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The aim of the *CJHP* is to be a respected international publication serving as a major venue for dissemination of information related to patient-centred pharmacy practice in hospitals and other collaborative health care settings in Canada and throughout the world.

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Pharmacists Are Medication Stewards

Cynthia A Jackevicius

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Pharmacists have long been key members of antimicrobial stewardship programs, having held leadership roles in such programs for more than 25 years, and more recently they have done the same in opioid stewardship programs. Now, we are hearing calls to action for the similar development of stewardship programs in anticoagulation, a field where hospital pharmacists have had extensive responsibility.[1] This issue of the *Canadian Journal of Hospital Pharmacy* is filled with many important examples of original research related to these types of stewardship, which are central to hospital pharmacy practice.

Stewardship programs have highlighted the unique insights and expertise of pharmacists, and our involvement in these programs has driven both health care and the pharmacy profession forward. The term "stewardship" continues to increase in popularity, not only within health care but even more broadly in society, as in environmental stewardship. In general terms, stewardship is an ethical value that embodies the responsible planning, management, and use of resources, often precious resources.[2]

In our case, as pharmacists, we have thus far been recognized as stewards of specific medications or classes of medications, and this recognition has fostered focused improvements in patient care, health systems, and research. Original research papers, many of which have been published in this Journal, have been critical in helping to disseminate our collective knowledge to move these fields forward for even more patient health advances. When pharmacists are seen as stewards functioning within the stewardship program for a particular medication class or therapeutic area (e.g., antibiotics, opioids, or anticoagulants), their role as medication experts is anticipated and easily understood. Thus far, however, only a few drug classes have been deemed worthy of being the focus of designated stewardship programs.

As the Institute for Safe Medication Practices Canada has reported, from 2015 to 2020, the top medications associated with harm incidents were pain relievers (opioids and acetaminophen), insulin, anticoagulants, methotrexate, furosemide, and metoprolol.[3] Stewardship programs already exist for some of these, and patients could likely benefit from stewardship for insulin, methotrexate, furosemide, and metoprolol as well, but should we have defined stewardship programs for each of these medications? Should there also be stewardship programs for critical care, for drug interactions, for drug dosing, all of which represent other areas of extensive pharmacist involvement and expertise? Although we could create an ever-increasing number of individual stewardship programs that further subdivide patients into individual medications or specialties, is this practically feasible? If we further "silo" a patient's care in relation to all of their constituent medications, we risk losing the holistic nature of pharmaceutical care.[4]

At our core, pharmacists are in fact stewards for all medications. We are ambassadors for optimizing medication use both for individuals and for the greater good of the population. Perhaps, as medication experts, pharmacists should capitalize on the importance that the term "stewardship" connotes and lead a movement to fully realize the shared value of pharmacists in our key role as the primary providers of global medication stewardship, without the need for drug-specific programs. As technology increases, thereby reducing the need for pharmacist involvement in medication dispensing, it is the ideal time to strengthen our role as clinicians and to make stewardship of medications a key part of this message. Let's empower ourselves to not only be the most trusted medication experts, but also embrace our key role as medication stewards. Furthermore, let's continue to make use of the Journal as a vehicle to share our journeys with one another as we continue to travel down exciting paths in hospital pharmacy practice.

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ON THE FRONT COVER

Sturgeon Lake, City of Kawartha Lakes, Ontario

Sunrise after the first snowfall on Sturgeon Lake, City of Kawartha Lakes, Ontario. This is Carolyn Dittmar's morning view from her home on the lake. The photo was taken on her Samsung Galaxy S21 5G mobile phone.

Carolyn is a semi-retired hospital pharmacist currently working in a Geriatric Assessment and Intervention Network (GAIN) clinic in Lindsay, Ontario. Carolyn most recently has extensive experience working in geriatrics and rheumatology. Carolyn is a CSHP Past President, CSHP Fellow, and recipient of the CSHP Distinguished Service Award. Some of her spare time is spent as the Managing Editor of the CSHP Hospital Pharmacy in Canada Survey.

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Les pharmaciens et la gérance des médicaments

par Cynthia A. Jackevicius

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Les pharmaciens sont depuis longtemps des membres clés des programmes d'intendance ou de gérance de l'utilisation des antimicrobiens, et occupent des rôles de leadership au sein de ces programmes depuis plus de 25 ans. Plus récemment, ils ont fait de même dans les programmes de gérance des opioïdes. Maintenant, nous entendons des appels à l'action pour le développement de programmes similaires en anticoagulation : un domaine où les pharmaciens hospitaliers ont eu une responsabilité importante.[1] Ce numéro du *Journal canadien de la pharmacie hospitalière* est rempli de nombreux exemples importants de recherches originales liées à ces types de gérance, qui sont au cœur de la pratique de la pharmacie hospitalière.

Les programmes de gérance ont mis en évidence les connaissances et l'expertise uniques des pharmaciens, et notre participation à ces programmes a fait progresser les soins de santé et la profession de pharmacien. Les notions d'intendance ou de gérance continuent de gagner en popularité, non seulement dans le domaine de la santé, mais encore plus largement dans la société, comme dans « intendance environnementale ». En termes généraux, il s'agit d'une valeur éthique qui incarne la planification, la gestion et l'utilisation responsables des ressources, souvent des ressources précieuses.[2]

Dans notre cas, en tant que pharmaciens, nous avons jusqu'à présent été reconnus comme les intendants de médicaments ou de classes de médicaments particuliers, et cette reconnaissance a favorisé des améliorations ciblées dans les soins aux patients, les systèmes de santé et la recherche. Des articles de recherches originales, dont beaucoup ont été publiés dans ce Journal, ont été essentiels pour aider à diffuser nos connaissances collectives afin de faire avancer ces domaines pour assurer encore plus de progrès dans la santé des patients. Lorsque les pharmaciens sont perçus comme des intendants qui fonctionnent au sein du programme de gérance pour une classe de médicaments ou un domaine thérapeutique particulier (par exemple, les antibiotiques, les opioïdes ou les anticoagulants), leur rôle en tant qu'experts en médicaments est anticipé et facilement compris. Jusqu'à présent, cependant, seules quelques classes de médicaments ont été jugées dignes de faire l'objet de programmes de gérance désignés.

Comme l'a rapporté l'Institut pour la sécurité des médicaments aux patients du Canada, de 2015 à 2020, les principaux médicaments associés aux incidents préjudiciables étaient les analgésiques (opioïdes et acétaminophène), l'insuline, les anticoagulants, le méthotrexate, le furosémide et le métoprolol[3]. Les programmes d'intendance existent déjà pour certains d'entre eux, et les patients pourraient probablement bénéficier de la gestion de l'insuline, du méthotrexate, du furosémide et du métoprolol; mais devrions-nous avoir des programmes de gérance définis pour chacun de ces médicaments? Devrait-il également y en avoir pour les soins intensifs, les interactions médicamenteuses et le dosage des médicaments, autant de domaines dans lesquels s'impliquent largement les pharmaciens et auxquels ils apportent leur expertise? Bien que nous puissions créer un nombre toujours croissant de programmes d'intendance individuels qui subdivisent davantage les patients en médicaments ou spécialités individuels, est-ce pratiquement faisable? Si nous « cloisonnons » davantage les soins d'un patient par rapport à tous ses médicaments constitutifs, nous risquons de perdre la nature holistique des soins pharmaceutiques.[4]

À la base, les pharmaciens sont en fait les intendants de tous les médicaments. Nous sommes les ambassadeurs de l'optimisation de l'usage des médicaments tant pour les individus que pour le plus grand bien de la population. Peut-être, en tant qu'experts en médicaments, les pharmaciens devraient-ils tirer profit de l'importance que le terme « intendance » implique et être à la tête d'un mouvement pour réaliser pleinement la valeur partagée des pharmaciens dans notre rôle clé en tant que principaux fournisseurs de la gestion globale des médicaments, sans avoir besoin de programmes spécifiques. À mesure du développement technologique, le besoin d'implication des pharmaciens dans la distribution des médicaments diminue; le moment est donc tout indiqué pour renforcer notre rôle de cliniciens et faire de l'intendance des médicaments un élément clé de ce message. Donnons-nous les moyens non seulement d'être les experts en médicaments les plus fiables, mais aussi d'assumer notre rôle clé en tant qu'intendants. De plus, continuons à utiliser le Journal comme un véhicule pour partager nos parcours les uns avec les autres alors que

nous continuons à parcourir des voies passionnantes dans la pratique de la pharmacie hospitalière.

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Pharmacy Practice in Quebec Emergency Departments: A Survey Study

Jessica Doiron, Madeleine Genest, Julie Morin, Jean-François Patenaude-Monette, Pierre-Olivier Monast, Nathalie Marceau, and Eric Villeneuve

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ABSTRACT

Background: According to a Canadian survey conducted in 2013, 37 of the 67 Quebec emergency departments (EDs) in hospitals with more than 50 beds reported having a pharmacist within the department. However, based on the 17 responses to the survey, it was not possible to determine patient care services offered by Quebec ED pharmacists, because the data were aggregated across all Canadian respondents. A provincial survey was undertaken to further define ED pharmacy practice within Quebec.

Objectives: To measure pharmacist involvement in EDs in the province of Quebec and to describe patient care services and interventions offered by these pharmacists.

Methods: A 47-question survey was sent to 33 directors of pharmacy departments, representing 90 hospitals and institutes with EDs in the province of Quebec. The directors of pharmacy were asked to forward the survey to an ED pharmacist for completion or to partially answer the survey themselves if their facilities had no pharmacists practising in the ED. The survey evaluated the presence of pharmacists in the ED, their training, the interventions they performed, and their involvement within the department. The presence and role of ED pharmacy technical staff were also evaluated.

Results: Of the 43 completed surveys received, 30 reported at least 1 pharmacist providing patient care within the facility's ED. The most common tasks performed by ED pharmacists were, in decreasing order of frequency, answering questions from the multidisciplinary team, adjusting medications according to patients' allergies or their renal or hepatic function, managing drug interactions, and clarifying prescriptions. Pharmacists also reported teaching pharmacy students and residents and supporting the team in the resuscitation area.

Conclusions: The majority of respondents reported having at least 1 pharmacist in the ED. Compared with previous Canadian results, this survey had more respondents from Quebec with better representation of ED pharmacy practice in the province. Patient care services provided by pharmacists were variable, possibly because of a lack of standardized practice guidelines.

Keywords: emergency, pharmacy, clinical services

RÉSUMÉ

Contexte : Selon une enquête canadienne menée en 2013, 37 des 67 services des urgences dans des hôpitaux québécois de plus de 50 lits ont déclaré avoir un pharmacien au sein de leur service. Cependant, à partir des 17 réponses de cette enquête, il n'a pas été possible de déterminer les services de soins aux patients offerts par les pharmaciens des services des urgences du Québec, car les données étaient agrégées pour tous les répondants canadiens. Une enquête provinciale a été menée pour mieux définir la pratique de la pharmacie au sein des services des urgences au Québec.

Objectifs : Mesurer l'implication des pharmaciens dans les services des urgences du Québec et décrire les services de soins aux patients et les interventions offerts par ces pharmaciens.

Méthodes : Un sondage comportant 47 questions a été envoyé à 33 chefs de départements de pharmacie, représentant 90 hôpitaux et instituts ayant un service des urgences au Québec. Les chefs de départements de pharmacie ont été invités à transmettre le sondage à un pharmacien du service des urgences pour qu'il y réponde; ou, si leur établissement ne comptait aucun pharmacien exerçant en service des urgences, à y répondre partiellement eux-mêmes. L'enquête a permis d'évaluer la présence des pharmaciens dans les services des urgences, leur formation, leurs interventions et leur implication au sein du département. La présence et le rôle du personnel technique en pharmacie des urgences ont également été évalués.

Résultats : Sur les 43 questionnaires remplis reçus, 30 indiquaient avoir au moins un pharmacien prodiguant des soins aux patients dans le service des urgences de l'établissement. Les tâches les plus courantes consistaient, par ordre décroissant de fréquence, à répondre aux questions de l'équipe multidisciplinaire, à adapter les médicaments selon les allergies des patients ou leur fonction rénale ou hépatique, à gérer les interactions médicamenteuses et à clarifier les ordonnances. Les pharmaciens ont également déclaré former les étudiants et les résidents en pharmacie et soutenir l'équipe dans la salle de réanimation.

Conclusions : La majorité des répondants ont déclaré avoir au moins un pharmacien au service des urgences. Par rapport aux résultats canadiens antérieurs, cette enquête comptait plus de répondants du Québec et indiquait une meilleure représentation de la pratique de la pharmacie au service des urgences dans la province. Les services de soins aux patients fournis par les pharmaciens étaient variables, peut-être en raison d'un manque de directives de pratique normalisées.

Mots-clés : urgence, pharmacie, services cliniques

INTRODUCTION

Previous research has shown that a pharmacist practising within the emergency department (ED) has a beneficial effect on patient outcomes in various clinical settings. For example, the presence of ED pharmacists is associated with reductions in medication errors and costs, as well as improvements in compliance with guidelines.[1] More specifically, examples of ED pharmacists' beneficial effects include reducing delays in administration of thrombolysis for stroke, of the first dose of antibiotics in sepsis, of analgesia in trauma, and of post-intubation analgesia.[2-5] Furthermore, pharmacists' involvement with the resuscitation team increases patient survival to hospital admission.[6]

Despite these proven benefits, the authors of a Canadian survey conducted in 2013 noted that only 37 (55%) of 67 Quebec hospitals with more than 50 acute care beds reported having a pharmacist practising within the ED, and only 17 of these 37 facilities responded to the survey.[7] Furthermore, almost half (43%) of the pharmaceutical services within Canadian EDs had been implemented within the previous 4 years, an indication that pharmacy practice within Canada was growing.[7] This national survey provided a general portrait of direct patient care services offered by Canadian ED pharmacists. The most commonly provided services were order clarification, troubleshooting, medication reconciliation, and assessment of renal dosing.[7]

To assess pharmacy practice within EDs in Quebec in greater detail, we conducted a survey of hospital pharmacy departments. The study objectives were to quantify the presence of pharmacists within EDs across Quebec and to describe the types of pharmaceutical services offered. More specifically, the survey sought information about the number of ED pharmacists employed, their training, types of pharmaceutical care activities offered, and involvement on resuscitation teams and in other activities, including teaching. We also aimed to identify the presence and roles of pharmacy technical staff within the ED. For departments without a pharmacy presence in the ED, we aimed to determine the main barriers to implementing this service.

METHODS

A 47-question survey was developed by a group of 3 ED pharmacists (J.D., J.M., J-F.P.-M.) and was then reviewed and validated by peers and members of the Association des pharmaciens des établissements de santé du Québec (A.P.E.S.), the mandatory association representing all Quebec hospital pharmacists. The questions and overall themes included in the survey were based on previously published surveys on pharmacy practice in the ED.[7,8] The full content of the survey is available upon request to the corresponding author. The survey was hosted on the SurveyGizmo platform (SurveyGizmo [now known as Alchemer]).

In January 2020, a link to the survey was sent to all directors of pharmacy of hospitals located in the province of Quebec through A.P.E.S. Reminders were sent 2 and 4 weeks before the survey deadline of February 18, 2020. The directors of pharmacy were asked to designate a pharmacist in charge of pharmacy activities in the ED to complete the questionnaire. This respondent had to answer for all of their colleagues and therefore had to have access to all data concerning pharmacists working in the ED (e.g., highest level of education, certifications, number of years working in the ED, percentage of time spent in the ED). If the facilities had no pharmacist practising in the ED, the director of pharmacy was asked to complete a shortened version of the survey. Participation in this study was voluntary, and no financial compensation was offered to participants. All answers were kept anonymous.

This study was approved by the McGill University Health Centre Research Ethics Board.

RESULTS

The invitation to participate in the survey was sent to 33 directors of pharmacy, representing 90 hospitals with EDs. The number of EDs was established through the annual report of *La Presse* (a French-language newspaper based in Montréal)[9] and was then adjusted to also include 6 institutes and pediatric or psychiatric hospitals that were excluded from the annual report but that have operational EDs. Of the 43 respondents who completed the survey, 30 (70%) reported having at least 1 pharmacist practising in the ED. The most common explanations for the absence of ED pharmacists are presented in Table 1.

Services Offered

The period over which pharmacy services had been offered in the ED, as well as the number of hours per week that a pharmacist was dedicated to the ED, varied among respondents. Across the 30 EDs, pharmacists began performing patient

TABLE 1. Reasons for Lack of a Pharmacist in the Emergency Department (ED)

Reason[a]	No. (%) of Respondents* (*n* = 13)
Lack of staff	10 (77)
Very short length of stay in the ED	5 (38)
Small volume of patients in the ED	4 (31)
Lack of funding	2 (15)
Lack of interest from the ED for a clinical pharmacist	2 (15)
Other	6 (46)

[a]Respondents could choose more than 1 option.

care activities within the previous 1 to 5 years in 5 EDs (17%), 5 to 10 years ago in 6 EDs (20%), 11 to 20 years ago in 15 EDs (50%), and more than 20 years ago in 4 EDs (13%). Nineteen pharmacy departments (63%) assigned a pharmacist to work 33 to 40 h/week in the ED, and 5 (17%) allocated more than 40 pharmacist-hours weekly. In all cases, pharmacists were scheduled in the ED during weekday shifts, with 1 pharmacy department also offering coverage that overlapped with the evening shift. In addition to pharmacists, 17 (57%) of the 30 EDs had pharmacy technical staff assigned specifically to the ED.

Pharmacy technical staff assigned to the ED performed a variety of tasks. In 14 (82%) of the 17 EDs with designated pharmacy technical staff, these personnel performed tasks related to the medication-use system, such as dispensing, prescription entry, and stock management, including refilling medication cabinets. In 7 (41%) of these 17 EDs, pharmacy technical staff assisted with medication reconciliation.

Pharmacists' Training and Experience

Of the 30 respondents from facilities with pharmacists assigned to the ED, 21 were pharmacists actually practising within the ED, whereas the other 9 were pharmacists filling various management positions, who answered on behalf of pharmacists practising in the ED. Respondents reported a total of 129 pharmacists who practised in the ED. For most of these pharmacists (n = 110, 85%), the highest completed level of education was a Master of Science (MSc), which is the hospital pharmacy residency program in Quebec (Table 2). The most common complementary training was Advanced Cardiac Life Support (ACLS), completed by 26 ED pharmacists (20%). The American College of Clinical Pharmacy (ACCP) offers several board certifications. Although board certification for emergency medicine pharmacy is not available, ED pharmacists in Quebec had ACCP certifications in other areas, specifically critical care, pharmacotherapy, oncology, and geriatrics.

Decentralized/Satellite Pharmacies

Of the 30 pharmacy departments providing pharmaceutical care in the ED, 5 (17%) reported having a decentralized pharmacy within the ED for order verification. Of these, 3 also dispensed medications directly from the satellite pharmacy. Including EDs with satellite pharmacies, 13 EDs (43%) had pharmacists performing order verification for some portion of their time; in the majority of these (9 of the 13), the pharmacists spent 20% or less of their time on this activity. Of note, 1 ED pharmacist allocated more than 80% of their time to verifying prescriptions. When asked if order verification by an ED pharmacist was of added value to the pharmaceutical care offered to patients, 18 (60%) respondents believed there was no added benefit.

Pharmaceutical Care Services

The ED pharmacists performed a wide variety of tasks while providing direct patient care. The most common activities, in decreasing order of frequency, were answering questions from the multidisciplinary team, adjusting medications according to the patient's allergies or their renal or hepatic function, managing drug interactions, clarifying drug prescriptions, evaluating adverse drug events, and taking part in activities in the resuscitation area (Table 3).

Most ED pharmacists (n = 22, 73%) reported having minimal involvement in the care of ambulatory care patients within the ED, typically seeing no more than 1 ambulatory patient per day.

Involvement in Resuscitation

As shown in Table 3, 23 (77%) of the 30 ED pharmacy teams offered support in the resuscitation area. More specifically,

TABLE 2. Training and Experience of Emergency Department (ED) Pharmacists

Training/Experience	No. (%) of Pharmacists (n = 129)
Highest level of education completed	
Undergraduate studies	13 (10)
Master of Science (MSc)	110 (85)
DPH	1 (1)
PGY-2	2 (2)
Master of Business Administration (MBA)	1 (1)
Graduate studies	1 (1)
Other	1 (1)
Complementary training and certification	
ACLS	26 (20)
Other ACCP board certification	7 (5)
BCCCP	4 (3)
ATLS	2 (2)
International health	1 (1)
Specialized emergency training	1 (1)
Experience in the ED (years)	
< 1	10 (8)
1–5	68 (53)
6–10	24 (19)
11–20	23 (18)
> 20	4 (3)
Time spent in the ED	
< 25%	54 (42)
25%–50%	64 (50)
51%–75%	8 (6)
76%–100%	3 (2)

ACCP = American College of Clinical Pharmacy, ACLS = Advanced Cardiac Life Support, ATLS = Advanced Trauma Life Support, BCCCP = Board of Certified Critical Care Pharmacists, DPH = Diplôme en pharmacie d'hôpital (diploma for hospital pharmacy practice before 1992), PGY-2 = postgraduate year 2.

the most commonly performed tasks related to resuscitation, in decreasing order of importance, were answering medication-related questions, preparing medications, obtaining patients' medication list and history, and taking part in therapeutic decision-making.

In addition to the support provided within the resuscitation area, 9 (30%) of the ED pharmacy teams were part of the hospital's "code blue" team.

Volume and Prioritization of Activities

Given high patient turnover in the ED, pharmacists' interventions may range from briefly intervening in a patient's medication regimen through answering questions to performing a complete analysis and management of a patient's pharmacotherapy. Most commonly, ED pharmacists performed 11 to 20 brief interventions (n = 13, 43%), answered 6 to 10 questions (n = 10, 33%) and performed complete pharmacotherapy management for 1 to 5 patients (n = 14, 47%) per day. "Brief interventions" are interventions targeted to a specific situation (e.g., clarifying an allergy, adjusting a dose, or modifying therapy because of an interaction) that are implemented without a complete review of the patient's chart. The frequency with which such brief interventions were performed daily was highly variable (Table 4).

TABLE 3. Pharmaceutical Care Activities Performed

Activity	No. (%) of EDs (n = 30)
Answering questions from nurses, physicians or other professionals	30 (100)
Evaluation and management of allergies	29 (97)
Evaluation of medication based on renal or hepatic function	29 (97)
Management of drug interactions	28 (93)
Clarification of orders	28 (93)
Evaluation of adverse drug events	27 (90)
Support in resuscitation area	23 (77)
Complete patient management and documentation in patient's chart	22 (73)
Medical and pharmaceutical history with patient	19 (63)
Patient follow-up	18 (60)
Medication reconciliation upon arrival	13 (43)
Preparation of medication	11 (37)
Patient counselling on discharge	4 (13)
Rounds	4 (13)
Development of protocols	3 (10)
Medication reconciliation at discharge	2 (7)
Warfarin management	1 (3)

ED = emergency department.

Respondents reported that their ED pharmacist provided pharmaceutical care to a median of 15 patients per day. Given that the daily number of patients visiting most Quebec EDs is greater than the number that can be seen by a single pharmacist in a day, 29 (97%) of the 30 ED pharmacists reported having to prioritize which patients they saw and which interventions they performed. The most commonly reported prioritization criteria were, in decreasing order of importance, patients with a medication-related problem detected by the pharmacist at the centralized pharmacy (25/29 [86%]), patients with a pharmacy consult requested by the medical team (25/29 [86%]), patients receiving care in the resuscitation area (18/29 [62%]), patients taking drugs with a narrow therapeutic index or taking high-risk medications (18/29 [62%]), and patients who were to be admitted to a ward (17/29 [59%]).

Survey respondents were asked to classify a prespecified set of interventions in order of importance according to actual practice and also according to how they believed these interventions should be prioritized. The difference in classification is presented in Table 5.

The standards of practice of the Ordre des pharmaciens du Québec specify that pharmacists' interventions be documented in patient charts.[10] However, this survey showed that the rate of documentation of ED pharmacists' activities was variable: 4 respondents (13%) reported a documentation rate of 1%–10%, 5 (17%) reported a rate of 26%–50%, 8 (27%) reported a rate of 51%–75%, and 13 (43%) reported a rate of 75%–100%.

Expanded Scope of Practice

The provincial Pharmacy Act (https://www.legisquebec.gouv.qc.ca/en/document/cs/p-10) was amended in 2015 (Bill 41) to

TABLE 4. Frequency of Pharmaceutical Activities during 8-Hour Shift in the Emergency Department (ED)

Activity and Frequency	No. (%) of EDs (n = 30)
Answer questions from multidisciplinary team	
2–5 times	6 (20)
6–10 times	10 (33)
11–15 times	7 (23)
> 15 times	7 (23)
Complete patient pharmacotherapy management	
0 times	2 (7)
1–5 times	14 (47)
6–10 times	9 (30)
11–20 times	4 (13)
> 20 times	1 (3)
Brief interventions	
1–5 times	3 (10)
6–10 times	5 (17)
11–20 times	13 (43)
> 20 times	9 (30)

Table 5. Current and Desired Importance of Interventions

Intervention	Importance[a]	
	Current	Desired
Answer questions from the multidisciplinary team (e.g., nurses, physicians)	1	2
Solve problems identified in the order verification process at the central pharmacy and transferred to the ED pharmacist	2	4
Adjust or suggest to adjust patients' medication	3	5
Respond to consults destined for the ED pharmacist	4	3
Ensure patient management and document interventions in patient's chart	5	1
Perform order verification in the ED	6	8
Complete medication histories or medication reconciliations with patients	7	6
Help nurses in the preparation of medication	8	7

ED = emergency department.
[a]Importance of interventions was rated from 1 to 8, according to current practice and according to how respondents thought the interventions should be prioritized.

allow for an expansion of pharmacists' scope of practice. Of the 30 survey respondents, 21 (70%) reported that their team of pharmacists performed activities allowed through this expansion of scope. Potential activities and their application are reported in Table 6.

Teaching

Pharmacy internships in the ED were offered by 27 (90%) of the 30 respondents. Among these 27 EDs, internships were offered to second-year entry-level PharmD students in 21 EDs (78%), to fourth-year entry-level PharmD students in 24 EDs (89%), and to pharmacy residents in 22 EDs (81%). Also, 11 (37%) of the 30 ED pharmacy teams had at least 1 member who taught at a university.

In addition to teaching and serving as preceptors within the pharmacy profession, 10 respondents (33%) reported that their team of pharmacists provided continuing education to other health care professionals within the ED team.

DISCUSSION

To the authors' knowledge, this survey is the first to specifically describe current pharmacy practice in Quebec EDs. The presence of pharmacists within the ED seems to be growing, with 5 additional hospitals having developed the service within the past 5 years. This trend toward increased pharmacist presence in the ED has also been observed in the United States.[11] Despite this development, approximately 30% of respondents to this survey still had no pharmacist presence within their ED. Of note, as reported in previous surveys,[7,8] the percentage of departments with a pharmacist was proportional to the number of stretchers, whereby 100% of EDs with more than 40 stretchers had a pharmacist present in the department.

The main limitations to development of pharmaceutical care services in the ED in Quebec were different from those underlined in the Canadian survey,[7] with a lack of pharmacists being one of the main limitations identified in our survey. The Canadian survey identified lack of training as a barrier to implementing this service,[7] but lack of training was not a perceived issue for our respondents. Of the pharmacists providing ED services in our survey, 86% had a general hospital residency (MSc, the Quebec graduate degree diploma for hospital pharmacy practice,

TABLE 6. Activities Related to Bill 41 (2015)

Pharmaceutical Activity	No. (%) of EDs (*n* = 30)
Request and interpret laboratory tests in a health care facility	20 (67)
Adjust or modify the dose of a prescribed medication to ensure patient safety	20 (67)
Adjust or modify the formulation, dosage, or quantity of a prescribed medication	19 (63)
Substitute a prescribed medication with another in the same therapeutic subclass during complete back orders in Quebec	15 (50)
Adjust or modify the dose of a medication to attain therapeutic goals	13 (43)
Extend a physician's prescription	11 (37)
Prescribe a medication when no diagnosis is needed	2 (7)
Administer a medication to demonstrate its correct use	1 (3)
Prescribe a medication for a minor condition (when the diagnosis and treatment are known)	0

ED = emergency department.

or, before 1992, DPH [Diplôme en pharmacie d'hôpital]). This proportion is higher than the 75% found in the 2013 Canadian survey.[7] However, the majority of pharmacists in our study had 5 years or less experience within the ED. In terms of additional training, several pharmacists had complementary training in ED-specific fields, such as ACLS. Some also had training or certification in fields outside of the ED. This non-ED training may reflect the broad spectrum of pharmaceutical needs of patients in the ED or the previous or concurrent practices of these ED pharmacists, given that most of them spent no more than 50% of their time in the ED.

The exercise of prioritizing activities according to actual and desired practice showed some important differences. For example, ED pharmacists reported wanting to prioritize patients' pharmacotherapy management and documentation of interventions in patient charts to a greater extent than in their current practice. Conversely, solving problems identified by and transferred from pharmacists in the central pharmacy, performing order verification, and making adjustments were being performed more often than what the ED pharmacists believed was necessary. The desired prioritization of these tasks was generally in line with current literature showing the added benefit of pharmacists in several ED clinical settings, such as resuscitation, trauma, stroke, and myocardial infarction. Being proactive in these specific settings allows the pharmacist to play an active role in preventing medication errors while providing medication information to the ED multidisciplinary team. The survey did not specifically ask whether pharmacists prioritized patients through manual screening or by using software integrating predetermined criteria.

The difference between tasks that pharmacists currently perform in the ED and those shown to have added benefit for patient care may reflect the evolution of ED pharmacy practice. For instance, the presence of a pharmacist within the resuscitation area in Quebec EDs was slightly higher than that reported in previous surveys, with 77% of respondents in the current provincial survey versus 61% in the 2013 Canadian survey.[7] This evolution of practice may not have been shared with or may be misunderstood by other members of the ED team or by non-ED pharmacist colleagues. There are currently no standards of practice or guidelines establishing the activities that an ED pharmacist in Quebec should be performing, which was reflected in variability among respondents. Interpretation of the definition of an ED pharmacist can also be variable, with 1 respondent reporting that more than 80% of the ED pharmacist's time was spent doing order verification. However, in 2021, the American Society of Health-System Pharmacists published guidelines on the practice of emergency medicine pharmacy services,[11] which could guide pharmacy and ED teams in establishing a standardized pharmaceutical service to be offered while local guidelines are developed.

Our survey had some limitations. The response rate of 48% was in line with the response rates in previous reports but may have biased our results. The reported proportion of EDs with pharmacists may have been overestimated, with a possible response bias in favour of EDs that had pharmacists. Also, among the respondents who reported that their facilities had ED pharmacists, 30% were not themselves providing clinical services in the ED but rather were working as pharmacy managers. This may have affected the accuracy of responses compiled for some questions regarding hands-on practice if the manager did not complete the survey with direct input from ED pharmacists. The reason for this deviation from the survey protocol is unknown, but it might be explained by lack of clarity in the wording of the survey instructions. Finally, because the roles and interventions of pharmacists in different clinical settings have not yet been clearly defined, certain elements of practice could be left to the respondent's interpretation, which may have led to confounding of some responses. For example, although most pharmacists can distinguish a brief intervention from a complete pharmacotherapy assessment, the exact components of each can vary, which may have influenced the volume of specific activities provided and reported in the survey.

CONCLUSION

The practice of pharmacy in Quebec EDs has evolved over recent years, with an increasing presence of pharmacists in this setting. However, their presence remains inconsistent because of a long-lasting shortage of hospital pharmacists in Quebec. The practice of ED pharmacists is also variable, possibly because of the lack of a standardized practice statement and differences in the training and experience of available staff. These results should help in the development of practice guidelines for Quebec emergency pharmacists and in the harmonization of pharmacist practice in the ED.

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Risk of Treatment Failure for Prosthetic Joint Infections: Retrospective Chart Review in an Outpatient Parenteral Antimicrobial Therapy Program

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ABSTRACT

Background: Prosthetic joint infections (PJIs) are a major complication of total joint replacement surgeries. Treatment includes surgical intervention with prolonged courses of IV antibiotics in outpatient parenteral antimicrobial therapy (OPAT) programs. The risk of PJI treatment failure is high and may be associated with various clinical factors.

Objectives: To determine the rate of PJI treatment failure and to identify potential risk factors for failure in patients admitted to an OPAT program.

Methods: A retrospective chart review was conducted for adult patients with PJI admitted to an OPAT program between July 1, 2013, and July 1, 2019. Treatment courses were deemed to have failed according to predetermined criteria. χ^2 tests and multiple linear regression were used to examine associations of comorbidities, pathogens, and antimicrobial regimens with treatment failure.

Results: In total, 100 patients associated with 137 PJI treatment courses in the OPAT program were included. Of these, 28 patients accounted for 65 of the treatment courses. Methicillin-susceptible *Staphylococcus aureus* was the most frequently isolated pathogen (31/137 or 22.6% of treatment courses). Patient comorbidities included body mass index of at least 30 kg/m^2 (58% of patients) and diabetes (41% of patients). The overall rate of treatment failure was 56.2% (77/137 treatment courses). Selected risk factors associated with treatment failure or success were diabetes (50.9% versus 29.8%; odds ratio [OR] 4.03, 95% confidence interval [CI] 1.38–12.88, $p = 0.013$) and depression (32.1% versus 14.9%; OR 5.02, 95% CI 1.30–22.89, $p = 0.025$).

Conclusions: The overall rate of PJI treatment failure in the study population was high. Patients with diabetes and depression experienced higher incidences of failure. Future investigations of comprehensive PJI management should be considered to ensure successful treatment and to minimize excessive use of health care resources.

