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Vol. 72, No. 4 July–August 2019
Pages 257–336
The Canadian Journal
of Hospital Pharmacy

Le Journal canadien
de la pharmacie hospitalière
Pages 257–336
Vol. 72, nº 4 juillet–août 2019

Cherry Hill Beach, Nova Scotia

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ADVERTISING/PUBLICITÉ
Canadian Society of Hospital Pharmacists
Publications Administrator / Agente des publications
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e-mail:
publications@cshp.pharmacy

PRODUCTION
Daren MacGowan
Graphic Design
Tel: 613.324.5294
Fax: 888.210.4630
e-mail: dmacgowan@sympatico.ca

Date of issue: August 2019
Date d'émission : août 2019

ISSN 1920-2903

WEBSITE / SITE WEB
www.cjhp-online.ca

CJHP
JCPH

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Grasping the Nettle: Why Pharmacists Must Lead Antibiotic Stewardship Initiatives

Christine M Bond

In an editorial in this Journal in 2015,[1] I highlighted the well-recognized public health crisis of increasing antimicrobial resistance. This problem could lead to a future where millions of people die as a result of infections associated with routine, straightforward surgical procedures, such as hip and knee replacements, heart surgery, childbirth, and cancer treatment, to name but a few. Infections such as pneumonia, sexually transmitted diseases, and tuberculosis, which are currently treatable with antibiotics, will be associated with increasing mortality rates, as in the pre-antibiotic era. According to the World Health Organization, antibiotic resistance is one of the biggest threats to global health, food security, and development today.[2] New data from the Canadian Institute for Health Information[3] show that antibiotics are prescribed more frequently in Canada than in other countries within the Organisation for Economic Co-operation and Development. Every day, about 20 out of every 1000 Canadians take a dose of antibiotics, and in Canada antibiotics are prescribed at a rate 133% of that in countries like the Netherlands, Sweden and Germany.

While the causes of antimicrobial resistance are multifactorial and include veterinary use (for food production and companion animals), personal hygiene and antibiotic prescribing for human use in the community and hospital settings are major contributors. Antibiotic stewardship in all health care settings—especially appropriate prescribing and hand-washing regimens—remains the best short-term strategy to tackle the problem. My 2015 editorial highlighted a role for the pharmacist to lead antibiotic stewardship initiatives and called for more research to demonstrate the effectiveness of this role. Sadly, 4 years later, little seems to have changed.

An article in this issue of the *Canadian Journal of Hospital Pharmacy* reports qualitative research from one province in Canada.[4] The researchers conducted focus groups and interviews with physicians, pharmacists, and nurses to assess their perceptions of antimicrobial use and stewardship in acute hospital settings. The results of this research suggest that practice is improving, but data from other studies do not support this perception. Routine statistics show that the rate of prescribing of antibiotics in Canada is not changing substantively.[5] Further, and therefore not surprisingly, rates of antimicrobial resistance are not dropping; instead, they remain well above levels seen at the beginning of the century.[4]

The authors acknowledge that their qualitative research study had limitations with respect to its generalizability.[4] Nonetheless, given that the 54 participants were recruited from regions across Nova Scotia, that the sites represented by participants included specialized and general regional hospitals, and that data saturation was reached, it is likely that most of the relevant issues were identified and reported. The article suggests that despite the high profile now given to antibiotic resistance, many organizations, including acute care hospitals, are not tackling the issue at a central level, and indeed some of the hospitals from which study participants were recruited did not themselves have organization-wide antibiotic stewardship initiatives. Barriers to improved prescribing included persistent knowledge gaps, failure to implement guidelines, time pressures, and challenges to continuity of care because of staff handovers (i.e., no practitioner wanted to change what another had started). Participants also reported a fear of liability for negligence in not prescribing an antibiotic (should subsequent events reveal that doing so would have been the correct decision) and pressure from patients and other members of the public. However, reassuringly, pharmacists who intervened with a prescriber and suggested amending a prescription in accordance with the guideline found that their interventions were well received.

These findings highlight that pharmacists, as a professional group, have not yet universally embraced an antibiotic stewardship role. Nonetheless, in some countries, progress is being made. In Scotland, specialist antibiotic pharmacists are highly

respected and have been credited[6] with some of the reductions in antibiotic prescribing we see today. The recently released UK 5-year national action plan to tackle antibiotic resistance highlights the increasing role that clinical pharmacists can play in antimicrobial stewardship in primary care.[7]

Given their status as self-proclaimed medicines experts, it is incumbent on pharmacists to demonstrate this expertise in the context of antibiotic prescribing, by acting as advocates to other health care providers and patients within the hospital and the local community. Systematic reviews have revealed that public knowledge and understanding of antibiotics and antibiotic resistance are still erroneous in many respects,[8] although evidence suggests that pressure from patients to prescribe is not as real as prescribers may perceive.[9] Pharmacists, as medicines experts and public health practitioners, can articulate to both patients and professionals the very real population risks that we face if practice does not change. Most prescribing of antibiotics is undertaken in primary care, which potentially creates a reservoir of resistance that can lie dormant until a patient is hospitalized and needs an affective antibiotic for a hospital-acquired infection. We should, as a profession, act across all care setting boundaries and be ambassadors for change. Hospital pharmacists could consider creating networks with their pharmacy colleagues in other settings to optimize antibiotic use, with mutual sharing of antibiotic stewardship initiatives and consistent messages.

Learning and implementing antibiotic stewardship is not a short-term measure. Although the immediate priority is to protect the effectiveness of our current antibiotics, we must think also about future scenarios. Intensive research is yielding promising results in the shape of new drug combinations and new approaches.[10] These treatments will be especially precious and will need our protection too.

So what needs to be done to empower our pharmacy colleagues to take on this leadership role? Applying the COM-B model,[11] they need to have the Capability, the Opportunity and the Motivation to effect Behavioural change. In terms of capability, they need to have the confidence to communicate their knowledge and the skills to do so in the most effective way. We know they have the opportunities, and the motivation must surely be there. Once again, we need more research to identify the best way to adopt this leadership role, but in the absence of evidence we cannot go wrong by spreading the message of what we all know to be the case. Antibiotics should be prescribed only for the right reason, at the right dose, for the right indication. All pharmacists should "grasp the nettle" to make this happen.

