a structurally dissimilar side chain. Despite this evidence, non-beta-lactam antibiotics (i.e., clindamycin and vancomycin) continue to be commonly prescribed for those with reported penicillin allergy.

Objective: The objective of this study is to evaluate the impact of revised order sets with antibiotic selection guidance (implemented on July 22, 2020) on appropriate antibiotic use in individuals with a reported beta-lactam allergy requiring GBS prophylaxis.

Methods: This is an interrupted time series analysis which included obstetric patients with beta-lactam allergies requiring GBS prophylaxis between April 2019 and July 2021 at Sunnybrook Health Sciences Centre. Patients were divided into pre-intervention (April 1, 2019–July 21, 2020) and post-intervention (July 22, 2020–July 31, 2021) groups. Data were collected retrospectively. Appropriateness was determined based on allergy history (type of beta-lactam and reaction) and the established side chain cross-reactivity risk. Monthly proportion of appropriate antibiotic use was analyzed using a Statistical Process Chart (p-chart).

Results: The study included 140 patients; 88 patients in the pre-intervention period and 52 patients in the post-intervention period. The proportion of patients receiving appropriate antibiotics was above the baseline median (53%) in 11 of the 12 post-intervention months, signifying special cause variation for improvement. Beta-lactam use significantly increased from 61% (54/88) in the pre-intervention period to 87% (45/52) in the post-intervention period (p=0.002). Drug-related hypersensitivity reactions were reported for one individual during the pre-intervention period and none in the post-intervention period.

Conclusions: Implementation of revised order sets significantly improved appropriate antibiotic prescribing and beta-lactam use in obstetric patients with beta-lactam allergies requiring GBS prophylaxis.

Meds to Beds: The Neonatal Intensive Care Unit Parent Perspective

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Background: Current literature describes medication concierge programs focused on patient outcomes. However, the impact of such programs on parents of infants in the Neonatal Intensive Care Unit (NICU) during transition home is lacking.

Objective: To describe the NICU parent experience related to discharge medication use, following implementation of a Meds to Beds program.

Methods: A qualitative descriptive study was utilized to explore parent experiences around medication use during the transition home. Eleven parents whose infants required prescription medications at time of transition home from a Level III NICU consented to participate in a semi-structured telephone interview post-discharge. The data was transcribed verbatim then coded line-by-line by study investigators with assistance from qualitative analysis software QSR NVivo. Data was analyzed using qualitative inductive content analysis to derive themes.

Results: Major themes nested within key stages of medication use in preparation for transition home from the NICU were identified: in-hospital preparation (practice early and often, Meds to Beds, and relationship with NICU clinical pharmacist), transition home (schedule and routine, strategies for medication administration) and post-discharge (refills and long-term medication management). Parents expressed that the Meds to Beds program increased confidence and knowledge around medications and reduced stress. Areas of improvement based on parent experiences include: empowering parents to prepare and administer medications prior to discharge, strategizing with parents around new home routines, incorporating medication therapy for fragile infants, post-discharge communication with parents to strategize concerns, and NICU pharmacist coordination of community compounding services and refills at community pharmacies, amongst others.

Conclusions: We provide a summary of parent experiences and insights, and based on this insight, suggest opportunities for system-level improvement. Great opportunities remain, from a medication perspective, to refine the transition home. Implementing any of these strategies could provide significant impact on patient care and parental stress during this crucial transition.

Encore Presentation

Monitoring Program of Surface Contamination with 11 Antineoplastic Drugs in 122 Canadian Hospitals

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Background: Occupational exposure to antineoplastic drugs can lead to long-term adverse effects on workers' health. Environmental monitoring is conducted once a year, as part of a Canadian monitoring program.

Objectives: To describe contamination with 11 antineoplastic drugs measured on surfaces in a monitoring program.

Methods: Twelve standardized sites were sampled in each hospital, six in oncology pharmacy and six in outpatient clinic. Samples were analyzed by high performance mass coupled liquid chromatography. The limits of detection (in ng/cm²) were: 0.0006 for cyclophosphamide; 0.001 for docetaxel; 0.04 for 5-fluorouracil; 0.0004 for gemcitabine; 0.0007 for irinotecan; 0.0009 for methotrexate; 0.004 for paclitaxel, 0.009 for vinorelbine, 0.02 for doxorubicine, 0.0037 for etoposide and 0.004 for the platinum (optional). The online REDCap® platform was used to collect centers' data.

Results: Hospitals sampled their surfaces from January 20th to June 8th, 2021. One hundred twenty-two Canadian hospitals participated. One thousand four hundred twelve compliant samples were analyzed. The antineoplastic drugs most frequently measured on surfaces were cyclophosphamide (451/1412, 32%) and gemcitabine (320/1412, 23%). The 90th percentile of the concentration measured on the surfaces was 0.0160 ng/cm² for cyclophosphamide and 0.0036 for gemcitabine. Less than 7% of surfaces were contaminated with the other nine drugs. The surfaces most frequently contaminated with at least one drug were the front grille inside the biological safety cabinet (BSC) (97/121, 80%), the armrest of patient treatment chair (92/118, 78%) and the floor in front of the BSC (79/121, 65%).

Conclusion: Traces of low concentration antineoplastic drugs persist on the surfaces of Canadian centers. This monitoring program allowed centers to benchmark their contamination with pragmatic contamination thresholds derived from the Canadian 90th percentiles. Problematic areas need corrective measures such as decontamination. The program helps to increase the workers' awareness and led to the creation of a community of practice in Quebec.

Pharmacogenetic Testing in Pediatric Neurology: A Pragmatic Study Evaluating Clinician and Patient Perceptions

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Background: Pharmacogenetics is an exponentially growing field; however, its integration into clinical practice has been limited to date. Pediatric epilepsy patients, in particular, could potentially benefit from pharmacogenetic testing as up to 40% of epilepsy patients are refractory to their initial treatment and children are generally more susceptible to adverse effects than adults.

Objectives: The primary objective of this study is to evaluate clinicians' perception of pharmacogenetic testing. Patients' and community pharmacists' perceptions are also evaluated in order to assess all participants in the clinical pharmacogenetic testing process.

Methods: This pragmatic prospective observational study comprises of mixed qualitative and quantitative methods. Neurologists from the study center were given access to pharmacogenetic tests for epilepsy patients with a follow up appointment within the study period. Three evaluation methods were used: 1) hospital pharmacists and neurologists participated in focus groups regarding pharmacogenetic testing; 2) patients who received pharmacogenetic testing completed surveys to assess their perception of these tests; and 3) community pharmacists responded to a survey on their perception of these tests. The documentation of test results was also measured.

Results: Most study participants had a positive view of pharmacogenetic testing. Three major themes were identified from the focus groups: receptiveness to pharmacogenetic testing, pharmacogenetic test characteristics and integrating pharmacogenetic tests into practice. Clinicians generally

consider that pharmacogenetic tests were relevant to their practice and the result reports were understandable. However, for these tests to become more commonly used in practice, reimbursement by insurance, an organizational structure to ensure cohesive use of test results and clinical decision support are necessary.

Conclusion: The views reported in this study are encouraging for the eventual implementation of pharmacogenetic tests in practice. Local integration of these tests is an essential step to eventually improve patient care and safety on a broader scale through personalized medicine.

Declarations: MA Pépin, AS Otis, Z Tremblay, M Boulé, and ME Métras received a PrecisionRx test from Dynacare ($200 value) with the objective to better understand the pharmacogenetic testing process for the present study. D Lebel participated in the Advisory Board of the Canadian Pharmacogenomics Network for Drug Safety. B Carleton received a grant from the Genomic Applications Partnership Program from Genome Canada, which requires an industry partner (Dynacare Next). JF Bussières received a grant from the Canadian Pharmacogenomics Network for Drug Safety. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the abstract apart from those disclosed.