Keywords: outpatient, IV therapy, prosthetic joint infection, treatment failure, antimicrobial, duration of therapy, comorbidities

RÉSUMÉ

Contexte : Les infections des prothèses articulaires (IPA) sont une complication majeure des arthroplasties totales. Le traitement comprend une intervention chirurgicale avec des séries prolongées d'antibiotiques IV dans le cadre de programmes de traitement antimicrobien parentéral ambulatoire (*outpatient parenteral antimicrobial therapy*; OPAT). Le risque d'échec du traitement des IPA est élevé et peut être associé à divers facteurs cliniques.

Objectifs : Déterminer le taux d'échec du traitement des IPA et identifier les facteurs de risque chez les patients admis dans un programme OPAT.

Méthodes : Un examen rétrospectif des dossiers de patients adultes atteints d'une IPA admis dans un programme OPAT entre le 1er juillet 2013 et le 1er juillet 2019 a été mené. L'échec d'un traitement était défini selon des critères prédéterminés. Des tests χ^2 et une régression linéaire multiple ont été utilisés pour examiner les associations de comorbidités, d'agents pathogènes et de régimes antimicrobiens avec l'échec du traitement.

Résultats : Au total, 100 patients associés à 137 séries de traitements des IPA au sein du programme OPAT étaient inclus. Parmi ceux-ci, 28 patients représentaient 65 des séries de traitement. Le *Staphylococcus aureus* sensible à la méthicilline était l'agent pathogène le plus fréquemment isolé (31/137 soit 22,6 % des séries de traitement). Les comorbidités des patients comprenaient un indice de la masse corporelle d'au moins 30 kg/m^2 (58 % des patients) et un diabète (41 % des patients). Le taux global d'échec thérapeutique était de 56,2 % (77/137 séries de traitement). Les facteurs de risque sélectionnés associés à l'échec ou à la réussite du traitement étaient le diabète (50,9 % contre 29,8 %; rapport de cotes [RC] 4,03, intervalle de confiance à 95 % 1.38-12.88, $p = 0,013$) et la dépression (32,1 % contre 14,9 %; RC 5,02, IC à 95 % 1.30-22.89, $p = 0,025$).

Conclusions : Le taux global d'échec du traitement de l'IPA dans la population étudiée était élevé. L'incidence des échecs chez les patients atteints de diabète et de dépression était plus élevée. Des enquêtes futures sur la prise en charge globale de l'IPA devraient être envisagées pour garantir la réussite du traitement et réduire au minimum l'utilisation excessive des ressources de soins de santé.

Mots-clés : ambulatoire, traitement IV, infection de prothèse articulaire, échec thérapeutique, antimicrobien, durée du traitement, comorbidités

INTRODUCTION

Prosthetic joint replacement is an effective intervention to restore function and improve quality of life for patients with arthritic or dysfunctional joints. In Canada, the number of joint replacement surgeries is expected to rise as the population ages. In its 2018-2019 report, the Canadian Joint Replacement Registry documented a 20% increase in hip and knee replacements over the previous 5 years and annual inpatient costs of $1.4 billion.[1] Although replaced joints should last 15–20 years before replacement is needed, some patients require early revisions, with associated inpatient costs of $42.1 million annually.[2] The most common problem leading to early revision surgery is prosthetic joint infection (PJI), accounting for over 30% of cases.[1,2] PJIs represent a serious complication of prosthetic joint replacement, resulting in readmission to hospital, prolonged length of stay, joint failure, and increased morbidity and mortality.[3,4] Management of PJIs includes revision surgery, source control, and prolonged courses of IV or highly bioavailable oral antibiotics.[1,5,6] Unfortunately, there is a high risk of relapse or re-infection following PJI treatment. In a retrospective study published in 2019, 33% of patients treated for hip or knee PJI experienced treatment failure within 4 years of revision surgery.[7] Both modifiable and nonmodifiable risk factors for PJI treatment failure have been reported in other studies.[8-17]

Risk factors associated with PJI treatment failure in previous studies have included infection due to *Staphylococcus aureus* or gram-negative bacilli, polymicrobial infections, pre-existing liver disease, obesity, smoking, and presence of a communicating sinus tract.[7-16] The risk of treatment failure among patients with retained implants is higher, with one study reporting a failure rate of 45% in patients with late PJI.[17]

To facilitate outpatient care in the community, patients requiring long-duration IV antibiotic therapy are enrolled in outpatient parenteral antimicrobial therapy (OPAT) programs. Unfortunately, there is a paucity of studies investigating PJI management in the OPAT setting, because previous studies investigating risk factors for treatment failure in such programs have included only small numbers of patients with PJI.[18-20] In Winnipeg, Manitoba, the Community IV Program (CIVP) provides OPAT services to patients requiring IV antimicrobials for an extended duration.

The purposes of this study were to determine the rate of PJI treatment failure and to identify risk factors for such failure in the Winnipeg OPAT population. Although previous studies have identified and reported rates of PJI treatment failure and associated risk factors, these data may not be reflective of Winnipeg's OPAT population. The frequency of specific pathogens and antibiotic data such as chosen regimens, duration of treatment, rationale for change in or early discontinuation of IV treatment, and use of oral antibiotics for infection suppression after IV treatment were also assessed.

METHODS

This retrospective chart review involved evaluation of the medical records of patients admitted to an OPAT program for treatment of PJI. A list of all patients treated from July 1, 2013, to July 1, 2019, was obtained from the Winnipeg CIVP's electronic medical record (EMR) system. The International Classification of Diseases, Ninth Revision (ICD-9), code 996.66 (for infection and inflammatory reaction due to internal joint prosthesis) was used to screen for PJI-related OPAT admissions. An admission was defined as the patient receiving a referral to the OPAT program for PJI treatment and receiving at least one dose of IV antibiotics through the program.

Patients were included in the study if they were 18 years of age or older when admitted to the OPAT program. Patients were excluded if they had amputation of the implicated limb before OPAT admission, if they had an infection involving nonjoint hardware, or if there was no documentation of the admission in the patient's EMR. If patients had more than one admission to the OPAT program within the study period, each admission was recorded as a separate treatment course. Separate treatment courses occurred if the patient was readmitted to the OPAT program after rehospitalization for any reason that disrupted the previous OPAT treatment course or if the patient was readmitted to the OPAT program at least 2 weeks after completing a previous IV antibiotic treatment course.

Patient data and potential risk factors for PJI treatment failure (Appendix 1, available from https://www.cjhp-online.ca/index.php/cjhp/issue/view/213) were extracted through a chart review of documentation in the OPAT EMR system. This documentation included demographic data (age, sex, body mass index [BMI], and estimated glomerular filtration rate), comorbidities, and use of immunosuppressant medications during the OPAT admission. Underlying comorbidities were determined through initial assessment by the OPAT nurse.

Information was collected about the prosthetic joint affected (knee, hip, or other) and the diagnostic indicators of PJI (specifically, presence of a sinus tract, purulence in affected joint, and at least 2 positive results on joint culture yielding the same organism). Any diagnostic indicator not documented in the chart was deemed not present. Data were also collected about the initial hospitalization, including duration of hospital stay and the date and type of surgical intervention. Microbiological data collected included all pathogens detected and the presence of bacteremia. Data collected about antimicrobial treatment included the type of antimicrobial regimen initiated in hospital and in the OPAT program, the intended and actual duration of treatment, and

the reasons for stopping or switching regimens. Use of long-term oral antibiotic therapy after the IV treatment course was also recorded, including intended duration of oral treatment.

Treatment courses that met any of the following criteria were classified as "treatment failure": readmission to the OPAT program for infection of the same joint, additional surgery outside of the original treatment plan, extension of IV antibiotic treatment beyond 8 weeks, persistence of symptoms, readmission to hospital for reasons related to the infection, and loss to follow-up before completion of treatment (Appendix 2, available from https://www.cjhp-online.ca/index.php/cjhp/issue/view/213). Treatment courses that did not meet these criteria were classified as "treatment success". To compare patient comorbidities in relation to treatment failure and success, each patient and their comorbidities were categorized into either the "treatment failure" or the "treatment success" group. For patients with failure of at least one treatment course, their comorbidities were categorized into the "treatment failure" group, and if they experienced only successful treatment courses, their comorbidities were categorized into the "treatment success" group.

The study was approved by the University of Manitoba Health Research Ethics Board and the Health Sciences Centre Research Impact Committee. The data were collected and analyzed by a single investigator (D.F.). Descriptive statistics were used, with dichotomous data represented as counts and percentages and non-normally distributed continuous data represented as median values and interquartile ranges (IQRs). The χ^2 test was used to examine associations between comorbidities, surgical interventions, pathogens, and antimicrobial regimens and treatment failure. The rate of treatment failure was determined by dividing the number of treatment courses that met any of the criteria for treatment failure by the total number of PJI treatment courses.

A post hoc analysis was performed using R software, version 4.2.0. This analysis involved a multiple logistic regression model to examine comorbidities for significant association with treatment failure. Odds ratios and confidence intervals (CIs) were determined, as well as the McFadden pseudo R^2 score to determine model fit. McFadden suggested that R^2 values between 0.2 and 0.4 represent a good fit of the model.[21]

RESULTS

Demographic Characteristics

For the period between July 1, 2013, and July 1, 2019, a total of 179 separate PJI treatment courses were identified by searching the EMR system. Of these, 42 were excluded: 18 courses had infection of nonjoint hardware, 16 courses had missing EMR documentation, and 8 courses occurred completely outside the study period. The remaining 137 PJI treatment courses, associated with 100 patients, were included in this study. Twenty-eight of the patients had more than one treatment course through the OPAT program and accounted for 65 (47.4%) of the included courses. Of the 28 patients with multiple treatment courses, 26 (92.9%) had infections in the same joint and 12 (42.9%) had infections with the same pathogen. The median age of all 100 patients was 65 years, and the most common comorbidities were BMI of 30 kg/m^2 or more (58%), diabetes mellitus (41%), smoking (25%), and depression (24%) (Table 1).

PJI Diagnosis and Surgical Intervention

Patients most commonly experienced PJI in the knee (52% of patients) and hip (41% of patients). Among the 137 treatment courses, the corresponding PJI was characterized by presence of a sinus tract in 23 (16.8%) cases, purulence in the affected joint in 55 (40.1%), and at least 2 positive culture results yielding the same organisms in 76 (55.5%). The most common pathogens isolated were gram-positive cocci (76/137 [55.5%]) (Table 2). *Staphylococcus aureus* was identified in association with 34 (24.8%) of the 137 treatment courses, with methicillin-sensitive *S. aureus* accounting for 31 of these cases. Bacteremia occurred in association with 15 (10.9%) of the treatment courses.

The most common initial surgical interventions to treat PJI were irrigation and debridement (for 65 [47.4%] of the 137 OPAT admissions) and 2-stage revision (49 [35.8%]). Single-stage revision (4 [2.9%]) and other surgeries (9 [6.6%]) were less common. For 10 treatment courses (7.3%), no surgical intervention was performed.

Antimicrobial Use

IV antimicrobials commonly initiated in hospital included cefazolin (37 [27.0%] of the 137 OPAT admissions) and vancomycin (30 [21.9%]). After hospital discharge, the most common initial IV antimicrobials administered in the OPAT program were ceftriaxone (65 [47.4%] of the 137 treatment courses) and vancomycin (41 [29.9%]). Oral and IV combination regimens were used in 11 treatment courses (8.0%). In 3 treatment courses (2.2%), oral rifampin was used with ceftriaxone. The overall median duration of IV antimicrobial treatment was 53 days (IQR 45–77 days).

Antimicrobial regimens were changed during OPAT treatment in 21 courses (15.3%), most commonly because of adverse drug reactions (9/21 [43%]) and physician-defined clinical treatment failure (4/21 [19%]). IV antibiotic treatment was stopped early in 18 courses (13.1%). The most common reasons for early discontinuation were adverse drug reaction (7/18 [39%]), readmission to hospital (5/18 [28%]), and patient non-adherence (5/18 [28%]).

Oral antibiotic therapy was initiated after 69 IV treatment courses (50.4%). The most common duration for oral antibiotic therapy was 1 year (17 [24.6%]), with lifelong suppressive therapy recommended after 4 treatment courses (5.8%). The duration of oral antibiotic therapy was not specified for 18 courses (26.1%).

TABLE 1. Unadjusted Risk Factors for Treatment Failure

Risk Factor	Group; No. (%) of Patients[a] All (*n* = 100)	Failure (*n* = 53)	Success (*n* = 47)	*p* Value[b]
Age (years) (median and IQR)	65 (59–71)	62 (56–68)	68 (59–74)	
Obesity (BMI ≥ 30 kg/m^2)	58 (58)	30 (56.6)	28 (59.6)	0.76
eGFR (mL/min/1.73 m^2)				
≥ 60	82 (82)	46 (86.8)	36 (76.6)	0.19
45–59	12 (12)	6 (11.3)	6 (12.8)	0.82
30–44	5 (5)	0 (0)	5 (10.6)	0.015
Sex, female	45 (45)	27 (50.9)	18 (38.3)	0.20
Concurrent condition				
Chronic liver disease	5 (5)	5 (9.4)	0 (0)	0.031
Diabetes mellitus	41 (41)	27 (50.9)	14 (29.8)	0.032
COPD	13 (13)	7 (13.2)	6 (12.8)	0.95
History of ischemic heart disease	14 (14)	5 (9.4)	9 (19.1)	0.16
Heart failure	9 (9)	5 (9.4)	4 (8.5)	0.87
Peripheral vascular disease	6 (6)	3 (5.7)	3 (6.4)	0.88
Rheumatoid arthritis	14 (14)	10 (18.9)	4 (8.5)	0.14
Active malignancy	2 (2)	1 (1.9)	1 (2.1)	0.93
Lymphedema	2 (2)	2 (3.8)	0 (0)	0.17
History of MRSA infection	8 (8)	7 (13.2)	1 (2.1)	0.042
Active smoker	25 (25)	16 (30.2)	9 (19.1)	0.20
Depression	24 (24)	17 (32.1)	7 (14.9)	0.045
Gout	14 (14)	5 (9.4)	9 (19.1)	0.16
Immunosuppressive agents				
Corticosteroid > 30 days	4 (4)	2 (3.8)	2 (4.3)	0.90
Methotrexate	3 (3)	2 (3.8)	1 (2.1)	0.63
TNF inhibitor	1 (1)	0 (0)	1 (2.1)	0.29

BMI = body mass index, COPD = chronic obstructive pulmonary disease, eGFR = estimated glomerular filtration rate, IQR = interquartile range, MRSA = methicillin-resistant *Staphylococcus aureus*, TNF = tumour necrosis factor.
[a]Except where indicated otherwise.
[b]χ^2 test.

Treatment Failure

As shown in Figure 1, 77 of the 137 treatment courses met at least one criterion for treatment failure, resulting in a 56.2% failure rate. Thirty-six courses (26.3%) met 2 or more criteria for treatment failure. Of the 100 patients included in the study, 53 (53%) had at least one course that resulted in treatment failure. The most common reasons for treatment failure (Figure 2) were extension of IV antibiotic therapy beyond 8 weeks (49 [35.8%] of 137 treatment courses) and readmission to the OPAT program for infection of the same joint (46 [33.6%] of 137 treatment courses).

Risk Factors for Treatment Failure

Patient comorbidities associated with treatment failure, as indicated by unadjusted χ^2 analysis, are shown in Table 1. The risk factors associated with treatment failure were diabetes mellitus (50.9% versus 29.8%; $p = 0.032$), chronic liver disease (9.4% versus 0%; $p = 0.031$), history of infection or colonization with methicillin-resistant *S. aureus* (MRSA) (13.2% versus 2.1%; $p = 0.042$), and depression (32.1% versus 14.9%; $p = 0.045$). There was no significant association of treatment failure with immunosuppressive therapy during OPAT treatment.

There was no significant difference in terms of treatment failure versus success for PJI of the knee (31/53 [58.5%] versus 21/47 [44.7%]; $p = 0.17$), the hip (20/53 [37.7%] versus 21/47 [44.7%]; $p = 0.48$), or other types of joints (2/53 [3.8%] versus 5/47 [10.6%]; $p = 0.18$). Diagnostic criteria, including presence of sinus tract, purulence in the affected joint, and at least 2 positive cultures yielding the same organism, were not significantly associated with treatment failure.

Pathogens associated with treatment failure are shown in Table 2. Gram-positive cocci were associated with treatment failure (63.6% for treatment failure versus 45.0% for treatment success; $p = 0.029$), but there was no significant association for gram-negative, anaerobic, or polymicrobial infections. Culture-negative infections were associated with treatment success (16.7% versus 5.2%; $p = 0.028$). The

TABLE 2. Frequency of Pathogens Associated with Failure of Treatment for Prosthetic Joint Infection

Pathogen	Group; No. (%) of Infections			
	All Infections[a] (*n* = 137)	Failure (*n* = 77)	Success (*n* = 60)	*p* Value[b]
Gram positive	76 (55.5)	49 (63.6)	27 (45.0)	0.029
Staphylococcus aureus	34 (24.8)	23 (29.9)	11 (18.3)	0.12
MSSA	31 (22.6)	22 (28.6)	9 (15.0)	0.06
MRSA	3 (2.2)	1 (1.3)	2 (3.3)	0.49
Coagulase-negative *Staphlyococcus*	19 (13.9)	13 (16.9)	6 (10.0)	0.25
S. simulans	1 (0.7)	1 (1.3)	0 (0)	0.38
S. epidermidis	6 (4.4)	5 (6.5)	1 (1.7)	0.17
MRSE	8 (5.8)	4 (5.2)	4 (6.7)	0.72
Resistant *S. haemolyticus*	4 (2.9)	3 (3.9)	1 (1.7)	0.44
Streptococcus	18 (13.1)	9 (11.7)	9 (15.0)	0.57
GAS	3 (2.2)	2 (2.6)	1 (1.7)	0.71
GBS	3 (2.2)	1 (1.3)	2 (3.3)	0.42
Group C/G streptococci	3 (2.2)	1 (1.3)	2 (3.3)	0.42
Viridans streptococci	8 (5.8)	5 (6.5)	3 (5.0)	0.71
S. pneumoniae	1 (0.7)	0 (0)	1 (1.7)	0.26
Enterococcus	5 (3.6)	4 (5.2)	1 (1.7)	0.27
E. faecalis	3 (2.2)	2 (2.6)	1 (1.7)	0.71
VRE	2 (1.5)	2 (2.6)	0 (0)	0.21
Gram-negative	7 (5.1)	3 (3.9)	4 (6.7)	0.46
Escherichia coli	4 (2.9)	2 (2.6)	2 (3.3)	0.80
Multidrug-resistant *E. coli*	1 (0.7)	0 (0)	1 (1.7)	0.26
Proteus	2 (1.5)	1 (1.3)	1 (1.7)	0.86
Anaerobes	4 (2.9)	1 (1.3)	3 (5.0)	0.20
Cutibacterium	1 (0.7)	0 (0)	1 (1.7)	0.26
Other	3 (2.2)	1 (1.3)	2 (3.3)	0.42
Polymicrobial	31 (22.6)	18 (23.4)	13 (21.7)	0.81
Other	1 (0.7)	0 (0)	1 (1.7)	0.26
Culture negative	14 (10.2)	4 (5.2)	10 (16.7)	0.028

GAS = group A *Streptococcus*, GBS = group B *Streptococcus*, MRSA = methicillin-resistant *Staphylococcus aureus*, MRSE = methicillin-resistant *Staphylococcus epidermidis*, MSSA = methicillin-susceptible *Staphylococcus aureus*, VRE = vancomycin-resistant *Enterococcus*.

[a]Four treatment courses (2 with treatment failure and 2 with treatment success) did not have documented culture results.

[b]χ^2 test.

presence of bacteremia was not associated with treatment failure (10/77 [13.0%] versus 5/60 [8.3%]; $p = 0.39$).

Surgical Interventions and Treatment Failure

Initial surgical intervention consisting of irrigation and debridement was not associated with treatment failure (41/77 [53.2%] versus 24/60 [40.0%]; $p = 0.12$). There was also no association of treatment failure or success with other types of surgeries or with no surgical intervention.

Antimicrobials and Treatment Failure

There were no associations of IV antimicrobial therapy with treatment failure, whether IV monotherapy, IV combination therapy, or oral–IV combination regimens. The median

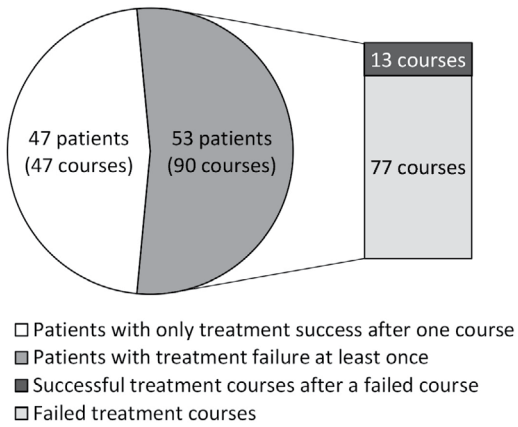

FIGURE 1. Patient outcomes and antibiotic treatment courses.

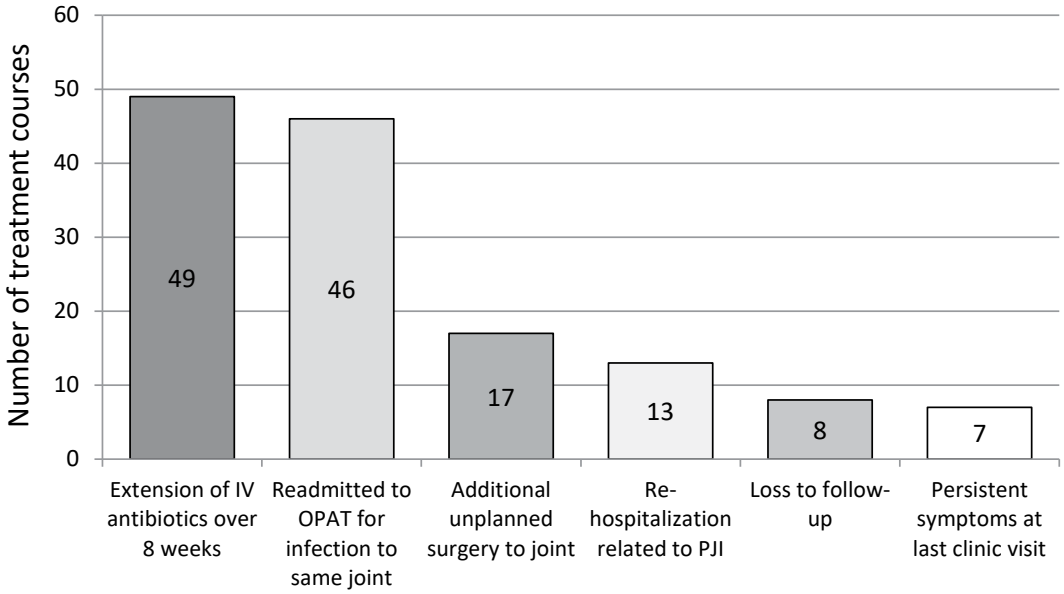

FIGURE 2. Incidence of treatments for prosthetic joint infection (PJI) that met criteria for treatment failure. A total of 36 courses (26.3%) met multiple criteria for treatment failure. OPAT = outpatient parenteral antimicrobial therapy.

duration of IV antimicrobial treatment was 71 days (IQR 46–95 days) for courses with treatment failure and 50 days (IQR 44–54 days) for courses with treatment success. When we excluded treatment courses defined as failure based on extension of IV antibiotic therapy beyond 8 weeks, the median duration of IV antimicrobial treatment was 63 days (IQR 44–86 days) for courses with treatment failure. Among patients with treatment failure due to extension of IV antibiotics beyond 8 weeks, the median duration of IV treatment extension beyond the 8-week mark was 28 days (IQR 18–62 days). Among patients who experienced treatment failure, the longest duration of IV antibiotic therapy occurred for PJI of the knee (median 81 days, IQR 50–110 days), whereas the median duration was 63 days (IQR 42–82 days) for hip PJI and 68 days (IQR 55–99 days) for PJIs affecting other joints.

Post Hoc Analysis

The multiple logistic regression analysis showed that diabetes (p = 0.013) and depression (p = 0.025) were significantly associated with treatment failure (Table 3). The McFadden pseudo R^2 score was 0.31, representing good model fit.

DISCUSSION

In Canada, PJI associated with hip and knee replacements accounted for over 30% of cases in which early revision surgery was required.[1,2] Early revision surgeries due to PJIs were also associated with higher average cost and longer length of hospital stay compared with non-PJI cases.[2] Additionally, the Canadian Institute for Health Information indicated that diabetes was a comorbidity in 24% of patients requiring early revisions due to PJI, compared with 12.7%–17% of early

TABLE 3. Logistic Regression Analysis of Association with Treatment Failure

Factor	Odds Ratio (95% CI)	*p* Value
Sex, female	1.47 (4.16–5.14)	0.54
Chronic liver disease	3.14×10^7 (0 – ∞)	0.99
Diabetes mellitus	4.03 (1.38–12.88)	0.013
COPD	2.76 (0.55–14.9)	0.22
History of ischemic heart disease	0.47 (0.09–2.21)	0.35
Heart failure	2.75 (0.50–16.56)	0.25
Peripheral vascular disease	2.04 (0.19–19.36)	0.53
Rheumatoid arthritis	6.09 (0.80–68.71)	0.09
Active malignancy	1.54 (0.02–142.61)	0.86
Lymphedema	3.23×10^7 (0 – ∞)	0.99
History of MRSA infection	3.42 (0.39–75.98)	0.32
Active smoker	0.60 (0.14–2.33)	0.47
Depression	5.02 (1.30–22.89)	0.025
Gout	0.52 (0.08–2.77)	0.46
Corticosteroid > 30 days	0.05 (1.01×10^{-3}–1.13)	0.07
Methotrexate	5.35 (0.20–376.35)	0.37
TNF inhibitor	1.75×10^{-9} (0 – ∞)	> 0.99

CI = confidence interval, COPD = chronic obstructive pulmonary disease, MRSA = methicillin-resistant *Staphylococcus aureus*, TNF = tumour necrosis factor, ∞ = infinity.

revisions due to other causes. [2] In our study of patients with PJI treated within the OPAT program, the treatment failure rate was 56.2%, which highlights the difficulty of eradicating PJI and the increased burden of infection. Risk factors associated with treatment failure were diabetes, depression, chronic liver disease, history of MRSA infection/colonization, and presence of gram-positive cocci.

In previous studies, the rate of PJI treatment failure has ranged from 12.2% to 63%,[15-17,22-41] including 33% after 4 years in patients treated with 1- or 2-stage exchange arthroplasty,[7] 42.1% in streptococcal PJI,[15] and 45% in late-acute PJI.[17] Most of these previous studies were retrospective and focused on subpopulations (such as patients who underwent specific surgical interventions or had particular pathogens) or investigated time to PJI relative to initial joint replacement surgery. The rate of treatment failure in our study (56.2%) was higher than the failure rates in most other studies,[15-17,22-28,36-41] but the difference is difficult to interpret because of differences in the criteria used to define treatment failure and the heterogeneous patient populations.

To date, it appears there is no universal definition of PJI treatment failure. Diaz-Ledezma and others[42] used a Delphi method to establish criteria for successful PJI treatment, which include (1) healing of the wound and no recurrence of infection, (2) no subsequent surgical intervention for infection, and (3) no PJI-related mortality. Data for these criteria were captured in our study and were used to identify treatment failure. Additionally, use of IV antibiotics beyond 8 weeks was used as a criterion for failure in our study, based on the 2013 Infectious Diseases Society of America guideline recommendations[5] for 2- to 6-week courses of IV antibiotics with allowance for scheduling changes or slight extensions. To our knowledge, no other studies have included prolonged duration of IV antibiotics as a criterion for treatment failure, perhaps overlooking the significant time and resource implications for both patients and OPAT programs. There also appear to be wide variations in antibiotic treatment strategies and durations in the literature and clinical practice, relative to the general guideline recommendations for IV antibiotics (specifically oral rifampin for staphylococcal PJI) for 2–6 weeks.[5] Factors contributing to this variability may be the lack of high-quality randomized studies comparing different durations of IV antibiotic treatment, the unknown efficacy of oral step-down therapy as an alternative to prolonged IV therapy, individual patient or logistic factors affecting optimal duration of treatment, and difficulty in managing comorbid conditions.

Our study also differed from previous literature by primarily focusing on PJI patients admitted to an OPAT program for infection management. These patients tend to constitute a high-risk population needing complex care; this complexity was highlighted by the 28% of patients who needed multiple treatment courses and accounted for 47.4% of the PJI treatment courses. Of note, the pathogens found in our study reflected PJIs described in previous literature.[7,23-25] However, our study also had a higher proportion of patients with diabetes (41%) than in other studies (8.8% to 26.3%).[15,17,22-28] The higher proportion of patients with diabetes in our study may have contributed to the higher rate of treatment failure that we observed.

Similar to our findings, comorbid conditions such as diabetes and depression have been found to be risk factors for PJI treatment failure.[16,27] In our study, these associations were confirmed as significant through the post hoc logistic regression analysis with a good model fit. Although chronic liver disease and history of MRSA infection were also associated with treatment failure in our study, the number of patients with either of these conditions was small. Diabetes is a well-known risk factor for development of PJI,[2,43] and Cancienne and others[16] found that diabetes was associated with risk of incomplete 2-stage procedures and death within 1 year after removal of an infected hip prosthesis. This situation is concerning, given that the number of Manitobans with a diagnosis of diabetes is expected to increase by 37% from 2018 to 2028,[44] at the same time as demand for hip and knee replacements is anticipated to increase with aging of the population. Physiologically, diabetes or hyperglycemia can lead to biofilm formation, decrease wound healing, impair leukocyte function, and decrease blood flow to the extremities because of microvascular changes.[45] Cancienne and others[16] also found that depression was associated with increased risk of repeat debridement and incomplete 2-stage procedures. Future studies should investigate coinciding treatment and optimization of comorbid risk factors during PJI treatment, as there are no current investigations in the literature.[43]

Our study had several limitations: it was a small, single-centre study, the researchers had EMR access only at the OPAT site, and IV antibiotic therapy duration greater than 8 weeks was used as a criterion for treatment failure. More specifically, this small, single-centre study was restricted to patients with PJI who were admitted to the Winnipeg OPAT program by a limited number of practitioners; as such, patients with PJI who were admitted to centres outside the Winnipeg OPAT may have been missed. In addition, we did not have access to hospital inpatient data for the initial surgery or subsequent hospital admissions. We also did not have access to information about oral antibiotic prescriptions after OPAT treatment, meaning such therapy may have been missed if it was not documented in the OPAT EMR. Finally, use of an arbitrary 8-week threshold criterion for treatment failure made it difficult to compare failure rates in this study with those from other studies.

CONCLUSION

The failure rate of PJI treatment in the Winnipeg OPAT population was 56.2%, higher than failure rates reported in most other studies. Patients with diabetes, depression,

chronic liver disease, or previous MRSA infection and those with PJIs involving gram-positive cocci experienced higher incidence of treatment failure. Opportunities for future investigations include assessment of the optimal duration of IV antibiotics and the efficacy of oral antibiotic step-down therapy, as these have yet to be defined. As the number of joint replacement surgeries in Canada continues to increase, this study and its high rate of treatment failure emphasize the need for future investigations of comprehensive PJI management to minimize the risk of treatment failure and to reduce excessive utilization of resources at the level of both patients and health care systems.

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Comparison of a Fully Weight-Based Protocol with a Non–Weight-Based Dosage Titration Protocol for IV Unfractionated Heparin: A Before-and-After Study

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ABSTRACT

Background: Unfractionated heparin (UFH) is used for the prevention and treatment of arterial or venous thromboembolism. The dosage for IV infusion of UFH is generally based on the patient's weight, with adjustment to a specific target for activated partial thromboplastin time (aPTT). In May 2019, the UFH protocols at the study institution were changed from being fully weight-based (i.e., for both initial dosing and subsequent dosage titrations) to weight-based initial dosing and non–weight-based dosage titrations, but the relative effectiveness of these 2 approaches was not known.

Objectives: The primary objective was to compare the effectiveness in achieving therapeutic aPTT with the fully weight-based and non–weight-based dosage titration protocols. The secondary objective was to compare the effectiveness of the non–weight-based dosage titration protocol with that of the previous fully weight-based one for patients with low-target aPTT.

Methods: A single-centre, retrospective, observational before-and-after study was conducted for patients receiving therapeutic UFH for any indication. Patients in the "before" group (fully weight-based protocol) were treated from January 2015 to October 2016, and those in the "after" group (non–weight-based titration) from January to October 2020.

Results: From a total of 1969 charts screened, 137 patients treated according to the fully weight-based protocols and 130 patients treated according to the non–weight-based titration protocols were included. In terms of the co-primary objective, the median number of dosage adjustments to achieve therapeutic anticoagulation was 1 in both groups ($p = 0.48$), and the proportion of patients with therapeutic anticoagulation at 24 h was similar (96.2% [125/130] with the non–weight-based titration protocols versus 99.3% [136/137] with the fully weight-based protocols; $p = 0.09$). Among patients treated according to the low-target UFH protocols, those with the non–weight-based titration protocol were less likely to have therapeutic anticoagulation at first measurement of aPTT than those with the fully weight-based protocol (37.9% [25/66] versus 44.6% [41/92], $p = 0.033$).

Conclusions: This retrospective, observational, before-and-after study showed that the effectiveness of the non–weight-based dosage titration protocols in achieving therapeutic aPTT was similar to that of fully weight-based UFH protocols.