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Competing interests: None declared.

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Prendre le taureau par les cornes : pourquoi les pharmaciens doivent être à la tête des initiatives consacrées à la gestion des antibiotiques

par Christine M. Bond

Dans un éditorial paru dans ce journal en 2015[1], je soulignais la crise de santé publique bien connue touchant l'augmentation de la résistance antimicrobienne. Ce problème pourrait mener à un futur où des millions de personnes meurent des suites d'infections associées à des procédures chirurgicales ordinaires, comme la mise en place d'une prothèse de la hanche et du genou, la chirurgie cardiaque, l'accouchement ou le traitement du cancer, pour n'en nommer que quelques-unes. Des infections, comme la pneumonie, les maladies sexuellement transmissibles et la tuberculose, actuellement traitables à l'aide d'antibiotiques, seront associées à des taux de mortalité croissants, comme à l'époque où les antibiotiques n'existaient pas. Selon l'Organisation mondiale de la Santé, la résistance aux antibiotiques est l'une des menaces les plus importantes qui pèsent sur la santé mondiale, la sécurité alimentaire et le développement actuel[2]. De nouvelles données de l'Institut canadien d'information sur la santé[3] démontrent qu'au Canada, on prescrit plus d'antibiotiques que dans d'autres pays de l'Organisation de coopération et de développement économiques. Chaque jour, environ 20 Canadiens sur 1000 prennent une dose d'antibiotiques, et les cliniciens du Canada prescrivent 33 % plus d'antibiotiques que ceux de pays comme les Pays-Bas, la Suède et l'Allemagne.

Bien que de nombreux facteurs expliquent les causes de la résistance antimicrobienne, notamment l'utilisation vétérinaire (pour la production alimentaire et les animaux de compagnie), l'hygiène personnelle et la prescription d'antibiotiques à des fins d'utilisation humaine dans les environnements hospitaliers et communautaires en sont les facteurs majeurs. La gestion des antibiotiques dans tous les environnements de soins de santé (particulièrement la prescription appropriée et le lavage des mains) reste la meilleure stratégie à court terme pour aborder le problème. Mon éditorial de 2015 soulignait le rôle du pharmacien : être le fer de lance des initiatives en matière de gestion des antibiotiques. Il appelait également à davantage de recherches afin de démontrer l'efficacité de ce rôle. Malheureusement, quatre ans plus tard, peu de choses semblent avoir changé.

Un article dans ce numéro du *Journal canadien de la pharmacie hospitalière* fait état d'une recherche qualitative menée dans une province canadienne[4]. Les chercheurs ont dirigé des séances de discussion et des entretiens avec des médecins, des pharmaciens et des infirmiers pour évaluer leur perception de l'utilisation et de la gestion des antimicrobiens dans un environnement hospitalier. Les résultats de cette recherche révèlent que la pratique s'améliore, mais les données provenant d'autres études n'étayent pas cette perception. Les statistiques courantes montrent que le taux de prescription d'antibiotiques au Canada ne change pas de manière substantielle[5]. De plus, et donc sans surprise, les taux de résistance aux antimicrobiens ne faiblissent pas, au contraire, ils restent bien au-delà des niveaux observés au début du siècle[4].

Les auteurs reconnaissent que leur recherche qualitative présentait des limites quant à la possibilité de les généraliser[4]. Néanmoins, étant donné que les 54 participants ont été recrutés dans toutes les régions de la Nouvelle-Écosse, que les sites d'où provenaient les participants comprenaient des hôpitaux régionaux spécialisés et généraux et que la saturation des données avait été atteinte, il est probable que les investigateurs aient décelé et rapporté la plupart des problèmes particulièrement pertinents. L'article laisse entendre que, malgré l'intérêt accordé de nos jours à la résistance aux antibiotiques, de nombreuses organisations, y compris les hôpitaux de soins actifs, n'abordent pas le fond du problème. En effet, dans certains hôpitaux d'où provenaient les participants, il n'y avait pas d'initiatives en place consacrées à la gestion des antibiotiques. Les obstacles qui empêchent l'amélioration de la prescription comprenaient des connaissances lacunaires persistantes, l'absence de lignes directrices, les contraintes de temps et les difficultés liées à la continuité des soins, en raison des transferts de personnel (c.-à-d. aucun praticien ne souhaite modifier ce qu'un autre a entamé). Les participants indiquent également la peur d'être accusés de négligence de n'avoir pas prescrit d'antibiotique (si des complications ultérieures devaient révéler que cette prescription aurait été la décision à prendre) ainsi que la pression des patients et

d'autres membres du public. Cependant, les pharmaciens qui sont intervenus auprès de médecins pour leur proposer de modifier une prescription, conformément aux lignes directrices, ont indiqué que leurs interventions étaient bien reçues.

Ces résultats démontrent que le groupe professionnel des pharmaciens n'assume pas encore universellement son rôle en matière de gestion des antibiotiques. Néanmoins, certains pays ont réalisé des progrès. En Écosse, les pharmaciens spécialisés sont très respectés et ils ont été reconnus[6] pour être à l'origine d'une certaine réduction des prescriptions d'antibiotiques observée aujourd'hui. Récemment rendu public, le plan d'action national quinquennal du R.-U., qui vise la résistance aux antibiotiques, souligne le rôle de plus en plus important que peuvent jouer les pharmaciens cliniciens dans la gestion de l'utilisation des antimicrobiens pour les soins primaires[7].