Portrayal of Autism Spectrum Disorder and Related Treatments in Printed Media

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Background: Although considerable progress in the diagnosis and treatment of autism spectrum disorder (ASD) has emerged over the last decade, negative media stereotypes about ASD and its treatments are amongst the most socially limiting stigma experiences reported by mental health service consumers and family members.

Objective(s): The main objectives of this study were to have a better understanding of the written media portrayal of ASD in Qatar, and to evaluate its influence on the public's understanding of ASD and its treatments.

Methods: A retrospective, quantitative, and qualitative content analysis of articles printed in Qatar's English and Arabic newspapers over one year was used. Quantitative descriptive analysis was employed to examine the extent of ASD media coverage. The qualitative analysis used a pre-determined coding approach derived from an extensive review of the literature to examine the discourse tone and assess the stigmatization of the main messages on the text. Articles discussing ASD treatments were analyzed separately, by reviewing the scientific evidence as outlined in the Qatar and the American Academy of Pediatrics (AAP) ASD treatment guidelines.

Results: A total of 178 ASD-related articles were found in 1 year of published articles. The quantitative analysis revealed that the overall attractiveness of ASD-related articles was poor, the majority were in relation to general news or local events and had a limited focus on the scientific aspects of this condition or its treatments. The discourse analysis revealed significantly more stigmatizing statements in articles in Arabic compared to those published in English newspapers. Based on current practice guideline recommendations, the majority of the ASD treatments discussed had insufficient or lacked scientific evidence.

Conclusion(s): Results from this study suggest that there is a need to improve how the print media addresses ASD. More scientific and responsible writing is needed, particularly when recommending treatments for this condition.

Encore Presentation

Probing Physicians' Perspectives on Pharmacist Prescribing Authority: 5P Study

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Background: Pharmacists' scope has expanded over the last decades in Nova Scotia (NS). Most recently, NS pharmacists were granted prescribing authority for uncomplicated cystitis, herpes zoster and contraception. Previous research has evaluated pharmacist perceptions and comfort with pharmacist prescribing, but scarce research exists assessing physicians' perspectives. This study investigated family physicians' perspectives on pharmacist prescribing.

Objectives: Determine physicians' comfort levels concerning pharmacist prescribing for uncomplicated cystitis, herpes zoster, and contraception, identify concerns and demographic factors associated with concerns.

Methods: A questionnaire was distributed online to family physicians in NS. Using a 5-point Likert scale, physicians indicated their comfort level with pharmacist prescribing, specific concerns, and perceived impact on patients, practice, and the healthcare system. Differences in comfort level were compared with Chi-square and one-way ANOVA. Thematic analysis was conducted on free-text responses.

Results: Overall, 131 (10.1%) NS family physicians responded. Most were uncomfortable with pharmacist prescribing for uncomplicated cystitis (79.4%), herpes zoster (66.4%), and contraception (79.4%). Concerns included diagnosis (70.2%), patient assessment (67.1%), unnecessary prescribing (61.1%) and documentation for physician records (58.0%). Comfort with prescribing for uncomplicated cystitis increased when physicians worked with pharmacists at least weekly compared to monthly (p=0.007). Major themes from physicians highlighted concerns that pharmacist prescribing may lead to misdiagnosis and inappropriate prescribing, pharmacist training is inadequate to complete a thorough clinical examination for diagnosis, and that pharmacist prescribing is an infringement on the physician scope of practice.

Conclusion: Family physicians in NS are uncomfortable with pharmacist prescribing. This partly stems from misconceptions about pharmacist training and scope. This data will help pharmacy organizations implement pharmacist prescribing and provide insight for physician education needs about the pharmacist scope.

Preliminary Results of an Intra-Hospital Study on the Reporting of Drug-Associated Adverse Events

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Background: Since December 2019, hospitals in Canada are required by Vanessa's Law to report all serious adverse events (AEs), e.g., life threatening. However, according to an international study, only 5% of AEs are reported to health authorities (e.g., Health Canada); the latter cannot

appropriately assess the risks-benefits ratio of drugs commercialized in Canada. This proportion remains unknown in Canada.

Objective: To investigate the proportion of AEs reported to Health Canada before and after Vanessa's Law.

Methods: We are conducting a descriptive study at Institut universitaire de cardiologie et de pneumologie de Québec-Université Laval. Five cohorts of 250 adult patients (n = 1250) who were hospitalized between 01/01/2018 and 12/31/2022 are included. Descriptive analyzes (median [minimum-maximum]; proportions) will help us to characterize the sample (sex, age, main diagnosis of hospitalization, length of stay, etc.), the drugs taken as well as AEs that occurred.

Results: So far, most patients were hospitalized for diseases of the circulatory (59–64%). The median length of stay was 3 days [min-max:<1-186 days]. The characteristics of the 99 patients in the 2018 cohort, our preliminary data, from which data have been extracted are: 48% female; median age: 74 years [min: 29-max: 93], body mass index: 27.4 kg/m^2 [19.1-46.7], number of comorbidities: 5 [2-26]. During their hospitalization, patients took 15 different drugs [6-28] and the number of AEs per patient was 4 [0-18]. None of these AEs have been reported to Health Canada.

Conclusion: Based on our preliminary data, no AEs were reported to Health Canada before the Vanessa's Law. Following complete data extraction (2022), it will be possible to assess the impact of the Vanessa's Law on AEs reporting. If Vanessa's Law is not an effective solution to improve the reporting of AEs, alternative solutions will have to be found to improve population safety related to drugs.

Professional Identity of Hospital Pharmacists

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Background: The question "So what do you do as a pharmacist?" would elicit a diverse number of responses — not only because of differences in training and various practice settings, but also due to an absence of a cohesive professional identity. Previous studies exploring pharmacists' professional identities have described many different roles. Currently, there is limited information on the professional identity of pharmacists practicing in hospital settings.

Objective(s): To identify hospital pharmacists' professional identity and to compare and contrast it to the professional identity of pharmacists practicing in other settings. To identify what changes in the culture and beliefs are necessary to enable hospital pharmacists to practice to their full scope.

Methods: This was a qualitative study that utilized key informant interviews with semi-structured interview questions. Maximum variation of sampling strategy was used to recruit a cross-section of pharmacists from different geographical areas in British Columbia who practiced in a variety of different roles. Questions asked during the interview were developed from a detailed literature search. Interviews were transcribed and were thematically analyzed.

Results: Nineteen pharmacists participated in the study. Seven themes pertaining to hospital pharmacists' professional identity were generated. These themes were medication expert, therapy optimizer, collaborator, educator, researcher, patient advocate, and unknown professional. Similarities between personas identified in community pharmacists were found. The ideal pharmacist was described as being a medication expert, collaborator and leader. The ideal practice setting was characterized as having collaboration opportunities, expanded pharmacist scope and adequate funding for staffing.

Conclusion(s): Hospital pharmacists' professional identity is based on being the medication expert who is seen as an essential member of a collaborative team. When compared to community pharmacists, hospital pharmacists identified with a less business oriented, dispensary-based practice.

Profil des décisions du conseil de discipline de l'Ordre des Pharmaciens du Québec de 1970 à 2021 : une étude descriptive

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Contexte : En vertu du Code des professions, le conseil de discipline d'un ordre professionnel saisi et juge toute plainte formulée contre un pharmacien pour une infraction aux lois et règlements encadrant l'exercice de la pharmacie. Au 31 mars 2021, l'Ordre des pharmaciens du Québec (OPQ) comptait 9859 membres.