Keywords: heparin, anticoagulants, partial thromboplastin time, nomogram

RÉSUMÉ

Contexte : L'héparine non fractionnée (HNF) est utilisée pour la prévention et le traitement de la thromboembolie artérielle ou veineuse. La posologie de la perfusion par IV d'HNF se base généralement sur le poids du patient, avec un ajustement à un objectif précis du temps moyen de céphaline activée (TCA). En mai 2019, les protocoles d'HNF de l'établissement à l'étude sont passés d'une approche entièrement basée sur le poids (à la fois pour la posologie initiale et les titrages posologiques ultérieurs) à une posologie initiale basée sur le poids, et à des titrages posologiques non basés sur le poids. Cependant, l'efficacité relative de ces 2 approches était inconnue.

Objectifs : L'objectif principal de l'étude consistait à comparer dans quelle mesure les protocoles entièrement basés sur le poids et les protocoles de titrage non basés sur le poids étaient efficaces pour atteindre le TCA thérapeutique. L'objectif secondaire consistait quant à lui à comparer l'efficacité du protocole de titrage de dose non basé sur le poids au protocole précédent entièrement basé sur le poids chez les patients ayant une faible cible de TCA.

Méthodes : Une étude monocentrique, rétrospective, observationnelle avant-après a été menée chez des patients recevant de l'HNF thérapeutique, toutes indications confondues. Les patients du groupe « Avant » (protocole entièrement basé sur le poids) ont été traités de janvier 2015 à octobre 2016, et ceux du groupe « Après » (protocole de titrage de dose non basé sur le poids) de janvier à octobre 2020.

Résultats : À partir de 1969 dossiers examinés, 137 patients traités selon les protocoles entièrement basés sur le poids et 130 patients traités selon les protocoles d'ajustement posologique non basés sur le poids ont été inclus. En ce qui concerne l'objectif co-principal, le nombre médian d'ajustements posologiques pour obtenir une anticoagulation thérapeutique était de 1 dans les deux groupes ($p = 0,48$), et la part de patients ayant une anticoagulation thérapeutique à 24 h était similaire (96,2 % [125/130] avec les protocoles non basés sur le poids contre 99,3 % [136/137] avec ceux entièrement basés sur le poids [$p = 0,09$]). Parmi les patients traités selon les protocoles HNF à faible cible, ceux avec le protocole de titrage non basé sur le poids étaient moins susceptibles de connaître une anticoagulation thérapeutique à la première mesure du TCA que ceux avec le protocole entièrement basé sur le poids (37,9 % [25/66] contre 44,6 % [41/92], $p = 0,033$).

Conclusions : Cette étude rétrospective et observationnelle avant-après a montré que l'efficacité des protocoles d'ajustement posologique non basés sur le poids pour obtenir un TCA thérapeutique était similaire à celle des protocoles d'HNF entièrement basés sur le poids.

Mots-clés : héparine, anticoagulants, temps de thromboplastine partiel, nomogramme

INTRODUCTION

Unfractionated heparin (UFH) is commonly used in the inpatient setting for various thromboembolic indications such as the prevention or treatment of arterial or venous thromboembolism in acute coronary syndrome, atrial fibrillation, or after heart valve surgery.[1] Consisting of polysaccharide chains from 3000 to 30 000 daltons, UFH may be administered by the subcutaneous or IV route, with the latter being most common.[1,2] Heparin exerts its pharmacodynamic effects by binding to antithrombin III, thereby inactivating clotting factors II, IX, X, and XII.[3] In terms of clearance, UFH is mostly eliminated through rapid and saturable depolymerization by endothelial cells and macrophages, with a small component of slow and nonsaturable renal elimination. The variable rates of saturable and nonsaturable elimination pathways for UFH result in a half-life of 30 to 150 min, depending on the dose.[1]

Although various methods exist for monitoring the pharmacodynamic effect of UFH, the activated partial thromboplastin time (aPTT) remains the most widely used, because of its convenience and availability. The aPTT is generally measured and the IV UFH dose adjusted every 6 h until aPTT within a target therapeutic range is achieved. Each institution typically has its own targets for aPTT based on reagent differences, but "normal" baseline aPTT is approximately 35 s, with therapeutic anticoagulation deemed to be 1.5–2 times above the baseline.[4] At our institution, we have 2 different aPTT target ranges for patients receiving IV UFH: low-target aPTT (50–70 s) and standard-target aPTT (60–90 s). The low-target aPTT protocol is indicated for patients with acute coronary syndrome or other situations where UFH is administered to prevent thromboembolism (e.g., atrial fibrillation, after heart valve surgery), whereas the standard-target aPTT protocol is indicated in cases where there is active thrombus (e.g., venous thromboembolism).

Historically, IV UFH dosing has followed non–weight based protocols, starting with a 5000-unit IV bolus, followed by 1000 units/h by infusion.[2] Protocols with weight-based initial dosing have been shown to reach therapeutic aPTT more quickly, with no difference in bleeding rates, relative to non–weight-based protocols,[5-8] but to date, there have been no comparative studies investigating weight-based and non–weight-based dosage titrations of IV UFH.

Before May 2019, our institution used fully weight-based IV UFH protocols (i.e., weight-based initial dosing and weight-based dosage titrations), including both low-target and standard-target protocols (target aPTT 50–70 s and 60–90 s, respectively) according to patients' actual body weight.[5-7] To prepare for the implementation of an electronic medical record (EMR), the various IV UFH protocols in the region were re-evaluated and consolidated, such that after May 2019, the fully weight-based UFH protocols were replaced with protocols that used weight-based initial dosing followed by non–weight based dosage titration protocols, to align with EMR order capabilities. Furthermore, the new low-target aPTT protocol had a lower initial weight-based dose (e.g., for an 80-kg patient, the new protocol used a 5600-unit bolus and 1100 units/h infusion initially, rather than the 6400-unit bolus and 1400 units/h infusion specified in the previous fully weight-based protocol). However, the effectiveness of the non–weight-based dosage titration protocols relative to the previous fully weight-based UFH protocols was not known.

METHODS

We conducted a retrospective, observational, before-and-after study comparing a non–weight-based dosage titration protocol with a fully weight-based IV UFH protocol, with each protocol incorporating low- and standard-target aPTT variations (for the complete protocols, see Appendices 1–4, available from https://www.cjhp-online.ca/index.php/cjhp/issue/view/213). Patients were identified using pharmacy dispensing records and were included if they were older than 18 years of age, had received therapeutic IV UFH for any indication, and had been admitted to a cardiology or cardiac surgery ward. Patients were excluded if the IV UFH had not been administered according to either the low-target or the standard-target protocol (e.g., dosage used for the protocol did not correspond to the patient's actual weight); also excluded were patients who had antiphospholipid antibody syndrome, active liver failure (defined as alanine aminotransferase levels 3 times the upper limit of normal at any time during IV UFH use), or any contraindications to IV UFH (including history of heparin-induced thrombocytopenia or allergy to heparin). Patients in the "before" group were those who received IV UFH (according to the fully weight-based protocol) between January 7, 2015, and October 14, 2016. Patients in the "after" group were those who received IV UFH (with weight-based initial dosing and non–weight-based dosage titration) between January 5 and October 16, 2020. The start date for the "after" group was 2 months following implementation of the EMR (which occurred in November 2019) to minimize risk of bias and confounding from the learning curve associated with changes during implementation of a new system.

The co-primary outcomes were (1) the number of dosage adjustments required to reach aPTT within the therapeutic range and (2) the proportion of patients with aPTT within the therapeutic range by 24 h after IV UFH initiation. At our institution, aPTT is measured every 6 h until a therapeutic level is achieved (and then every 24 h thereafter), with therapeutic aPTT defined as 50–70 s for the low-target protocol and 60–90 s for the standard-target protocol (based on our laboratory standards). The secondary outcome was the proportion of patients treated according to

the low-target protocol who reached therapeutic aPTT after the first aPTT measurement (at least 6 h after the initiation of UFH).

Data were collected for patient age, sex, weight, baseline aPTT, indication for heparin (post-lytic, acute coronary syndrome, atrial fibrillation, venous thromboembolism, after valve surgery), aPTT target of the protocol used (low or standard target), and dose of heparin. All aPTT values and heparin doses received while on therapy, including the initial bolus (if used), were recorded.

Ethics approval was obtained from the Providence Health Care Research Institute Office of Research Ethics (H20-02807).

Statistical Analysis

The convenience sample was obtained by reviewing and selecting the charts sequentially by date and screening sufficient records to ensure similar numbers in the "before" and "after" groups. Descriptive statistics were calculated for the baseline characteristics. Parametric data were analyzed by 2-sample *t* test, whereas nonparametric data were analyzed by the Wilcoxon rank-sum test. For categorical data, *p* values were calculated by χ^2 test. Between-group differences were calculated and adjusted for age, sex, and weight. Poisson regression models, logistic regression models, and multinomial logistic regression models were used for count, binary, and ordinal data, respectively. The co-primary outcomes were considered significant if the *p* value was less than 0.025 for each outcome individually, for a total *p* less than 0.05 for primary outcomes combined. A *p* value less than 0.05 was considered significant for the secondary outcome. All data were analyzed using Statistical Analysis Software (SAS) version 9.4.

RESULTS

In total, 1969 records were screened for eligibility, and 267 patients were included, 137 in the fully weight-based UFH protocol ("before") group and 130 in the non–weight-based dosage titration ("after") group (Figure 1). The baseline characteristics of the 2 groups were similar (Table 1). Overall, the mean age was 65.6 (standard deviation [SD] 14.0) years, mean body weight was 82.8 (SD 20.5) kg, and 82 (30.7%) were female. The most common indications for IV UFH were unstable angina/non-ST elevation acute coronary syndrome and atrial fibrillation. Fewer patients were treated according to the low-target protocol in the non–weight-based dosage titration group than in the fully weight-based dosage titration group (50.8% versus 67.2%).

With regard to the co-primary outcomes, for comparison of the non–weight-based dosage titration protocols with the fully weight-based protocols, there were no significant differences in terms of the median number of dosage adjustments required to reach therapeutic aPTT (median 1, interquartile range [IQR] 0–2, range 0–5, versus median 1, IQR 0–1, range 0–5; $p = 0.48$) or the proportion of patients achieving therapeutic aPTT at 24 h (96.2% versus 99.3%, $p = 0.09$) (Figure 2 and Table 2). The results of multivariable analysis for these outcomes were also nonsignificant (for number of adjustments to first therapeutic aPTT, relative risk [RR] 1.23, 95% confidence interval [CI] 0.95–1.58, $p = 0.12$; for proportion with therapeutic aPTT at 24 h, odds ratio [OR] 0.18, 95% CI 0.02–1.60, $p = 0.12$) (Table 3).

With regard to the secondary outcome, 158 (59.2%) of the 267 patients received UFH according to one of the low-target protocols, and the proportion of patients reaching therapeutic aPTT range by the first aPTT measurement

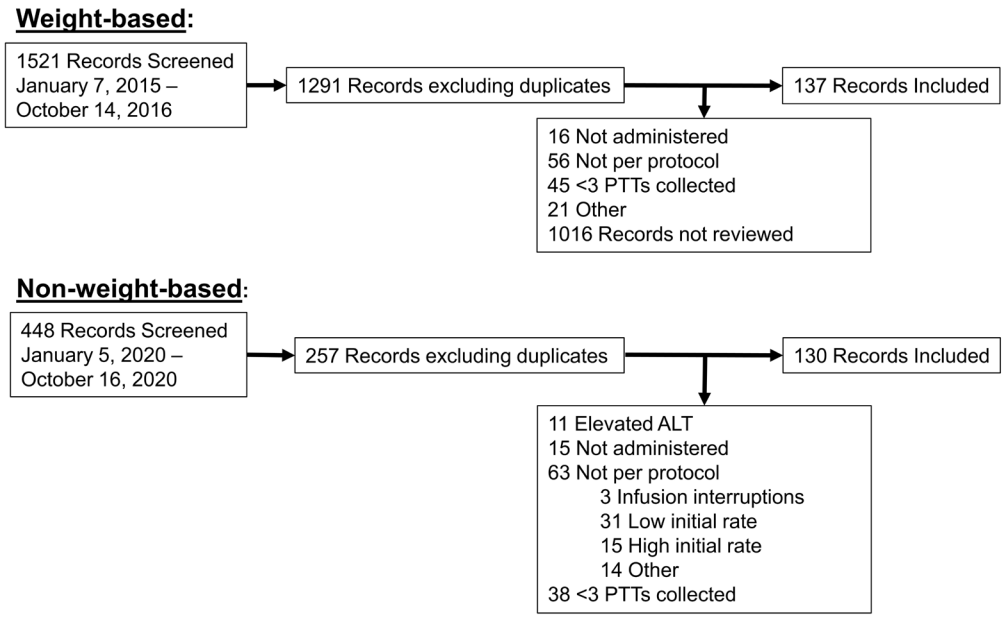

FIGURE 1. Flow diagram of chart review. ALT = alanine aminotransferase, PTT = partial thromboplastin time.

TABLE 1. Baseline Characteristics

Characteristic	Group; No. (%) of Participants[a]		
	Total (*n* = 267)	Non–Weight-Based (*n* = 130)	Weight-Based (*n* = 137)
Age (years) (mean ± SD)	65.6 ± 14.0	66.2 ± 13.4	65.1 ± 14.5
Sex, female	82 (30.7)	40 (30.8)	42 (30.7)
Weight (kg) (mean ± SD)	82.8 ± 20.5	82.6 ± 21.6	83.0 ± 19.5
Indication for UFH			
UA + NSTE-ACS	75 (28.1)	29 (22.3)	46 (33.6)
STE-ACS	31 (11.6)	28 (21.5)	3 (2.2)
Atrial fibrillation	109 (40.8)	49 (37.7)	60 (43.8)
Heart valve	19 (7.1)	13 (10.0)	6 (4.4)
Other	33 (12.4)	11 (8.5)	22 (16.1)
Protocol			
Low-target	158 (59.2)	66 (50.8)	92 (67.2)
Standard-target	109 (40.8)	64 (49.2)	45 (32.8)

NSTE-ACS = non-ST elevation acute coronary syndrome, SD = standard deviation, STE-ACS = ST-elevation acute coronary syndrome, UA = unstable angina, UFH = unfractionated heparin.
[a]Except where indicated otherwise.

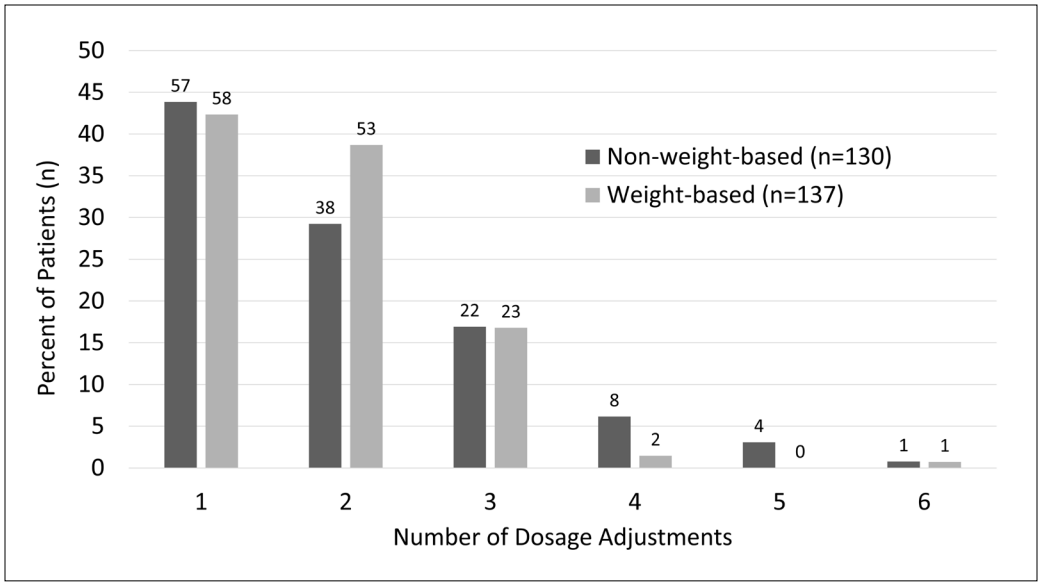

FIGURE 2. Dosage adjustments to reach therapeutic activated partial thromboplastin time.

(i.e., achieving target aPTT of 50–70s by 6 h after initiation of IV UFH) was lower in the non–weight-based dosage titration protocol group than in the fully weight-based protocol group (37.9% versus 44.6%, $p = 0.033$) (Table 2). Of those who were not at target, more patients in the non–weight-based titration protocol group than in the fully weight-based protocol group had subtherapeutic aPTT at first aPTT measurement (61.0% [25/41] versus 35.3% [18/51]). According to the multivariable analysis, patients treated according to the low-target non–weight-based dosage titration protocol were more likely to have aPTT below target than within target at first aPTT measurement relative to those treated according to the fully weight-based protocol (OR 2.23, 95% CI 1.00–4.99, $p = 0.051$).

DISCUSSION

In this retrospective, observational, before-and-after study of various IV UFH protocols at a single institution, protocols involving weight-based initial dosing and non–weight-based dosage titration were compared with fully weight-based protocols. These 2 dosing approaches resulted

TABLE 2. Summary of Outcomes

Outcome	Non–Weight–Based (*n* = 130)	Weight-Based (*n* = 137)	*p* Value
Primary outcome 1: Total number of adjustments to reach first therapeutic aPTT (median and IQR)	1 (0–2)	1 (0–1)	0.48
Primary outcome 2: Number (%) of patients with therapeutic aPTT at 24 h	125 (96.2)	136 (99.3)	0.09
Secondary outcome 1, for low-target patients	*n* = 66	*n* = 92	
Number (%) therapeutic at first aPTT			
Yes	25 (37.9)	41 (44.6)	0.033
No	41 (62.1)	51 (55.4)	
Number (%) above target (> 70 s)	16 (24.2)	33 (35.9)	
Number (%) below target (< 50 s)	25 (37.9)	18 (19.6)	

aPTT = activated partial thromboplastin time, IQR = interquartile range.

TABLE 3. Multivariable Analyses

Outcome	RR or OR (95% CI)	*p* Value
Primary outcome 1: Total number of adjustments to reach first therapeutic aPTT	RR 1.23 (0.95–1.58)	0.12
Primary outcome 2: Patients with therapeutic aPTT at 24 h	OR 0.18 (0.02–1.60)	0.12
Secondary outcome 1: Among low-target patients, therapeutic at first aPTT		
Above-target versus in-target	OR 0.73 (0.33–1.62)	0.44
Below-target versus in-target	OR 2.23 (1.00–4.99)	0.051
Above-target versus below-target	OR 0.33 (0.14–0.78)	0.012

aPTT = activated partial thromboplastin time, CI = confidence interval, OR = odds ratio, RR = risk ratio.

in a similar number of dosage adjustments required to reach the target for therapeutic aPTT and a similar proportion of patients achieving therapeutic aPTT by 24 h. To our knowledge, this is the first study comparing a non–weight-based dosage titration protocol with a fully weight-based protocol for IV UFH.

The median of 1 dose adjustment required to reach therapeutic aPTT in both groups was consistent with a previous study investigating weight-based heparin nomograms.[6] Previous studies of IV UFH protocols found that weight-based nomograms achieved therapeutic aPTT at 24 h for 72%–97% of patients.[5,7,8] Our study also demonstrated that therapeutic aPTT was achieved at 24 h for a large proportion of patients (> 96%), which is consistent with previous literature. The results of our study may suggest that weight-based initial dosing is important in achieving therapeutic aPTT and that weight-based dosage adjustments may be less important.

With regard to patients treated according to the low-target UFH protocols, more patients in the non–weight-based titration protocol group had subtherapeutic first aPTT values than in the fully weight-based protocol group. These results might be due to the fact that the non–weight-based titration protocol also had a lower initial weight-based dose. In a previous study using a weight-based protocol (60 units/kg bolus and 12 units/kg/h initial infusion) for low-target heparin therapy (aPTT 50–70 s), 51% of patients reached therapeutic aPTT at first measurement of aPTT.[7] In contrast, in our study, 37.9% of patients in the non–weight-based titration protocol group and 44.6% of those in the weight-based protocol group reached therapeutic aPTT at first measurement. Given that the data on low-target dosing and initial aPTT results were not analyzed head-to-head in the same population or study, there is no consistent evidence of optimal initial low-target heparin dosing.

With regard to limitations, our study was retrospective and observational, and it had a small sample size; hence, there was a risk of bias and confounding. Although we used a convenience sample, we coincidentally achieved a sample size similar to those of previous heparin nomogram studies.[5,8] In addition, the study was undertaken during implementation of an EMR system, which may unpredictably bias or confound the performance of the protocols, given the learning required after a system-wide change in practice; we attempted to mitigate this concern by excluding data from the first 2 months after EMR implementation. Also, we did not collect data for bleeding or thrombotic outcomes and thus cannot draw conclusions as to whether the achievement of aPTT targets was correlated with clinical outcomes.

CONCLUSION

This single-centre, retrospective, observational before-and-after study showed that for therapeutic IV UFH, a non–weight-based dosage titration protocol was similarly effective in achieving therapeutic aPTT relative to a fully weight-based protocol in terms of the median number of dose adjustments required to reach target aPTT and the proportion of patients reaching the therapeutic target at 24 h.

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Opioid and Sedative Coprescription: Prescribing Patterns after an ICU Admission

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ABSTRACT

Background: Opioid misuse constitutes a health care crisis in Canada, and coprescription of opioids with sedatives has been associated with adverse events. Opioids and sedatives are frequently administered in the intensive care unit (ICU). The rate of continuation of opioid–sedative combinations after an ICU admission at the study institution was unknown.

Objectives: To determine the rates of opioid and sedative coprescriptions following an ICU admission and to identify factors associated with continuation of hospital-initiated opioid–sedative coprescriptions at ICU transfer and hospital discharge.

Methods: This retrospective chart review involved patients admitted to ICUs at a tertiary care centre between April 1, 2018, and March 31, 2019. Baseline characteristics were obtained from a clinical database and medication information from medication reconciliation forms. An opioid coprescription was defined as prescription of an opioid in combination with a sedative (benzodiazepine, z-drug, gabapentinoid, tricyclic antidepressant, or antipsychotic), and hospital-initiated coprescriptions encompassed various predefined scenarios of therapy started or modified before ICU transfer. Factors associated with hospital-initiated opioid coprescription were analyzed by multivariable logistic regression.

Results: A total of 735 patients met the inclusion criteria. At ICU transfer, 23.0% (169/735) of the patients had an opioid coprescription, and 87.0% (147/169) of these coprescriptions were hospital-initiated. At hospital discharge, 8.6% (44/514) of the patients had an opioid coprescription, and 56.8% (25/44) of these coprescriptions were hospital-initiated. Male sex, home opioid coprescription, surgical patient, prolonged hospital stay, and in-hospital death were significantly associated with hospital-initiated opioid coprescription at the time of ICU transfer. Home opioid coprescription was significantly associated with opioid coprescription at the time of hospital discharge.

Conclusions: Hospital-initiated opioid coprescriptions accounted for the majority of opioid coprescriptions at ICU transfer and hospital discharge. Pharmacists should assess all opioid coprescriptions to determine whether discontinuation and/or dose reduction is appropriate.

Keywords: opioid coprescription, opioid, sedative, intensive care, critical care, associated factors

RÉSUMÉ

Contexte : L'abus d'opioïdes est une crise sanitaire au Canada, et les opioïdes coprescrits avec des sédatifs ont été associés à des événements indésirables. Les opioïdes et les sédatifs sont fréquemment utilisés en unité de soins intensifs (USI). Sur le lieu de l'étude, on ne connaissait pas le taux de maintien de l'utilisation de la combinaison opioïdes-sédatifs après une admission en USI.

Objectifs : Déterminer les taux de coprescription d'opioïdes et de sédatifs suite à une admission en USI et identifier les facteurs associés au maintien de l'utilisation des coprescriptions d'opioïdes et de sédatifs amorcées par l'hôpital au moment du transfert hors de l'USI et du congé hospitalier.

Méthodes : Cet examen rétrospectif des dossiers portait sur des patients admis en USI d'un centre de soins tertiaires entre le 1er avril 2018 et le 31 mars 2019. Les caractéristiques de base ont été obtenues à partir d'une base de données clinique et des informations sur les médicaments à partir des formulaires de bilan comparatif des médicaments. Une coprescription d'opioïdes a été définie comme « La prescription d'un opioïde associée à un sédatif (benzodiazépine, médicament z, gabapentinoïde, antidépresseur tricyclique ou antipsychotique) ». Les « coprescriptions amorcées par l'hôpital » correspondaient à des coprescriptions initiées ou modifiées avant le transfert hors de l'USI, selon des scénarios préalablement définis. Les facteurs associés à la coprescription d'opioïdes amorcée par l'hôpital ont été analysés par régression logistique multivariée.

Résultats : Au total, 735 patients répondaient aux critères d'inclusion. Lors du transfert hors de l'USI, des opioïdes étaient coprescrits à 23,0 % (169/735) d'entre eux; de ces coprescriptions, 87,0 % (147/169) étaient amorcées par l'hôpital. Au moment du congé hospitalier, des opioïdes étaient coprescrits à 8,6 % (44/514) d'entre eux; de ces coprescriptions, 56,8 % (25/44) étaient amorcées par l'hôpital. Le sexe masculin, la coprescription d'opioïdes à domicile, l'admission en chirurgie, le séjour prolongé à l'hôpital et le décès à l'hôpital étaient fortement associés à la coprescription d'opioïdes amorcée par l'hôpital au moment du transfert hors de l'USI. La coprescription d'opioïdes à domicile était fortement associée à la coprescription d'opioïdes au moment du congé de l'hôpital.

Conclusions : Les coprescriptions d'opioïdes amorcées par l'hôpital représentaient la majorité des coprescriptions au moment du transfert hors de l'USI et au moment du congé de l'hôpital. Les pharmaciens doivent évaluer toutes les coprescriptions d'opioïdes pour déterminer si l'arrêt et/ou la réduction de la dose est appropriée.

Mots-clés : coprescription d'opioïdes, opioïde, sédatif, soins intensifs, facteurs associés

INTRODUCTION

Opioid misuse is a major health care concern in Canada, and long-term opioid use increases the risk of opioid use disorder, overdose, and death.[1] In Nova Scotia, where this study was conducted, opioids are prescribed at a higher rate than the national average.[2] Most patients admitted to an intensive care unit (ICU) are exposed to opioids,[3] and the use of opioids is promoted by guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in ICU patients.[3] These guidelines recommend an analgesia-first (analgesic used before a sedative) or analgesia-based (analgesic used instead of a sedative) approach.[3]

Sedatives are prescribed in the ICU for various indications,[3] but emerging evidence suggests that concurrent administration of sedatives and opioids intensifies the risk of opioid-related harm.[4-10] For example, coprescription of opioids with benzodiazepines has been associated with increased risk of adverse outcomes, including death, relative to opioids or benzodiazepines alone.[5,11-15] Despite their known risks, such as delirium, benzodiazepines are frequently prescribed in the ICU for their sedative effects.[3,16,17] The Canadian guideline for opioids for chronic noncancer pain states that opioids and benzodiazepines should very rarely be prescribed together because of the risks of enhanced depressant effects.[18]

Other sedatives, such as z-drugs, gabapentinoids, tricyclic antidepressants (TCAs), and antipsychotics, may be prescribed in combination with opioids in the ICU. Z-drugs, which are benzodiazepine receptor agonists, are commonly prescribed as sleep aids. Medications such as gabapentinoids and TCAs are recommended as part of a multimodal approach for management of neuropathic pain in the ICU.[3] Antipsychotics are used to treat delirium in the ICU, although there is a lack of evidence for efficacy.[3,19-21] Coprescription of opioids with these sedatives has also been associated with an increased risk of adverse events.[6-12,22,23]

The ICU may be a source of initiation of opioid coprescriptions, defined as the combination of an opioid with a sedative. Local prescribing patterns for opioid coprescriptions after an ICU admission were previously unknown. The purposes of this study were to evaluate the proportions of patients with opioid coprescriptions at the time of ICU transfer and hospital discharge and to determine factors associated with hospital-initiated opioid coprescriptions. Understanding prescribing patterns and associated factors could inform future strategies for determining appropriate use, deprescribing, and opioid and sedative stewardship.

METHODS

This retrospective study involved patients admitted to the medical–surgical and medical–surgical–neurological ICUs of the Queen Elizabeth II Health Sciences Centre (QEII HSC) at Nova Scotia Health in Halifax, Nova Scotia, from April 1, 2018, to March 31, 2019. The QEII HSC is a tertiary care centre with two level 1 ICUs, one 12-bed medical–surgical–neurological ICU, and one 8-bed medical–surgical ICU. The ICUs serve patients from across the Atlantic provinces, are staffed by intensivists, have a 1:1 nurse-to-patient ratio, and are staffed by clinical pharmacists 5 days a week for 8 h/day.

Patients included in the analysis were 16 years of age or older, had survived to ICU transfer, and had complete hospital admission and ICU transfer medication reconciliation forms. For patients with multiple hospital admissions during the study period, each admission was assessed separately; for patients with multiple ICU admissions during their hospital stay, only the last ICU admission was included.

This study was approved by the Nova Scotia Health Research Ethics Board on March 5, 2020 (file 1025396), and the need for participant consent was waived.

Outcome Measures

The primary outcomes were the proportions of patients with an opioid coprescription at ICU transfer and at hospital discharge, as well as the proportions of opioid coprescriptions that were hospital-initiated at these time points. The proportion of patients with opioid coprescriptions at hospital discharge included those for whom the medications were prescribed at ICU transfer and subsequently continued at hospital discharge. Opioid coprescriptions initiated after patients were transferred out of the ICU (before discharge from hospital) were not included. The appropriateness of medication use was not assessed.

An opioid coprescription was defined as the concurrent prescription of at least one opioid with at least one sedative. Sedatives included benzodiazepines, z-drugs, gabapentinoids, TCAs, and antipsychotics (for a complete list of the drugs considered in this study, see Appendix 1, available from https://www.cjhp-online.ca/index.php/cjhp/issue/view/213). Patients' home medications before admission and medication changes made in hospital were analyzed to determine whether opioid coprescriptions were hospital-initiated. Opioid coprescriptions were considered hospital-initiated in the following scenarios: the patient was receiving neither an opioid nor a sedative at home, and both were initiated in hospital; the patient was receiving an opioid at home, and a sedative was initiated in hospital; the patient was receiving a sedative at home, and an opioid was initiated in hospital; the patient was receiving an opioid and a sedative at home, and the opioid dose was increased in hospital; the patient was receiving an opioid and a sedative at home, and another sedative was initiated in hospital; and the patient was receiving an opioid and a sedative at home, and a different sedative was initiated in hospital. An increase in sedative dose was not a criterion for hospital-initiated opioid coprescription, because dose-related adverse effects have been established for benzodiazepines[5,24] and

gabapentinoids[7,8] but not for the other sedative drug classes, and dose conversion between the sedative drug classes has not been established.

The secondary outcome consisted of factors associated with hospital-initiated opioid coprescription at ICU transfer and hospital discharge. Data were collected for the following characteristics: age, sex, comorbidities (AIDS, cirrhosis, hepatic failure, immunosuppression, leukemia/multiple myeloma, lymphoma, and metastatic cancer), long-term dialysis, home opioid coprescriptions, patient type (medical or surgical), Acute Physiology and Chronic Health Evaluation (APACHE) IV predicted mortality, duration of invasive mechanical ventilation, presence of delirium (according to the Confusion Assessment Method in the ICU) in the 24 h before ICU transfer, level of sedation (according to the Richmond Agitation-Sedation Scale) in the 24 h before ICU transfer, ICU length of stay, number of readmissions to the ICU, hospital length of stay, and hospital discharge location.

Data Collection and Procedures

The ICU clinical database was used to generate a list of patients admitted to the QEII HSC ICUs from April 1, 2018, to March 31, 2019, who were 16 years of age or older and who survived to ICU transfer.

The digital patient record (OneContent by Allscripts Healthcare) was used to view medication reconciliation forms at the time of admission, ICU transfer, and hospital discharge and to collect medication names, routes of administration, and doses. For patients discharged from hospital directly from the ICU, the hospital discharge medication reconciliation form was also considered their ICU transfer medication reconciliation form. Total daily doses were collected for opioids, benzodiazepines, and gabapentinoids because dose-related risks have been identified with these medications.[5,7,8,24,25] For medications prescribed on an "as needed" basis or with dose or frequency ranges, the maximum possible total daily dose was collected. Opioid doses were converted to morphine milligram equivalents (MME),[18] and benzodiazepine doses were converted to diazepam milligram equivalents (DME).[26] Data collection was performed by the principal investigator (T.T.), and 10% of patient records were reviewed by a co-investigator (H.N. or S.B.) to ensure accuracy. The categorization of opioid coprescriptions as hospital-initiated was performed by the principal investigator (T.T.) and confirmed by a co-investigator (H.N. or S.B.).

Data Analysis

Baseline characteristics and primary outcomes were summarized descriptively. For the secondary outcome, patients were divided into 2 groups: those with and those without hospital-initiated opioid coprescription. Variable data collected from the ICU clinical database were tested for association with hospital-initiated opioid coprescription at ICU transfer and hospital discharge. Univariable nonparametric analyses at each time point were performed using all variables. For the multivariable logistic regression analyses, one variable for every 10 cases was used to reduce the potential effect of overfitting.[27] After the univariable analysis, variables were ranked in order of importance in predicting the outcome, on the basis of clinical expert reasoning and variables found to be significant in the literature.[27] Variables were ranked as follows, beginning with the highest importance: home opioid coprescription, patient type (medical or surgical), ICU length of stay, hospital length of stay, APACHE IV predicted mortality, duration of invasive mechanical ventilation, sex, age, hospital discharge location, presence of delirium, comorbidities, level of sedation, number of ICU readmissions, and long-term dialysis. Multivariable logistic regression was conducted for each time point to determine significant factors ($p < 0.05$) independently associated with hospital-initiated opioid coprescription. All data were analyzed in IBM SPSS Statistics for Windows, version 26.0.