Étant donné leur statut d'experts autoproclamés en médicaments, il incombe aux pharmaciens de démontrer cette expertise dans le contexte de la prescription des antibiotiques, en agissant comme porte-parole auprès des autres fournisseurs de soins de santé et des patients au sein des hôpitaux et de la communauté locale. Des examens systématiques ont dévoilé que les connaissances et la compréhension du public à l'égard des antibiotiques et de la résistance face à ces derniers sont encore erronées à bien des égards[8], alors que les données probantes démontrent que la pression exercée par les patients pour obtenir ce type de médicaments n'est pas aussi réelle que la perception qu'en ont les prescripteurs[9]. À titre d'experts en médicaments et praticiens en santé publique, les pharmaciens peuvent expliquer aux patients et aux professionnels les risques réels auxquels nous serons confrontés si la pratique ne change pas. La plupart des prescriptions d'antibiotiques s'effectuent dans le cadre des soins primaires, ce qui génère un réservoir potentiel de résistance qui peut demeurer latent jusqu'à ce que le patient soit hospitalisé et nécessite un antibiotique contre une infection contractée en milieu hospitalier. Dans le cadre de notre profession, nous devons agir dans tous les environnements de soins et être des ambassadeurs du changement. Les pharmaciens hospitaliers pourraient songer à créer des réseaux avec leurs collègues pharmaciens qui œuvrent dans d'autres environnements pour optimiser l'utilisation des antibiotiques, en mettant en commun les initiatives axées sur la gestion des antibiotiques et en diffusant des messages cohérents.

L'apprentissage et la mise en place d'une gestion des antibiotiques n'est pas une mesure à court terme. Bien que la priorité immédiate consiste à protéger l'efficacité de nos antibiotiques actuels, nous devons songer aux scénarios de demain. Des recherches intensives livrent des résultats prometteurs qui prennent la forme de nouvelles combinaisons de médicaments et de nouvelles approches[10]. Ces traitements seront particulièrement précieux et devront également bénéficier de notre protection.

Alors, qu'est-ce qui doit être fait pour que nos collègues pharmaciens assument leur rôle de leader? Pour la mise en œuvre du modèle « COM-C »[11], ils doivent avoir la Capacité, l'Opportunité et la Motivation d'entraîner un changement de Comportement. En termes de capacité, ils doivent avoir la confiance leur permettant de communiquer leurs connaissances et compétences de la manière la plus efficace possible. Nous savons qu'ils ont les opportunités de le faire et que la motivation est sûrement bien présente. Répétons-le, des recherches supplémentaires sont nécessaires pour déterminer la meilleure manière pour le pharmacien d'assumer ce rôle de leadership. Mais en l'absence de preuve, on ne se trompera jamais en diffusant le message de ce que nous savons tous être le cas : les antibiotiques doivent être prescrits uniquement pour les bonnes raisons, à la bonne dose et pour la bonne indication. Tous les pharmaciens doivent « saisir le taureau par les cornes » pour que cela se concrétise.

[Traduction par l'éditeur]

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Health Care Providers' Perceptions of Antimicrobial Use and Stewardship at Acute Care Hospitals in Nova Scotia

Emily K Black, Lindsay MacDonald, Heather L Neville, Kim Abbass, Kathryn Slayter, Lynn Johnston, and Ingrid Sketris

ABSTRACT

Background: Antimicrobial use is the major factor in the development of antimicrobial resistance. Antimicrobial stewardship has been recommended as a strategy to improve antimicrobial use.

Objective: To learn about health care providers' perceptions of current antimicrobial use and stewardship, including barriers and facilitators to improving antimicrobial use at acute care hospitals in Nova Scotia.

Methods: This qualitative research study was conducted at acute care hospitals in Nova Scotia using focus groups and semistructured interviews. Health care providers (nurses, nurse practitioners, pharmacists, pharmacy students, and physicians) were invited to participate. Focus groups and interviews were conducted at each participant's place of employment. Interviews and focus groups were facilitated with an interview guide, audio-recorded, and transcribed verbatim. Transcripts were independently coded by 2 investigators and analyzed using thematic analysis.

Results: A total of 9 focus groups and 3 individual interviews were conducted between June and August 2017. Fifty-four health care professionals and trainees (24 pharmacists and pharmacy students, 14 physicians, and 16 nurses and nurse practitioners) from 5 hospitals participated. The following themes were identified: current practices, prescribing influences, access to information, collaboration and communication, resources, and antimicrobial stewardship. Within each theme, barriers and facilitators to improving antimicrobial use were identified as subthemes.

Conclusion: Participants identified current barriers to appropriate use of antimicrobials and suggested facilitators that might improve the use of these drugs. The results of this study could be used by antimicrobial stewardship teams and decision-makers to improve antimicrobial use and stewardship initiatives throughout Nova Scotia, and may be applicable to hospitals outside the province.

Keywords: antimicrobial stewardship, infectious disease, antibiotic, antimicrobial

RÉSUMÉ

Contexte: L'utilisation des antimicrobiens est le principal facteur de développement de la résistance à cette classe de médicaments. La gestion des antimicrobiens a été recommandée comme stratégie visant à améliorer leur utilisation.

Objectif : Découvrir la perception des fournisseurs de soins de santé au sujet de l'utilisation et de la gestion actuelles des antimicrobiens, y compris les obstacles et les moyens destinés à favoriser l'amélioration de leur utilisation dans des hôpitaux de soins actifs en Nouvelle-Écosse.

Méthodes : Cette recherche qualitative a été menée dans des hôpitaux de soins actifs en Nouvelle-Écosse à l'aide de groupes de discussion et d'entretiens semi-structurés. Les fournisseurs de soins de santé (infirmières, infirmières praticiennes, pharmaciens, étudiants en pharmacie et médecins) ont été invités à y participer. Les groupes de discussion et les entretiens ont été menés sur chaque lieu de travail des participants. Ils ont été facilités grâce à un guide d'entretien. Ils ont aussi été enregistrés (audio) et retranscrits textuellement. Les transcriptions ont été codées de façon indépendante par deux enquêteurs et étudiées à l'aide d'une analyse thématique.