Objectif : Décrire le profil des décisions rendues par le Conseil de discipline de l'OPQ (CDOPQ).

Méthode : Étude descriptive rétrospective portant sur les décisions rendues par le CDOPQ de janvier 1970 à juin 2021. Les éléments suivants ont été codifiés par décision : année, numéro de permis, sexe de l'intimé, région, nombre de chefs d'infraction et de culpabilité, infractions recodées selon neuf thématiques et 35 libellés, nombre de mois de radiation, valeur totale des amendes.

Résultats : 1488 décisions ont été revues et codifiées (32±24/année) avec un top-10 annuel décroissant en 1980 (n=127, 9%), 1976 et 1978 (n=79, 5%), 1975 (n=64, 4%), 1988 (n=66, 4%), 2011 (n=57, 4%), 1977 et 1984 (n=49, 3%), 2020 (n=45, 3%) et 1990 (n=41, 3%). Les décisions portaient sur des pharmaciens (n=561, 38%), des pharmaciennes (n=255, 17%) ou le sexe n'était pas spécifié (n=672, 45%). Une majorité (n=1005, 68%) des décisions permettait d'identifier le pharmacien impliqué avec son numéro de permis. Les principaux libellés d'infractions (>5% des chefs d'accusation) étaient : erreurs de dispensation (n=287, 19%), absence de pharmacien sur place (n=214, 14%), publicité professionnelle (n=167, 11%), vente de médicaments de l'annexe I sans ordonnance (n=93, 6%) et omission d'analyser le dossier pharmacologique (n=90, 6%). La médiane de la somme des amendes imposées par année civile était de 134 642$ [min : 200$ en 1974; max : 630 500$ en 2011].

Conclusion : Chaque année, un nombre limité de pharmaciens sont reconnus coupables d'une infraction aux lois et règlements encadrant l'exercice de la pharmacie. Une diversité d'infractions a été identifiée.

Physician and Nurse Practitioner Perceptions of the Routine Opioid Outcome Monitoring (ROOM) Tool

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Background: The Routine Opioid Outcome Monitoring (ROOM) Tool was developed and validated in community pharmacies in Australia. It facilitates pharmacists' screening and brief interventions regarding an individual's opioid use for chronic pain. An adapted version was piloted at University Health Network's outpatient pharmacies. The tool's value to prescribers caring for patients living with chronic pain who are prescribed opioids is unknown.

Objectives: The primary objectives were: 1) identify prescribers' perspectives on aspects of the tool that facilitates its use in clinical practice; 2) identify barriers and limitations to the integration of the tool into their practice. The secondary objective was to identify perspectives on the impact of the tool on patient care and safety.

Methods: The study involved focus groups with prescribers from the Toronto Western Hospital Family Health Team. These participants work in a setting where they may receive a ROOM Tool. Qualitative content analysis of transcripts was performed to identify themes.

Results: Six prescribers were interviewed and themes were organized into the following categories. *Facilitators*: comprehensive and valuable information, enables collaboration between pharmacist and prescriber, integrated mode of communication, ease of use; *Barriers*: lack of clarity regarding action items for prescribers, form too long, administrative and communication barriers, perceived redundancy in healthcare provider roles; *Recommendations*: optimize content and format, enhance pharmacist brief interventions; *Impact on patient care and safety*: prioritize population at greatest risk, optimize pharmacist role and expertise in improving safe patient care, harm reduction.

Conclusion: The ROOM Tool has potential value in supporting pharmacist collaboration with prescribers to improve care for patients who are prescribed opioids for chronic pain. There are opportunities to refine the tool which may increase its utility to prescribers, and may enhance the impact on patient care and safety.

Declaration: Christine Papoushek is a member of the advisory board/ speaker bureau of the Canadian Stroke Best Practice Advisory Committee.

Revue d'utilisation des opioïdes au CHU Sainte-Justine : prescriptions émises au congé à la suite d'une chirurgie

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Contexte : Au cours des 20 dernières années, l'augmentation de mésusage des opioïdes prescrits chez les jeunes a été corrélée avec l'augmentation du nombre de prescriptions d'opioïdes. Une portion importante des prescriptions est destinée au soulagement de la douleur postopératoire. Le profil de prescription est mal connu.

Objectif : Décrire le profil des prescriptions remises au congé à la suite d'une chirurgie.

Méthode : Revue rétrospective. Inclusion : Prescriptions des patients âgés de moins de 18 ans, naïfs aux opioïdes, du 1er avril au 31 août 2021. Sélection du plus grand nombre de chirurgies et de prescripteurs différents. Profil décrit à l'aide des caractéristiques suivantes : présence de coanalgésie, détails de la posologie, précision de la quantité maximale permise, format et type de prescripteurs.

Résultats : Cent-cinquante prescriptions ont été incluses: orthopédie (n=34; 23%), plastie (n=34; 23%), ORL (n=34; 23%), urologie (n=33; 22%), neurochirurgie (n=8; 5%), gynécologie (n=7; 4%). La morphine était l'opioïde le plus prescrit (n=141; 94%) et une coanalgésie était prévue sur 146 (97%) des prescriptions. Le nombre de prescriptions permettant un écart de doses est de 15 (10%) ou un écart d'intervalle est de 64 (43%). Le nombre de prescriptions avec un intervalle régulier est de 7 (5%) ou au besoin est de 143 (95%). La quantité maximale était précisée en comprimés ou en millilitres de solution sur 18 (12%) ou en nombre de doses maximales sur 127 (85%); la durée maximale était précisée sur 24 (16%) des prescriptions. Le nombre de prescriptions pré-rédigées est de 72 (48%) et la quantité totale est exprimée en lettres sur 49 (33%) des prescriptions. Les prescripteurs étaient majoritairement des résidents (n=89; 59%).

Conclusion : Différentes pratiques de prescription sont observées. La description des prescriptions pourra servir de point de départ de discussion sur les possibilités d'optimisation avec les équipes cliniques.

Stability of Voriconazole 10 mg/mL in Isopto® Tears 0.5% Stored in Glass Vials and Low-Density Polyethylene Droppers at 4°C and 25°C for 28 Days

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Background: Voriconazole ophthalmic drops are used for the treatment of deep or superficial fungal eye infections. There is no stability data for voriconazole in Isopto Tears 0.5%.

Objective: To evaluate the stability of voriconazole 10 mg/mL reconstituted with Isopto Tears 0.5% over 28 days at 4°C and 25°C in the original glass vials and low-density polyethylene (LDPE) eye dropper bottles.

Methods: On day 0, 12 vials of 200 mg voriconazole were reconstituted with 19mL of Isopto tears 0.5%. Six were retained in the original glass vials and six were transferred into sterile LDPE droppers. Three containers of each type were stored at 4°C and 25°C. Concentration and physical inspection were completed on study days 0,1,3,7,10,14,21 and 28.

Results: Samples stored at 4°C remained clear and colourless for the 28-day period. However, samples stored at 25°C developed flocculation on day 1 that remained throughout the study. The analytical method separated degradation products from voriconazole such that the concentration was measured specifically, accurately (deviations from known averaged 1.78%) and reproducibly (replicate error averaged 0.85%). Multiple linear regression revealed significant differences in percent remaining due to day (p=0.003), but not temperature (p=0.94) or container (p=0.77). Analysis of variance did not identify significant differences in percent remaining due to temperature (p=0.95), study day (p=0.26), or container (p=0.79). The study was capable of detecting a <1% difference in percent remaining due to study day, container or temperature. The calculated beyond use date exceeded 28 days for both temperatures and containers.