RESULTS

Overall, 848 adults were admitted to the QEII HSC ICUs between April 1, 2018, and March 31, 2019, and survived to ICU transfer. Of those screened, 735 were included, and 514 (69.9%) of these were discharged from the QEII HSC with legible discharge medication reconciliation forms and were included in the hospital discharge analysis (Figure 1). The median age of included patients was 63 years, and 61.0% were male (Table 1). Before hospital admission, 11.6% (85/735) of the patients had opioid coprescriptions. The median ICU length of stay was 2.45 days, and 69.1% of patients received mechanical ventilation.

The proportion of patients with an opioid coprescription at ICU transfer was 23.0% (169/735), and 87.0% (147/169) of these opioid coprescriptions were hospital-initiated (Table 2). Of the patients with a hospital-initiated opioid coprescription at ICU transfer, 40.1% (59/147) had not been receiving an opioid or a sedative at home (before the hospital stay), 36.7% (54/147) had been receiving a sedative only, and merely 3.4% (5/147) had been receiving an opioid only. At hospital discharge, the proportion of patients with an opioid coprescription was 8.6% (44/514), and 56.8% (25/44) of these opioid coprescriptions were hospital-initiated (Table 2). All patients who were discharged with a hospital-initiated opioid coprescription had been receiving a sedative (18/25) or both an opioid and a sedative (7/25) at home. Patients with opioid coprescription at home and categorized as having a hospital-initiated opioid coprescription most commonly met the definition because their opioid dose had been increased (26/29 at ICU transfer and 7/7 at hospital discharge).

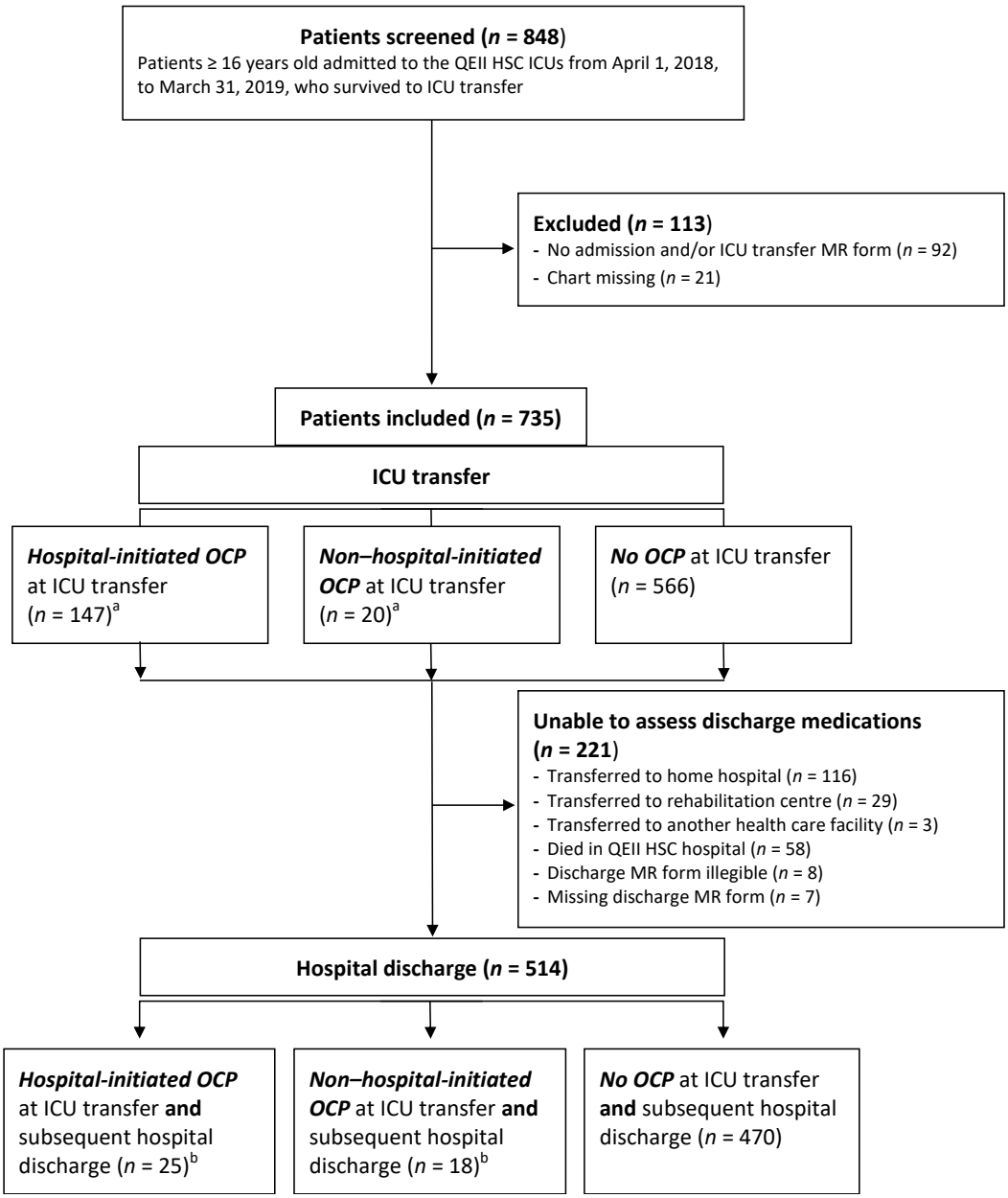

FIGURE 1. Patient flow chart. ICU = intensive care unit, MR = medication reconciliation, OCP = opioid coprescription, QEII HSC = Queen Elizabeth II Health Sciences Centre. [a]For 2 patients, unable to assess whether OCP met hospital-initiated criteria because medication information was missing. [b]For 1 patient, unable to assess whether OCP met hospital-initiated criteria because medication information was missing.

Median daily doses of opioids, benzodiazepines, and gabapentinoids were higher at ICU transfer than at hospital discharge (Table 3). Benzodiazepines (46.3%) and antipsychotics (38.8%) were the sedatives most commonly prescribed at ICU transfer, whereas benzodiazepines (72.0%), z-drugs (28.0%), and gabapentinoids (28.0%) were most commonly prescribed at hospital discharge. Hospital-initiated opioid coprescriptions with multiple sedatives were common at ICU transfer (36.7%) and hospital discharge (60.0%) (Table 3).

In the multivariable logistic regression at ICU transfer, up to 14 variables could be tested in the model with 147 cases. Male sex, home opioid coprescription, surgical patient, prolonged hospital stay, and in-hospital mortality were significantly associated with a hospital-initiated opioid coprescription (Table 4). The multivariable logistic regression at hospital discharge, with 25 cases, tested the 2 highest-ranking variables. Home opioid coprescription was significantly associated with hospital-initiated opioid coprescription (Table 5). The ICU transfer model explained 12.1% (Nagelkerke R^2) of the variance in the outcome, and the hospital discharge model explained 4.8% (Nagelkerke R^2) of the variance in the outcome.

TABLE 1 (Part 1 of 2). Baseline and Hospital Stay Characteristics

Characteristic	No. (%) of Patients[a]
Age (years) (median and IQR)	*n* = 735 63 (51–71)
Sex	*n* = 735
Male	448 (61.0)
Female	287 (39.0)
Medications prescribed at home[b]	*n* = 735
No opioid or sedative	438 (59.6)
Opioid	131 (17.8)
Sedative	251 (34.1)
Opioid coprescription	85 (11.6)
APACHE IV comorbidities[b]	*n* = 721
None	593 (82.2)
AIDS	6 (0.8)
Cirrhosis	34 (4.7)
Hepatic failure	17 (2.4)
Immunosuppression	33 (4.6)
Leukemia/multiple myeloma	10 (1.4)
Lymphoma	20 (2.8)
Metastatic cancer	47 (6.5)
Long-term dialysis	*n* = 721 41 (5.7)
ICU admission source	*n* = 732
Direct admission	18 (2.5)
Emergency department	234 (32.0)
Medicine	81 (11.1)
Obstetrics	3 (0.4)
Operating room/postoperative recovery area	326 (44.5)
Psychiatry	2 (0.3)
Surgery	1 (0.1)
Other unit	67 (9.2)
ICU admission location	*n* = 735
Medical–surgical ICU	270 (36.7)
Medical–surgical–neurological ICU	465 (63.3)
Patient type	*n* = 730
Medical	368 (50.4)
Surgical	362 (49.6)
ICU diagnosis	*n* = 731
Cardiovascular	118 (16.1)
Gastrointestinal	122 (16.7)
Genitourinary	38 (5.2)
Hematologic	5 (0.7)
Metabolic/endocrine	6 (0.8)
Musculoskeletal/skin	22 (3.0)
Neurological/neurosurgical	131 (17.9)
Respiratory	153 (20.9)
Sepsis	59 (8.1)
Transplant	19 (2.6)
Trauma	58 (7.9)

TABLE 1 (Part 2 of 2). Baseline and Hospital Stay Characteristics

Characteristic	No. (%) of Patients[a]
APACHE IV predicted mortality	*n* = 693
Low (< 20%)	425 (61.3)
Medium (20%–80%)	250 (36.1)
High (> 80%)	18 (2.6)
Mechanical ventilation	*n* = 734
No. (%)	507 (69.1)
Duration (days) (median and IQR)	0.80 (0–2.11)
CAM-ICU in the 24 h before ICU transfer	*n* = 707
Positive (delirious)	134 (19.0)
Negative (not delirious)	573 (81.0)
Level of sedation in the 24 h before ICU transfer	*n* = 733
RASS –5 to –2 (sedated or comatose)	51 (7.0)
RASS –1 to +1 (target range)	595 (81.2)
RASS +2 to +4 (agitated)	12 (1.6)
Declassed[c]	75 (10.2)
ICU length of stay (days) (median and IQR)	*n* = 735 2.45 (1.26–4.84)
ICU transfer location	*n* = 735
Home	45 (6.1)
Medicine	264 (35.9)
Obstetrics	3 (0.4)
Psychiatry	4 (0.5)
Surgery	397 (54.0)
Other	22 (3.0)
ICU readmissions	*n* = 735
None	702 (95.5)
1	28 (3.8)
2	4 (0.5)
3	1 (0.1)
Hospital length of stay (days) (median and IQR)	*n* = 727 14.72 (7.46–35.07)
Hospital discharge location	*n* = 734
Home	581 (79.2)
Long-term care facility	18 (2.5)
Rehabilitation centre	39 (5.3)
Another hospital	30 (4.1)
Morgue (died in hospital)	66 (9.0)

APACHE = Acute Physiology and Chronic Health Evaluation, CAM-ICU = Confusion Assessment Method for the Intensive Care Unit, ICU = intensive care unit, IQR = interquartile range, RASS = Richmond Agitation and Sedation Scale.

[a]Except where indicated otherwise.

[b]Sum of percentages is greater than 100 because some patients are included in more than one group.

[c]Level of sedation was not documented for patients who were declassed to a lower level of care.

TABLE 2. Proportions of Opioid Coprescriptions at ICU Transfer and Hospital Discharge

Outcome	No. (%) of Patients
Opioid coprescription at ICU transfer	169/735 (23.0)
Hospital-initiated opioid coprescription at ICU transfer[a]	147/169 (87.0)
Opioid coprescription at ICU transfer and subsequent hospital discharge	44/514 (8.6)
Hospital-initiated opioid coprescription at ICU transfer and subsequent hospital discharge[b]	25/44 (56.8)

ICU = intensive care unit
[a]For 2 patients, unable to assess whether opioid coprescription met hospital-initiated criteria because of missing medication information.
[b]For 1 patient, unable to assess whether opioid coprescription met hospital-initiated criteria because of missing medication information.

TABLE 3. Characteristics of Hospital-Initiated Opioid Coprescriptions

Characteristics	No. (%)[a] At ICU Transfer (*n* = 147)	No. (%)[a] At Hospital Discharge (*n* = 25)
Daily dose (median and IQR)		
Opioid (MME)	128 (64–308)[b]	72 (48–128)[b]
Benzodiazepine (DME)	32 (20–120) (*n* = 68)	20 (10–33) (*n* = 18)
Gabapentin (mg)	800 (300–900) (*n* = 26)	600 (500–2100) (*n* = 5)
Pregabalin (mg)	225 (138–338) (*n* = 10)	188 (*n* = 2)
Type of sedative		
Benzodiazepine	68 (46.3)	18 (72.0)
Z-drug	29 (19.7)	7 (28.0)
Gabapentinoid	36 (24.5)	7 (28.0)
Tricyclic antidepressant	13 (8.8)	3 (12.0)
Antipsychotic	57 (38.8)	6 (24.0)
No. of sedatives		
1	93 (63.3)	10 (40.0)
≥ 2	54 (36.7)	15 (60.0)

DME = diazepam milligram equivalent, ICU = intensive care unit, IQR = interquartile range, MME = morphine milligram equivalent.
[a]Except where indicated otherwise.
[b]Two doses were unknown.

DISCUSSION

To our knowledge, the rate of opioid coprescription after an ICU admission has not been previously studied. In our study, almost one-quarter of patients were transferred out of the ICU with an opioid coprescription, the majority of which were hospital-initiated. The proportion of patients with an opioid coprescription at discharge was much lower, and over half of these were hospital-initiated. While it is encouraging that the proportion of patients with opioid coprescriptions drastically decreased from ICU transfer to hospital discharge, previous studies have found risks associated with opioid coprescriptions during hospital admissions,[10,23] so assessment of opioids and sedatives and their doses is essential at every transfer of care. A higher proportion of patients had opioid coprescriptions before hospital admission than at hospital discharge. When considering these results, it is important to highlight that the group analyzed at admission and ICU transfer was different from (and smaller than) the group analyzed at hospital discharge, because for 221 patients, discharge medication reconciliation forms were not available.

Benzodiazepines were the most common sedative in hospital-initiated opioid coprescriptions. This may not be surprising, given that benzodiazepines and related drugs were prescribed at a higher rate in Nova Scotia relative to the Canadian average.[2] Opioid coprescriptions with benzodiazepines have been reported in the literature,[5,11-15] and have been associated with twice the risk of emergency room visits or inpatient admissions[15] and higher rates of overdose.[3,5,13,14] Despite recommendations against the use of benzodiazepines for sedation and recommendations to avoid concomitantly prescribed opioids,[3,18,28,29] opioids and benzodiazepines were commonly prescribed together at our institution.

Gabapentinoids, which were present in one-quarter of hospital-initiated opioid coprescriptions in this study, have been associated with twice the odds of opioid-related death compared with opioids alone.[7,8] In 2019, Health Canada issued a safety alert advising caution in the concomitant use of opioids and gabapentinoids.[30] In contrast, gabapentinoids are recommended as adjuncts to opioids for neuropathic pain in critically ill patients, in part because of their opioid-sparing abilities.[3] We did not assess medication appropriateness, so could not determine whether the benefits of this combination outweighed the risks for the patients in this study.

The risks of adverse outcomes of z-drugs, antipsychotics, and TCAs in combination with opioids are less well documented. Among patients receiving opioid maintenance treatment, z-drugs were associated with 1.6 times the risk of overdose death compared with opioid maintenance treatment alone.[31] Long-term concomitant use of antipsychotics with opioids has been found to put men at higher risk of fractures.[9] TCAs, like gabapentinoids, may have been appropriately prescribed for neuropathic pain[5] in our patient population. However, TCAs were included in a group of sedatives that were associated with increased risk of cardiopulmonary and respiratory arrest in hospital when combined with opioids, relative to opioids or sedatives alone.[10] There is also evidence that treatment with more than one sedative in combination with an opioid may result in greater

TABLE 4. Factors Associated with Hospital-Initiated Opioid Coprescription (HI-OCP) at ICU Transfer

Factor	No. (%)[a] No HI-OCP	HI-OCP	*p* Value	B	Adjusted OR (95% CI)	*p* Value
Age (years) (median and IQR)	*n* = 586 63 (51–72)	*n* = 147 60 (50–69)	0.064	–0.007	0.993 (0.980–1.006)	0.29
Sex	*n* = 586	*n* = 147				
Female	240 (41.0)	46 (31.3)	0.040		–	
Male	346 (59.0)	101 (68.7)		0.422	1.525 (1.005–2.313)	0.047
Opioid coprescription at home	*n* = 586 54 (9.2)	*n* = 147 29 (19.7)	0.001	1.119	3.063 (1.795–5.227)	< 0.001
APACHE IV comorbidities[b]	*n* = 577	*n* = 142				
None	476 (82.5)	116 (81.7)	0.92			
AIDS	4 (0.7)	2 (1.4)	0.75			
Cirrhosis	31 (5.4)	3 (2.1)	0.16			
Hepatic failure	13 (2.3)	4 (2.8)	0.93			
Immunosuppression	28 (4.9)	5 (3.5)	0.65			
Leukemia/multiple myeloma	9 (1.6)	1 (0.7)	0.70			
Lymphoma	15 (2.6)	4 (2.8)	> 0.99			
Metastatic cancer	37 (6.4)	10 (7.0)	0.93			
Long-term dialysis	*n* = 577 31 (5.4)	*n* = 142 10 (7.0)	0.57			
Patient type	*n* = 583	*n* = 145				
Medical	311 (53.3)	57 (39.3)	0.003		–	
Surgical	272 (46.7)	88 (60.7)		0.880	2.411 (1.544–3.764)	< 0.001
APACHE IV predicted mortality (median and IQR)	*n* = 550 13.95 (4.18–32.06)	*n* = 142 12.48 (4.41–32.80)	0.89			
Duration of mechanical ventilation (days) (median and IQR)	*n* = 585 0.75 (0.00–1.93)	*n* = 147 1.00 (0.00–2.68)	0.028	0.084	1.088 (0.981–1.207)	0.11
CAM-ICU in 24 h before ICU transfer	*n* = 567	*n* = 138				
Positive (delirious)	103 (18.2)	31 (22.5)	0.30			
Negative (not delirious)	464 (81.8)	107 (77.5)				
Level of sedation in 24 h before ICU transfer	*n* = 585	*n* = 146				
RASS –5 to –2 (sedated or comatose)	40 (6.8)	11 (7.5)	0.51			
RASS –1 to +1 (target)	471 (80.5)	123 (84.2)				
RASS +2 to +4 (agitated)	10 (1.7)	2 (1.4)				
Declassed	64 (10.9)	10 (6.8)				
ICU length of stay (days) (median and IQR)	*n* = 586 2.38 (1.29–4.66)	*n* = 147 2.84 (1.17–6.22)	0.15			
ICU readmissions	*n* = 586	*n* = 147				
None	562 (95.9)	138 (93.9)	0.21			
1	21 (3.6)	7 (4.8)				
2	3 (0.5)	1 (0.7)				
3	0 (0.0)	1 (0.7)				
Hospital length of stay (days) (median and IQR)	*n* = 580 14.15 (7.22–31.81)	*n* = 145 21.71 (9.81–50.16)	< 0.001	0.005	1.005 (1.001–1.009)	0.021
Hospital discharge location	*n* = 585	*n* = 147				
Home	474 (81.0)	105 (71.4)	0.033		–	0.043
Long-term care facility	16 (2.7)	2 (1.4)		–1.768	0.171 (0.019–1.523)	0.11
Rehabilitation centre	26 (4.4)	13 (8.8)		0.646	1.908 (0.894–4.072)	0.10
Another hospital	22 (3.8)	8 (5.4)		0.430	1.537 (0.595–3.966)	0.37
Morgue (died in hospital)	47 (8.0)	19 (12.9)		0.644	1.904 (1.012–3.582)	0.046

APACHE = Acute Physiology and Chronic Health Evaluation, CAM-ICU = Confusion Assessment Method for the Intensive Care Unit, CI = confidence interval, ICU = intensive care unit, IQR = interquartile range, OR = odds ratio, RASS = Richmond Agitation and Sedation Scale.

[a]Except where indicated otherwise.

[b]Sum of percentages is greater than 100 because some patients are included in more than one group.

TABLE 5. Factors Associated with Hospital-Initiated Opioid Coprescription (HI-OCP) at Hospital Discharge[a]

Factor	No. (%)[b] No HI-OCP	No. (%)[b] HI-OCP	*p* Value	B	Adjusted OR (95% CI)	*p* Value
Age (years) (median and IQR)	*n* = 488 63 (52–63)	*n* = 25 54 (50–60)	0.002			
Sex	*n* = 488	*n* = 25				
Female	295 (60.5)	14 (56.0)	0.82			
Male	193 (39.5)	11 (44.0)				
Opioid coprescription at home	*n* = 488	*n* = 25				
	52 (10.7)	7 (28.0)	0.020	1.130	3.096 (1.160–8.262)	0.024
APACHE IV comorbidities[c]	*n* = 482	*n* = 24				
None	388 (80.5)	16 (66.7)	0.17			
AIDS	4 (0.8)	0 (0.0)	> 0.99			
Cirrhosis	20 (4.1)	1 (4.2)	> 0.99			
Hepatic failure	11 (2.3)	3 (12.5)	0.019			
Immunosuppression	28 (5.8)	0 (0.0)	0.45			
Leukemia/multiple myeloma	7 (1.5)	0 (0.0)	> 0.99			
Lymphoma	13 (2.7)	1 (4.2)	> 0.99			
Metastatic cancer	41 (8.5)	4 (16.7)	0.32			
Long-term dialysis	*n* = 482	*n* = 24				
	26 (5.4)	2 (8.3)	0.88			
Patient type	*n* = 487	*n* = 24				
Medical	236 (48.5)	7 (29.2)	0.10		–	
Surgical	251 (51.5)	17 (70.8)		0.904	2.470 (0.996–6.124)	0.051
APACHE IV predicted mortality (median and IQR)	*n* = 462 11.84 (3.65–25.38)	*n* = 25 8.16 (2.94–22.52)	0.34			
Duration of mechanical ventilation (days) (median and IQR)	*n* = 487 0.67 (0.00–1.47)	*n* = 25 1.12 (0.60–3.19)	0.016			
CAM-ICU in 24 h before ICU transfer	*n* = 475	*n* = 25				
Positive (delirious)	61 (12.8)	4 (16.0)				
Negative (not delirious)	414 (87.2)	21 (84.0)	0.88			
Level of sedation in 24 h before ICU transfer	*n* = 487	*n* = 25				
RASS –5 to –2 (sedated or comatose)	27 (5.5)	2 (8.0)	0.88			
RASS –1 to +1 (target)	407 (83.6)	21 (84.0)				
RASS +2 to +4 (agitated)	7 (1.4)	0 (0.0)				
Declassed	46 (9.4)	2 (8.0)				
ICU length of stay (days) (median and IQR)	*n* = 488 2.11 (1.16–3.83)	*n* = 25 1.93 (0.99–5.39)	0.73			
ICU readmissions	*n* = 488	*n* = 25				
None	471 (96.5)	23 (92.0)	0.39			
1	15 (3.1)	2 (8.0)				
2	2 (0.4)	0 (0.0)				
3	0 (0.0)	0 (0.0)				
Hospital length of stay (days) (median and IQR)	*n* = 487 11.84 (6.63–22.58)	*n* = 25 22.86 (9.79–42.04)	0.015			
Hospital discharge location	*n* = 488	*n* = 25				
Home	480 (98.4)	24 (96.0)	0.92			
Long-term care facility	8 (1.6)	1 (4.0)				
Rehabilitation centre	0 (0.0)	0 (0.0)				
Another hospital	0 (0.0)	0 (0.0)				
Morgue (died in hospital)	0 (0.0)	0 (0.0)				

APACHE = Acute Physiology and Chronic Health Evaluation, CAM-ICU = Confusion Assessment Method for the Intensive Care Unit, CI = confidence interval, ICU = intensive care unit, IQR = interquartile range, OR = odds ratio, RASS = Richmond Agitation and Sedation Scale.

[a]The 2 highest-ranked variables (home coprescription and patient type) were entered in the multivariable logistic regression model.

[b]Except where indicated otherwise.

[c]Sum of percentages is greater than 100 because some patients are included in more than one group.

risks.[4,7,8,11,25,32] One report described a higher risk of overdose when benzodiazepines and z-drugs were combined with opioids, relative to opioids and a single sedative.[11]

In one study of outpatients for whom opioids were dispensed, the odds of death were higher for patients with daily MME of at least 50 relative to patients with doses of 1–19 MME.[25] Based on opioid dose alone, the majority of patients in our study were potentially at increased odds of death, given that the median doses were above 50 MME. Benzodiazepines and gabapentinoids have been reported to have a dose-related impact on the odds of opioid-related death.[5,7,8] Based on the dose-related risks of these medications, clinicians should aim to prescribe the lowest effective dose.

Identification of characteristics associated with hospital-initiated opioid coprescription will help focus efforts to discontinue opioid coprescriptions after an ICU admission. Factors associated with prescription of opioids and some sedatives in the ICU and general inpatient population have been studied.[20,21,33-39] In the current study, home opioid coprescription was the factor most strongly associated with hospital-initiated opioid coprescription at both time points. Similarly, Yaffe and others[33] identified preadmission opioid use as a factor associated with opioid use after an ICU admission. An ICU stay may be associated with pain and increased opioid requirements, and many home opioid coprescriptions were categorized as hospital-initiated because the opioid dose was increased during the hospital stay.

Male sex was significantly associated with hospital-initiated opioid coprescription at ICU transfer. In one study, men were more likely to have an antipsychotic initiated in the ICU.[34] Our results may be explained by the high proportion of hospital-initiated opioid coprescriptions with antipsychotics at ICU transfer; however, without more data, the significance of male sex as a factor associated with hospital-initiated opioid coprescription is unknown. Surgical patients, relative to medical patients, were more likely to have a hospital-initiated opioid coprescription at ICU transfer. This may be partially explained by the need for pain control after surgery.

Hospital length of stay and in-hospital death may be correlated with severity and complexity of illness, and sicker patients may have been more likely to require opioids and sedatives. Therefore, it is not surprising that prolonged hospital stay and in-hospital death were identified as significant factors at ICU transfer in our study. A longer hospital stay was also associated with long-term opioid use after an ICU admission at our institution.[33] It is unknown whether longer hospital stays led to hospital-initiated opioid coprescriptions or if patients remained in hospital longer because of their opioid and sedative regimen. The possibility that hospital-initiated opioid coprescriptions led to higher mortality cannot be ruled out.

Opioids and some sedatives have valid indications for use in the ICU[3]; however, there is a lack of guidance on the appropriateness of their use after an ICU admission. Emerging data indicate that pharmacists can play an important role in reducing opioid coprescribing through opioid and sedative stewardship. In one study, intervention by a pharmacist resulted in the discontinuation of approximately half (8/17) of ICU-initiated antipsychotics after ICU transfer.[38] In another study involving patients with opioid and benzodiazepine coprescriptions at a primary care clinic in Ontario, a pharmacist-led intervention decreased MME by 11% and DME by 8%, whereas the control group's MME increased by 15% and DME decreased by 4%.[40] Although assessing the appropriateness of opioid coprescriptions was beyond the scope of our work, it is recommended to evaluate the use of this combination to reduce unnecessary medication-related risks.

This study had limitations. We were unable to assess ICU-initiated medications because medication reconciliation was not consistently completed upon admission to ICU. Therefore, a detailed definition of hospital-initiated opioid coprescription was developed to focus on the opportunity for intervention at the time of ICU transfer. This study was conducted at 2 tertiary care ICUs, and the results may not be generalizable to other institutions; however, the study population was large. We were unable to access the discharge medication reconciliation forms of patients transferred to other facilities outside the QEII HSC. Reliance on the medication reconciliation forms for data collection presented 2 limitations. First, in Nova Scotia, outpatient opioid prescriptions must be written on a separate prescription and hence may not be documented on the discharge medication reconciliation form, which may have resulted in an underestimate of opioid coprescriptions at hospital discharge. Second, because we collected data from medication reconciliation forms, we did not obtain information about actual use of medications prescribed "as needed" or with dose or frequency ranges, and we collected doses as the maximum possible dose. The reliance on collecting data retrospectively is a limitation; however, data accuracy was enhanced by the audit of 10% of data collected from the medication reconciliation forms; in addition, the ICU clinical database has strong quality controls in place. The logistic regression analysis for opioid coprescription at discharge was limited to 2 variables in the model because of the small number of cases. Both logistic regression analyses explained a small amount of the variability in the models, which suggests the presence of unmeasured confounders. Finally, the indications for opioid and sedative prescriptions were not collected, which prevented an assessment of appropriateness.

CONCLUSION

Nearly one-quarter (23%) of ICU patients had opioid coprescriptions at ICU transfer, and 9% had opioid coprescriptions at hospital discharge, the majority of which were

hospital-initiated. Pharmacists can play a role as stewards of opioid and sedative therapy by assessing all opioid coprescriptions to determine whether discontinuation and/or dose reduction is appropriate to minimize potential risks. Male sex, opioid coprescriptions at home (before the hospital stay), surgical admission, and prolonged hospital stay were associated with higher odds of hospital-initiated opioid coprescription. The identified factors should be evaluated to determine barriers for discontinuation and to identify alternative management strategies for opioid and sedative stewardship.

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Development of Quality Indicators to Evaluate the Appropriateness of Empiric Antimicrobial Use in Pediatric Patients

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ABSTRACT

Background: Use of quality indicators is one strategy recommended to assess antimicrobial prescribing for pediatric inpatients.

Objective: To achieve consensus from infectious diseases clinicians on quality indicators that characterize appropriate empiric antimicrobial use for the management of infectious syndromes in pediatric inpatients.

Methods: This study was completed using the Delphi technique. The research team developed an initial list of quality indicators, informed by a literature search. A multidisciplinary group of health care providers with expertise in infectious diseases was invited to participate. The list was disseminated to this panel of experts using Opinio survey software. The experts were asked to rate the indicators on a 9-point Likert scale in relation to the following criterion: "The importance of each item in determining appropriateness considering benefit or harm at the individual or population level". Consensus was defined as at least 75% agreement and a median score of 7 or higher.

Results: Twelve of 31 invited experts completed at least 1 round of the survey, and 10 completed all rounds. Consensus was achieved on 28 of 31 proposed indicators after 3 rounds. Indicators with consensus were categorized under "empiric choice" (n = 12 indicators), "dose" (n = 5), "duration" (n = 2), "administration" (n = 4), "diagnosis" (n = 2), and "documentation" (n = 3). Six of the indicators for which consensus was achieved were rephrased by the experts.

Conclusions: Consensus was achieved on quality indicators to assess the appropriateness of empiric antimicrobial use in pediatric patients. Clinicians and researchers can use these consensus-based indicators to assess adherence to best practice.

Keywords: antimicrobial use, pediatrics, quality indicators

RÉSUMÉ

Contexte : L'utilisation d'indicateurs de qualité est l'une des stratégies recommandées pour évaluer la prescription d'antimicrobiens aux patients pédiatriques hospitalisés.

Objectif : Parvenir à un consensus, entre les cliniciens des maladies infectieuses, portant sur les indicateurs de qualité qui caractérisent l'utilisation empirique appropriée des antimicrobiens pour la prise en charge des syndromes infectieux chez les patients pédiatriques hospitalisés.

Méthodes : Cette étude a été réalisée à l'aide de la technique Delphi. L'équipe de recherche a dressé une liste initiale d'indicateurs de qualité éclairée par une recherche documentaire. Un groupe multidisciplinaire de prestataires de soins de santé ayant une expertise dans le domaine des maladies infectieuses a été invité à participer. La liste a été diffusée à ce panel d'experts à l'aide du logiciel d'enquête Opinio. Les experts ont été invités à noter les indicateurs sur une échelle de Likert de 9 points par rapport au critère suivant : « L'importance de chaque élément pour déterminer la pertinence compte tenu du bienfait ou du dommage à l'échelle individuelle ou de la population ». Le consensus était défini comme « Un accord d'au moins 75 % et un score médian d'au moins 7 ».

Résultats : Douze des 31 experts invités ont terminé au moins 1 cycle de l'enquête et 10 les ont tous terminés. Un consensus a été atteint pour 28 des 31 indicateurs proposés après 3 cycles. Les indicateurs qui ont atteint le consensus ont été classés en « choix empirique » (n = 12 indicateurs), « dose » (n = 5), « durée » (n = 2), « administration » (n = 4), « diagnostic » (n = 2) et « documentation » (n = 3). Six indicateurs faisant consensus ont été reformulés par les experts.

Conclusions : Un consensus a été atteint pour les indicateurs de qualité visant à évaluer l'utilisation empirique appropriée des antimicrobiens chez les patients pédiatriques. Les cliniciens et les chercheurs peuvent utiliser ces indicateurs basés sur le consensus pour évaluer le respect des meilleures pratiques.

Mots-clés : utilisation d'antimicrobiens, pédiatrie, indicateurs de qualité

INTRODUCTION

Antimicrobial resistance is an increasing threat to human health worldwide. In Canada, more than a quarter of infections are currently resistant to the antimicrobial agents typically used to treat them, and this proportion is expected to rise to 40% by 2050.[1] Antimicrobial resistance is also a growing concern in the United States. More than 2.8 million antimicrobial-resistant infections and 35 000 related deaths occur each year in the United States alone.[2] Without

action, many life-saving medical advances will no longer be available.[1,2] Antimicrobial resistance also has significant socioeconomic implications. A decline in gross domestic product is projected to result from decreased labour productivity. Broader societal concerns have also been suggested, including a decrease in quality of life, social trust, and equality.[1]

Inappropriate antimicrobial use contributes to development of antimicrobial resistance and negative health outcomes, including increased risk of death.[3,4] Antimicrobial stewardship, defined as "coordinated interventions designed to improve and measure the appropriate use of antibiotic agents", is an important strategy to combat these negative outcomes.[5] Data on the appropriateness of antimicrobial use, in addition to standard surveillance of antimicrobial utilization, is needed to inform stewardship efforts[6,7]; however, definitions of "appropriate use" or "appropriateness" are inconsistent.[4]

The proportion of antimicrobial use considered appropriate varies according to the investigators' definition. A recent systematic review reported a large range of inappropriate antimicrobial use, from as low as 14.1% to as high as 78.9%, in hospitalized patients with severe infection.[4] Data from a point prevalence survey of children's hospitals in the United States showed that a quarter of pediatric patients were receiving suboptimal antibiotic therapy.[8] Studies have often used a qualitative assessment of appropriateness based on clinician judgment; however, this approach may lead to differences in opinion because of the subjective nature of the assessment.[9]

The use of quality indicators is one strategy to objectively evaluate the appropriateness of antimicrobial use. A standardized list of indicators provides consistency in factors that should be considered when evaluating appropriateness. According to the Agency for Healthcare Research and Quality (US), quality indicators are "standardized, evidence-based measures of health care quality".[10] Quality indicators to evaluate the appropriateness of antibiotic use in a variety of settings have been published; however, these indicators were not specifically developed for use in the pediatric population after admission to hospital.[11-15] When evaluating antimicrobial use in the pediatric population, unique considerations related to patient assessment (e.g., guidelines and recommendations for screening and diagnosis of infectious diseases, etiology of disease) and choice of antimicrobial agent (considering age, weight, and route of administration) should be considered, given the known differences between pediatric and adult populations. Monitoring of the appropriateness of antimicrobial use in the pediatric population, using standardized process measures, to assess the impact of stewardship efforts and to identify areas for quality improvement is therefore needed.