Résultats : Neuf groupes de discussion et trois entretiens individuels ont été menés entre juin et août 2017. Cinquante-quatre professionnels et stagiaires de la santé (24 pharmaciens et étudiants en pharmacie, 14 médecins, 16 infirmières et infirmières praticiennes) provenant de cinq hôpitaux y ont participé. Les thèmes suivants ont été soumis à la discussion : pratiques actuelles, influences en matière de prescription, accès aux informations, collaboration et communication, ressources et gestion des antimicrobiens. Chaque thème comportait deux sous-thèmes abordant les obstacles et les mesures favorisant l'amélioration de l'utilisation des antimicrobiens.

Conclusion : Les participants ont relevé les obstacles actuels nuisant à une bonne utilisation des antimicrobiens et ont proposé des moyens pour améliorer l'utilisation de ces médicaments. Les résultats de cette étude pourraient être utilisés par les équipes de gestion des antimicrobiens ainsi que par les décideurs qui doivent favoriser l'amélioration de l'utilisation des antimicrobiens et les initiatives relatives à leur gestion partout en Nouvelle-Écosse. Ils sont aussi applicables aux hôpitaux extérieurs à la province.

Mots-clés : gestion des antimicrobiens, maladies infectieuses, antibiotiques, antimicrobiens

Can J Hosp Pharm. 2019;72(4):263-70

INTRODUCTION

The international community has recognized antimicrobial resistance as a growing health concern.[1] Without action, about 10 million deaths per year worldwide will be attributable to antimicrobial resistance by the year 2050.[2] Infection with antimicrobial-resistant organisms has been associated with increased morbidity, mortality, cost, and burden to the health care system.[3]

Antimicrobial use is the major factor contributing to the development of antimicrobial resistance.[4,5] Antimicrobial stewardship (AMS) has been suggested as a strategy to improve use of these drugs and is a core component of the pan-Canadian framework on tackling the problem of resistance.[6,7] Successful AMS has resulted in several benefits, including reductions in antimicrobial use and associated costs, decreases in length of hospital stay, and improvements in adherence to prescribing policies.[6,8]

Despite the recognized value of AMS, further research is needed. In a recently published international consensus paper, identifying barriers and facilitators to implementing AMS programs and specifying activities in current programs were listed as priority areas requiring urgent scientific investigation to optimize AMS programs.[9] Research on barriers and facilitators to implementation of interventions, with input from stakeholders on the design of programs, has also been recommended.[8]

A 2015 point prevalence survey of antimicrobial use in Nova Scotia identified targets for quality improvement.[10] The objective of the qualitative study reported here was to explore the perceptions of stakeholders regarding barriers and facilitators to appropriate antimicrobial use and successful stewardship to guide effective implementation of AMS interventions.

METHODS

Study Design

A qualitative study was completed using focus groups and individual interviews for which a study-specific interview guide was developed and piloted before data collection began. Transcripts of both types of discussion were analyzed using thematic analysis. The study was part of a larger mixed-methods project and was informed by the results of the point prevalence survey.[10] Potential participants were invited to attend a focus group or to complete an individual interview. The study was conducted in accordance with ethical standards of the responsible committees on human experimentation and the Helsinki declaration and was approved by the research ethics boards at the Nova Scotia Health Authority (file 100287) and the IWK Health Centre (file 1020269). Participants provided written informed consent.

Participant Selection

The participants in focus groups and interviews were health care providers (nurses, nurse practitioners, pharmacists, and physicians) working at acute care hospitals in Nova Scotia. Pharmacy students were permitted to participate if they were completing a rotation with an invited participant. Health professionals were selected to receive an invitation on the basis of their role in direct care of patients with infectious diseases or their involvement and/or leadership in AMS initiatives at acute care hospitals in the province. Health care providers were purposely sampled from a range of specialities, specifically internal medicine, infectious diseases, infection control, surgery, pediatrics, emergency medicine, critical care, obstetrics, women's and newborn health, and leadership/administration. Health care providers were invited verbally or through e-mail communication by site investigators at each hospital. Communication included information about the study objectives, study design, and expectations of participants. The e-mail invitation was sent to 122 individuals, and additional participants were invited verbally at one of the study sites. Participants were grouped by profession, with nurses, nurse practitioners, pharmacists, and pharmacy students participating jointly in focus groups, but separately from physicians. These groupings were based on feedback from the pilot phase, to increase participants' willingness to contribute openly and to minimize perceived differences in authority.

Settings

All hospitals in Nova Scotia are part of the Nova Scotia Health Authority (NSHA), except the IWK Health Centre, which is a specialized hospital providing care to women, children, youth, and families.[11] The study sites consisted of 2 specialized tertiary hospitals in large population centres and 3 regional hospitals in small to medium population centres. The sites were chosen to provide geographic representation from health care providers throughout the province. The IWK Health Centre established an AMS program in 2015, and the NSHA launched a provincial AMS program around the time of data collection in 2017 (http://www.cdha.nshealth.ca/nsha-antimicrobial-stewardship). All sites had treatment guidelines for select infectious syndromes. The IWK Health Centre launched an electronic application for disseminating guidelines a few months before data collection and provided prospective audit and feedback on antimicrobial prescribing for inpatients. At the time of data collection, the other sites were providing or were in the process of implementing prospective audit and feedback to select units within the health authority.

Data Collection

The focus groups and interviews took place at the participants' respective places of employment using the study-specific interview guide, which was developed by members of the research team, who had expertise in infectious disease and pharmacotherapy, as well as experience with qualitative research. Additional feedback

on the guide was sought from a qualitative researcher who was not otherwise involved in the study. The guide was piloted with 4 pharmacists and revised on the basis of feedback received. During each discussion, the moderator/interviewer provided participants with an overview of the research team, objectives of the current study, reasons for completing this project, and background on previously completed research evaluating antimicrobial use in Nova Scotia. Personal opinions and assumptions of the research team were not shared with participants. Focus groups and interviews were continued until representation from a diverse range of providers from different professions and specialities throughout Nova Scotia was obtained.