Conclusions: We conclude that 10 mg/mL voriconazole in Isopto Tears 0.5% is chemically stable for at least 28 days at 4°C and 25°C in the original glass vial and LDPE droppers. We recommend storage at 4°C to minimize microbial growth and due to physical incompatibility when stored at 25°C.

Declaration: William Perks is a consultant to Medisca. There are no conflicts of interest to declare with respect to this project.

Status of Validation for Accuracy of Blood Pressure Devices Sold in Community Pharmacies in Qatar

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Background: Digital blood pressure (BP) devices sold in community pharmacies are commonly used for home blood pressure monitoring. Devices validated for accuracy are important for management of hypertension. Non-validated devices are more likely to be inaccurate and could potentially lead to poor BP control and compromise patient-safety.

Objectives: We wanted to 1) determine the proportion of validated BP devices sold in community pharmacies in Qatar and 2) to determine the relationship between the validation status of devices and cuff location and price.

Methods: We visited 28 community pharmacies including the 2 major pharmacy chains in Qatar. The following data were collected about BP devices: brand/model, validation status on the package, cuff location, and price. Validation status was checked in an internationally recognized registry on automated BP monitors (Medaval: https://medaval.ie/blood-pressure-monitors/). Descriptive and inferential statistics were used as appropriate.

Results: A total of 83 distinct models of BP devices from 19 different brands are sold in Qatar community pharmacies. The majority are upper arm devices (76%) while the rest are wrist devices (24%). Among all models, only 36% are validated while an equal proportion is not validated. Thirty five percent of upper-arm devices and 40% of wrist devices are validated. Importantly, 41% of lower priced (QAR 250-500) devices are not validated while 60% of higher priced (QAR 501-750) devices are validated (P<0.01). Among 31 devices indicated as "not validated" on medaval.ie, packages of 16 of these devices indicated they were validated. The validation status for 22% of the devices is under audit while information was not available for 4 devices.

Conclusions: A high proportion of BP devices sold in community pharmacies are not validated for accuracy, a finding that has the potential to compromise patient safety. Pharmacists should advocate for the clinical use of validated BP devices.

The Drug Interactions between Tacrolimus and Fluconazole or Voriconazole in Heart Transplant Patients

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Background: Transplant patients undergo prolonged immunosuppression and are at risk of acquiring fungal infections. Tacrolimus, an immunosuppressor used in heart transplant patients, as CYP3A4 substrate, is frequently involved in drug interactions with antifungals. The azole antifungals increase tacrolimus serum concentrations, putting patients at risk for toxicities. Thus, to improve pharmaceutical care of patients, the impacts of these interactions on the doses of tacrolimus must be better characterized.

Objective(s): The main objective was to investigate the drug interaction between azole antifungals and tacrolimus in heart transplants patients treated at IUCPQ-UL, specifically comparing potential changes in tacrolimus dosage when an azole antifungal is used concomitantly.

Methods: This study used a longitudinal descriptive design with retrospective data collection including heart transplant patients who received concomitant azole antifungals (fluconazole or voriconazole) and tacrolimus for 5 days or more. Serum concentrations of tacrolimus were analyzed at 3 times before, 9 time during and 3 times after the antifungal treatment.

Results: Preliminary data included 22 heart transplant patients who received fluconazole-tacrolimus (n=13) or voriconazole-tacrolimus (n=9) drug combinations. When combined with voriconazole treatment, the doses of tacrolimus were initially reduced by 33%. Serum levels of tacrolimus increased more with voriconazole than with fluconazole (p = 0.0001). Among the 9 patients using voriconazole and tacrolimus, 8 required further dose reduction to maintain tacrolimus concentrations within goal of targeted level. On average, a cumulative reduction of 75% in the dosage of tacrolimus was necessary to maintain serum concentrations within goal.

Conclusion(s): This study documented larger variations in tacrolimus serum concentrations when used in combination with voriconazole than with fluconazole. Although they need further validation upon completion of the study, these preliminary results suggest that closer attention should be given to dosage adjustments, potentially mounting to an average reduction of 75% in the tacrolimus dose when voriconazole is used concomitantly.

Declaration: Julie Methot received funding from the foundation of the Institut universitaire de cardiologie et de pneumologie de Québec—Université Laval.

The Emotional Impact of Medication-Related Patient Safety Incidents on Canadian Hospital Pharmacists: A Mixed Methods Study

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Background: Patient safety incidents are cited as the third leading cause of death in Canada. These occurrences have negative consequences for patients and the wellbeing of healthcare professionals as well as adding a financial burden on the healthcare system. Several organizations focus on minimizing patient safety incidents, however an area requiring additional research is evaluating the emotional impact of medication-related patient safety incidents (MRPSIs) on Canadian hospital pharmacists. This research project aims to describe the psychological burden on pharmacists when facing MRPSIs and identify supportive strategies.

Medication-related patient safety incident (MRPSI): a preventable, unintended outcome that was the result of medication management as opposed to an underlying disease. Consequences may result in no harm, temporary harm, prolonged hospital stays, disability or death.

Objectives:

1. Describe the emotional impact of MRPSIs on Canadian hospital pharmacists;
2. Identify factors influencing Canadian hospital pharmacists' emotional burden following MRPSIs;
3. Identify current and desired support strategies that can assist hospital pharmacists with their emotional burden following MRPSIs.

Methods: This mixed methods study included a voluntary survey of hospital pharmacists (N=179) and structured individual interviews (N=18). Survey respondents scored their emotional distress on the Impact of Events Scale (IES), a validated self-reported tool used to assess the impact of traumatic life events. Interviewees' responses were analyzed qualitatively.

Results: Eighty-two percent of pharmacists had a significant score (>8) on the IES, indicating that the MRPSI was an impactful event. Commonly reported factors contributing to the event were heavy workload, interruptions and inexperience. The most desired support strategies included: talking to a colleague, compassionate notification of the event through management and involvement in team debriefs.

Conclusions: Emotional impact reported by Canadian hospital pharmacists is significant. The majority of participants felt that increased support to overcome emotional burden related to MRPSIs is needed.

PHARMACY PRACTICE / PRATIQUE PHARMACEUTIQUE

Customization of Order Alerts through Filters: Impact on Pharmacists' Override Rate and Perceptions of Alert Fatigue

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Background: Clinical decision supports (CDS) in electronic medication order systems help identify important alerts for clinicians. However, CDS may cause alert fatigue. Alert fatigue is the tendency for clinicians to ignore prompts presented by CDS due to excessive numbers and/or their perceived limited clinical significance. Alert fatigue may increase the risk of missing important alerts and decrease work efficiency.

Description: At North York General Hospital, pharmacists managed over 50% of all medication CDS alerts amounting to approximately 60 alerts per day per pharmacist. Pharmacists' override rate was over 90% indicating a high likelihood of alert fatigue. As such, we decided to attempt to reduce pharmacists' alert fatigue.

Action: Utilizing a visual analytics dashboard, high frequency alerts were tabulated with type, volume and override rate. With this data and discussions with pharmacists, three targeted interventions were designed and implemented to suppress non-significant alerts for duplicate orders and drug interactions.

First, a filter to suppress duplicate checking for specific medications ordered multiple times in one session. Second, a filter targeting selected medications commonly ordered both as scheduled and as needed. Lastly, we customized how long discontinued drugs are eligible for CDS checking.