The objective of this study was to achieve consensus within a group of pediatric specialists on a list of quality indicators to evaluate the appropriateness of empiric antimicrobial use for pediatric patients admitted to hospital.

METHODS

Study Design

This study was completed using the Delphi technique, a method that uses a series of questionnaires to achieve consensus of opinion among individuals within an area of expertise. This technique allows participants to adjust their opinion after considering group feedback in successive rounds and also allows individuals to provide their opinions anonymously and without the influence of dominant individuals.[16,17] This method was employed in our study as we aimed to obtain consensus virtually on a list of quality indicators of appropriate empiric antimicrobial use from experts throughout North America.

This study was approved by the IWK Health Research Ethics Board.

Questionnaire Development

A questionnaire was developed on the basis of published literature and the expertise of our research team. This team was composed of researchers and pediatric infectious diseases physicians and pharmacists (who are the authors of this article). A literature search was completed in the PubMed database to identify studies that described quality indicators suitable for evaluating the appropriateness of empiric antimicrobial prescriptions. The search strategy was designed by our team, which included clinicians and researchers with experience in completing systematic reviews. The search terms included combinations of antibiotic, antibacterial agent, or bacterial infection combined with terms for quality indicators. This search was consistent with the approach used by Kallen and Prins[15] in completing a systematic review of quality indicators for determining the appropriateness of antibiotic use in adult inpatients. The reference lists of retrieved full-text articles were also searched by hand to identify relevant publications. Studies that reported on antimicrobial quality indicators or prescribing survey tools and checklists were retained for use in developing the questionnaire.

Based on the results of the literature search[12,18-22] and the expertise of the research team, a questionnaire consisting of 25 indicators for evaluating the appropriateness of antimicrobial use in pediatric patients admitted to hospital was developed. The questionnaire was piloted by 5 pharmacists who had experience in infectious diseases or survey design and were not participating in the Delphi panel and was then adapted according to their feedback. Changes based on piloting of the survey included incorporation of formatting suggestions and rewording of some of the quality indicators for clarity and consistency. The pharmacists who peer reviewed the questionnaire also suggested

reducing the basis for rating quality indicators from 2 criteria to a single criterion. This suggestion was accepted, and the criterion for rating indicators is described below, under "Data Collection".

Participants

Potential participants were invited to complete the questionnaire on the basis of their expertise in providing care to pediatric patients with infectious syndromes. Experts were purposively sampled to obtain diverse representation from a multidisciplinary group of health care providers. Experts invited to participate included infectious diseases physicians, pharmacists, microbiologists, and administrators representing antimicrobial stewardship programs at various stages of implementation. Experts in Canada and the United States were considered for inclusion, to ensure broad geographic representation throughout North America. Experts were identified through the team's professional networks and were invited to participate through email communication by a member of the research team. The initial list of experts was identified from previous work by members of our team (K.T., M.S.), who used the Delphi technique to develop quality indicators for evaluating antimicrobial stewardship programs.[23] All participants provided consent through the online consent statement at the beginning of the questionnaire.

Data Collection

Experts who agreed to participate were asked to complete consecutive rounds of the Delphi process to establish consensus on the indicators. In each round, the experts were asked to review and rate each indicator listed in the questionnaire, which was disseminated through the survey tool Opinio, housed by Dalhousie University. The following criterion was used to rate the indicators: "The importance of each item in determining appropriateness considering benefit or harm at the individual or population level".

During the first round, the experts were asked to rate the indicators on a scale from 1 to 9, where 1 = very unimportant and 9 = very important. The experts were also given the opportunity to comment on the indicators, suggest changes to wording, or add new indicators. In the second round, each expert received an individualized questionnaire that included, for each indicator, their previous rating, the aggregate mean rating (with standard deviation), the aggregate median rating (with interquartile range), the mode, and anonymous comments from the other experts. Newly suggested indicators were also added to the second-round questionnaire. The experts were asked to again rate the indicators on a scale from 1 to 9. In addition, the experts were provided with wording changes suggested by participants in round 1 and asked to indicate if they agreed or disagreed with the proposed changes (yes/no). An additional third version of the questionnaire was circulated for experts to rate the indicators with remaining disagreement after round 2.

Data Analysis

The results were summarized using descriptive statistics. Indicators with a median score of 7 or higher with no disagreement after 2 rounds of rating were retained and included in the final list of indicators for assessing appropriateness. Based on previously published related Delphi studies[23-26] and published guidelines,[27] disagreement was defined as less than 75% of panelists assigning a score of 7 or higher.

RESULTS

The 3 versions of the questionnaire were distributed to the expert panel in 3 rounds of the Delphi process between July and December 2018. Thirty-one experts were invited to participate in an attempt to recruit 15–20 participants, and 17 experts agreed to participate. Of those who agreed to participate, 12 completed at least 1 round of the questionnaire, with 10 of the 12 experts completing all rounds. Panelists who agreed to participate were infectious diseases physicians (n = 5) and infectious diseases pharmacists (n = 7). Most of the experts (n = 8) were practising in Canada.

A total of 25 indicators included in the initial questionnaire and 6 indicators suggested by the expert panelists were assessed during the 3 rounds (Table 1). After the initial round, consensus was achieved for 23 of the initial 25 indicators, and 6 new indicators were suggested. The 2 indicators with disagreement in round 1 were included in subsequent rounds. Six of the indicators with agreement also had suggested changes to wording; these indicators were rephrased, incorporated into the second round, and accepted by the experts (Table 2). After completion of 3 rounds, consensus was reached for 24 of the 25 quality indicators originally proposed and 4 of the 6 indicators suggested by expert panelists in the first round, and these 28 indicators were retained. The indicators for which consensus was reached were grouped under the categories of "empiric choice" (n = 12), "dose" (n = 5), "duration" (n = 2), "administration" (n = 4), "diagnosis" (n = 2), and "documentation" (n = 3).

The highest-ranking indicators, which had 100% agreement by the experts and a median score of 9, were the following:

- "Empiric choice of antimicrobial agents for pediatric patients should be active against most likely causative pathogens."
- "Antimicrobial agents for pediatric patients with sepsis should be started intravenously."
- "Broad spectrum intravenous empiric antimicrobials should be administered to pediatric patients with severe sepsis and septic shock within 1 hour of identification."

TABLE 1 (Part 1 of 3). Rating and Assessment of Quality Indicators by Experts

Indicator[a]	Round 1 (*n* = 12)		Round 2 (*n* = 10)		Round 3 (*n* = 10)		Conclusion
	No. (%) Strong Agreement	Median Score	No. (%) Strong Agreement	Median Score	No. (%) Strong Agreement	Median Score	
Empiric choice							
Empiric choice of antimicrobial agents for pediatric patients should be active against most likely causative pathogens.	12 (100)	9	–	–	–	–	Retain
Empiric choice of systemic antimicrobial therapy in pediatric patients should consider local susceptibilities (local antibiogram).	–	–	10 (100)	8.5	–	–	Retain
Pediatric patients with a history of anaphylaxis after penicillin therapy should be prescribed an alternative drug class.	10 (83)	8.5	–	–	–	–	Retain
Empiric choice of systemic antimicrobial therapy for pediatric patients should be prescribed according to local guidelines. If no local guidelines exist, choice of therapy should be prescribed according to national or international guidelines (where available).	12 (100)	8	–	–	–	–	Retain
Previous microbiology results should be considered in empiric choice of systemic antimicrobial therapy in pediatric patients.	11 (92)	8	–	–	–	–	Retain, rephrased
Contraindications (including medical conditions and medication use) should be taken into account when antimicrobials are prescribed to pediatric patients.	10 (83)	8	–	–	–	–	Retain, rephrased
Allergy status and history of adverse drug reactions should be taken into consideration when selecting empiric antimicrobial agents for pediatric patients.	9 (75)	8	–	–	–	–	Retain
Previous history of infection should be considered in empiric choice of systemic antimicrobial therapy in pediatric patients.[b]	8 (67)	8	–	–	8 (80)	8	Retain, rephrased
Empiric choice of systemic antimicrobial therapy in pediatric patients should consider individual travel history.	–	–	10 (100)	7.5	–	–	Retain
Empiric choice of systemic antimicrobial therapy in pediatric patients should include data on local public health outbreaks.	–	–	8 (80)	7	–	–	Retain
Empiric choice of systemic antimicrobial therapy in pediatric patients does not include unnecessary duplication of therapy.	–	–	6 (60)	7.5	7 (78) (*n* = 9)	7	Retain
Empiric choice of systemic antimicrobial therapy should consider previous antimicrobial use in pediatric patients.	9 (75)	7	–	–	–	–	Retain, rephrased
Empiric choice of systemic antimicrobial therapy in pediatric patients should consider vaccination status.	–	–	5 (50)	7	4 (40)	6	Exclude
Empiric choice of systemic antimicrobial therapy in pediatric patients should consider previous environment exposures.	–	–	5 (50)	6.5	4 (40)	6	Exclude

TABLE 1 (Part 2 of 3). Rating and Assessment of Quality Indicators by Experts

Indicator[a]	Round 1 (*n* = 12)		Round 2 (*n* = 10)		Round 3 (*n* = 10)		Conclusion
	No. (%) Strong Agreement	Median Score	No. (%) Strong Agreement	Median Score	No. (%) Strong Agreement	Median Score	
Dose							
Dose and dosing interval of systemic empiric antimicrobials should be adapted to pediatric patient renal function.	11 (92)	8	–	–	–	–	Retain
Antimicrobial agents that require therapeutic drug monitoring (such as vancomycin and gentamicin) should be managed according to guidelines.	10 (91) (*n* = 11)	8	–	–	–	–	Retain
Dose and dosing interval of systemic empiric antimicrobials should be adapted to the pediatric patient's age.	10 (83)	8.5	–	–	–	–	Retain
Dose and dosing interval of systemic empiric antimicrobials should be prescribed according to guidelines.	10 (83)	8	–	–	–	–	Retain
Dose and dosing interval of systemic antimicrobials should be adapted to the pediatric patient's weight.	10 (83)	8	–	–	–	–	Retain
Duration							
Duration of surgical prophylaxis for pediatric patients should not exceed 24 hours.	11 (92)	9	–	–	–	–	Retain
Intended duration of systemic empiric antimicrobial therapy for pediatric patients should be compliant with guidelines.	10 (91) (*n* = 11)	8	–	–	–	–	Retain
Administration							
Antimicrobial agents for pediatric patients with sepsis should be started intravenously.	12 (100)	9	–	–	–	–	Retain
Broad spectrum intravenous empiric antimicrobials should be administered to pediatric patients with severe sepsis and septic shock within 1 hour of identification.	12 (100)	9	–	–	–	–	Retain
Timelines of administration of antimicrobial therapy and prophylaxis for pediatric patients should be compliant with guidelines.	11 (92)	8.5	–	–	–	–	Retain
Empiric antimicrobial agents for pediatric patients should be administered via the appropriate route as recommended by guidelines.	11 (92)	8	–	–	–	–	Retain
Diagnosis							
When starting systemic antimicrobial therapy for pediatric patients, specimens for culture from suspected sites of infection should be taken as soon as possible, preferably before antimicrobial agents are started (if applicable).	11 (92)	9	–	–	–	–	Retain
Microbiological investigations should be performed according to guidelines.	10 (83)	8	–	–	–	–	Retain
Two sets of blood cultures should be taken before antimicrobial administration when bacteremia is suspected in pediatric patients.	7 (58)	7	3 (30)	6	–	–	Exclude

TABLE 1 (Part 3 of 3). Rating and Assessment of Quality Indicators by Experts

Indicator[a]	Round 1 (*n* = 12)		Round 2 (*n* = 10)		Round 3 (*n* = 10)		Conclusion
	No. (%) Strong Agreement	Median Score	No. (%) Strong Agreement	Median Score	No. (%) Strong Agreement	Median Score	
Documentation							
Allergy status (including nature and severity) should be documented in the medical records when antimicrobials are prescribed for pediatric patients.	12 (100)	8.5	–	–	–	–	Retain
Antimicrobial therapy for pediatric patients that deviate[s] from guidelines should be justified.	10 (83)	8.5	–	–	–	–	Retain, rephrased
An antimicrobial plan should be documented for pediatric patients in the medical record at the start of systemic antimicrobial treatment. (Antimicrobial plan in indication, name, dose, route, and interval of administration.)	9 (75)	8	–	–	–	–	Retain, rephrased

Note: Dashes are used for indicators not included in a particular round of the Delphi process.
[a]For the 6 indicators with rephrasing (as noted in col. 3), the entry shown here incorporates the revised wording. See Table 2 for original wording.
[b]Indicator omitted in error during round 2, but consensus was achieved in round 3.

The only indicator originally proposed to the experts that was ultimately rejected was "Two sets of blood cultures should be taken before antimicrobial administration when bacteremia is suspected in pediatric patients".

Ratings for each indicator during the 3 rounds of the Delphi process are presented in Table 1.

DISCUSSION

To the authors' knowledge, this study is the first to seek and achieve consensus on quality indicators to characterize the appropriateness of empiric antimicrobial use for the management of infectious syndromes in hospitalized pediatric patients. Panel representation included experts throughout North America with experience providing direct care to pediatric patients with infectious syndromes. All indicators included in this study were process-related measures that aimed to assess the quality of antimicrobial use. Most approved indicators were categorized as relating to "empiric choice". High agreement after the first round by experts who worked as clinicians suggests that the indicators initially proposed are clinically important and relevant to improving the quality of patient care.

Indicators for determining appropriateness of use of antimicrobial agents in hospitalized patients have been developed by others. Monnier and others[11] published 51 generic quality indicators for responsible antibiotic use in the inpatient setting. A broad range of stakeholders were included in that study; however, few participants were from North America (*n* = 5/25).[11] In another study, a European panel of experts developed quality indicators for evaluating the appropriateness of antimicrobial use in hospitalized adults.[12] Neither of these studies specifically focused on management of infectious diseases or antimicrobial use in pediatric patients.[11,12] Considerations when determining appropriateness of antibiotic use in the management of infectious diseases in this patient population were therefore needed. Pediatric patients are not small adults: they exhibit differences in the spectra of infections that they may acquire, and their presentations differ from those of adults. Children, especially neonates, require special consideration when determining choice of antimicrobial therapy, including unique precautions and contraindications, as well as differences in dosing and formulation.

Many generic quality indicators related to empiric antimicrobial use that were published by Monnier and others[11] and van den Bosch and others[12] were used in development of our survey, with tailoring for the pediatric population. Retained quality indicators in our study overlap with previously published indicators; however, our expert panel also suggested additional indicators that focus on specific considerations in choosing the most appropriate empiric antimicrobial agent. These indicators are more tailored and may prompt further consideration of appropriateness at an individual patient level.

Our expert panel rejected the indicator "Two sets of blood cultures should be taken before antimicrobial administration when bacteremia is suspected in pediatric patients," although this indicator was included and retained by previously published studies.[11,12] Determining the rationale for indicator ranking was not within the scope of our study; however, it is postulated that respondents may have rejected the indicator given difficulty with venous access, especially in neonates. The need for adequate sample volume is the most important consideration for detection of bacteria when performing blood cultures. In children, the

TABLE 2. Accepted Changes in Wording of Original Quality Indicators

Original Wording	Suggested Wording Change	No. (%) in Agreement (n = 10)
Empiric choice of systemic antimicrobial therapy is appropriate for pediatric patients considering previous history of infection.	Previous history of infection should be considered in empiric choice of systemic antimicrobial therapy in pediatric patients.	10 (100)
Empiric choice of systemic antimicrobial therapy is appropriate for pediatric patients considering previous antimicrobial use.	Empiric choice of systemic antimicrobial therapy should consider previous antimicrobial use in pediatric patients.	10 (100)
Empiric choice of systemic antimicrobial therapy is appropriate for pediatric patients considering previous microbiology results.	Previous microbiology results should be considered in empiric choice of systemic antimicrobial therapy in pediatric patients.	10 (100)
Contraindications (including concomitant medical conditions and medication use) should be taken into account when antibiotics are prescribed to pediatric patients.	Contraindications (including medical conditions and medication use) should be taken into account when antimicrobials are prescribed to pediatric patients.	9 (90)
An antimicrobial plan should be documented for pediatric patients in the case notes at the start of systemic antimicrobial treatment. (Antibiotic plan is indication, name, dose, route, and interval of administration.)	An antimicrobial plan should be documented for pediatric patients in the medical record at the start of systemic antimicrobial treatment. (Antimicrobial plan in indication, name, dose, route, and interval of administration.)	10 (100)
Antibiotic therapy for pediatric patients that deviate[s] from guidelines should be justified.	Antimicrobial therapy for pediatric patients that deviate[s] from guidelines should be justified.	10 (100)

volume should be determined on the basis of the patient's age and weight. In pediatrics especially, there must be a balance between volume of blood collected and the patient's clinical condition.[28,29]

Our study had several strengths. The expert consensus panel comprised infectious diseases specialists and pharmacists with experience caring for pediatric patients with infectious syndromes within a North American context. The indicators presented in the first round were designed as process measures for clinicians and researchers to evaluate antimicrobial use and assess the impact of antimicrobial stewardship interventions. Furthermore, the indicators are detailed and provide opportunities to clearly identify areas for improvement in the processes of prescribing and administering antimicrobial agents.

Despite these strengths, a number of limitations should be considered. The expert panel included only pharmacists and physicians, as we were unable to recruit any microbiologists. Thus, our study yielded the perspectives of only pharmacists and physicians, although we recognize that other health care providers have valuable expertise to contribute to assessing appropriateness of antimicrobial use. Furthermore, the indicators were developed on the basis of evidence and guidelines current at the time. Since dissemination of our survey, pediatric guidelines in the Surviving Sepsis Campaign have been published, which recommend starting antimicrobials as soon as possible and within 3 hours for children with sepsis-associated organ dysfunction and no signs of shock.[30] The Surviving Sepsis Campaign recommendation is reported to have a very low quality of evidence[30]; however, use of our indicators should be combined with consideration of the most recent evidence when evaluating appropriateness of antibiotic use. Finally, our study included only experts from North America and, as a result, the findings may not be generalizable to other geographic regions. Given overlap of retained indicators from the current study with those from European and other international Delphi studies, however, we expect that our findings may be relevant to other regions of the world.

CONCLUSION

To our knowledge, this is the first study to report on process-related quality indicators for assessing the appropriateness of empiric antimicrobial use in pediatric patients admitted to hospital on which consensus was achieved by an expert panel. Our findings may provide a standardized list of measures that infectious diseases clinicians, antimicrobial stewardship teams, institutions, and researchers can use when evaluating the effect of various interventions on the quality of antimicrobial use.

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Evaluating the Influence of IV Ketamine on Postoperative Opioid Use for Surgical Patients at a Tertiary Care Centre

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ABSTRACT

Background: Subanesthetic doses of ketamine have been shown to improve the efficacy of opioids, increase pain control, and exemplify opioid-sparing effects when used as postoperative analgesia for adults.

Objectives: To determine, for surgical patients, the impact of IV ketamine infusions on opioid use in hospital, overall and within 24 h before discharge, as well as pain scores.

Methods: A retrospective matched cohort study was conducted, in which surgical patients exposed to ketamine were compared with those not exposed to ketamine, among admissions from January 1, 2018, to February 28, 2020. Patients were matched for age, surgical service, and sex.

Results: A total of 104 patients were included in the study. Overall, there was no significant difference in mean total opioid use in hospital for patients exposed and not exposed to ketamine (171.7 mg versus 115.5 mg oral morphine equivalent [OME], $p = 0.09$), nor was there any difference in opioid use in the 24 h before discharge (28.2 mg versus 18.2 mg OME, $p = 0.14$). Patient-reported pain scores did not differ between groups. More patients in the ketamine group experienced hallucinations than in the group not exposed to ketamine (5 versus 0, $p = 0.024$).

Conclusions: Overall, subanesthetic doses of IV ketamine used postoperatively in surgical patients did not decrease opioid use or patient-reported pain. More patients who received ketamine had documented hallucinations. These results will help guide postoperative analgesia practice and strategies to reduce opioid use.

Keywords: ketamine, pain management, postoperative pain, opioid-sparing, opioid stewardship

RÉSUMÉ

Contexte : Il a été démontré que des doses sous-anesthésiques de kétamine améliorent l'efficacité des opioïdes, augmentent le contrôle de la douleur et illustrent les effets d'épargne des opioïdes lorsqu'elles sont utilisées comme analgésie postopératoire chez l'adulte.

Objectifs : Déterminer, pour les patients chirurgicaux, l'impact des perfusions de kétamine IV sur la consommation d'opioïdes à l'hôpital en général et dans les 24 h précédant la sortie, ainsi que les scores de douleur.

Méthodes : Une étude de cohorte rétrospective appariée a été menée dans laquelle on a comparé, chez les patients chirurgicaux admis du 1er janvier 2018 au 28 février 2020, ceux qui ont été exposés à la kétamine à ceux non exposés à la kétamine. Les patients ont été appariés selon l'âge, le service chirurgical et le sexe.

Résultats : Au total, 104 patients ont été inclus dans l'étude. Dans l'ensemble, il n'y avait pas de différence significative dans la consommation totale moyenne d'opioïdes à l'hôpital pour les patients exposés et non exposés à la kétamine (171,7 mg contre 115,5 mg d'équivalents de morphine orale [OME], $p = 0,09$), ni de différence dans la consommation d'opioïdes dans les 24 h avant la sortie (28,2 mg contre 18,2 mg OME, $p = 0,14$). Les scores de douleur rapportés par les patients ne différaient pas entre les groupes. Plus de patients du groupe kétamine que du groupe non exposé à la kétamine ont eu des hallucinations (5 contre 0, $p = 0,024$).

Conclusions : Dans l'ensemble, les doses sous-anesthésiques de kétamine IV utilisées après l'opération chez les patients chirurgicaux n'ont pas diminué l'utilisation d'opioïdes ni la douleur signalée par les patients. Plus de patients ayant reçu de la kétamine avaient des hallucinations documentées. Ces résultats aideront à guider la pratique de l'analgésie postopératoire et les stratégies visant à réduire l'utilisation d'opioïdes.

Mots-clés : kétamine, gestion de la douleur, douleur postopératoire, épargne des opioïdes, gestion des opioïdes

INTRODUCTION

The opioid crisis is a well-known public health concern. Routine postoperative use of opioids may result in discharge prescriptions for opioids and serves as a means of introducing opioids into the community. A variety of studies have demonstrated a link between opioid use/abuse and opioid prescriptions written by surgeons. Two studies concluded that 6% to 7% of opioid-naive patients for whom opioids were prescribed after discharge following surgery became persistent users.[1,2] The need for postoperative opioid stewardship is evident.

Non-opioid analgesia is one strategy to reduce postoperative opioid use. Ketamine is a non-competitive *N*-methyl-D-aspartate (NMDA) receptor antagonist that possesses anesthetic properties at high doses and analgesic properties at low doses.[3] Laskowski and others[4] completed a meta-analysis of randomized placebo-controlled trials evaluating the role of IV ketamine in decreasing postoperative pain. Their results suggested that ketamine may improve the efficacy of opioids and pain control and may exemplify opioid-sparing effects when used in adults as postoperative analgesia, irrespective of the type of intraoperative opioid administered. Additionally, a Cochrane review of 113 studies using perioperative IV ketamine for acute postoperative pain found that participants treated with ketamine consumed 7.6 mg less morphine equivalent opioid (95% confidence interval [CI] −8.9 to −6.4) in the first 24 h after surgery.[5] US consensus guidelines on the use of IV ketamine infusions for acute pain management support the use of low-dose ketamine for pain control in patients undergoing surgery where postoperative pain is likely to be severe.[6]

Ketamine, however, is known to have adverse effects. Many studies have shown that ketamine is associated with adverse central nervous system (CNS) effects, such as hallucinations, nightmares, delirium, and cognitive impairment.[6-8] It is, however, difficult to differentiate between the adverse effects caused by ketamine and those caused by other drugs used in the perioperative setting (e.g., opioids, antiemetics) or by the surgery itself. Although side effects are less likely with low doses of ketamine relative to the higher doses used for anesthesia, the clinical impact of these adverse events can be significant.[6]

In many hospitals, the use of IV ketamine is restricted to the operating rooms, the intensive care units (ICUs), and/or the acute pain service. In August 2019, our institution introduced a new policy allowing the unrestricted use of low-dose IV ketamine infusions (less than or equal to 0.3 mg/kg/h) for pain control on the wards as an opioid-alternative strategy. This study was undertaken to determine the impact of IV ketamine infusions on opioid use in hospital (entire stay) and within 24 h before discharge, as well as postoperative pain scores in surgical patients.

METHODS

Study Design

This study was a retrospective chart review. Patients admitted to the Orthopedic, Trauma, and General Surgery services at Sunnybrook Health Sciences Centre in Toronto, Ontario, from January 1, 2018, to February 28, 2020 were eligible for inclusion. Approval was obtained from the hospital's Research Ethics Board.

Data Sources

Consecutive surgical patients exposed to analgesic doses of IV ketamine were identified and screened for inclusion criteria using the hospital's Health Records database. Information was collected from the hospital's electronic patient medical record system (Sunnycare, Sunnybrook Health Sciences Centre) and the scanned patient chart system (Sovera, CGI Technologies and Solutions Inc).

Inclusion and Exclusion Criteria

Patients 18 years of age or older who were admitted from home for surgery under the Orthopedics, Trauma, or General Surgery service were eligible for the study. General surgeries primarily consisted of appendectomies and cholecystectomies, and orthopedic surgeries primarily consisted of lower-extremity and spinal surgeries. The following patients were excluded because they did not represent the typical postoperative surgical patient: patients with opioid use before admission, those who left against medical advice, those discharged from the short-stay unit, those who died during the hospital admission, those admitted to critical care for longer than 48 h, those with ketamine use beyond 4 days, and those with oral ketamine use.

Patient Characteristics and Data Collection

Health Records generated extensive lists of patients from the prespecified surgical services according to whether they did or did not receive ketamine. A convenience sample of approximately 100 patients was chosen. Fifty-two patients who met the inclusion criteria and received IV ketamine for pain were randomly selected from this list. These patients were then matched (by age, sex, and surgical service) to an additional 52 patients who met the inclusion criteria but were not exposed to ketamine. Ketamine for pain was defined as a continuous infusion of ketamine at a dosage less than 0.3 mg/kg/h. Baseline demographic data, including age, sex, and comorbidities, were collected. Comorbidity data were based on the Charlson Comorbidity Index, along with the presence or absence of chronic pain or cancer before admission. The Injury Severity Score was collected for patients who underwent trauma surgery. Data on analgesic use and pain scores were collected for the day of surgery and 3 days postoperatively (4 days in total) and for the 24 h before discharge. Data were also captured for reason for admission, length of stay, procedure type, procedure date, and whether the Acute Pain Service (an interprofessional team at our institution specializing in pain management) was consulted. For each day of data collection, drug, dose, and total daily use were collected for all IV ketamine, opioid, and non-opioid analgesia (acetaminophen, non-steroidal anti-inflammatory drugs, gabapentanoids, and antidepressants, such as amitriptyline, nortriptyline, and duloxetine). The highest pain score on each day was noted. Data on postoperative epidural use were collected, and the occurrence of delirium or hallucinations was noted. Although gastrointestinal symptoms are also a common adverse effect of ketamine, we chose not to collect such

data, given the concomitant medications and medical conditions that could be expected to contribute to nausea and vomiting in this population. Administration of naloxone was used as a surrogate for opioid toxicity.

Outcomes

There were 3 primary outcomes of interest for surgical patients exposed to postoperative IV ketamine relative to those without ketamine exposure. The first was mean postoperative opioid use on day 0 (defined as the day of surgery) and on days 1 through 3, displayed in terms of both individual days and the sum of all days. The second outcome of interest was mean opioid use within the 24 h before discharge, as a reflection of opioid requirements at discharge. We chose not to collect data for discharge opioid prescriptions because a previous study at our institution suggested that the total quantity of opioids prescribed at discharge was greater than the amount of opioids consumed in the 24 h before discharge.[9] All opioid doses were converted to the oral morphine equivalent (OME).[10,11] The third primary outcome was pain scores on days 0 through 3, along with pain score in the 24 h before discharge. Pain scores were reported on a Numerical Rating Scale (NRS) from 0 to 10, where 10 was maximum pain. The NRS is a validated pain score and is incorporated into the nursing documentation at our institution.[12,13]

Secondary outcomes of interest were the use of naloxone and the presence of hallucinations or delirium.

Statistical Analysis

Descriptive statistics (mean, standard error) were used to summarize continuous variables, such as age, Charlson Comorbidity Index, length of stay, opioid use, and pain scores. The Student *t* test (Excel spreadsheet software, Microsoft Corporation) was used to compare the means of continuous variables, with 2-sided tests used for all statistical analyses. Categorical variables, such as sex, cancer, and chronic pain before admission, and involvement of the Acute Pain Service were described using frequency counts and proportions. Tests of proportions were used to compare proportions between the study groups, and χ^2 tests were used to study correlations between pairs of categorical variables. Results were deemed significant when p was less than 0.05. Descriptive statistics were also used to summarize the adverse CNS effects of delirium and hallucinations.

RESULTS

In total, 404 patient charts were reviewed, and 104 patients met the inclusion criteria. Fifty-two patients who received IV ketamine for analgesia were randomly selected and matched with 52 patients for whom IV ketamine was not prescribed, matched by age range, sex, and surgical service. Baseline characteristics were similar between the groups (Table 1). Important characteristics such as ICU admission and Charlson Comorbidity Index were also similar between the groups, and among trauma patients there was no difference in the Injury Severity Score. Patients in the ketamine group had a longer mean length of stay than those who did not receive ketamine (8.4 days versus 6.1 days, $p = 0.005$). Patients in the ketamine group also had more involvement of the Acute Pain Service (50 patients versus 12 patients, $p < 0.001$) and therefore had a higher rate of epidural use and a larger number of adjunct analgesics (Table 1). For patients receiving ketamine, the median dosage of this drug was 0.1 mg/kg/h (range 0.05–0.1 mg/kg/h), and the median duration of use was 44 h (range 8–83 h).

All opioid doses are reported as OME.[11,12] There was no significant difference in the mean total opioid use over the period from day 0 (the day of surgery) to postoperative day 3 between patients exposed to IV ketamine and those not exposed (171.7 mg [range 0–950 mg] versus 115.5 mg [range 0–558 mg], $p = 0.09$), nor were there significant differences on day 0, day 1, or day 2 (Figure 1). However, there was a significant difference in opioid use on postoperative day 3, with those exposed to ketamine having higher mean opioid use than those not exposed (33.9 mg [range 0–200 mg] versus 13.8 mg [range 0–80 mg], $p = 0.007$). There was no difference in overall mean opioid use in hospital (postoperative days 0 through 3) by service (Figure 2).

In the 24 h before discharge, there was no significant difference in opioid use between those exposed to ketamine and those not exposed (28.2 mg [range 0–160 mg] versus 18.2 mg [range 0–150 mg], $p = 0.14$) (Figure 3).

Similarly, there was no significant difference in maximum reported pain scores on the day of surgery or on postoperative days 1 through 3 (Figure 4).

Safety outcomes are detailed in Table 2, specifically naloxone use and the presence of delirium or hallucinations. Three patients in the ketamine group, but none in the "no ketamine" group, received naloxone. Delirium was reported for the same number of patients in each group ($n = 5$). Five patients in the ketamine group, but none in the "no ketamine" group, experienced hallucinations.

DISCUSSION

The aim of this study was to determine the impact of IV ketamine on opioid use postoperatively and in the 24 h before discharge, as well as pain scores, for surgical patients.

The results demonstrated that ketamine had no clinically or statistically significant impact on opioid use. The only result that reached statistical significance was greater opioid use on postoperative day 3 among patients exposed to ketamine, but this may have been the result of type II error, rather than a clinically relevant difference. For all other days of data collection, there was no difference in opioid use. This analysis does not support the hypothesis that

TABLE 1. Patient Characteristics

Characteristic	Group; No. (%) of Patients[a]		*p* value
	Ketamine (*n* = 52)	No Ketamine (*n* = 52)	
Age (years) (mean ± SD)	53.3 ± 18.2	52.4 ± 18.2	0.97
Sex, female	23 (44)	23 (44)	> 0.99
Type of surgery			
Orthopedic	18 (35)	18 (35)	> 0.99
Trauma	18 (35)	18 (35)	> 0.99
Injury Severity Score[b] (mean ± SD)	17.0 ± 7.7	14.6 ± 7.5	0.25
General	16 (31)	16 (31)	> 0.99
Length of stay (days) (mean ± SD)	8.4 ± 4.6	6.1 ± 3.3	0.005
Charlson Comorbidity Index (mean ± SD)	2.6 ± 2.8	2.1 ± 2.3	0.36
Chronic pain before admission	2 (4)	3 (6)	0.65
Active cancer diagnosis	13 (25)	7 (13)	0.14
Discharge to rehabilitation	10 (19)	11 (21)	0.81
APS involvement	50 (96)	12 (23)	< 0.001
Epidural use	15 (29)	2 (4)	0.001
ICU stay at any time during admission	13 (25)	9 (17)	0.34
Duration of IV ketamine (hours) (mean ± SD)	44 ± 21.7	NA	< 0.001
Maximum no. of adjunct agents per day (mean ± SD)	2.4 ± 0.9	1.5 ± 0.9	< 0.001

APS = Acute Pain Service, ICU = intensive care unit, NA = not applicable, SD = standard deviation.
[a]Except where indicated otherwise.
[b]For patients undergoing trauma surgery only.