The focus groups and interviews were conducted between June and August 2017. All discussions took place in person, except for one telephone interview. Each focus group lasted about an hour, and the individual interviews lasted 30 minutes. Aside from the participants, only the principal investigator (E.B.) and a research assistant (L.M.) were present during discussions. Focus groups and interviews were moderated by the principal investigator, who maintains an active pharmacy practice licence, has completed a hospital pharmacy residency and Doctor of Pharmacy degree, holds an appointment as an Assistant Professor at Dalhousie University (with a research program focusing on antimicrobial use and stewardship), and provided about 100 h of clinical services with the infectious disease team at the Queen Elizabeth II Health Sciences Centre during the year before data collection. The research assistant was a pharmacy student who assisted by audio-recording the sessions and taking notes.

Data Analysis

The data were interpreted using a thematic analysis. The analysis began during the interview or focus group process, with the interviewer/moderator asking probing questions as preliminary themes emerged. After each focus group or interview, the principal investigator and research assistant debriefed to discuss the emerging themes and perceived similarities and differences among interviewees and focus group participants. The research assistant then transcribed the recorded interviews verbatim. Each transcript was read in full by the principal investigator and the research assistant to better understand the discussion, followed by coding.[12]

Each transcript and related field notes were independently reviewed and coded in Microsoft Word (Microsoft Corporation, Redmond, Washington) by the 2 members of the research team (E.B., L.M.) who were present during interviews and focus groups. Coding was guided by a cyclic process, as described by Saldaña.[13] The codes were initially determined with a process of open-coding, and emerging themes were noted thereafter. The principal investigator and research assistant each generated a code list, which included a description of code contents; they then compared and refined these 2 initial lists to create a unified codebook. The principal investigator functioned as the "codebook editor" and maintained the master list of codes.[13] Transcripts were reviewed and independently recoded a minimum of 3 times by the principal investigator and research assistant. After each cycle of coding, the codes in the master codebook were further compared and refined. Before the final analysis was completed, the codebook was reviewed and revised by the full research team. After the third round of coding, a final list of themes and subthemes was prepared. During the final stage of analysis, codes were analyzed for similarities and differences by type of health care professional. Transcripts were not returned to participants for comment.

RESULTS

Study Participants

Nine focus groups and 3 interviews were completed with a total of 54 individuals, most of whom (n = 40) were unknown to the principal investigator; however, the principal investigator had a pre-existing relationship with 14 participants through undergraduate pharmacy training, committee involvement, clinical work, or research collaboration. All regions of Nova Scotia were represented. Baseline characteristics of participants are outlined in Table 1. Of those who did not participate, the proportions who were unavailable versus unwilling are unknown.

Themes

The following 6 themes were identified: current practices, prescribing influences, access to information, collaboration and communication, resources, and antimicrobial stewardship. For all of the themes, factors that affect antimicrobial use were identified (Figure 1). Within each theme, several individual-level and organizational or system-level barriers and facilitators to improve antimicrobial use were discussed by study participants. With the exception of one individual interview, each of the 6 themes was discussed in every focus group and interview. At sites where AMS initiatives were in place, discussions focused more extensively on facilitators and examples of success in improving antimicrobial use, whereas barriers and challenges formed the main topics of discussion at sites lacking those services and resources.

Saturation of ideas occurred after 7 focus groups and 2 interviews. However, 2 additional focus groups and 1 additional interview were completed, to ensure geographic representation and inclusion of a diverse range of perceptions. Each theme is discussed below with representative quotations.

Current Practices

All groups recognized challenges with antimicrobial use. Suboptimal prescribing was most extensively discussed by focus groups involving pharmacists and nurses; however, physicians also acknowledged this challenge. Other challenges included inappro-

Table 1. Demographic Characteristics of Participants in Focus Groups and Interviews in a Study of Antimicrobial Stewardship in Nova Scotia Acute Care Hospitals

Characteristic	No. (%) of Respondents (*n* = 54)
Location of employment	
IWK Health Centre (228 acute care beds)	13 (24)
Nova Scotia Health Authority Central Zone (706 acute care beds)	14 (26)
Nova Scotia Health Authority Eastern Zone (239 acute care beds)	8 (15)
Nova Scotia Health Authority Northern Zone (124 acute care beds)	7 (13)
Nova Scotia Health Authority Western Zone (137 acute care beds)	12 (22)
Hospital type	
Regional hospital in small to medium population centre	27 (50)
Specialty/tertiary hospital in large population centres	27 (50)
Type of health care provider	
Nurse or nurse practitioner	16 (30)
Pharmacist or pharmacy student*	24 (44)
Physician	14 (26)
Experience (years) (mean ± SD)	14.3 ± 11.2
Area of specialty	
Administrative	5 (9)
Critical care, emergency medicine	8 (15)
Infectious disease, infection control	10 (19)
Medicine	11 (20)
Multiple clinical areas	5 (9)
Obstetrics/women's health, general pediatrics, newborn health	6 (11)
Surgery	8 (15)
Unknown	1 (2)

SD = standard deviation.
*Pharmacy students numbered fewer than 5.

priate microbiological testing, antimicrobial resistance, and lengthy use of medical devices such as catheters and drains.

> "The course of treatment. I can almost guarantee people overtreat everything in terms of course." [Physician 36]

> "That's a full-time position right there to deal with the amount of urine cultures that go to the [microbiology laboratory] and identify whether they actually have symptoms or not." [Nurse 22]

Specific barriers impeding improvement in antimicrobial use included prescribers' resistance to recommendations from other health care providers at the individual level and lack of continuity of care at the organization/system level. Nurse/pharmacist focus groups primarily discussed prescriber resistance. Continuity of care, both in the hospital and upon discharge, was listed as a barrier across focus groups at the regional hospitals outside urban centres.

> "Our patients are covered by multiple physicians that change over on certain days. They come on and say, 'Well I'm just covering the weekend so you know, complete antibiotics until after the weekend.' " [Pharmacist 30]

Despite these barriers, the majority of participants reported increasingly judicious antimicrobial prescribing in recent years, and they were generally optimistic about future improvements in antimicrobial use.