Evaluation: After implementation, alerts decreased from 59.7 to 27.1 alerts per day per pharmacist. Pharmacists perceived a reduction of unnecessary CDS alerts and found they had more time to review alerts. Review of medication incidents found no increase in medication errors after changes. However, override rate was minimally reduced from 98.1% to 97.3%. Most pharmacists surveyed felt that there was still room for improvement in the CDS system.

Implications: Customization of CDS filters can be an effective strategy to reduce non-meaningful alerts without increasing medication errors. It is imperative that hospital pharmacies review alert data and re-assess CDS settings periodically to manage non-clinically significant alerts to minimize pharmacists' alert fatigue.

Comprehensive Medication Reviews for Children with Medical Complexity

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Background: Children with medical complexity (CMC) are at increased risk for drug-related adverse events due to polypharmacy, complicated regimens with specialized dosage forms, multiple prescribers, and a lack of pediatric-specific evidence regarding safe and effective drug therapy. CMC stand to benefit from comprehensive medication assessment, but clinical pharmacist services were limited to inpatient care at BC Children's Hospital (BCCH).

Description: The Complex Care program at BCCH provides coordinated care for CMC. Our goal was to incorporate a pharmacist into the Complex Care outpatient program and provide comprehensive medication reviews.

Action: The Pharmacy Department provided one half-day per week of pharmacist services. Patients were scheduled for a virtual appointment in the weeks before their annual comprehensive review with Complex Care. The pharmacist met with the patient/family to gather medication history, identify and resolve drug therapy issues, and provide education. A written medication history and recommendations were provided to the Complex Care team, primary care provider, and patient/family.

Evaluation: Over the 38 weeks of this program to date, 24 patients attended appointments and five cancelled or did not attend. The most common drug therapy issues identified were adverse effects (46% of patients), unnecessary drug therapy (33%) and insurance coverage (33%). The most frequent interventions were education about drug therapy and medication safety (63% and 54% respectively), and stopping a medication or changing its dose (38% each). A satisfaction survey of families is in progress and expected to have results in the coming weeks.

Implications: The high frequency of drug therapy issues identified demonstrates the need for pharmacist assessment of CMC outside the acute inpatient setting. In addition, duplication of effort collecting medication history was avoided, allowing other clinicians to focus on different aspects of care. The introduction of this pharmacist role has facilitated high-quality, longitudinal care for CMC.

Decreasing Antibiotic Use in the Neonatal Intensive Care Unit by Limiting Time to Blood Culture Results to 36 Hours

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Background: Many infants in Neonatal Intensive Care Units (NICU) receive empiric broad spectrum antibiotics because of high infection risk. However, most of these infants do not suffer from actual bacterial infections. Antibiotic over-use in neonates risks the development of antibiotic-resistant bacteria as well as short- and long-term adverse events related to early-life microbiome perturbations. Sunnybrook Health Sciences Centre's (SHSC) NICU-Antimicrobial Stewardship Program (NICU-ASP) and Division of Microbiology collaborated to reduce the NICU's antibiotic usage rate (AUR) by 20% over 2 years by implementing a change to facilitate earlier antibiotic discontinuation based on neonatal blood culture results reported at 36 hours rather than 48 hours.

Description: A Plan-Do-Study-Act (PDSA) cycle was designed to measure the effect of earlier blood culture reporting, from 48 to 36 hours. AUR was an outcome measure. Late bacterial infections, a balancing measure.

Action: Time to positivity data for all neonatal blood culture results was collected and collaboratively analyzed for 1 year. After reviewing this data with all stakeholders and providing unit-wide education, a practice change was implemented to reduce neonatal blood culture reporting time to 36 hours.

Evaluation: By basing the decision to discontinue antibiotics on a 36-hour rather than a 48-hour blood culture result, SHSC's NICU was able to decrease AUR by a relative 28% (15.8 to 11.3 antibiotic days per 100 patient days), over a span of 2 years. Despite discontinuing antibiotics sooner, the incidence of late bacterial infection was not impacted (6.9% to 6.4%). Identified challenges include a delay in blood culture reports due overnight and a lack of an automated mechanism to stop antibiotics.

Implications: By shortening the time to receive blood culture reports from 48 hours to 36 hours, SHSC's NICU was able to reduce antibiotic use by 28% over 2 years without any increase in late bacterial infections.

Development and Validation of a Clinical Guide for the CannabisCareRx Program

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Background: Pharmacists are uniquely positioned to provide integrated care to the one-quarter of people in Canada who report using cannabis. A reported lack of comfort with their own cannabis-related knowledge is one of the barriers limiting this role.

Description: This project aimed to develop and validate a cannabis-focused clinical guide to support pharmacists in the delivery of a novel integrated care program, CannabisCareRx.

Action: We developed a cannabis-focused clinical guide by consolidating and adapting existing resources and clinical expertise. It was designed with suggested phrasing to minimize stigma and a motivational approach to behavior change. We included the best available clinical information to support pharmacists to gather information, assess risk, review drug interactions, provide brief interventions (including harm reduction, product selection and dose titration), make referrals, and provide follow-up.

Evaluation: Nine pharmacists participated in virtual interviews to rate content relevance, assess face value, and provide recommendations for improvement as part of an iterative 3 round process with 3 participants per round. Participants rated aspects of the guide using a Likert scale to determine face validity. We performed thematic content analysis to summarize participant feedback. Content validity scores improved after revision. Over 89% of participants rated each face validity statement as "agree" or "strongly agree". Thematic content analysis revealed strengths (e.g., valuable information, patient-centered approach, logical flow) and areas for improvement (e.g., clarity of pharmacist role/action, process for collaboration with primary care provider, format).

Implications: A cannabis-focused clinical guide to support pharmacists in the delivery of integrated care was developed and evaluated. Content validity of the clinical guide neared universal agreement and face validity was high. A planned pilot implementation of the cannabis-focused clinical guide in pharmacies as part of the CannabisCareRx program will contribute to the iterative development process.

Declarations: Avery Loi received funding from the Canadian Foundation for Pharmacy Innovation Fund. Andrea Furlan received an unrestricted educational grant to maintain the online opioid self-assessment program from the Canadian Generic Pharmaceutical Association. The funding organization has no role in the preparation, approval, or data analysis of the course content. Responsibility for the course content is solely that of authors. Maria Zhang developed a CCCEP accredited program for cannabis education to Ontario pharmacists through the University of Toronto.

Implementation of a Pharmacist-Led Proton Pump Inhibitor Deprescribing Assessment (PDA) Initiative in Complex Continuing Care Patients

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Background: Proton pump inhibitors (PPIs) are one of the most commonly prescribed drugs with between 40% and 65% of hospitalized patients in the United States and Australia respectively lacking documented indication for PPI therapy. There are a number of adverse effects associated with continued PPI use such as impaired vitamin B12 absorption, hypomagnesemia, *Clostridium difficile* infection, and fractures. The Canadian Deprescribing Network published recommendations to reduce unnecessary use of PPIs. PPI deprescribing is stopping or decreasing the dose of a patient's PPI with the intent of reducing medication burden and chances of developing adverse effects in a supervised process.

Description: The objective of this pharmacy practice study was to evaluate and implement a PPI deprescribing assessment (PDA) for hospitalized complex continuing care patients at a community hospital led by a pharmacist.

Action: The pharmacy team in collaboration with the utilization committee developed the PDA based on published evidence-based guidelines. The deprescribing rate, refractory patients who required re-initiation of a PPI, and number of PPI doses were tracked pre- and post-implementation.