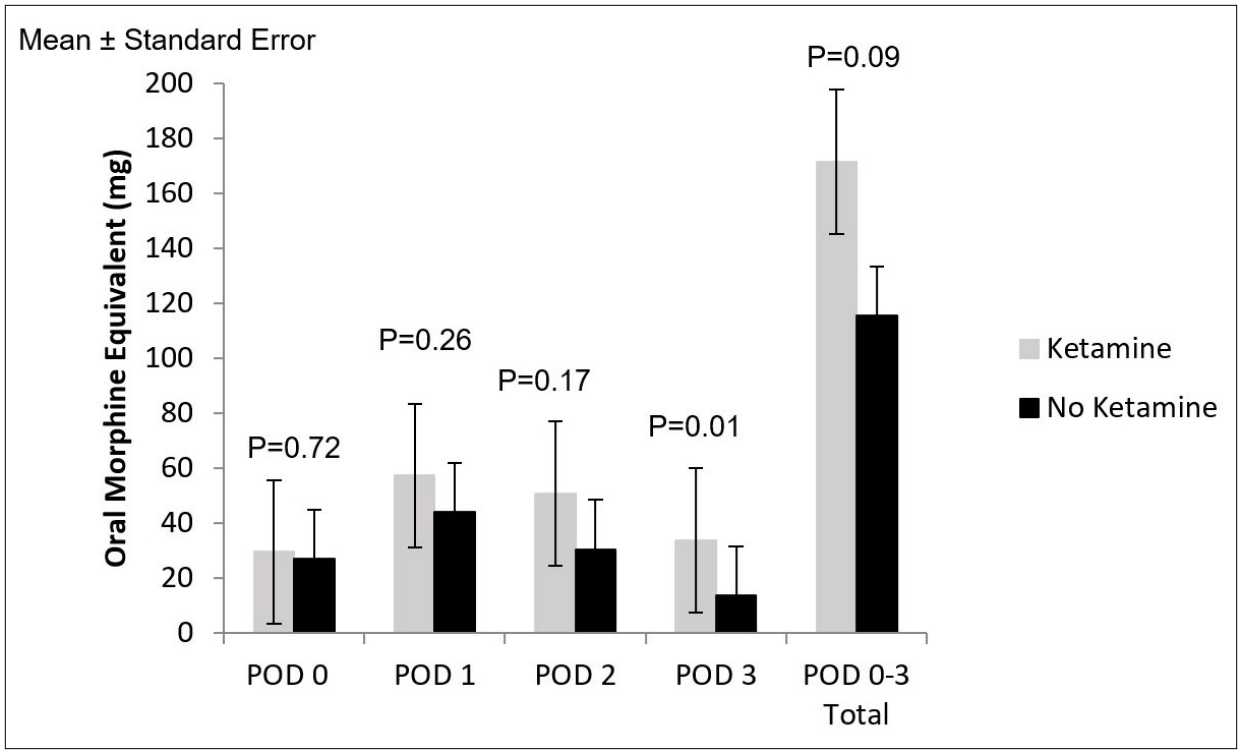

FIGURE 1. Mean daily opioid use in hospital. POD = postoperative day.

subanesthetic doses of IV ketamine lower opioid use either postoperatively or in the period just before discharge. We therefore speculate that postoperative IV ketamine will not decrease the amount of opioids prescribed at discharge and therefore will not reduce the amount of opioids introduced into the community. These results do not align with the meta-analysis by Laskowski and others,[4] which suggested that ketamine may improve the efficacy of opioids and exemplify opioid-sparing effects when used as postoperative analgesia in adults.

Our results also failed to demonstrate a difference in patient-reported pain scores between patients exposed and not exposed to ketamine. This result held true for all the days on which data were collected. In contrast, in their Cochrane review on perioperative IV ketamine for postoperative pain, Brinck and others[5] found that pain scores measured with a visual analogue scale (0–100 mm) were 5 mm lower after ketamine treatment (95% CI −6.6 to −3.6) relative to participants receiving the control treatment. One hypothesis is that regardless of whether

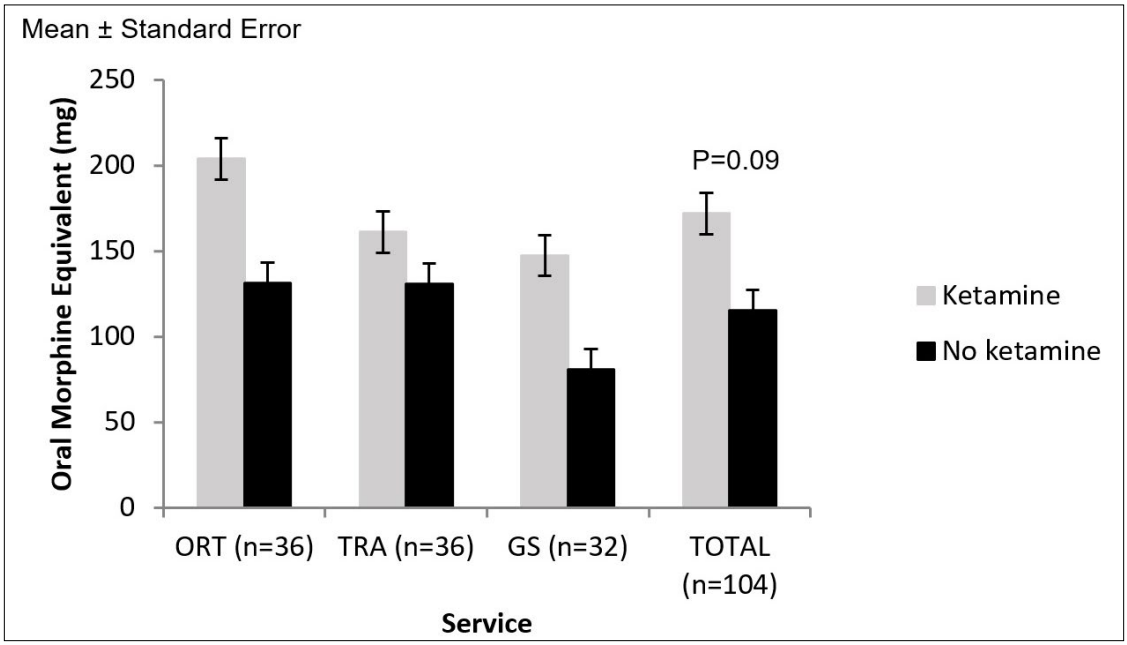

FIGURE 2. Mean total opioid use (postoperative days 0–3) in hospital, by service. ORT = orthopedic surgery, TRA = trauma surgery, GS = general surgery.

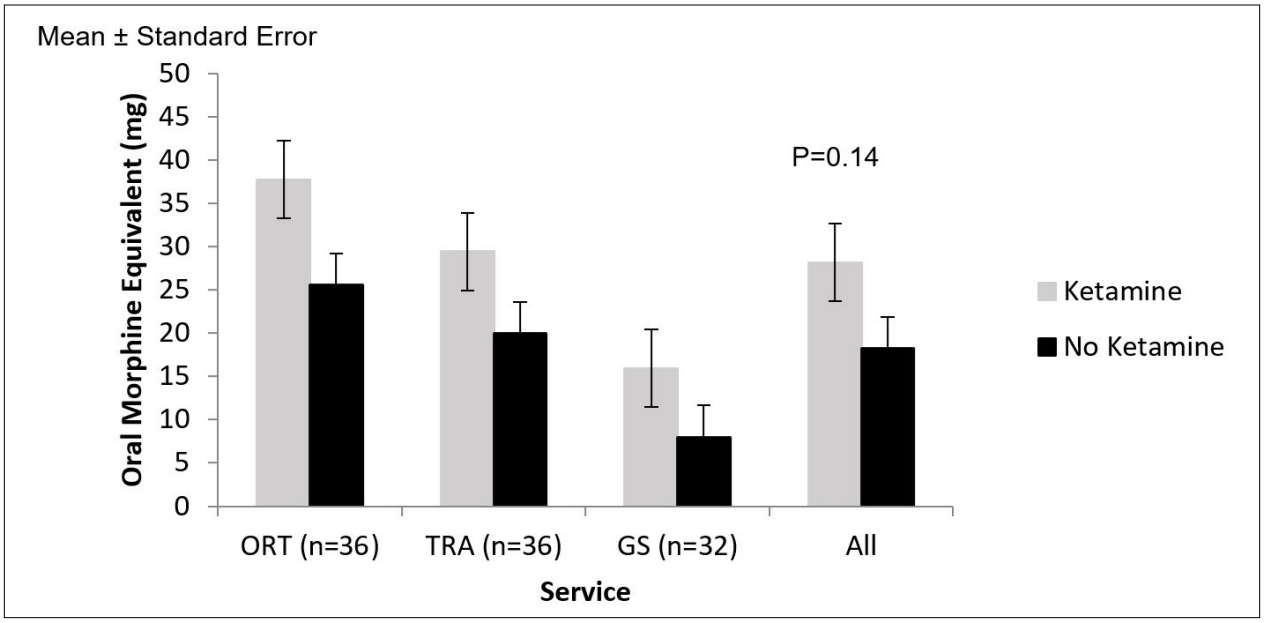

FIGURE 3. Mean opioid use in the 24 h before discharge, by service. ORT = orthopedic surgery, TRA = trauma surgery, GS = general surgery.

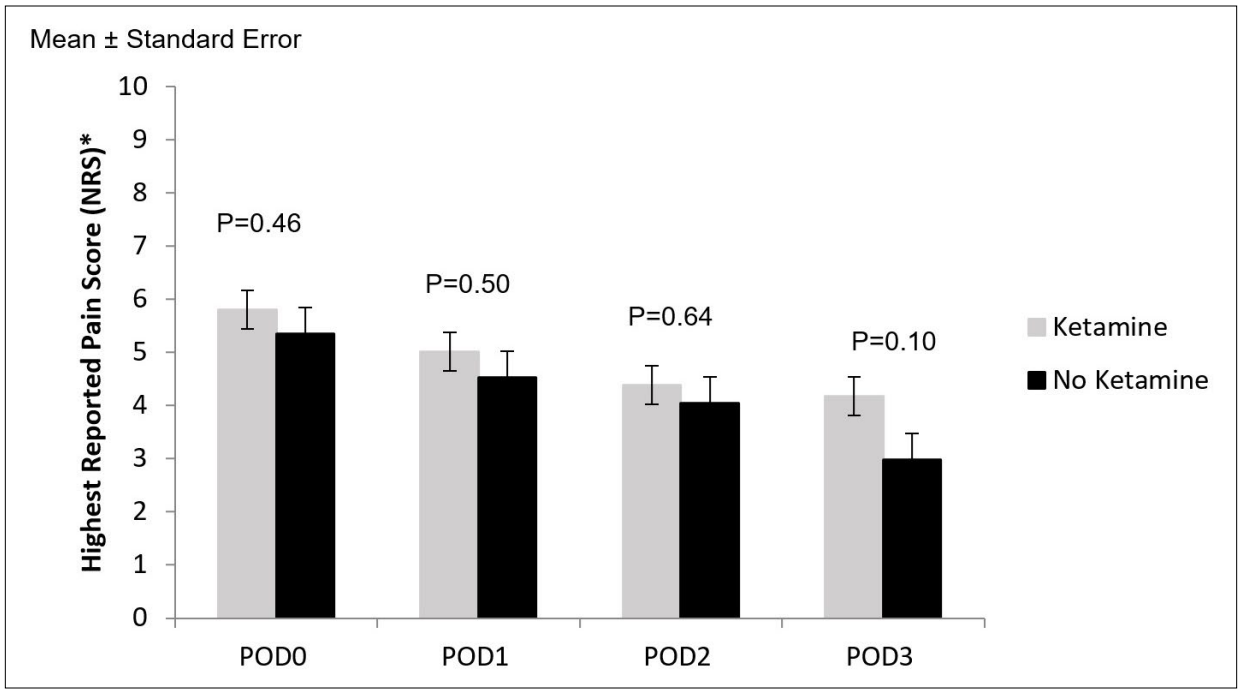

FIGURE 4. Mean maximum pain score. *Pain score reported according to the Numerical Rating Scale (NRS), from 0 to 10, where 10 is maximum pain. POD = postoperative day.

TABLE 2. Secondary Outcomes: Safety

	Group; No. with Effect		
Adverse Effect	Ketamine (n = 52)	No Ketamine (n = 52)	p Value
Naloxone use	3	0	0.08
Delirium	5	5	> 0.99
Hallucinations	5	0	0.024

ketamine lowers opioid use, it may reduce the pain that patients experience. It is important to note, however, that patient-reported pain is highly subjective and can be difficult to capture retrospectively.

There is little research on the influence of postoperative ketamine use for pain in surgical patients. In a study of patients with chronic opioid use who underwent surgery, those receiving IV ketamine had a 13.5% decrease from preoperative pain score to postoperative pain score, whereas the placebo group experienced a 15.5% increase (p = 0.0057).[14] It is difficult to directly compare our results with this previous study, as patients receiving opioids before admission were excluded from our study. In their Cochrane review, Brinck and others[5] found that among participants receiving ketamine, consumption of morphine equivalent opioid was 7.6 mg less (95% CI −8.9 to −6.4) and 12.6 mg less (95% CI −15.1 to −10.2) in the first 24 and 48 h after surgery, respectively. However, those authors looked at the use of perioperative IV ketamine, whereas our study analyzed only postoperative IV ketamine use. In the same review, when only the studies that administered ketamine in the postoperative setting were analyzed, ketamine treatment was found to reduce opioid consumption at 24 h by 9 mg (95% CI −13.8 to −3.5) morphine equivalents compared with control.[5] However, the authors did note that the quality of evidence was only moderate because all of the included studies had fewer than 50 patients. Our results were not consistent with those of the Cochrane review.

Our study did demonstrate more instances of hallucinations among patients who were exposed to ketamine relative to those not exposed. This result was not surprising and is consistent with current literature.[6-8] In contrast, there was no difference in instances of delirium between the 2 groups, which again was not surprising, given that both opioids and ketamine, along with surgery itself, can increase the risk of delirium. With no difference in opioid use or pain control, but an increase in adverse effects, IV ketamine may not be an appropriate strategy for opioid conservation.

Our study had some limitations, the first being the small sample of 104 patients from a single institution. To compensate for the limited sample size, we matched for characteristics related to severity of illness, which might predict increased opioid requirements. Baseline characteristics such as ICU admission and Charlson Comorbidity Index were similar between the groups, and among trauma patients there was no difference in the Injury Severity Score. Additionally, our study may not reflect prescribing practices

for patients undergoing same-day surgery or those with a long ICU stay, given that such patients were excluded. The study was retrospective, and therefore we were unable to investigate potential cause-and-effect relationships. Incomplete documentation, specifically for patient-reported pain scores, also limited the reliability of data collection. Including the Acute Pain Service and the specific surgical procedure as criteria for matching the patients would have allowed for more equal distribution of baseline characteristics. We speculate that patients with greater actual or expected pain were likely referred to the Acute Pain Service, which may have explained their higher opioid use. Adjunctive medications, which may lower opioid use and pain scores, were not evenly distributed between the groups. It would have been difficult to match patients for these medications in a retrospective trial, and excluding them would have drastically lowered our sample size. Interestingly, although patients in the ketamine group used more analgesics than those in the "no ketamine" group, their pain control and opioid use did not differ. Lastly, although the mean ketamine dosage was 0.1 mg/kg/h, we analyzed results according to the presence or absence of ketamine use. Therefore, we cannot draw any conclusions about the relationship between total amount of ketamine exposure and opioid use. In the future, a prospective randomized trial looking at postoperative opioid use and pain scores is required to accurately determine the true relationship between opioid use and ketamine exposure.

The results of our study are important in the quest to find opioid alternatives, given the opioid crisis that our country faces. We focused on patients who were not routinely using opioids before admission. Alam and others[1] studied opioid-naive adult patients undergoing surgery and found that those receiving an opioid prescription within 7 days after surgery were 44% more likely to become long-term opioid users within 1 year compared with those who received no opioid prescription (adjusted odds ratio 1.44, 95% CI 1.39 to 1.50). The need for postoperative opioid stewardship is evident. However, our study suggests that subanesthetic doses of IV ketamine administered postoperatively may not be the answer.

Our study supports the need for ongoing research in the field of opioid reduction in the postoperative period. While patients require adequate pain control following surgery, the health care system requires a solution that is safe for both patients and the community. The use of alternative and adjunctive analgesic medications is only one avenue for reducing opioid use in the community. Additional opioid stewardship strategies include individualized opioid discharge prescriptions based on opioid use within hospital, part-fill prescriptions, outpatient follow-up with pain specialists as necessary, changing expectations of acceptable levels of postoperative pain, and broad education for both health care prescribers and patients.[15,16]

CONCLUSION

This study showed that subanesthetic doses of IV ketamine administered postoperatively in surgical patients did not decrease opioid use in the overall postoperative period or within 24 h before discharge and had no effect on patient-reported pain scores. Although the incidence was small, hallucinations were documented more frequently among those who received ketamine. The study was limited by its small sample size, its retrospective nature, and an imbalance in baseline characteristics, specifically the involvement of the Acute Pain Service. The results of this study will help to guide future postoperative analgesia and strategies to reduce opioid use.

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The Role of Home Care Pharmacists in the Edmonton Zone: A Retrospective Study

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ABSTRACT

Background: Despite the rising demand for home-based health care services in Canada and the increasing medical complexity of elderly patients, there is limited literature exploring the role of home care pharmacists and the clinical activities they perform.

Objectives: The primary objective was to describe the types and frequencies of clinical activities (both interventions and recommendations) performed by home care pharmacists upon initial consultation. The secondary objective was to determine which patient characteristics resulted in the highest number of clinical activities.

Methods: This study was a retrospective review of adult patients who had an initial in-person or telemedicine consultation with home care pharmacists from June 2018 to May 2019 in the Edmonton Zone of Alberta Health Services.

Results: Of the 355 patients whose records were screened, 318 (89.6%) were included in the analysis. Of these, 191 (60.1%) were female, and the median age was 79 years (interquartile range [IQR] 68–86 years). The median numbers of medical conditions and medications were 6 and 10, respectively. Of the total of 1172 clinical activities, there was a median of 3 (IQR 2–5) per patient, irrespective of the patient's medical conditions, including those with the most common conditions. The most common activities were patient counselling (n = 160, 13.7%), collaboration with another health care professional (n = 157, 13.4%), and deprescribing (n = 140, 11.9%). Across all activities, pharmacists performed a total of 562 interventions and made 610 recommendations. Each additional year of age and each additional medication on a patient's medication list resulted in an increase in the number of clinical activities (by 0.01 for each additional year of age [p = 0.003] and by 0.03 for each additional medication [p < 0.001]).

Conclusions: Home care pharmacists in the Edmonton Zone performed a wide range of clinical activities, particularly for older patients and those with more medications. Further research is required to evaluate the outcomes of pharmacist consultations.

Keywords: clinical pharmacy service, home care pharmacist, clinical activity, pharmacy practice, Alberta, home visit

RÉSUMÉ

Contexte : Malgré l'augmentation de la demande de services de soins de santé à domicile au Canada et la complexité médicale croissante des patients âgés, il existe peu de documentation examinant le rôle des pharmaciens au sein de l'équipe de soins à domicile et leurs activités cliniques.

Objectifs : L'objectif primaire consistait à décrire le type et la fréquence des activités cliniques (interventions et recommandations) effectuées par les pharmaciens à domicile lors de la consultation initiale. L'objectif secondaire consistait quant à lui à déterminer les caractéristiques des patients qui ont entraîné le plus grand nombre d'activités cliniques.

Méthodes : Cette étude était une revue rétrospective de patients adultes ayant eu une première consultation en personne ou par télémédecine avec des pharmaciens de soins à domicile de juin 2018 à mai 2019 dans la zone d'Edmonton des services de soins de santé de l'Alberta.

Résultats : Sur les 355 patients dont les dossiers ont été examinés, 318 (89,6 %) ont été inclus dans l'analyse. Parmi eux, l'âge médian était de 79 ans (écart interquartile [IQR] 68–86) et 191 (60,1 %) étaient des femmes. Le nombre médian de problèmes médicaux et de médicaments était respectivement de 6 et 10. Sur les 1172 activités cliniques au total, le nombre médian était de 3 activités (IQR 2-5) par patient, indépendamment de ses problèmes médicaux, y compris ceux présentant les maladies les plus courantes. Les activités les plus courantes étaient le conseil aux patients (n = 160, 13,7 %), la collaboration avec un autre fournisseur de soins de santé (n = 157, 13,4 %) et la déprescription (n = 140, 11,9 %). Toutes activités confondues, les pharmaciens ont effectué 562 interventions et fait 610 recommandations. Chaque année d'âge supplémentaire et chaque médicament ajouté à la liste des médicaments donnaient lieu à une augmentation du nombre d'activités cliniques (de 0,01 pour chaque année d'âge supplémentaire [p = 0,003] et de 0,03 pour chaque médicament supplémentaire [p < 0,001]).

Conclusions : Les pharmaciens de soins à domicile de la zone d'Edmonton effectuaient un large éventail d'activités cliniques, en particulier pour les patients âgés et ceux prenant plus de médicaments. Des recherches supplémentaires sont nécessaires pour évaluer les résultats des consultations des pharmaciens.

Mots-clés : service de pharmacie clinique, pharmacien de soins à domicile, activité clinique, pratique de la pharmacie, Alberta, visite à domicile

INTRODUCTION

The increasing costs of delivering acute care health services has prompted a shift toward optimizing the care of community-dwelling patients.[1] These efforts are aimed at keeping patients in their own homes for longer, to avoid unnecessary hospitalizations and emergency room visits.[1,2] As the number of older adults (over the age of 65 years) continues to rise in the next decade, the strains on the health care system will be further magnified, and the utilization of alternatives to facility-based care will parallel this increase.[3,4] The changing landscape of health service delivery, with greater emphasis on community-based care, is in line with the preferences of many older Canadians, who wish to live in their own homes for as long as they are able.[5]

Continuing care programs across the country seek to address this demand by providing an array of nursing and medical services to enable individuals to receive care within the safety and comfort of their own homes.[5] Data gathered from home care programs in Canada have revealed that many home care patients are older adults, living with multiple medical conditions and correspondingly complex medication regimens.[2,4] In 2011, approximately 24% of older adults reported having 3 or more formally diagnosed chronic conditions, and according to public drug program data, nearly two-thirds of adults over the age of 65 had claims for more than 5 medications.[4] Furthermore, older adults are at increased risk of hospitalization due to adverse drug events.[6-8] Many of these adverse drug events may be preventable at transitions of care from the hospital to the community.[7] Once in the community, these patients may be seen by different prescribers and may be unable to regularly access office-based primary care services for a variety of reasons, including physical limitations.[9,10]

Thus, home care pharmacists have the opportunity to optimize drug therapy management for patients who are at increased risk of adverse medication-related events and serve as a critical link between inpatient and community care by reconciling medication-related issues. Not only do home visits allow pharmacists to connect face to face with patients who may be unable to travel or leave their homes, but they also allow the pharmacists to gain insight into patients' use of compliance aids and medication storage.[11] Pharmacists in Alberta, in particular, are uniquely positioned to independently address multiple medication- and health-related concerns. With their expanded scope of practice in the province, pharmacists have the ability to administer drugs by injection, prescribe Schedule I medications, and order laboratory tests.[12,13]

In the Edmonton Zone, home care services encompass professional consultative service providers (e.g., pharmacists, registered dieticians, speech language pathologists, occupational therapists, physical therapists, nurse practitioners, respiratory therapists, and recreation therapists) and various support services, such as personal care services (e.g., bathing, grooming).[14] As personnel functioning within a consult-based service, Edmonton Zone home care pharmacists receive patient referrals from home care case managers for any actual or perceived medication-related concerns. Case managers are responsible for assessing and managing all aspects of a patient's care. Given that pharmacists serve as core members on consultative teams, they commonly work with other home care health professionals and make clinical recommendations or initiate interventions. In this practice, pharmacists are generally involved in patient care for a limited time, addressing specific medication-related concerns relayed by the case manager. Within Alberta, no assessment has been done to qualify patient characteristics that are more likely to result in pharmacist interventions and recommendations.

Over the past 2 decades, various iterations of pharmacist-delivered services in the home setting have been described in the literature; these have largely consisted of pilot programs and research-based initiatives.[10,11,15-25] The context of service delivery has ranged from post–hospital discharge visits by community pharmacists to referral-based and structured medication review programs.[15,16,18,26] In general, findings from these studies have revealed that pharmacists were engaged in providing a number of clinical services, mostly consisting of medication reviews and medication reconciliation.[15] Other clinical activities have included deprescribing, patient education, assessment of cognition, compliance support, and recommendations for laboratory monitoring.[15] Notably, these services represent only a portion of the activities authorized under Alberta's scope of practice for pharmacists.[27]

The current published literature provides limited insight into the range of clinical activities performed by pharmacists as members of a multidisciplinary home care team. Therefore, the primary objective of this study was to describe the types and frequencies of clinical activities (both interventions and recommendations) performed by home care pharmacists in the Edmonton Zone upon initial consultation. The secondary objective was to determine which patient characteristics resulted in the highest number of clinical activities.

METHODS

Study Design and Patient Population

This study was a retrospective chart review of home care patients referred by case managers for home care pharmacist services in the Edmonton Zone from June 1, 2018, to May 31, 2019. Patients were eligible for inclusion if they were registered under 1 of the 4 Edmonton Zone Home Care Networks and had received home care pharmacy services during the study timeframe. Patients were excluded if they were younger than 18 years of age, did not have a

pharmacist involved in their care, or did not have clinical documentation in their chart.

Data Sources and Data Collection

A list of patients registered to receive pharmacy services from June 1, 2018, to May 31, 2019, was generated from the electronic charting system (Meditech). Data were obtained from the electronic chart of each patient. In each case, the pharmacist's clinical documentation was obtained from the initial consultation notes, scanned documents (such as medication reconciliation records), and faxed consultation notes to physicians, at or near the time of the first consultation during the study time period. If patients had multiple consultations during the study period, only the first consultation was included. The following data were entered directly into a Research Electronic Data Capture (REDCap) database: age at time of initial consultation or home care pharmacy service, sex assigned at birth, main home care network, number and type of medical conditions, number of medications, type and frequency of clinical activities (see Appendix 1, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/213), and number of pharmacist-initiated interventions or recommendations.

Outcomes

The primary outcome was the overall median number (with interquartile range [IQR]) of pharmacist clinical activities performed per patient at the time of initial consultation; the activities were also detailed as the proportion of each type of clinical activity performed in relation to all activities (Appendix 1). The clinical activities encompassed both interventions and recommendations. A clinical activity was classified as an intervention if the pharmacist initiated an action or was actively managing the patient's therapy. A clinical activity was classified as a recommendation if the pharmacist made suggestions for changes to patient therapy or management. For example, provision of patient education and making changes to drug therapy were classified as interventions, whereas a suggestion to use an over-the-counter or nonprescription medication was classified as a recommendation. Pharmacists' recommendations were provided to other care providers, which could include the case manager, nurse practitioner, home care physician, primary care physician, or specialist physician, or were given directly to the patient. Therefore, the clinical activities analyzed in this study encompassed both recommendations made by the pharmacist and interventions or changes initiated by the pharmacist. Other examples of clinical activities included prescribing, changing a medication dose, ordering a laboratory test, and providing seamless care.

Secondary outcomes included the disease states for which the most clinical activities were performed, the median number of clinical activities performed per patient for each of the 5 most common medical conditions, and the median number of pharmacist-initiated interventions and recommendations per patient. Another set of secondary outcomes consisted of the differences in number of clinical activities performed for patients stratified by age, sex, number of medications, and whether they were receiving Medication Assistance Program (MAP) services. The MAP is a program available to home care patients who require assistance to take their medications. Before any patient receives MAP services, medication reconciliation is completed by a health care professional.

Statistical Analysis

Descriptive statistics generated in REDCap and Microsoft Excel software were used to define the study group. Percentages and medians (with IQR) are reported, where applicable. Poisson regression was performed by Alberta Strategy for Patient Oriented Research (using R software, version 4.0.0) to determine the influence of the following patient characteristics on the number of clinical activities: age, sex, number of medications, and whether patients received MAP services. This study was approved by the University of Alberta Health Research Ethics Board (Pro00094658).

RESULTS

Patient Characteristics

From among the 355 patient records screened, 318 (89.6%) patients were included in the study; the other 37 patients were excluded because pharmacists' clinical documentation was not available in the chart. The median age was 79 years, and 191 (60.1%) of the patients were female (Table 1). The median number of medical conditions was 6 (IQR 4–8). The 5 most prevalent medical conditions were hypertension (62.9%), followed by type 2 diabetes (39.9%), osteoarthritis (39.6%), depression (29.2%), and dyslipidemia (28.9%). The median number of medications was 10 (IQR 7–14), and 53.5% of patients were receiving MAP services at the time of the initial pharmacist consultation. Most of these patients required full assistance and supervision (level 3 MAP) to administer at least 1 medication (Table 1).

Clinical Activities

Pharmacists performed a total of 1172 clinical activities at initial consultation, with a median of 3 (IQR 2–5) clinical activities per patient. The most common clinical activities were patient/caregiver counselling (13.7%), collaborating or intending to collaborate with another health care professional (13.4%), deprescribing (11.9%), and adjusting medication doses (9.4%) (Table 2). There were no differences in the median number of clinical activities performed per patient among those with any of the 5 most common medical conditions (median of 3 clinical activities per patient).

Furthermore, for each additional year of age and each additional medication, there was an increase in the number

TABLE 1. Demographic Characteristics of Home Care Patients Who Received Clinical Pharmacy Services

Characteristic	No. (%) of Patients[a] (*n* = 318)	
Age (years) (median and IQR)	79	(68–86)
Sex, female	191	(60.1)
No. of medications (median and IQR)	10	(7–14)
Medication Assistance Program client[b]	170	(53.5)
Level 1	2	(1.2)
Level 2	23	(13.5)
Level 3	145	(85.3)
No. of medical conditions (median and IQR)	6	(4–8)
Most common medical conditions		
Hypertension	200	(62.9)
Diabetes mellitus, type 2	127	(39.9)
Osteoarthritis	126	(39.6)
Depression	93	(29.2)
Dyslipidemia	92	(28.9)
Hypothyroidism	82	(25.8)
Chronic obstructive pulmonary disease	79	(24.8)
Gastroesophageal reflux disease, peptic ulcer disease, gastritis	79	(24.8)
Chronic pain	63	(19.8)
Coronary artery disease	58	(18.2)
Cognitive decline, unspecified	52	(16.4)
Atrial fibrillation	49	(15.4)
Chronic kidney disease	46	(14.5)
Osteoporosis	45	(14.2)
Congestive heart failure	45	(14.2)

IQR = interquartile range.
[a]Except where indicated otherwise.
[b]Indicates the highest level of medication assistance required for any medication, where level 1 (reminder) = the patient requires a verbal reminder to take their medications and is otherwise independent; level 2 (some/partial assistance) = the patient does not require supervision to take their medications as they are able to manage their own medications with minimal assistance, but the patient may require assistance opening containers; and level 3 (full assistance) = a health care aide takes medications out of the packaging and assists and supervises the patient to ensure the medications are taken. The percentage for each level is based on the number of patients who were clients of the program (*n* = 170).

of clinical activities performed: by 0.01 (95% confidence interval [CI] 0.001–0.014) for each additional year of age ($p = 0.003$) and by 0.03 (95% CI 0.01–0.04) for each additional medication on their medication list ($p < 0.001$). A small effect of sex on pharmacist clinical activities was also observed, whereby female sex was correlated with a slightly higher number of clinical activities (1.24 activities/patient among female patients versus 1.11/patient among male patients, 95% CI for the ratio 0.95–1.31, $p = 0.08$). In contrast, receiving medication assistance through the MAP was associated with a slightly lower number of clinical activities performed (0.86/patient, 95% CI 0.74–1.01, $p = 0.012$).

TABLE 2. Clinical Activities Performed by Home Care Pharmacists and Frequency of Total Clinical Activities Per Patient[a]

Clinical Activity[b]	No. (%) of Activities (*n* = 1172)	
Patient/caregiver counselling or education	160	(13.7)
Collaborate or intent to collaborate with another health care professional	157	(13.4)
Deprescribe/discontinue medication	140	(11.9)
Medication dose change	110	(9.4)
Recommend an over-the-counter/ nonprescription medication	109	(9.3)
Formulation or medication change	86	(7.3)
Referral to another health care professional	84	(7.2)
Prescribing	76	(6.5)
Order laboratory test(s)	71	(6.1)
Seamless care	66	(5.6)
Change in medication timing	58	(4.9)
Medication adherence	54	(4.6)
Administer injection[c]	1	(0.1)
No. of clinical activities per patient (median and IQR)	3	(2–5)

IQR = interquartile range.
[a]Clinical activities were performed for a total of 304 patients.
[b]Definitions of the clinical activities appear in Appendix 1 (available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/213).
[c]Home care pharmacists are generally not involved in administering or assisting with the administration of medications, including injections.