> "Over the last number of years we've seen them [prescribers] not jump to antibiotics right away. They seem to be rationalizing it a bit more." [Pharmacist 3]

Prescribing Influences

Participants shared a number of prescribing influences they perceived as affecting antimicrobial use. Knowledge, past experience, and external factors (such as patient pressure or perceptions of other health care providers) were influences that represented individual-level barriers or facilitators, depending on context.

> "We're seeing such diverse transition of physicians coming in, sometimes a locum … from out of province. They [prescribers] are nailing everybody with big guns because that is what they typically were used to." [Nurse 11]

> "I think sometimes what's happening in a busy family practice is that you sort of succumb to the will of the parent demanding the antibiotics when maybe you don't even feel like the patient actually needs it." [Physician 52]

Diagnostic uncertainty, patient complexity, and prescriber fear were other individual-level barriers described in the study. Additionally, a few participants listed professional liability as both an individual-level and an organizational/system-level barrier that influenced prescribing. Other influences were patient-related factors, including clinical status, cost and convenience of the

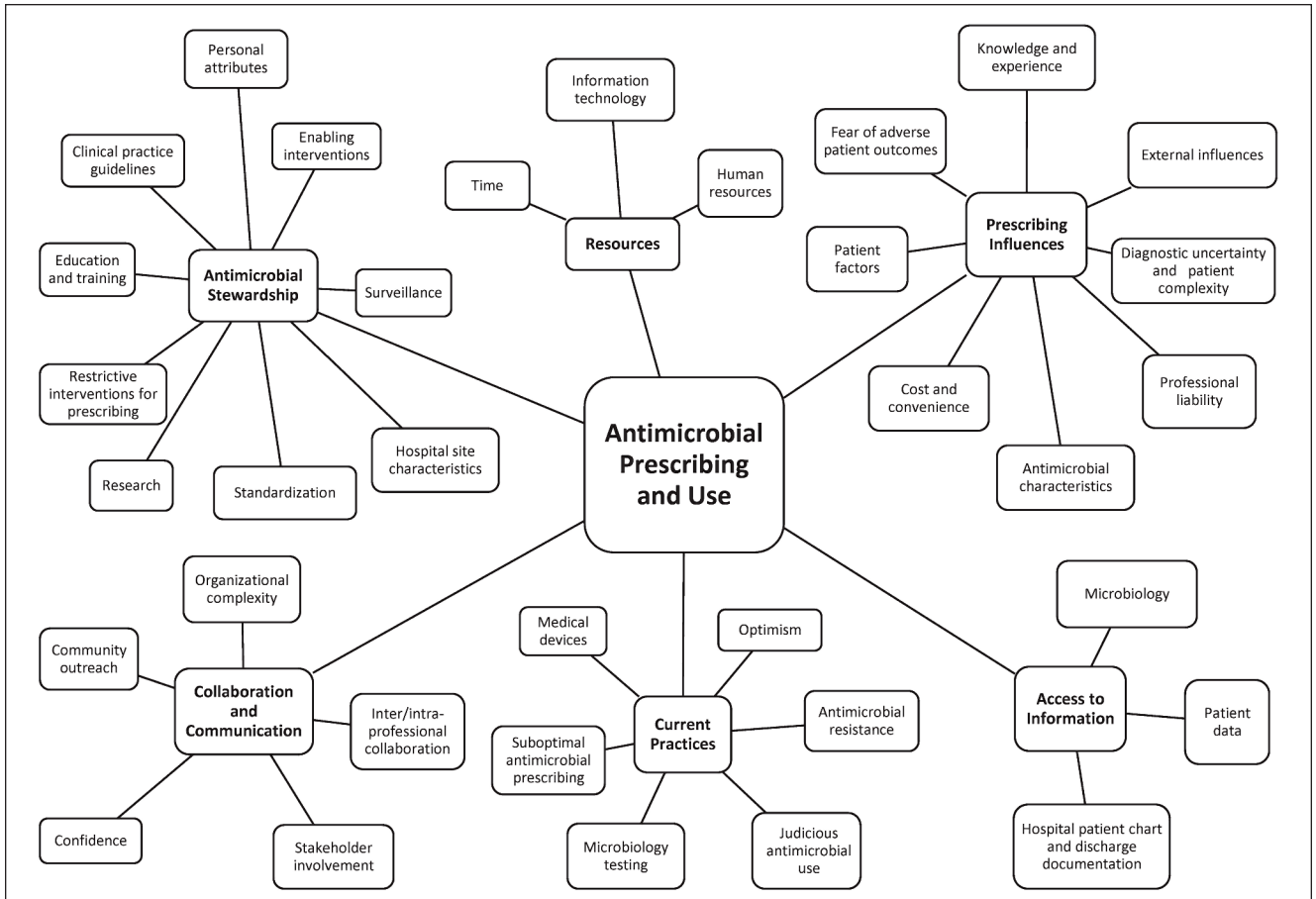

Figure 1. Themes and factors identified from health care providers' perceptions of antimicrobial prescribing and use.

antimicrobial agent, antimicrobial characteristics, and local patterns of antimicrobial resistance.

> "Empiric antibiotic use we're comfortable with, but it's the uncertainty when you're unsure what infection you are treating. That's one of the decisions around antimicrobial use or discontinuation that becomes the most challenging." [Physician 51]
>
> "In emerg [sic] I guess everyone's just scared, so go broad just in case." [Pharmacist 37]

Access to Information

Access to information was primarily discussed as a barrier at the organizational/system level. The most extensively discussed problem of this kind was lack of documentation in the health record, leading to challenges with inter- and intra-professional collaboration and extended duration of antimicrobial use. In contrast, some participants acknowledged that chart documentation in hospitals had improved recently.

> "The indication not being included, it's difficult for nursing and pharmacists to help, to be included in that therapy." [Pharmacist 30]

Participants also reported challenges with accessing patient data, including current or previous antimicrobial use (at other institutions or in the community) and microbiology reports.