Evaluation: In the 4 sites of the hospital where PDAs were implemented, 179 PDAs were completed. Of that, 163 (91%) recommendations by the pharmacist were accepted by the most responsible prescriber (MRP). From the PDAs completed, 58 patients (32%) were deprescribed successfully, 8 patients (5%) required step-up therapy after initially being deprescribed, and 113 patients (63%) had no change in their PPI therapy.

Implication: Approximately one third of hospitalized patients admitted into complex continuing care on a PPI did not meet indication for chronic PPI therapy. Deprescribing unnecessary PPI resulted in the reduction of medication burden, cost, and a decreased risk of the downstream adverse events. A targeted deprescribing approach, such as the PDA, was an effective practice and promotes future deprescribing efforts in other therapeutic areas.

Medication Safety Training: An Opportunity for Virtual Interactive Case System Innovation

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Background: Current literature on virtual cases illustrates increased student self-directed learning and satisfaction. Yet, the use of virtual cases has not been explored in the context of patient or medication safety.

Description: The Virtual Interactive Case (VIC) System allows educators to create online clinical reasoning scenarios with a bridge between theory and practice. We aimed to share our experience in the development and evaluation of 3 VIC teaching modules on patient or medication safety.

Action: We created VIC training modules on medication incident disclosure, root cause analysis (RCA), and failure mode and effects analysis (FMEA). We piloted tested them during the COVID-19 pandemic.

Evaluation: We administered a 16-item online questionnaire from May 22, 2020, to June 8, 2020 and obtained feedback from pharmacy students and practitioners in Ontario, Canada. Most of our 18 respondents had 1-5 years of practice experience. Their practice settings ranged from associations, academia, to community pharmacies and hospitals. Respondents found the VIC platform easy to navigate. They perceived the content to be relevant and easy to implement in patient care settings. Majority of them indicated that they were confident in carrying out incident disclosure, RCA, and FMEA at their practice settings.

Implications: The VIC System can be used to educate students and practitioners on patient or medication safety. It is a safe and user-friendly platform to support patient safety in virtual pharmacy care.

Encore Presentation

Redevelopment of Clinical Orientation to Encourage Self-Reflection and Assessment

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Background: A provincial Clinical Orientation (C.O.) has been offered to all new pharmacists in our organization to ensure consistent orientation to clinical practice since 2010.

Description: In 2018, revisions to the C.O. program helped address changes in the pharmacy curriculum and scope of practice, increased diversity in experience of new hires and the desire for our pharmacists to build upon skills in self-reflection and self-directed learning alongside their peers.

Action: The overarching goal of the new framework was to develop a foundation of clinical knowledge and skills through facilitated discussions, peer support, reflection and self-assessment. The desired outcomes were to help increase confidence, integration and the formation of peer-to-peer linkages. The three half-day virtual sessions include the following topics: Clinical Vision and Expectations, Acute Kidney Injury, Pharmacokinetics, Infectious Disease and Transitions in Care. After completion, six monthly Transition to Practice Support (TIPS) peer-supported sessions are offered to each cohort of new pharmacists. The purpose of TIPS is to create a community of practice for new practitioners, providing a safe place to meet and share practice challenges and interesting cases.

Evaluation: On-line surveys conducted pre and post C.O. revealed a substantial decrease in attendees feeling not or only somewhat confident performing key clinical activities. Evaluation of the TIPS sessions revealed that the overwhelming majority of respondents reported feeling comfortable contributing and sharing during the sessions. Most felt confident or very confident that participation helped identify opportunities to enhance their practice and almost all indicated they would recommend TIPS to a new practitioner.

Implications: The revised C.O. program has been successful and well received by the participants. The sessions will continue to be offered twice yearly to address the clinical orientation needs of new pharmacists. Evaluation of the longer-term impact of this program is currently being planned.

Working from Home for Clinical Pharmacists during the COVID-19 Pandemic

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Background: While many employees worked from home during the COVID-19 pandemic, it was difficult for frontline clinical pharmacists ("pharmacists"). However, situations such as quarantine, emergency childcare, and the switch to virtual clinics required the implementation of an alternative work solution to support continuity of clinical pharmacy services.

Description: Facilitated by secure access to the hospital's electronic health information system, EPIC®, a Work from Home (WFH) program was implemented. Pharmacists signed an Agreement and completed a daily workload tracker. A key element of the program was continued provision of high-quality clinical pharmacy services.

Action: To evaluate the program, data was collected on the number of pharmacists who worked from home and the reason, from March 2020 to May 2021. The pharmacists were then surveyed to gain their perspective on the new program, and to learn about their daily clinical activities.

Evaluation: Overall, 77% (24/31) of pharmacists worked from home at least once during the study period, representing 304 shifts. Reasons for WFH are represented in Figure 1. Fifteen pharmacists worked from home more than 5 times. Of this group, 40% indicated they could complete 90 to 100% of their clinical role while working from home.

Implications: The majority of pharmacists preferred to work in-person in order to complete their full clinical role. However, by leveraging EPIC®, working remotely from home is an alternative work solution for clinical pharmacists that supports continuity of clinical pharmacy services, during and after a pandemic.

For the figure that goes with this abstract, please see Abstract Appendix, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/208

CASE REPORTS / OBSERVATIONS CLINIQUES

Ceftaroline Induced Neutropenia in the Setting of Methicillin Resistant *Staphylococcus aureus* Bacteremia Salvage Therapy: A Case Report

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Background: Ceftaroline is a 5th generation cephalosporin, available in Canada via the Special Access Program, indicated for treatment of bacterial skin infections and community acquired pneumonia. Ceftaroline offers coverage for Methicillin Resistant *Staphylococcus aureus* (MRSA) and can be used at off-label doses as salvage therapy in serious MRSA infections. While hematological adverse effects rarely occur with cephalosporins, there is limited information on the incidence with off-label ceftaroline use.

Case Description: A 27-year-old presented with MRSA bacteremia and endocarditis with septic emboli to the lungs. When blood cultures failed to clear after 6 days of vancomycin, therapy was switched to daptomycin. Two days later, ceftaroline 600 mg IV every 8 hours was added. Clearance of blood cultures was achieved. Leukocyte and neutrophil counts began to decline on day 16 of ceftaroline therapy. Ceftaroline was stopped on day 17 due to suspected ceftaroline-induced neutropenia. Two days after reaching nadir (day 18 absolute neutrophil count = 0.1x109/L), cell counts began to recover. No granulocyte colony-stimulating factor was given.

Assessment of Causality: Upon stopping ceftaroline this case of neutropenia quickly resolved. This case received a score of 4 (possible adverse drug reaction) on the Naranjo Probability Scale. As per the WHO-UMC Causality Assessment, it is probable ceftaroline was responsible for the neutropenia.

Literature Review: A series of 37 case reports involving ceftaroline induced neutropenia found an incidence of 12% in patients exposed for ≥7-14 days (range 7%-18%). Median time from ceftaroline start to development of neutropenia was 25 days. A retrospective analysis concluded ceftaroline-associated adverse events appear to occur at higher rates than reported in clinical trials which may be due to off-label, prolonged use.

Importance to Practitioners: Off-label, extended duration ceftaroline use may be significantly associated with a risk of neutropenia. Close monitoring for laboratory abnormalities is warranted.