Pharmacist-Initiated Interventions and Recommendations

In this study, pharmacists initiated a total of 562 interventions for 284 patients, for a median of 2 (IQR 1–3) per patient (Table 3). A large proportion of pharmacist-initiated interventions involved patient education/counselling (28.5%) and collaborating with another health care professional (27.9%).

Pharmacists also made 610 recommendations for 216 patients (median of 2 [IQR 1–4] per patient). Deprescribing was the most frequent type of recommendation (21.1%) (Figure 1, Table 3). Recommending an over-the-counter or nonprescription medication was the second most commonly suggested change to drug therapy (17.9 %).

DISCUSSION

In this study, older patients with multiple medications were more likely to have greater involvement of pharmacists in their care. The pharmacists' substantial role in

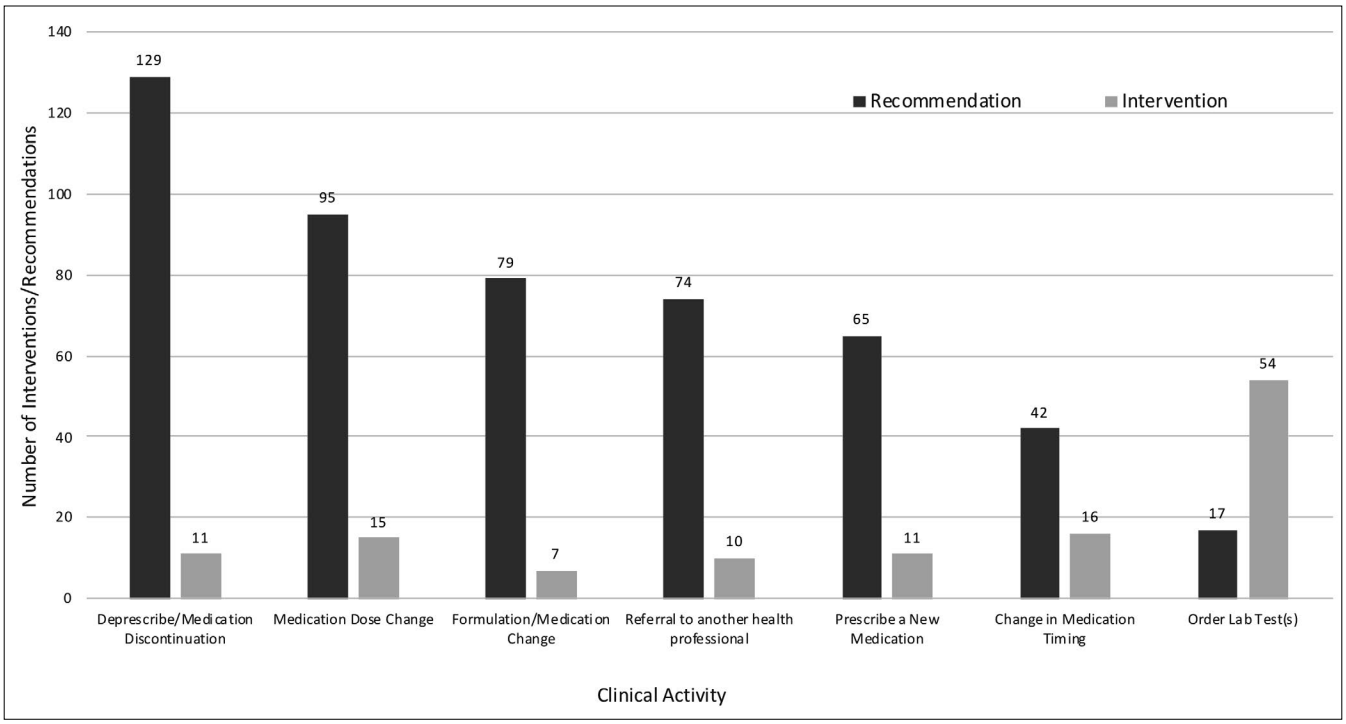

FIGURE 1. Relative frequency of selected pharmacist-initiated activities that could be classified as either an intervention or a recommendation.

managing medication therapy for home care patients is further supported by previous findings that advanced age and higher number of medications are risk factors for adverse medication-related events.[28] Furthermore, although many patients had cardiovascular disease, an array of other medical conditions was seen in this population. Considering that the median number of clinical activities was the same for patients with the 5 most common medical conditions as for all patients combined, the presence or absence of certain disease states is not a good indicator to identify patients who should be referred to a home care pharmacist. Case managers who are triaging patients requiring professional care services could instead consider placing greater emphasis on the patient's age or number of medications when determining whether to initiate a referral for pharmacy services.

The overall characteristics of our patient population were similar to those of other home care patient populations in Canada and those observed in previous studies examining in-home pharmacy services.[2,4,6,28] Patients referred for home care pharmacy services were generally elderly individuals, with a complex array of medications and medical conditions, as well as high rates of hypertension (62.9%) and diabetes (39.9%). Many also had higher-level care needs, often requiring assistance with medication administration; as such, they constituted a population at risk for adverse medication-related events. Although patient education (13.7%) and collaborating with another health care professional (13.4%) were the most common clinical activities, pharmacists provided a number of other services, with the frequencies of these activities being fairly evenly distributed.

In addressing medication-related issues, home care pharmacists made recommendations and performed interventions. Almost two-thirds of all pharmacist recommendations (62.7% [410/610]) involved a suggestion to alter medication therapy in some way. This total encompassed recommendations to change medication doses, timing, or formulation, as well as recommendations for prescribing and deprescribing medications. Pharmacists also made use of their expanded scope of practice in Alberta to perform a variety of active interventions, including preparation of laboratory test requisitions to monitor medication therapy. Home-bound patients may be unable to easily access laboratory services; therefore, home care pharmacists have the opportunity to initiate in-home lab collections and ensure timely monitoring of patients' health status and response to medications. Home care pharmacists were also largely involved in recommending or initiating deprescribing, thus demonstrating their role in mitigating polypharmacy. The use of multiple medications continues to be a growing concern among elderly patients because of the increased risk of drug-related problems.[28,29] Our findings suggest that home care pharmacists may play an important role as liaisons between primary and tertiary care, as well as providing care to patients who may home-bound or unable to regularly visit other health care providers.

The need for patient education among home-bound patients is illustrated by the fact that approximately half of all patients received medication-related education, similar to rates described in previous studies of home visit and consultant pharmacy programs.[15,26] Home care pharmacists

TABLE 3. Frequency of Pharmacist Interventions and Recommendations

Intervention or Recommendation	No. (%)
Intervention	*n* = 562
Patient/caregiver counselling or education	160 (28.5)
Collaborate or intent to collaborate with another health care professional	157 (27.9)
Seamless care	66 (11.7)
Medication adherence	54 (9.6)
Order laboratory test(s)	54 (9.6)
Change in medication timing	16 (2.8)
Medication dose change	15 (2.7)
Prescribing	11 (2.0)
Deprescribing	11 (2.0)
Referral to another health care professional	10 (1.8)
Formulation/medication change	7 (1.2)
Administer injection	1 (0.2)
No. of interventions per patient (*n* = 284 patients)	Median 2 (IQR 1–3)
Recommendation	*n* = 610
Deprescribing	129 (21.1)
Recommend over-the-counter or nonprescription medication	109 (17.9)
Medication dose change	95 (15.6)
Formulation/ medication change	79 (13.0)
Referral to another health care professional	74 (12.1)
Prescribing	65 (10.7)
Change in medication timing	42 (6.9)
Order laboratory test(s)	17 (2.8)
No. of recommendations per patient (*n* = 216 patients)	Median 2 (IQR 1–4)

IQR = interquartile range.

may also play a role in reinforcing medication education for patients recently discharged from hospital. These individuals may be at a particularly increased risk of medication errors upon discharge as a result of misunderstandings related to medication changes during the hospital stay.[30] This finding emphasizes that the home care pharmacist's role in patient care goes beyond the number of medication changes or interventions made or recommended, and further illustrates how pharmacists may facilitate care in the transition between inpatient and outpatient care settings. The ability to speak directly with other caregivers in the home, assess the patient's living environment, and review medication adherence techniques and storage of medications gives the home care pharmacist valuable opportunities to evaluate and address potential or actual drug-related problems.

Interprofessional collaboration was another highly prevalent activity in home care pharmacy practice. These findings are in alignment with a recent review of 75 studies, which concluded that a majority of home visit programs involved pharmacist collaboration with a physician or other health care professional.[15] Beyond communicating with the referring case manager, home care pharmacists also frequently engaged with other providers to promote collaboration, with a view to resolving concerns and facilitating continuity of care. Given the pharmacist's role as a consultant on the home care team and the varied level of interprofessional collaboration with other providers, each pharmacist exercises discretion in determining the appropriateness of initiating an intervention and/or making a recommendation. In some instances, the pharmacist is involved in the patient's care for only a brief period and thus performs a consultative role and relays recommendations to other health care providers, whereas in other instances the pharmacist will implement clinical activities. This is exemplified by the balance seen in terms of the overall proportions of clinical activities that were classified as interventions (48%) and recommendations (52%).

Our study had some limitations. As it was a retrospective record review, we were reliant on documentation within the patients' charts. Also, the clinical activities that we identified could not be linked to specific medical conditions or medications. Therefore, the frequency of clinical activities for patients with the top 5 medical conditions reflected the overall number of clinical activities performed, rather than activities directed at optimizing the management of particular medical conditions. Given that our study was designed to capture initial consultations, we did not follow charts forward to determine whether pharmacists' recommendations were implemented. Our inability to quantify economic, clinical, or humanistic outcomes was an additional limitation. Finally, the study was limited to patients served within the greater Edmonton Zone, and the findings will have limited generalizability to other home care programs.

CONCLUSION

To our knowledge, this is the first study in Alberta to elucidate the role of home care pharmacists and to capture the clinical activities that they perform. Limited international studies have outlined the role of the pharmacist in an established home care team.[6,15,26] This study demonstrates that home care pharmacists are engaged in various clinical activities, including activities related to an expanded scope of practice, such as prescribing, which underlines the need for medication management services among home care patients. In collaboration with the multidisciplinary home care team, home care pharmacists play a large role in optimizing therapy for older patients who are taking several medications, and future referrals by case managers should target such patients. Optimizing the referral process will lead to more efficient use of limited pharmacist resources for the patients who need them most. Further research is warranted to determine the rates of acceptance and implementation of pharmacist recommendations and their

impact in achieving treatment targets for various medical conditions alongside desired clinical outcomes, as well as to measure patient satisfaction with services.

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Discerning Clinician Perceptions of an Established Opioid Stewardship (DISCLOSE) Program

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ABSTRACT

Background: The Opioid Stewardship Program (OSP) was created to promote safe and rational prescribing of opioids, where the risks associated with providing opioids for patients must be balanced against the risk of patients experiencing uncontrolled pain. The pharmacist-led OSP was established at 2 Fraser Health Authority (FHA) sites, British Columbia, to provide clinical services through patient referrals and screening. The rate of acceptance of OSP pharmacists' recommendations has been high, but there was a need to assess clinicians' perceptions of the program.

Objectives: To assess the perceptions of health care professionals at FHA hospitals offering the OSP regarding various aspects of the program and to identify areas of the program that could be modified to further optimize service delivery.

Methods: A prospective cross-sectional survey was distributed to about 250 targeted health care professionals, who answered questions regarding their perceptions of the OSP. Data were analyzed using simple descriptive statistics.

Results: A total of 71 respondents initiated the survey, of whom 59 were included in the final analyses. Most participants indicated that the OSP pharmacists' suggestions were valuable for optimizing pain management (52/57, 91%) and preventing adverse events (49/56, 88%). Most participants were satisfied with the quality of communication (51/56, 91%), timeliness to consults (51/52, 98%), and recommendations provided (52/55, 95%). Increasing knowledge transfer, improving communication about intentions for patient follow-up, and expanding services at current sites and to other sites were recommended to improve the OSP.

Conclusions: Clinicians responding to the survey reported a high level of satisfaction with and positive views of the pharmacist-led OSP. Providing more education and clarifying intentions for patient follow-up are modifications that could be made to improve the program.

Keywords: opioids, stewardship, pharmacist, perception, survey, questionnaire

RÉSUMÉ

Contexte : L'Opioid Stewardship Program (OSP) *[programme de gestion des opioïdes]* a été mis sur pied pour encourager la prescription sûre et rationnelle d'opioïdes qui permet de peser les risques associés à leur délivrance contre les risques que le patient ressente une douleur incontrôlée. L'OSP, dirigé par les pharmaciens, a été mis en place sur 2 sites de la Fraser Health Authority (FHA) (Colombie-Britannique) afin de fournir des services cliniques par l'entremise de l'aiguillage et du dépistage des patients. Le taux d'acceptation des recommandations des pharmaciens de l'OSP était élevé, mais il était nécessaire d'évaluer la perception des cliniciens à l'égard du programme.

Objectifs : Évaluer les perceptions des professionnels de la santé dans les hôpitaux de la FHA offrant l'OSP à l'égard de divers aspects du programme et cerner ceux qui pourraient être modifiés pour optimiser la prestation de services.

Méthodes : Une enquête prospective transversale a été distribuée à environ 250 professionnels de la santé ciblés, qui ont répondu à des questions portant sur leur perception de l'OSP. Les données ont été analysées à l'aide de statistiques descriptives simples.

Résultats : Au total, les réponses de 71 répondants ont fait l'objet d'analyses. La plupart des participants ont indiqué que les suggestions des pharmaciens de l'OSP étaient utiles pour optimiser la gestion de la douleur (52/57, 91 %) et prévenir les événements indésirables (49/56, 88 %). La plupart des participants étaient satisfaits de la qualité de la communication (51/56, 91 %), de la rapidité des consultations (51/52, 98 %) et des recommandations fournies (52/55, 95 %). Les recommandations suivantes ont été formulées pour améliorer l'OSP : amélioration du transfert des connaissances; amélioration de la communication sur les intentions de suivi des patients; et élargissement des services sur les sites actuels et à d'autres sites.

Conclusions : Les cliniciens qui ont répondu au sondage ont fait état d'un niveau élevé de satisfaction et d'opinions positives à l'égard de l'OSP dirigé par les pharmaciens. Une formation accrue et la clarification des intentions quant au suivi des patients sont des modifications qui pourraient être apportées en vue d'améliorer le programme.

Mots-clés : opioïdes, gestion, pharmacien, perception, sondage, questionnaire

INTRODUCTION

Opioid stewardship has been described as "coordinated interventions designed to improve, monitor, and evaluate the use of opioids in order to support and protect human health".[1] Opioid prescribing practices in Canada have changed in recent years, with trends toward reduced prescribing and increased tapering.[2] Although seemingly positive, these trends signal a possible shift toward opiophobia. In response to the identified need to optimize opioid use, the Fraser Health Authority (FHA) initiated the first pharmacist-led inpatient Opioid Stewardship Program (OSP) in British Columbia. Two clinical pharmacy specialists (K.C., K.N.) were hired at the 2 largest hospitals in the FHA: the first at Royal Columbian Hospital in 2018 and the second at Surrey Memorial Hospital in 2019. These pharmacists provide daytime coverage on weekdays, without backfilling for days off. Each pharmacist has completed a Canadian Pharmacy Residency Board hospital residency program and has earned a Doctor of Pharmacy degree, with additional self-training in pain and opioid stewardship. The objectives of the FHA OSP are to prevent opioid-related adverse outcomes by promoting optimal opioid prescribing in hospital and on hospital discharge without compromising pain management, and to provide immediate local impact and long-term community improvements in opioid use.

The FHA OSP is delivered by means of direct clinical care, quality improvement work, research, and education. The clinical portion of the FHA OSP was modelled after the audit and feedback method of antimicrobial stewardship programs (i.e., prospective case review and feedback). In a cross-sectional survey aiming to gather information about opioid-related hospital practices, 23% of 133 responding hospitals reported having an opioid stewardship program,[3] but only 9 of the 133 hospitals reported having a prospective screening process. Most of these hospitals were in the United States. Some OSP programs in North America are led by pharmacists.[4,5] In British Columbia, a similar OSP exists within a different health authority, incorporating an audit and feedback process led by a pharmacist and a physician.[6]

Clinical work began in March 2019 at Surrey Memorial Hospital and June 2019 at Royal Columbian Hospital. The OSP pharmacists identified patients at high risk of opioid-related adverse outcomes using the following criteria: personal or family history of substance use disorder, psychiatric illness, opioid-related aberrant behaviour, increased risk of overdose (e.g., pulmonary disease), morphine milligram equivalent above 50 mg/day, concurrent use of opioid and benzodiazepines or other sedatives, long-acting opioid use by opioid-naive patients, escalating opioid use without apparent cause, and non-decreasing opioid requirements for management of acute pain.[7,8] The OSP pharmacists also accept patient referrals from prescribers, pharmacists, and patient care coordinators (i.e., unit-based nurse managers). Patients whose care is managed by the addiction medicine, palliative care, or acute pain services are generally excluded from OSP pharmacist care. Optimization of opioid use throughout the hospital stay, referrals to outpatient clinical pharmacists, and handover to community prescribers provide opportunities for the OSP pharmacists to influence opioid prescribing in the community.

The FHA OSP recorded an overall 92.5% acceptance rate for the 3026 recommendations put forth between August 2019 to July 2020 (unpublished data). A total of 1408 patients received interventions in this period. Most of these patients were identified through screening (62% of those at the Royal Columbia Hospital, 70% of those at Surrey Memorial Hospital) rather than referral. At the Royal Columbian Hospital, there was an almost equal split between medicine and surgical cases (42% versus 57%), whereas at Surrey Memorial Hospital, most of the patients who received an intervention were admitted under the medicine service (67%), with a smaller proportion from the surgical service (31%). The number of patient referrals increased over the same period, with the total number of referrals across both sites reaching 453 for the year. Patient referrals were made by physicians/nurse practitioners (43%), pharmacists (41%), and patient care coordinators (16%).

Successful delivery of the OSP is reliant on cooperation among clinicians. The literature indicates that the implementation of antimicrobial stewardship programs may be impeded by concerns about threatened autonomy among prescribers, a hierarchical hospital culture, and lack of support.[9] Such concerns were expected to be elucidated by this study, which aimed to determine whether the OSP pharmacists have been successful in offering a collaborative, supportive service that encourages opioid optimization.

The primary objective of the study was to assess the perceptions of health care professionals at FHA hospitals offering the OSP regarding various aspects of the program. The secondary objective was to identify areas that could be modified to further optimize the program.

METHODS

Local research ethics boards approved this research, which was in accordance with the Helsinki Declaration. Participants provided written consent.

Study Design and Participants

The study was based on a prospective cross-sectional survey developed using REDCap software, version 9.1.0.[10,11] A convenience sample from the 2 study sites was sought. The Royal Columbian Hospital and Surrey Memorial Hospital are regional hospitals with 490 and 650 acute care beds, respectively. Both hospitals provide primary, secondary,

and tertiary care, and both have addiction medicine, palliative care, and acute pain services, all without clinical pharmacists on the team. The following groups of health care professionals were invited to participate in the survey: attending (or staff) physicians, medical fellows, medical residents, nurse practitioners, pharmacists, and patient care coordinators. These potential participants represent health care providers who may have had contact with OSP pharmacists, through either pharmacist screening or referrals. Providers who were not aware of the OSP or the purpose and types of interventions completed by the OSP pharmacists, as well as those who indicated that they had never had any interaction with the OSP pharmacists, were excluded from the majority of the study; however, they were able to complete demographic questions, a question about the types of interactions they had with the OSP pharmacists (if applicable), and a question about how valuable they perceived the OSP pharmacists could be to their practice (based on a description of the OSP provided within the survey). Similarly, we targeted health care professionals working on units where the OSP pharmacists provide routine screening, including the clinical teaching unit, general surgery, neurosurgery, orthopedic surgery, trauma, vascular surgery, cardiac surgery, psychiatry, infectious diseases, general medicine, pain services, and addiction services. It was anticipated that the survey would be disseminated to approximately 250 health care professionals.

Survey Tool

The anonymized survey used 7 rating-scale, 10 Likert-type, 8 multiple-choice, 1 ranking, and 7 yes/no questions to elucidate participants' demographic characteristics and to assess the primary and secondary objectives. Four mandatory free-text questions allowed participants to provide additional feedback. The questionnaire was developed according to recommendations in the literature,[12] and feedback was provided by 2 pharmacists who were aware of the OSP program and pilot-tested the tool. The survey was anticipated to take approximately 15 minutes to complete. Reliability and validity were not formally assessed.

Medical department heads, patient care coordinators, and pharmacy department administrative staff were contacted by email and asked to disseminate the study invitation to their team members. A letter containing the questionnaire link with an embedded consent form was sent by email by the pharmacy administration assistant 3 times between November 2020 and February 2021. Respondents had 4 months to complete the questionnaire. There were no incentives for participants; however, the overall benefits of optimizing the OSP were discussed in the invitation letter.

Analytical Plan

A convenience sample was used because this survey research was not data-driven. Most individual survey questions were optional. Responses were analyzed on the basis of the number of respondents answering each question, not the total number of survey respondents. Participants who indicated having no awareness of the program or the purpose and type of interventions and those reporting no previous contact with the OSP pharmacists were excluded from completing most of the survey. At minimum, each respondent had to answer at least one question other than those for demographic characteristics for that respondent's data to be included in the analysis.

Planned subgroup analyses compared responses according to each participant's profession, hospital site, and prescriber specialty, as well as those with frequent (> 7) versus infrequent (≤ 7) interactions with the OSP pharmacists. Simple descriptive statistics were used for most responses. REDCap version 9.1.0,[10,11] a secure electronic data capture tool, was used to report these frequencies, and Excel spreadsheet software (Microsoft Corporation) was used to analyze the responses. Two investigators (C.R., K.C.) identified recurrent and unique opinions in the free text.

RESULTS

The survey was distributed to an estimated 250 individuals. A total of 75 clinicians initiated the survey (estimated response rate 30%), and 71 (95%) of these answered the required questions to be included in at least some of the final analyses. Demographic information is presented in Table 1.

Awareness

Nearly all 71 participants were aware of the OSP (Table 2). Individuals who indicated a lack of awareness of the OSP (either the program or associated interventions) or had no previous interaction with the OSP pharmacists were then given a description of the OSP. Two-thirds of these individuals (8/12 [67%]) thought this program would be valuable to their practice.

Of the 71 participants included in the analyses, 63 indicated that they had interacted with the OSP pharmacists in the following ways: reading an OSP pharmacist's note in a patient's chart (56/63 [89%]), consulting the OSP pharmacists (47/63 [75%]), and/or being contacted by their OSP pharmacist (39/63 [62%]). Participants were asked to rank various reasons for consulting with the OSP pharmacists, by assigning each reason a rank from 1 (high importance) to 7 (low importance). In terms of reasons with high importance (rank = 1), 42% (24/57) of participants identified opioid use management, 38% (21/55) identified optimizing pain management, 29% (16/56) identified opioid tapering, 17% (9/53) identified patient education, 13% (7/54) identified discharge assistance, and 11% (6/55) identified opioid risk assessment. Among participants who completed the entire survey (n = 59), more than half had interacted with their OSP pharmacist more than 7 times (35/58 [60%]).

Main Perceptions

Value and Satisfaction

Most participants indicated that they thought the OSP pharmacists were valuable for optimizing pain management and preventing opioid-related adverse events (Table 3, Figure 1), and most participants were satisfied with the quality of services provided by the OSP (Figure 2). The majority consensus was that the OSP pharmacists are easily accessible. A few respondents stated that the service is missed when there is no OSP coverage. One pharmacist reported that they occasionally had concerns that the OSP recommendations tended toward polypharmacy. One prescriber reported being unsatisfied with the recommendations and interventions, indicating a perception that the OSP pharmacists lacked clinical experience in this area. Conversely, another prescriber stated that they now suggest that all attending physicians consult the OSP pharmacist. A common sentiment is illustrated by the following quote: "The OSP [pharmacist] is a valuable colleague with deeper understanding of opioid use, and collaboration helps in optimization of patient care."

The majority of respondents (50/52 [96%]) did not perceive the OSP pharmacists to have limited their own autonomy. Overall, 90% (46/51) of participants reported that they often or always agreed with OSP recommendations and were very or extremely comfortable following the recommendations (46/52 [88%]). Only 1 respondent (the prescriber who reported a lack of satisfaction with OSP recommendations) indicated rarely agreeing with recommendations and being only slightly comfortable following OSP recommendations. The most frequent reason for not accepting OSP recommendations was "having new information that the OSP pharmacist did not have" (14/59 [24%]; Table 4).

TABLE 1. Participant Characteristics by Profession, Specialty, Hospital, and Duration of Work

Category	No. (%) of Participants[a]
Profession	*n* = 68 (96)
Physician	31 (46)
Pharmacist	29 (43)
Patient care coordinator	4 (6)
Nurse practitioner	3 (4)
Medical resident	1 (1)
Medical fellow	0
Prescriber[b] specialties	*n* = 35 (49)
Medicine + subspecialties[c]	21 (60)
Surgery[d]	5 (14)
Addictions	6 (17)
Psychiatry	3 (9)
Hospital	*n* = 71 (100)
Royal Columbian Hospital only	41 (58)
Surrey Memorial Hospital only	28 (39)
Both hospitals	2 (3)
Duration of work (years)	*n* = 67 (94)
< 1	4 (6)
1–5	19 (28)
> 5	44 (66)

[a]The first row of each section shows the number of respondents who answered the specific question (and percentage of 71 participants). In subsequent rows of each section, the percentages are based on the number of respondents for the question.
[b]Prescribers consisted of 31 physicians, 3 nurse practitioners, and 1 medical resident.
[c]Medicine + subspecialties = general medicine, internal medicine, hospitalist practice, geriatric medicine.
[d]Surgery = general surgery, thoracic surgery, orthopedic surgery, vascular surgery, neurosurgery.

Services

With respect to follow-up by the OSP pharmacist, most participants named tapering medications (42/59 [71%]) as the top scenario in which such follow-up would be required. A small number of participants believed that OSP follow-up would be required only if specifically requested (Table 5). Several participants noted a lack of clarity about whether the OSP pharmacist was providing one-time interventions or ongoing follow-up throughout a patient's hospital stay.

Study participants indicated that patients with the following characteristics would be most likely to benefit

TABLE 2. Participants' Awareness of the Opioid Stewardship Program (OSP)

Question[a]	Group; No. (%) of Participants				
	Total Group (*n* = 71)	Hospital A (*n* = 43)	Hospital B (*n* = 30)	Prescribers (*n* = 35)	Pharmacists (*n* = 29)
Are you aware that there is an OSP in this hospital?	70 (99)	43 (100)	29 (97)	35 (100)	29 (100)
Are you aware of the purpose and types of interventions made by the OSP pharmacists?	61 (86)	35 (81)	28 (93)	28 (80)	27 (93)
Is it clear to you when you would consult the OSP versus addiction medicine, acute pain service, or palliative care?	55 (77)	31 (72)	25 (83)	24 (69)	26 (90)

[a]Answering "no" to either of the first 2 questions in this table led to participant's exclusion from subsequent analyses. Overall, after application of all exclusions (including those not represented in this table), 59 of the initial 71 participants had complete survey responses and were included in the final analyses.

from OSP services: those at high risk of opioid use disorder (47/50 [94%]), those with difficult-to-control pain (43/50 [86%]), those with psychiatric illnesses (38/49 [78%]), those with opioid-seeking tendencies (46/50 [92%]), those receiving high doses of opioids (46/50 [92%]), those taking concomitant benzodiazepines or other sedatives (38/49 [78%]), and those at high risk of adverse effects (41/50 [82%]).

Common themes for the most helpful aspects of OSP services were completing a thorough assessment of the patient's pain history and/or opioid use (mentioned by 5 participants), exploring multiple modalities to target pain (mentioned by 4 participants), and assisting with the management of complex pain and/or opioid-seeking tendencies (mentioned by 6 participants). The least helpful

TABLE 3. Value of OSP Pharmacists' Suggestions Reported as ≥ 7 for 2 Outcomes[a]

	Group; No. (%) of Participants				
Question	**Total Group**	**Hospital A**	**Hospital B**	**Prescribers**	**Pharmacists**
How valuable do you feel the OSP pharmacist suggestions are to optimizing pain management?	52/57 (91)	33/35 (94)	21/24 (88)	22/27 (81)	25/25 (100)
How valuable do you feel the OSP pharmacist suggestions are in preventing adverse events related to opioid use?	49/56 (88)	31/34 (91)	20/24 (83)	22/27 (81)	22/24 (92)

OSP = Opioid Stewardship Program.
[a]Value of suggestions was graded from 1 (not very valuable) to 10 (very valuable).

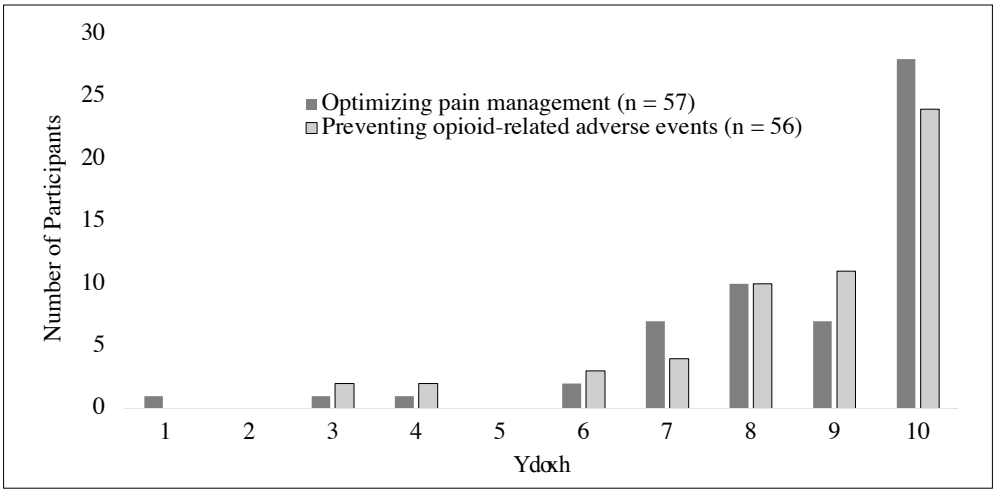

FIGURE 1. Value of suggestions made by the Opioid Stewardship Program pharmacists for 2 outcomes. Value was graded from 1 (not very valuable) to 10 (very valuable).

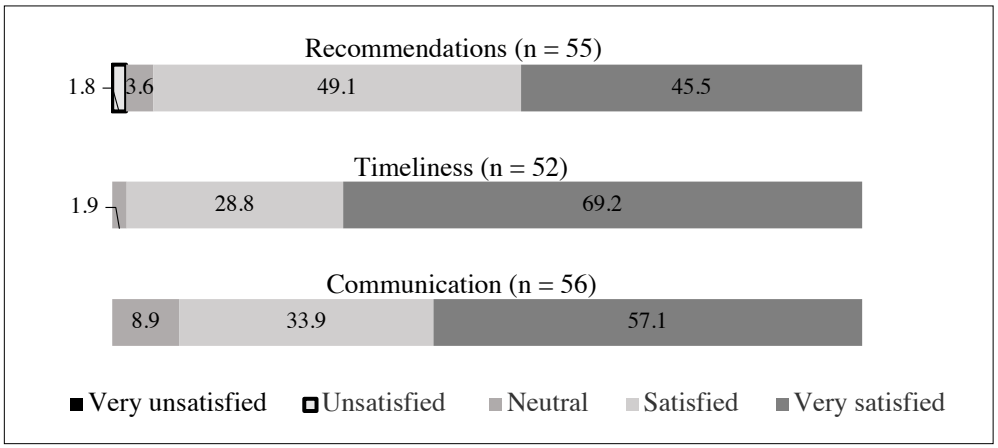

FIGURE 2. Satisfaction with various aspects of the Opioid Stewardship Program, specifically recommendations provided, timeliness to consultations, and quality of communication.

aspect was lack of follow-up after providing an intervention (mentioned by 3 participants).

Prescribing Patterns

Among prescribers, 58% (15/26) agreed and 31% (8/26) were neutral when asked whether the OSP pharmacists had influenced their opioid prescribing patterns. Respondents were mostly either in agreement (31/51 [61%]) or neutral (17/51 [33%]) when asked whether the OSP pharmacists had influenced their approach to pain management; a small number of respondents disagreed with this statement (3/51 [6%]).

Participants thought that OSP involvement promoted safer opioid use, with 96% (50/52) indicating that such involvement was moderately to extremely effective at achieving this goal. Equal numbers of participants (23/51 [45%]) thought that the OSP pharmacists' attitude toward prescribing long-term opioid therapy tended toward an avoidance of prescribing as thought that these pharmacists took a balanced approach (i.e., neither avoided prescribing nor engaged in overprescribing). More than two-thirds of participants believed the OSP pharmacists took a balanced approach to acute pain management (35/51 [69%]). One prescriber reported that the OSP pharmacists might be overly conservative with their analgesic approach.

Expansion of the OSP

Most participants indicated that the current OSP model, combining screening and referrals, was the most effective method of service delivery (44/49 [90%]). There was consensus regarding this combination approach among participating pharmacists (21/21 [100%]), whereas a few prescribers put higher value on clinician referrals (3/25 [12%]). As illustrated in Table 6, most respondents reported that they were more likely to prioritize pain as a medical issue after interacting with their OSP pharmacist than beforehand, and indicated that they were likely to consult their OSP pharmacist again and to recommend the OSP to colleagues. Most participants believed that the OSP should be expanded to other institutions. The most common suggestions for additional OSP services were providing more educational presentations, creating patient handouts, and expanding services to support patients with chronic benzodiazepine use.