> "So you have a patient coming from [another town] and they've had a nasopharyngeal swab for influenza. No one can access the results, so they send another one from here." [Nurse 43]

Most participants indicated that these barriers need to be overcome to facilitate improvements in antimicrobial use.

Collaboration and Communication

Some participants listed inter- and intra-professional collaboration as an individual-level barrier to improving antimicrobial use. Conversely, other participants attributed success in this area to local collaboration among health care providers at their institution. Similarly, stakeholder involvement in developing policies or guidelines and community outreach were identified by some participants as a system-level barrier and by others as a facilitator, depending on their respective experiences.

> "Whenever I've gotten a call from a pharmacist [to] bring to my awareness you know, IV [sic] or spectrum [of activity], I always appreciate it." [Physician 33]

"To have a physician that will step in, physician-to-physician, and to have the conversation is huge." [Nurse 20]

A few pharmacists also felt that a lack of confidence on the part of some health care providers to interact with physicians represented an individual-level barrier to improving antimicrobial use. One group discussed organizational complexity as a barrier that impeded efforts to improve antimicrobial use.

Resources

Lack of resources was identified as a barrier to improving the use of antimicrobials. Availability of adequate personnel and time were discussed extensively. Specific challenges with human resources included an inadequate number of health care providers with relevant expertise (infectious disease physicians, pharmacists, and AMS team members) and an inadequate number of experts to see the volume of patients requiring assessment. Some participants indicated that lack of time to contribute to initiatives in a busy clinic setting was a barrier. In contrast, a few groups indicated that access to dedicated AMS personnel or infectious disease specialists at their respective sites had facilitated successful implementation of AMS at the organizational level.

"Locally we just lost our infectious disease specialist … I think that really had a hit on our antimicrobial [use]." [Physician 24]

"I think we tried to pseudo-implement something before [our AMS pharmacist] showed up … but it was difficult. We didn't have somebody specifically delegated and now, you have somebody you can go to and their attention isn't divided to other things." [Pharmacist 2]

Use of information technology was recognized as a facilitator that might address some barriers. Specific suggestions to improve access to information and prescribing included implementation of electronic medical records, physician order entry, computerized clinical decision support, and use of electronic applications (apps) to distribute clinical practice guidelines.

"I do find the peds [sic] residents, in particular, are very excited to have this app and they do use it regularly … That's their go-to in terms of writing out their starting orders." [Pharmacist 4]

Antimicrobial Stewardship

Most AMS initiatives were identified as facilitators that might improve antimicrobial use. Participants indicated a desire for prescribing supports, including implementation of guidelines and provision of enabling AMS interventions such as audit and feedback. Education and training for a variety of audiences, including health care providers and the general public, were also viewed favourably. Current gaps in knowledge and guideline uptake were listed as ongoing barriers that slowed progress in improving antimicrobial use.

"Guidelines, having our own-specific guidelines [for the institution] and now the app, it's just huge … even I'm finding myself changing therapy that is appropriate to slightly more appropriate." [Pharmacist 1]

"When you went to nursing school one of the first things they taught you was if the patient is confused or if their urine smelled or was cloudy you should send that, when that's really not the case now in 2017 so I think it's a lot of education for nursing staff as well." [Nurse 22]

Other system-level facilitators that were identified included research, surveillance of antimicrobial use, antimicrobial resistance, monitoring and reporting on the impact of AMS interventions, and the size of the facility. At the individual level, personal attributes of health care providers, including expertise, respect, and collegiality in delivering initiatives, were recognized as facilitators of success.

"Having someone who's pleasant and friendly and engages with other people really well and in a non-threatening, non-confrontational way. I think that's really critical when you're trying to convince people to change practice." [Physician 51]

Health care providers' perceptions of restrictive interventions, including pre-authorization, were variable. Several participants indicated that previous attempts to implement restrictive interventions had led to poor relationships and "policing" of antimicrobial prescribing. Other participants felt that restrictive interventions would improve prescribing if delivered properly. Additional standardization of services was identified as a current system-level barrier that needed to be addressed to facilitate delivery of initiatives and improve antimicrobial use.

"We used to have restrictions and we got rid of them because it required a lot of policing [on] pharmacy's part." [Pharmacist 10]

DISCUSSION

Health care providers who participated in this study provided insights into antimicrobial use and stewardship in Nova Scotia. Barriers to and facilitators of improvements in antimicrobial use were underlying subthemes that crossed all major themes discussed. Participants recognized a number of modifiable barriers that need to be addressed to improve antimicrobial use. Despite these challenges, many participants indicated that progress had already been made in improving antimicrobial use. The findings from this study will be shared with members of AMS teams in Nova Scotia and used to inform more research on developing and implementing AMS interventions.

Although many of the barriers and facilitators identified in this study were consistent with those reported in the literature,[14-21] our findings contribute in several ways to a growing body of knowledge on AMS. Previously published qualitative studies were primarily completed in countries outside Canada, under different health care systems.[14-19,21] In addition, few studies

considered the perceptions of stakeholders from interdisciplinary teams in rural settings.[18,19,21] A Canadian study by Pasay and others,[20] which evaluated the perceptions of pharmacy staff about AMS policies and resources, highlighted the lack of generalizability to other professions. An Australian study by Bishop and others[21] concluded that centralized organizations (as in Nova Scotia) should have a good understanding of local context, given specific considerations identified in regional hospitals. Consistent with recently published priorities for AMS research,[9] our study adds to the literature by reporting the barriers and facilitators identified by an interdisciplinary group of stakeholders working in rural and urban publicly funded hospitals in a Canadian context.

Successful implementation of AMS interventions has been attributed to adequate resources and infrastructure, in addition to the establishment of relationships, with strong communication between AMS programs and clinical teams.[22] However, one of the most widely discussed barriers in this study was lack of adequate personnel with expertise in infectious disease and/or AMS. To overcome this barrier, additional personnel with dedicated time to deliver interventions and increased access to infectious disease specialists, particularly in regional hospitals, are needed. Financial constraints may hinder attempts to increase personnel. Solutions for overcoming this barrier in resource-limited settings include providing further training for the current workforce, streamlining processes to reallocate clinician time to focus on AMS-related interventions, and use of technology such as telehealth. Incorporating these suggestions may capitalize on appropriate use of human resources.