Dapsone-Associated Methemoglobinemia Treated with Cimetidine: A Case Report

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Background: Exposure to oxidizing agents can convert hemoglobin to methemoglobin, a configuration that cannot bind or deliver oxygen. Dapsone is a major cause of drug-induced methemoglobinemia. Various cytochrome P450 (CYP450) enzymes are involved in the metabolism of dapsone to its oxidizing hydroxylamine metabolites. Oxidizing agents can also induce hemolysis, which is exacerbated in those who are glucose-6-phosphate dehydrogenase (G6PD)-deficient. Through competitive inhibition of CYP450 enzymes, oral cimetidine can mitigate dapsone-associated methemoglobinemia by limiting production of toxic metabolites.

Case Description: A 28-year-old woman receiving high-dose corticosteroids required prophylaxis for pneumocystis jirovecii pneumonia. Following an allergic reaction to sulfamethoxazole-trimethoprim, therapy was switched to dapsone 100 mg daily, which she took for 10 days before presenting to hospital with shortness of breath, lethargy, hematuria, and petechiae. She was found to have hemolytic anemia and a methemoglobin level of 15.9%. Dapsone was held, and supportive care was provided. Given dapsone's long half-life and enterohepatic recirculation, cimetidine 300 mg jirovecii pneumonia was administered every 8 hours to inhibit further production of hydroxylamine metabolites. Over 8 days, the patient's methemoglobin level decreased to 1.0%. Following her admission, she was confirmed to be G6PD deficient.

Assessment of Causality: This case of dapsone-associated methemoglobinemia received a score of 7 on the Naranjo scale, indicating a probable association. It is not possible to conclude the extent of cimetidine's role in the patient's recovery.

Literature Review: Available case series in adults and children support that dapsone is commonly implicated in methemoglobinemia. Case reports support that cimetidine 400 mg three times daily can lead to a significant and sustained drop in methemoglobin for patients on chronic dapsone therapy.

Importance to Practitioners: Cimetidine presents an accessible, convenient, and relatively safe treatment option for dapsone-associated methemoglobinemia. This case also demonstrates successful treatment of methemoglobinemia in a patient with G6PD deficiency, where methylene blue is contraindicated.

Erroneous Computerized Interpretation of Corrected QT Interval and Influence on a Patient's Drug Therapy

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Background: A prolonged QT interval from drug interactions increases the risk of torsades de pointes. Twelve lead electrocardiograms (ECG) calculate a corrected QT interval (QTc), however this computerized calculation can be inaccurate.

Case Description: A 64-year-old female with a history of heart failure, atrial fibrillation, anxiety and chronic kidney disease was hospitalized with urosepsis and treated with piperacillin/tazobactam. Concurrent medications included amiodarone, bisoprolol, spironolactone, furosemide, mirtazapine, venlafaxine and apixaban. Her baseline creatinine was 178 mmol/L, potassium 2.9 mmol/L, magnesium 0.7 mmol/L and baseline ECG showed sinus rhythm, biphasic p waves, t wave inversion and computer calculated QTc of 465 msec. On day 2, piperacillin/tazobactam was changed to oral ciprofloxacin. A repeat ECG was ordered on day 5 (Figure 1). The repeat ECG was similar to baseline but with a computer calculated QTc of 684 msec, suggesting a significant drug-drug interaction with ciprofloxacin.

Assessment: Based on manual assessment of the repeat ECG, the computer erroneously interpreted the biphasic p waves as part of the QT interval, thus miscalculating the QTc. The correct, manually assessed QTc was 448msec and thus no changes to the patient's drug therapy were warranted.

Literature Review: Computerized calculation of QTc has known to be inaccurate, especially with abnormal or poor quality ECGs. Previous literature and guidelines recommend manual interpretation of QTc.

Importance to Practitioners: Pharmacists should not be solely rely on computer calculated QTc and QTc should be manually assessed if drug interactions are identified.

Metronidazole and Mebendazole Combination Therapy for Treatment of Chronic Giardia in a Pediatric Patient with Immunodeficiency

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Background: Chronic Giardia, defined as infection persisting for over two months, can lead to severe diarrhea, malnutrition and extraintestinal manifestations. Patients with severe immunodeficiency or malnutrition can be more susceptible to chronic Giardia. For infections that become resistant to standard antimicrobial monotherapy, the use of combination antimicrobials with different mechanisms of actions may exert synergistic effects to maximize therapeutic benefit.

Case Description: A 15-year-old male with common variable immunodeficiency (CVID) and autoimmune enteropathy presented with chronic Giardia, malnutrition and failure to thrive. The patient had a two-year history of treatment refractory Giardia, failing four trials of oral metronidazole and two trials of albendazole. Given the history of treatment failure, combination antimicrobial therapy with metronidazole 10mg/kg IV every 8 hours and mebendazole 200mg oral three times daily for 10 days was trialed, resulting in successful eradication of the Giardia.

Assessment of Causality: This case demonstrated successful treatment of refractory Giardia using combination therapy in a patient with immunodeficiency. After completion of the 10-day course of metronidazole and mebendazole, the patient's endoscopy biopsy and stool test were negative for Giardia. In addition, the patient improved clinically in the following months with resolution of diarrhea and improved nutritional status.

Literature Review: There are limited randomized control trials studying the benefit of combination therapy in chronic Giardia. Observational studies demonstrate that combination of a 5-nitroimidazole and a benzimidazole may be more effective treatment for metronidazole-resistant infections than repeated courses of monotherapy. A case series with 22 patients demonstrated a 7-day course of albendazole and metronidazole combination therapy compared to albendazole monotherapy had a higher cure rate in treating metronidazole-resistant Giardia.

Importance to Practitioners: Refractory Giardia infections can be difficult to treat due to increasing resistance to metronidazole. Combination therapy with mebendazole and metronidazole may be an effective, accessible and affordable alternative to standard monotherapy.

Severe Pancytopenia Secondary to Azathioprine

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Background: Thiopurines (azathioprine and 6-mercaptopurine) are commonly used in inflammatory bowel disease to induce and maintain remission. The metabolism of thiopurines in the body varies according to genetic differences in enzymatic activity. Loss-of-function alleles in the thiopurine methyltransferase *(TPMT)* and the nudix-type motif 15 *(NUDT15)* genes are associated with increased risk of toxic adverse effects including leukopenia, neutropenia, and myelosuppression.

Case Description: A 15-year-old girl of Southeast Asian descent, with a history of ulcerative colitis was hospitalized for right-sided pneumonia in the context of severe pancytopenia. Prior to admission the patient was initiated on azathioprine 50 mg daily to help manage a disease flare. Routine blood work taken two weeks after initiating azathioprine detected the pancytopenia and the medication was discontinued. Patient presented to hospital a few days later. Genotype testing revealed normal functioning alleles in the *TPMT* gene and a homozygous loss-of-function allele (c.415C>T) in the *NUDT15* gene.

Assessment of Causality: Based on the Naranjo Scale, this case is considered a probable adverse drug reaction (score = 6).

Literature Review: Significant literature exists detailing the link between deficiencies in the *TPMT* gene and increased incidence of myelosuppression. This has led to the development of guidelines detailing genotype test interpretation to individualize dosing. Recommendations to screen for genetic polymorphisms in *TPMT* prior to initiating thiopurines are also included in many European and American clinical practice guidelines. A newer link was demonstrated between myelosuppression and loss-of-function alleles in the *NUDT15* gene, more commonly observed in East and Southeast Asians. Although less widespread, updated recommendations exist supporting testing for both genes to improve clinical outcomes.

Importance to Practitioners: Myelosuppression is a serious and potentially fatal adverse effect of thiopurines. Performing regular blood work and routinely incorporating pharmacogenomic screening into clinical practice in Canada can help mitigate harm, particularly in at risk populations.