DISCUSSION

To the authors' knowledge, this is the first study to explore clinician perceptions of a pharmacist-led inpatient OSP that combines screening and consultations. The demographic characteristics of the participants closely reflected those of

TABLE 4. Reasons for Disagreement with OSP Pharmacists' Recommendations

	Group; No. (%) of Participants				
Reason[a]	Total Group (*n* = 59)	Hospital A (*n* = 35)	Hospital B (*n* = 26)	Prescribers (*n* = 27)	Pharmacists (*n* = 27)
Disagreed with OSP pharmacist rationale	5 (8)	3 (9)	2 (8)	3 (11)	2 (7)
Patient disagreed with OSP pharmacist rationale	10 (17)	6 (17)	4 (15)	5 (19)	5 (19)
New patient information that OSP pharmacist did not have	14 (24)	8 (23)	7 (27)	6 (22)	8 (30)
Personal preference	8 (14)	4 (11)	4 (15)	4 (15)	4 (15)
Did not want to write opioid prescription	0	0	0	0	0
Never disagreed	10 (17)	8 (23)	2 (8)	6 (22)	2 (7)

OSP = Opioid Stewardship Program.
[a]Participants could select more than one option.

TABLE 5. Scenarios for Which Follow-Up Is Thought to Be Necessary

	Group; No. (%) of Participants				
Scenario[a]	Total Group (*n* = 59)	Hospital A (*n* = 35)	Hospital B (*n* = 26)	Prescribers (*n* = 27)	Pharmacists (*n* = 27)
Tapering	42 (71)	25 (71)	19 (73)	23 (85)	16 (59)
Changing acute pain medication	36 (61)	23 (66)	14 (54)	15 (56)	19 (70)
Directing opioid discharge prescribing	25 (42)	17 (49)	8 (31)	14 (52)	9 (33)
No follow-up necessary unless requested	2 (3)	2 (6)	0	1 (4)	1 (4)

[a]Participants could select more than one option.

the main users of the OSP, based on unpublished statistics collected by the program, which strengthens the validity of the results. Among participants, there was an almost universal awareness of the OSP, and most were frequent users of the OSP. At the time of this study, delivery of OSP clinical services had been available for just over 1 year. These results indicate that the current OSP model can quickly achieve wide program awareness and strong receptiveness.

The results of this survey indicated a strong consensus among participants regarding the value of a pharmacist-led OSP in optimizing patient care and preventing opioid-related harms. Survey responses indicated that most recommendations provided by the OSP met with agreement, which is congruent with the high acceptance rate observed in the first year of program implementation. Collaboration with OSP pharmacists was largely appreciated, especially in the care of patients with complex medical needs, where meticulous history gathering is time-consuming but necessary. Although many participants reported being likely to prioritize pain as a medical issue after their interaction with the OSP pharmacists, a notable percentage of participants still responded that they would not prioritize pain in this way. This may indicate that some prescribers prefer to delegate pain management to the OSP pharmacists. Ultimately, clinicians felt confident that recommended OSP interventions were in each patient's best interest.

The approach to pain management may require the use of multiple non-opioid analgesic agents to reduce opioid dosages. This may be perceived as polypharmacy or a conservative strategy, as indicated by some respondents. A single participant expressed the belief that the OSP pharmacists lacked the clinical experience to provide pain recommendations, but this opinion was at odds with the vast majority of feedback. There can be resistance when a new program is introduced, especially if collaboration has not been requested through consultation. The FHA OSP is run by pharmacists without dedicated opioid stewardship physicians. Nonetheless, the program appears to be effective at both sites where it has been implemented. This is likely because the pharmacists have expertise in optimizing appropriate use of medications and monitoring response to drug therapy, and are therefore well equipped to be advocates for opioid stewardship. In fact, the literature provides supporting evidence regarding clinical pharmacists and how they improve quality and safety of care.[13,14] Since program inception, the OSP has aimed to be perceived as a patient care service rather than a policing entity. Survey responses aligned with this orientation, in that most participants did not perceive the OSP as limiting their professional autonomy. Clinicians likely appreciated the efficiency of having opioid-related assistance by means of systematic screening, without being required to seek help each time.

The overarching goal of programs like the OSP is to broadly influence the culture of opioid use and shift practice toward evidence-based opioid prescribing. This study supports the provision of OSP clinical services through both screening and consultation as a successful approach to achieving positive perceptions of recommendations among providers. Notably, participants suggested offering more education related to opioid stewardship as a way to improve the program. According to conclusions drawn in the antimicrobial stewardship literature, passive education (e.g., presentations) alone was inferior to active screening (audit and feedback) in achieving stewardship goals.[15,16] However, adding passive education to existing clinical services may help in achieving OSP goals.

Some participants expressed confusion about whether OSP pharmacists provide follow-up on the interventions they recommend. In some straightforward cases, a single intervention may be sufficient, whereas longer-term monitoring (e.g., follow-up phone call) may be required in other cases. Clearly indicating intentions for follow-up in the chart notes may help to avoid misunderstandings in the future.

A final common suggestion was to expand OSP services to other hospitals, as well as within the current hospitals to ensure constant OSP pharmacist coverage. This would reduce the number of patients who might benefit from OSP pharmacist interventions but are missed because of pharmacist unavailability.

Survey research has inherent limitations. Volunteer bias might have resulted in poor representation of the attitudes of the various groups. However, although the response rate was low (in relation to the number of potential participants), the total number of responses ($n = 71$) was relatively

TABLE 6. Participants' Beliefs about Expansion of the Opioid Stewardship Program (OSP)

	Group; No. (%) of Participants				
Question	**Total Group**	**Hospital A**	**Hospital B**	**Prescribers**	**Pharmacists**
Would you consult the OSP pharmacist in the future (or again)?	49/50 (98)	31/31 (100)	20/21 (95)	25/25 (100)	21/21 (100)
Do you believe the OSP should be expanded to other institutions?	48/50 (96)	30/31 (97)	20/21 (95)	24/25 (96)	21/21 (100)
Would you recommend the OSP to colleagues?	49/50 (98)	31/31 (100)	20/21 (95)	25/25 (100)	21/21 (100)
Are you more likely to prioritize pain as a medical issue after interacting with the OSP team?	38/49 (78)	23/30 (77)	16/21 (76)	18/24 (75)	17/21 (81)

high for this type of survey. Participation by pharmacists and physicians was nearly equal, whereas few individuals from other health care professions responded to the survey. This may have skewed the opinions represented, given that the OSP is a pharmacist-led program. Ideally, there would have been equal numbers of respondents from each health care profession; however, analyses of the various subgroups revealed attitudes that were mostly congruent with the total group. Finally, given time and resource constraints, the survey was not validated, and piloting was limited to 2 pharmacists. However, the questions were created with generic wording to ensure that the context would be appropriate for each profession.

The FHA OSP has had largely positive reviews, which supports its success as a novel program. Addressing the feedback for program improvement, continuing to advocate for opioid stewardship, and supporting clinicians to safely prescribe opioids are crucial to ensure continued program growth. Future research to assess recommendation acceptance rates and perceptions of the OSP will be instrumental in further strengthening this program and optimizing patient care.

CONCLUSION

Inpatient health care providers at the 2 FHA hospital sites believed that the pharmacist-led OSP had a positive impact on optimizing pain management and preventing opioid-related harms. After 1 year of implementation, the OSP pharmacists were perceived to have influenced clinicians' approach to pain management. Increasing knowledge transfer, improving the clarity of communication regarding patient follow-up, and expanding services were recommended as ways to improve the program.

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Cultural Competency Education for Health Care Providers: A Literature Review to Guide Canadian Pharmacy Residency Programs

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ABSTRACT

Background: The need for cultural competency education has been emphasized for health care professionals in Canada. According to the Canadian Pharmacy Residency Board accreditation standards, pharmacy residents must be able to provide culturally competent care for their patients, further building upon the education received during their undergraduate pharmacy programs. Although these standards exist, guidance for their implementation in pharmacy residency programs is lacking.

Objectives: To review the available literature and develop recommendations for pharmacy residency coordinators and directors on cultural competency training for pharmacy residents.

Data Sources: A literature search was conducted to explore the literature concerning cultural competency education for pharmacy residents. The search was expanded to encompass literature involving pharmacy students and medical residents for information that could be applied to pharmacy residents.

Data Synthesis: The initial literature search did not yield any results for cultural competency education provided to pharmacy residents. The expanded search yielded information about methods used to educate pharmacy students and medical residents, including didactic lectures, online modules, experiential learning rotations, seminars, workshops, patient simulations and case discussions, and guest lectures by experts in the field or by patients.

Conclusions: It is recommended that interactive education methods be used to train pharmacy residents in cultural competency, to match the experiential learning structure of residency training programs. Methods that could be implemented include offering online modules or readings, arranging for guest speakers, contacting local experts and community members for guidance on creation of a suitable curriculum, and providing immersive rotations focused on diverse populations.

Keywords: cultural competency, pharmacy residency, education methods

RÉSUMÉ

Contexte : La nécessité d'une formation portant sur les compétences culturelles s'adressant aux professionnels de la santé a été soulignée au Canada. Selon les normes d'agrément du Conseil canadien de la résidence en pharmacie, les résidents en pharmacie sont tenus de prodiguer des soins culturellement adaptés à leurs patients, renforçant leur formation pendant les programmes de premier cycle en pharmacie. Malgré ces normes, les directives encadrant leur mise en œuvre dans les programmes de résidence en pharmacie font défaut.

Objectifs : Examiner la documentation disponible et préparer des recommandations à l'intention des coordonnateurs et des directeurs de résidence en pharmacie sur la formation en compétences culturelles pour les résidents en pharmacie.

Sources des données : Une recherche documentaire a été menée pour étudier la littérature portant sur l'éducation en matière de compétences culturelles pour les résidents en pharmacie. La recherche a été élargie pour englober la littérature impliquant des étudiants en pharmacie et des résidents en médecine afin d'obtenir des informations pouvant être appliquées aux résidents en pharmacie.

Synthèse des données : La recherche documentaire initiale n'a donné aucun résultat en ce qui concerne l'enseignement des compétences culturelles offert aux résidents en pharmacie. La recherche élargie a quant à elle fourni des informations sur les méthodes utilisées pour former les étudiants en pharmacie et les résidents en médecine, y compris des conférences didactiques, des modules en ligne, des stages d'apprentissage expérientiel, des séminaires, des ateliers, des simulations de patients et des discussions de cas ainsi que des conférences d'experts invités dans le domaine ou de patients.

Conclusions : Il est recommandé d'utiliser des méthodes d'éducation interactives pour aider les résidents en pharmacie à acquérir des compétences culturelles pour que celles-ci correspondent à la structure d'apprentissage expérientiel de ces programmes. Les méthodes qui pourraient être mises en œuvre comprennent l'offre de modules ou de lectures en ligne, l'organisation de conférenciers invités, la prise de contact avec des experts locaux et des membres de la communauté pour obtenir des conseils sur la création d'un programme approprié et l'offre de stages d'immersion axés sur les diverses populations.

Mots clés : compétence culturelle, résidence en pharmacie, méthodes d'enseignement

INTRODUCTION

Racism is a major contributing factor to health inequities for racialized Canadians.[1] In particular, Indigenous and Black Canadians experience higher rates of health inequities than White Canadians.[1,2] More specifically, Black Canadians experience higher rates of diabetes and overall worse health than White Canadians.[1] Additionally, Indigenous people experience higher rates of arthritis, asthma, diabetes, and obesity than non-Indigenous people.[2] Given Canada's diverse population, it is crucial that pharmacists be capable of providing culturally competent care to all patients to reduce these health disparities.[3] In 2015, the Truth and Reconciliation Commission of Canada published 94 calls to action, directed to various levels of government in Canada, to advance reconciliation with the country's Indigenous peoples.[4] There are 8 health-related calls to action, including one specifically directed toward education: "We call upon all levels of government to: … provide cultural competency training for all health care providers."[4]

In the 2017 update of its educational outcomes, the Association of Faculties of Pharmacy of Canada acknowledged the calls to action set out by the Truth and Reconciliation Commission of Canada and included cultural competency and cultural safety education as a required competency in undergraduate pharmacy curriculums.[5] Canadian pharmacy residency programs are to further develop the cultural competency education that pharmacy students receive during their undergraduate training, moving residents from "competent" to "proficient". The Canadian Pharmacy Residency Board, in its *Accreditation Standards for Pharmacy (Year 1) Residencies*, has also acknowledged the Truth and Reconciliation Commission of Canada's calls to action, and requirement 3.1.4 outlines that pharmacy residents are to practise in a culturally safe manner.[6]

This emphasis on the importance of incorporating cultural competency training into pharmacy education programs across Canada prompted a review of the literature to assess the resources and methods available to implement cultural competency education in Canadian pharmacy (year 1) residency programs. Information gathered from the available literature was then used to develop guidance for pharmacy residency coordinators and directors on strategies for implementing cultural competency training for residents and preceptors.

METHODS

A literature search was conducted in the MEDLINE and Embase databases. The search terms used were "education, pharmacy, continuing", "pharmacy residencies", "education, pharmacy", "pharmacy", "education, pharmacy, graduate", or "intern and residency" combined with "cultural competency" using the "and" function. Title and abstract screening was performed to exclude irrelevant articles.

Articles describing methods for implementing cultural competency education were included in the review. Articles with an experiential learning component were also included, to align with the typical structure of pharmacy residency programs. Articles with information about medical residency programs relating to cultural competency education were also screened for potential applicability to pharmacy practice. Articles concerning cultural competency training provided to nurses were not considered, because nurses do not undergo residency training, which limits the applicability of the nursing literature to pharmacy residency practice.

RESULTS

The initial literature search yielded 189 results from MEDLINE and 27 from Embase (after omission of duplicates) (see Figure 1). The search did not yield any studies describing cultural competency education for pharmacy residency programs or, with the search terms used, any results related to the Truth and Reconciliation Commission of Canada's 94 calls to action. The search did identify some studies describing methods of implementing cultural competency education into undergraduate pharmacy programs (n = 2) and medical residencies (n = 7); these 9 studies are summarized in Table 1.

Methods used in undergraduate pharmacy programs included presenting didactic lectures, offering mandatory service learning rotations at community sites that work with culturally diverse populations, teaching how to work with interpreters, encouraging understanding of cross-cultural communication strategies, facilitating reviews of patient cases in which culture may affect the care plan,

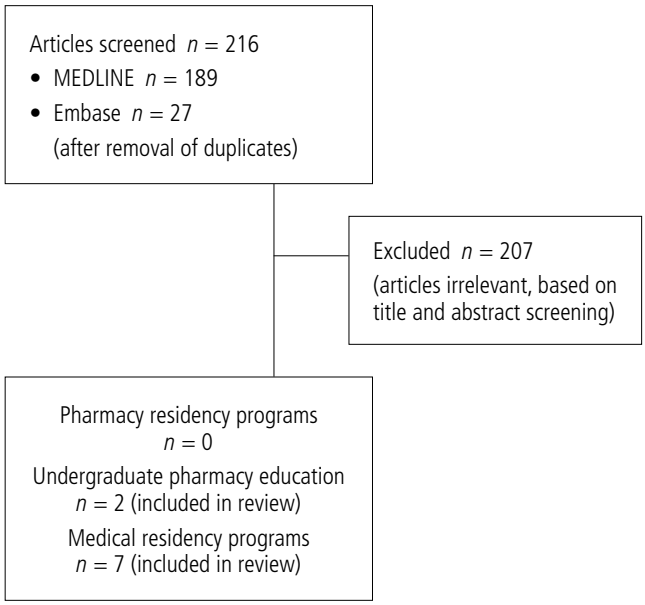

FIGURE 1. Description of article distribution.

TABLE 1. Summary of Studies

Source	Population and Sample Size	Methods
Haack and Phillips (2012)[7]	Pharmacy students (n = 135)	Implementation of a course series in an undergraduate curriculum
Lorenzen (2017)[8]	Pharmacy students[a]	Commentary on methods that can be used to teach cultural competency
Changoor et al. (2019)[9]	Surgical residents (n = 15) and attending surgeons (n = 16)	Structured interviews to gauge perceptions of cultural competency training
Jacobs et al. (2019)[10]	Family medicine residents (n = 22)	Implementation of a longitudinal curriculum over the span of the residency program
Kesler et al. (2015)[11]	Public health and general preventive medicine residents (n = 24)	Education on a niche topic regarding a specific cultural group
Lappen et al. (2014)[12]	Obstetrician–gynecologist medical residents[a]	Exposure to housing court to experience determinants of health of the local population
Talati et al. (2018)[13]	Obstetrician–gynecologist medical residents[a]	Exposure to housing court, group discussion with a panel of patients to learn the patient experience, and driving in the local neighborhood to visualize living conditions
Staton et al. (2013)[14]	Internal medicine residents (n = 28)	Implementation of a conference series, webinars, small-group sessions, multicultural social gatherings, grand round presentations, and case-based programs to teach cultural competency
Mechanic et al. (2017)[15]	Emergency medical residency programs (n = 73)	Distribution of a survey to determine training methods used to teach residents cultural competency; methods reported included structured didactic lectures, webinars, journal clubs, and simulations

[a]Sample size not available.

offering mandatory culturally diverse experiential learning,[7] incorporating culturally diverse patients into laboratory simulations, and offering course electives with a cultural competency focus.[8]

Beyond the profession of pharmacy, the search yielded literature regarding the implementation of cultural competency education into medical residency programs. Within this literature, some studies have documented a proven increase in cultural competency. The methods used by these programs have been variable. Changoor and others[9] stated that, when learning about cultural competency, surgical residents preferred interactive to didactic methods, as engagement was better maintained. The residents also suggested that simulated clinical scenarios would be valuable for cultural competency training.[9] Jacobs and others[10] conducted a longitudinal study in which they implemented an experimental curriculum and assessed the change in cultural competency knowledge over the span of a 3-year family medicine residency. Residents completed either day-long workshops focusing on health disparities, experiential learning workshops with an underserved population, or seminars led by guest speakers from the community. The residents also attended annual seminars, with an additional workshop during the second year. The residents were evaluated with pre- and post-tests at each workshop or seminar to evaluate knowledge gained, confidence, and attitudes. Annual surveys were also completed to assess the residents' confidence and attitudes regarding cultural competency. The absolute increase in post-test scores for cultural competency was 31.0% ($p < 0.0001$) after the workshops and 28.8% ($p < 0.0001$) after the seminars. After the 3-year curriculum, there were absolute increases in participants' awareness of obstacles faced by people of colour accessing health care services of 50.9% ($p = 0.024$) and in their knowledge of cultural factors that influence nursing care of 80.9% ($p = 0.0003$).[10]

Other articles assessed residents' self-reported level of confidence after the training intervention. One method involved education on a niche topic for a specific culture. For example, Kesler and others[11] described training residents in the traditional healing practices of the local Mexican population. The authors did not report outcomes experienced by residents after the training, but they explained that cultural competency was evaluated by individual mentors throughout the residency.[11] Similar to the experiential learning practices used to teach cultural competency, an obstetrics and gynecology residency program implemented a unique immersive experience for their residents to observe housing court, which encouraged an understanding of health disparities influenced by social determinants of health for the people in their community.[12,13] The residents were instructed to reflect on their experience, and overall the experience facilitated the development of empathy for patients.[12,13] A 1-week training session in an internal medicine residency program implemented mandatory online modules, conferences over lunch hours, grand rounds with a national expert, a webinar with an expert panel, and small-group discussions. After this week-long education session, a survey showed that 33% of

participants "agreed" and 48% "strongly agreed" that their confidence in cross-cultural encounters had improved.[14] Other methods used in different programs, without clear results to support their efficacy, included guest speakers, presentations from patients explaining their experience in the health care system, journal clubs, clinical simulations, and immersive rotations in the community.[9,12,13,15]

DISCUSSION

Pharmacy residency programs in Canada have an experiential basis,[6] which may limit the use of didactic-style education for cultural competency training. Some of the methods described in the literature follow a didactic structure but likely still have a place in cultural competency education for pharmacy residents. Online modules, guest speakers, or required pre-readings are methods that could be used to prepare residents before they begin patient interactions or other experiential learning. As described above, surgical residents preferred training by interactive methods rather than didactic methods,[9] and this preference may also extend to pharmacy residents. Interactive methods include immersion within the diverse community where the resident will be working, learning about cultures that are prevalent in their community, understanding how patients might be involved in their own care, training to work with interpreters, hearing patient narratives describing their experience with the health care system, and being exposed to a variety of patient cases in which culture might have affected the care plan.

A limitation to the potential implementation into pharmacy residency programs of the cultural competency training described for medical residents is the shorter duration of pharmacy residency programs. Most Canadian pharmacy residency programs are 1 year long, whereas medical residency programs often span multiple years. Some medical curriculum literature described interventions that took place over 3 years,[10] which may not be feasible for all pharmacy residencies. However, it is likely that cultural competency education can be modified to fit within the time frame of pharmacy residency programs. Other barriers to implementing cultural competency training, described by Mechanic and others,[15] include a lack of dedicated time to implement structured cultural competency education, a lack of buy-in or support from surrounding staff members, and concerns about funding these activities. Suggested solutions to these barriers include involving all staff pharmacists and residency preceptors in the cultural competency training opportunities offered to residents, prioritizing available funding for cultural competency training, and scheduling dedicated time for cultural competency education during less busy times in the residency year (e.g., during the orientation period).

The literature search conducted for this article did not yield any results specifically describing implementation of cultural competency education into pharmacy residency programs. This represents a gap in the literature, and further research should be conducted to determine the optimal way to provide cultural competency training to pharmacy residents. Ideally, future research will evaluate patient outcomes related to cultural competency training.

This review had some limitations. Only 2 databases, MEDLINE and Embase, were searched to find references on the topic. The search initially focused on the literature related to pharmacy residency programs and was then expanded to capture literature related to undergraduate pharmacy programs and medical residencies.

The following recommendations for pharmacy residency programs are based on the information for undergraduate pharmacy programs and medical residency programs (Box 1). Local experts should be consulted when constructing a cultural competency curriculum to capture the relevant health concerns of the local population. Providing mandatory readings or online modules related to the local population (for example, information about Indigenous history and the effects of colonialism or information about the health inequities experienced by local Indigenous populations) can help to establish a strong baseline knowledge while also aiding in preparation for rotations and the provision of resources for future use. In addition, incorporating a longitudinal approach to cultural competency education, rather than a single lecture or short-term lecture series, may help to ensure that the knowledge and skills are consistently developed and maintained. Teaching cultural competency concepts on each clinical rotation will allow the resident to apply the information they have been taught, and the residents can then adapt this information to different clinical environments. This approach also allows preceptors to longitudinally assess cultural competency and provide ongoing feedback to the resident.

CONCLUSION

Literature about the provision of cultural competency education to pharmacy residents is lacking, despite the current

BOX 1. Summary of Recommendations

Use local experts to train pharmacy residents in the health needs of the local population.
Develop online modules or required readings for pharmacy residents to provide background knowledge on cultural competency or the health needs of the local population.
Provide cultural competency education using a longitudinal approach, with education sessions throughout the residency program, allowing residents to apply the training to various areas of practice and allowing cultural competency to be assessed at formal evaluations.

emphasis on the importance of such education for health care providers. The information available is largely related to undergraduate pharmacy programs and medical residencies, and further research is needed to determine the optimal method to educate pharmacy residents in this area. Based on the information summarized here, reasonable methods for implementing cultural competency education for pharmacy residents would be online modules or required pre-readings about practising culturally competent care, to allow residents to establish a baseline knowledge and skill set before entering clinical practice rotations. In addition, having experts in the content area as guest speakers or inviting patients to present narrative sessions outlining their experiences may be beneficial in terms of guiding residents on how to provide culturally competent care. Providing cultural competency training in all rotations throughout the residency year will allow residents to apply their knowledge directly in clinical practice and will provide opportunities for cultural competence to be assessed.

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Correction apportée à l'article « Pénuries de médicaments au Canada au cours des 24 derniers mois : la situation ne fait que qu'empirer »

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Veuillez noter qu'une erreur s'est produite lors de la préparation de cet article aux fins de publication. Il s'ensuit que l'un des mots dans le titre se répète. Le titre de l'article devrait se lire comme suit : « Pénuries de médicaments au Canada au cours des 24 derniers mois : la situation ne fait qu'empirer ». L'article a été corrigé (voir https://doi.org/10.4212/cjhp.v74i1.3076).

In Need of a North Star for Canadian Pharmacy Practice

Zack Dumont

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You know the old saying, "If you've seen one pharmacy practice model, you've seen … one pharmacy practice model". As pandemic restrictions loosen and we begin to gather again, I worry that we aren't coming together to address the important issue of variation in pharmacy practice models across the country.

Through various channels, I've had the opportunity to attend two recent international conferences: the ASHP Summer Meetings and the Global Conference of the American College of Clinical Pharmacists (ACCP). In my role with the CSHP, I'm also part of discussions involving the Society's board, affiliated boards, task forces, and committees. Being part of such a variety of meetings is a privilege, and I'm forever indebted. As well as sharing learnings from these events with my Canadian colleagues, I have the added responsibility of taking action. My aim in writing this commentary is to point out that your (yes, your!) vision for a health-system pharmacy practice model is different from the next person's, whose vision is different from that of the person next to them, and so on.

The issue of variant models of pharmacy practice isn't unique to Canada. At the ASHP and ACCP conferences, it became obvious that we're all working on similar, but slightly different, plans. Though we share the same *ultimate* goal—to improve patient outcomes—we don't necessarily agree on how to accomplish it. Some feel that pharmacists should be responsible for every aspect of a patient's medication therapy and should address every drug-related problem (DRP), while others feel that certain aspects of medication therapy should be prioritized, with others de-prioritized and followed-up after discharge. It's no wonder the corresponding practice models are different! Some models deliberately target the main DRP and admitting diagnosis, while others rely on the attending physician for those aspects and focus instead on all other DRPs. One model is heavily reliant on regulated pharmacy technicians, while the other struggles with recruitment … which leads to my next point.

Perhaps the models are justified in being different. All hospitals are different. They evolved from different pasts. They're funded differently. The corresponding health care providers' practices are different. Maybe even patients' goals of therapy are different. But I worry that these explanations are just rationalizations for keeping the status quo. It can be difficult to look outward, reflect inward, and recognize that we need to change. But with such an approach, we can do more to control the situation, rather than having it entirely dictated by external factors.

You might be thinking, "Hey Zack, back off. Where I come from, we live and breathe vision and change." If you do, that's great. Yet I would still ask, "Where are these changes taking you? How do you know it's where others think we should be going?" Perhaps your North Star is the International Pharmaceutical Federation Basel Statements on the Future of Hospital Pharmacy (https://www.fip.org/files/content/pharmacy-practice/hospital-pharmacy/hospital-activities/basel-statements/fip-basel-statements-on-the-future-of-hospital-pharmacy-2015.pdf) or the ASHP long-range vision for the pharmacy workforce in hospitals and health systems (https://www.ashp.org/-/media/assets/policy-guidelines/docs/endorsed-documents/pharmacy-workforce-long-range-vision.pdf). Or maybe the visioning work of Jorgenson and others (https://pubmed.ncbi.nlm.nih.gov/29123593/) resonates with you: "Pharmacy professionals providing proactive, interprofessional or team-based, patient-centred care that optimizes drug therapy outcomes". These are all important documents. Yet we aren't talking about them. What do they mean? How can we use them? In my most recent commentary (DOI: 10.4212/cjhp.v75i1.3256), I borrowed the quote "If you want to go fast, go alone; if you want to go far, go together", and I'm reiterating it now.

Together, we can really get somewhere. We need to layer on the detail. We need to consolidate our plans for comprehensive medication management, determine pharmacist ratios, specify technician roles, and more.

If I may speak frankly, we're spoiled in Canada. We have, essentially, a noncompetitive health care system without the burden of ensuring profitability. We have the CSHP Hospital Pharmacy in Canada Survey. We're the birthplace of clinical pharmacy key performance indicators. We have

a "town square" in CSHP, our community of not-for-profit pharmacy professionals who work to improve patient outcomes, and we should be doing this work in ways that are more similar than different. COVID-19 has kept us apart these past few years, and now we must come together again, hardened by battle, and reignite our conversations on the future of pharmacy practice. Finding a pharmacy practice North Star cannot wait.

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Besoin d'une étoile polaire pour guider la pratique de la pharmacie canadienne

par Zack Dumont

https://doi.org/10.4212/cjhp.3428

Vous connaissez le vieil adage : « Quand on a vu un modèle de pratique pharmaceutique, on … en a vu qu'un seul ». Alors que les restrictions imposées par la pandémie se relâchent et que nous recommençons à nous rassembler, je crains que nous ne nous réunissions pas pour aborder l'important problème de la variation des modèles de pratique pharmaceutique au pays.

J'ai eu l'occasion d'assister à deux conférences internationales récentes : les Réunions d'été de l'ASHP et la Conférence mondiale de l'American College of Clinical Pharmacists (ACCP). Dans mon rôle au sein de la SCPH, je participe également aux discussions impliquant le conseil d'administration de la Société, les conseils affiliés, les groupes de travail et les comités. Faire partie d'une telle variété de réunions est un privilège, et j'en serai éternellement reconnaissant. En plus de partager les enseignements tirés de ces événements avec mes collègues canadiens, j'ai la responsabilité supplémentaire d'agir. Mon but, en rédigeant ce commentaire, est de souligner que votre (oui, votre!) vision d'un modèle de pratique pharmaceutique du système de santé est différente de celle d'une autre personne, dont la vision est elle-même différente de celle d'une autre, et ainsi de suite.

La question des variantes des modèles de pratique ne se limite pas au Canada. Lors des conférences de l'ASHP et de l'ACCP, il est devenu évident que nous travaillons tous sur des plans semblables, mais légèrement différents. Bien que nous partagions le même objectif *ultime* – l'amélioration des résultats pour les patients – nous ne sommes pas nécessairement d'accord sur la manière d'y parvenir. Certains estiment que les pharmaciens devraient être responsables de tous les aspects de la pharmacothérapie d'un patient et devraient s'attaquer à tous les problèmes liés aux médicaments (PLM); d'autres estiment que certains aspects de la pharmacothérapie devraient être prioritaires, tandis que d'autres devraient moins l'être et faire l'objet d'un suivi après le congé de l'hôpital. Il n'est pas étonnant que les modèles de pratique correspondants soient différents! Certains modèles ciblent délibérément le PLM principal et le diagnostic d'admission, tandis que d'autres s'appuient sur le médecin traitant pour ces aspects et se concentrent plutôt sur tous les autres PLM. Un modèle dépendra fortement des techniciens en pharmacie réglementés, tandis que l'autre aura du mal à recruter… ce qui m'amène au point suivant.

Peut-être que la différence entre les modèles se justifie. Tous les hôpitaux sont différents. Leurs antécédents sont différents. Leur financement est différent. Les pratiques des prestataires de soins correspondants sont différentes. Peut-être même que les objectifs thérapeutiques des patients sont différents. Mais je crains que ces explications ne soient que des rationalisations pour maintenir le statu quo. Il peut être difficile de regarder autour de soi, de s'interroger et de reconnaître que le changement est nécessaire. Mais avec une telle approche, nous pouvons faire plus pour contrôler la situation, plutôt que de la laisser être entièrement dictée par des facteurs externes.

Vous pensez peut-être : « Hé, Zack, laisse-nous tranquilles. D'où je viens, nous vivons et respirons la vision et le changement. » Si c'est le cas, bravo. Pourtant, je vous demanderais quand même : « Où ces changements vous mènent-ils? Comment savez-vous que c'est à cet endroit que les autres pensent que nous devrions nous rendre? » Votre étoile polaire est peut-être les Déclarations de Bâle sur l'avenir de la pharmacie hospitalière de la Fédération internationale pharmaceutique (https://www.fip.org/files/content/pharmacy-practice/hospital-pharmacy/hospital-activities/basel-statements/fip-basel-statements-on-the-future-of-hospital-pharmacy-2015.pdf) ou la vision à long terme de l'ASHP pour l'effectif pharmaceutique dans les hôpitaux et les systèmes de santé (https://www.ashp.org/-/media/assets/policy-guidelines/docs/endorsed-documents/pharmacy-workforce-long-range-vision.pdf). Ou encore le travail de Jorgenson et collègues (https://pubmed.ncbi.nlm.nih.gov/29123593/) trouve-t-il écho chez vous : « Les professionnels de la pharmacie qui fournissent des soins proactifs, interprofessionnels ou en équipe, centrés sur le patient, qui optimisent les résultats de la pharmacothérapie ». Ces documents sont tous importants. Pourtant, nous n'en parlons pas. Que signifient-ils? Comment les utiliser? Dans mon dernier commentaire (DOI : 10.4212/cjhp.v75i1.3255), j'ai emprunté la citation « Si vous voulez aller vite, partez

seul; si vous voulez aller loin, partons ensemble », et je le répète maintenant.

Ensemble, nous pouvons arriver quelque part. Nous devons nous concentrer sur les détails. Nous devons consolider nos plans de gestion globale des médicaments, déterminer les ratios des pharmaciens, préciser les rôles des techniciens, etc.

Si je peux parler franchement, nous sommes gâtés au Canada. Nous avons, essentiellement, un système de soins de santé non concurrentiel sans devoir porter le fardeau de la rentabilité. Nous avons le Sondage sur les pharmacies hospitalières canadiennes de la SCPH. Nous sommes le berceau des indicateurs clés de performance pour la pharmacie clinique. Nous avons un « forum » à la SCPH – notre communauté de professionnels de la pharmacie à but non lucratif qui travaillent pour améliorer les résultats des patients – et nous devrions faire ce travail de manière plus similaire que différente. La COVID-19 nous a séparés ces dernières années, et maintenant nous devons nous réunir à nouveau, aguerris par le combat, et relancer nos conversations sur l'avenir de la pratique de la pharmacie. Trouver l'étoile polaire de la pratique pharmaceutique ne peut attendre.

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