Successful Use of Edoxaban for Resolution of Left Ventricular Thrombus

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Background: Historically, warfarin has been the drug of choice for treating left ventricular thrombus (LVT). Patient specific factors may make the use of direct oral anticoagulants (DOACs) a more feasible option; however, they have not been extensively studied in this disease state.

Case Description: A 71-year-old female presented with shortness of breath, chest pain and elevated troponin. She was diagnosed with an acute myocardial infarction and an echocardiogram identified an LVT. Warfarin was deemed inappropriate for this patient and edoxaban was chosen as an alternative. The patient was subsequently admitted five months later for congestive heart failure and an echocardiogram was repeated. There was no LVT noted and edoxaban was stopped.

Assessment of Causality: Prior to her second admission, she was compliant with her edoxaban and was not taking any other form of anticoagulation. She did not experience another thrombotic event during this time or any adverse events.

Literature Review: There is consistently new evidence for use of DOACs in LVT emerging. The current evidence for this topic is mostly made up of observational studies and case reports. There have been a few meta-analyses done on literature surrounding this topic, which have all suggested DOACs may be a reasonable alternative to warfarin; however, some retrospective reviews have shown negative outcomes. There has been one case report published on edoxaban use in this context, which resulted positively in resolution of the patient's LVT.

Importance to Practitioners: Although warfarin is standardly used for the treatment of LVT, it may not be appropriate for all patients. This case report strengths evidence for edoxaban for treatment of LVT and may be considered as an alternative to warfarin.

Overstretched to Overcapacity

Tania Mysak

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As we enter the third year of the pandemic, and the Omicron variant threatens our health care system (again), none of us want to hear about "resiliency" or "pivoting" anymore. We are rightfully exhausted from dealing with the disruption to our professional and personal lives. When exhausted, the short-term treatment needs to be rest, and the longer-term strategy should have us reflecting and re-evaluating where our future energies are best applied.

Writing this in early 2022, much of the discourse is about capacity in our health care systems. Omicron quickly overwhelmed testing and tracing capacity. Hospital capacity is also threatened, in part, from decades of structuring our systems to provide a vast array of services as leanly as possible. With growing populations and advancements in practice, pharmacy practice has grown. We see these trends reflected in the Hospital Pharmacy in Canada Survey—we have expanded clinically into ambulatory clinics and emergency rooms, we have added clinical duties for pharmacy technicians, and distribution services are providing more unit dose and integrating more technology. With an eye to efficiency, we have cultured ourselves to offer these services as thinly as possible.

Looking forward, we may wish to rethink the idea of the notion that all growth is good, and that leaner is always better. Have we spread ourselves too thinly? If we have no flexibility in our systems, no redundancies, we are susceptible to small surges, causing us to cut back on services we will advocate as "essential" in good times, but "expendable" during times of crisis (e.g., cutting back clinical services to support distribution if someone calls in sick). Can we realistically be all things to all patients while providing quality services, always?

Imagine a department where strategic redundancies allowed for innovation—time for project work, quality assurance efforts, precepting, or research. Would this enhance staff satisfaction and alleviate burnout as well?

Similarly, the Canadian Society of Hospital Pharmacists has been having conversations about what exactly our core businesses are, and how we determine the best way to prioritize them to enhance what we have, as opposed to growing into more. There are many excellent ideas of what we *could* do and of what we might be pretty great at doing. But the real question is whether we *should* be pursuing those activities, and if we have the resources to do them well in addition to our core businesses. Examples like government lobbying, large public education campaigns, specialized clinical practice tools—these are costly, could be done better by others, or have unclear benefits. We may be wiser to make strategic investments in solid infrastructure to share developed resources (as opposed to developing them ourselves), and to invest in strategies that will enhance current member value (as opposed to chasing ideas for new members).

It's all about values, priorities, and choices—all worthy of our reflection to place ourselves in a position of greater strength for the future.

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De la surtension à la surcapacité

par Tania Mysak

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Alors que nous entamons la troisième année de la pandémie et que la variante Omicron menace (à nouveau) notre système de santé, personne ne veut plus entendre parler de « résilience » ou de « pivotement ». Nous sommes, à juste titre, épuisés de faire face à la perturbation de nos vies professionnelles et personnelles. Une fois épuisé, le repos constitue le traitement à court terme prescrit, et la stratégie à plus long terme devrait nous amener à réfléchir et à réévaluer là où notre énergie future sera la mieux appliquée.

Alors que j'écris ces quelques lignes au début de 2022, on parle beaucoup de la capacité de nos systèmes de soins de santé. La variante Omicron a rapidement submergé notre capacité à effectuer des tests et en matière de traçage. La capacité des hôpitaux est également menacée, en partie à cause des dizaines d'années passées à structurer nos systèmes afin de pouvoir offrir une vaste gamme de services de la manière la plus simple possible. En réponse à la croissance démographique et aux progrès de la pratique, la pratique de la pharmacie s'est elle aussi développée. Nous constatons que ces tendances se reflètent dans le Sondage sur les pharmacies hospitalières canadiennes : nous avons étendu nos activités cliniques aux cliniques ambulatoires et aux salles d'urgence, nous avons distribué des tâches cliniques supplémentaires aux techniciens en pharmacie, et les services de distribution fournissent plus de doses unitaires et intègrent davantage de technologies. Dans un souci d'efficacité, nous nous sommes attachés à proposer ces services de la façon la plus allégée (lean) possible.

À l'avenir, nous souhaiterons peut-être repenser la notion selon laquelle toute croissance est bénéfique et la gestion allégée toujours meilleure. Faisons-nous fausse route? Si nos systèmes ne sont ni flexibles ni redondants, nous sommes alors à la merci de petites embuches qui nous poussent à réduire des services que nous préconisons comme étant « essentiels » en période faste, mais « facultatifs » en période de vaches maigres (par exemple, réduire certains services cliniques pour soutenir la distribution si quelqu'un est malade). Pouvons-nous, de façon réaliste, tout faire pour tous les patients, tout en offrant toujours des services de qualité?

Imaginez un service où les redondances stratégiques favoriseraient l'innovation : du temps pour travailler sur un projet, des efforts en matière d'assurance de la qualité, de préceptorat ou de recherche. Est-ce que la satisfaction du personnel s'améliorerait? L'épuisement professionnel diminuerait-il?

De même, la Société canadienne des pharmaciens d'hôpitaux a eu des conversations sur la nature de ses activités fondamentales et sur sa manière de les prioriser pour renforcer les acquis, plutôt que de les développer. Les excellentes idées sur ce que nous *pourrions faire* et sur ce que nous pourrions même très bien faire abondent. Mais la vraie question consiste à savoir si nous *devrions* poursuivre ces activités, et si nous disposons des ressources pour les mener à bien en plus de nos activités fondamentales. Le lobbying auprès du gouvernement, les grandes campagnes de sensibilisation du public, les outils spécialisés de la pratique clinique sont, par exemple, des initiatives coûteuses, qui pourraient être mieux entreprises par d'autres ou dont les avantages restent à éclaircir. Nous pourrions faire preuve d'une plus grande sagesse en investissant de manière stratégique dans une infrastructure solide pour partager les ressources développées (au lieu de les développer nous-mêmes) et en investissant dans des stratégies qui amélioreront la valeur des membres actuels (au lieu de nous lancer à la poursuite d'idées pour de nouveaux membres).

Tout est question de valeurs, de priorités et de choix qui méritent tous notre attention afin de pouvoir occuper une meilleure position à l'avenir.

Tania Mysak, B. S. P., Pharm. D., est présidente sortante et agente de liaison pour la vision de la Société canadienne des pharmaciens d'hôpitaux.