Implementation of AMS was generally viewed as a facilitator. Consistent with our findings, specific interventions viewed favourably in previously published qualitative studies include enabling interventions such as audit and feedback delivered in a safe learning environment by content experts,[16] educational initiatives,[15,17] and guideline implementation.[15,18] Restrictive interventions were listed as a barrier by some participants in our study and as a facilitator by others. Although restrictive interventions have shown benefit in terms of adherence to policies, they may lead to challenges in communication and trust between health care providers and can result in a delay in treatment.[8] If restrictive interventions are being implemented, careful consideration of methods to ensure best delivery is suggested.

Limitations

This study had several limitations. A pharmacist conducted the interviews and moderated the focus groups, which may have influenced participant response. In addition, the pharmacist who moderated the interviews had a pre-existing relationship with some of the participants. However, excluding participants known to the research team might have led to bias and poor validity through the omission of views of key stakeholders. We do not believe that facilitation of interviews by the principal investigator significantly affected the results, as similar themes were discussed across all groups. The funding available for this study did not support hiring additional research personnel with experience in qualitative research to facilitate the interviews and focus groups or to analyze the transcripts; however, members of our team, including the principal investigator, have previous experience in completing qualitative studies. Finally, results from this study represent the opinions of the study participants and may not be generalizable to other groups of health care providers or health care providers in other provinces. Despite these limitations, the themes discussed were relatively consistent across groups and likely represent accurately the perceptions of antimicrobial use and stewardship in Nova Scotia hospitals.

CONCLUSION

Findings from this study provide evidence of targets for improvement in a Canadian context, in both urban and rural publicly funded inpatient settings. Although the study identified numerous challenges in antimicrobial use, optimism was apparent. Modifiable barriers should be addressed to optimize the impact of AMS initiatives.

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Funding: This study was funded by a Development/Innovative Grant from the Nova Scotia Health Research Foundation. As a summer research student, Lindsay MacDonald received payment from the Nova Scotia Health Research Foundation and a Dalhousie University, Faculty of Health Professions establishment grant, to complete data collection.

Competing interests: Other than the funding outlined above, no competing interests were declared.

Acknowledgements: The authors would like to acknowledge Steve Smith and Andrea Kent, of the Nova Scotia Health Authority, for their assistance in recruiting participants. The authors would also like to acknowledge Olga Kits from the Research Methods Unit at the Nova Scotia Health Authority for her support in reviewing the interview guide and advising on the analysis.

Developing Preliminary Steps in a Pharmacist Communication – Patient Outcome Pathway

Bernadette Chevalier, Bernadette M Watson, Michael A Barras, and William N Cottrell

ABSTRACT

Background: Nonadherence to medication therapy has been associated with poor health outcomes and increased health care costs. The literature describes pharmacists as key health care professionals in identifying and addressing nonadherence issues but does not explain how and why effective pharmacist-patient communication affects patients' medication adherence. Previously published pathways used in linking effective physician-patient communication to patient outcomes are proposed for the context of pharmacist-patient communication.

Objectives: To develop preliminary steps in a pharmacist communication – patient outcome pathway, adapted from a physician-patient communication pathway,

Methods: This longitudinal descriptive study, which took place in a large quaternary hospital, involved hospital pharmacists and patients. Patients' assessment of pharmacist communication behaviours and reporting of patient satisfaction occurred after the pharmacist-patient consultation. Medication-taking behaviour questionnaires were administered before the consultation and again 4 weeks after discharge. Developing the preliminary pathway (based on previously established physician communication pathways) involved 2 steps, with investigation of the following associations: (1) between patient-reported effective communication by pharmacists, as per the Communication Accommodation Theory (CAT), and patient satisfaction; and (2) between patient-reported pharmacist communication and satisfaction and patients' medication-taking behaviour.

Results: Twelve pharmacists and 48 patients participated. For step 1, almost all patient-reported pharmacist communication behaviours were positively correlated with patient satisfaction statements. Strong associations between CAT-related pharmacist communication behaviours and patient satisfaction highlighted the pharmacists' behaviours that are important to patients and necessary for effective conversations to take place. In step 2, there were fewer correlations of medication-taking behaviour indices with pharmacist communication behaviours and patient satisfaction.

Conclusions: This study showed how a preliminary pharmacist communication – patient outcome pathway could be successfully adapted from existing physician communication pathways. Such pathways provide an initial platform upon which future pharmacist communication – patient outcome research can be built.

RÉSUMÉ

Contexte : Le non-respect de la pharmacothérapie a été associé à de mauvais résultats sur la santé et à une augmentation des coûts des soins de santé. La documentation actuelle décrit les pharmaciens comme étant les professionnels de la santé les mieux placés pour déceler les problèmes de non-respect de la prise de médicaments et pour y répondre. Toutefois, elle n'explique pas comment ni pourquoi une communication efficace entre le pharmacien et le patient incite le patient à respecter sa médication. Les parcours qui ont aidé les médecins à améliorer l'efficacité de la communication avec leurs patients sont désormais proposés aux pharmaciens dans le contexte de leur relation avec le patient.

Objectifs : Développer les étapes préliminaires d'un parcours de communication entre le pharmacien et le patient adapté à partir des résultats tirés du parcours de communication entre le médecin et le patient.

Méthodes : Cette étude descriptive longitudinale, qui s'est déroulée dans un important hôpital de soins quaternaires, portait sur les pharmaciens d'hôpitaux et les patients. L'évaluation par les patients des comportements de communication des pharmaciens et le rapport sur la satisfaction du patient se sont déroulés après la consultation qui a eu lieu entre le pharmacien et le patient. Les questionnaires relatifs à la prise de médicaments ont été administrés avant la consultation et à nouveau quatre semaines après le congé hospitalier. L'élaboration du parcours préliminaire (basée sur les parcours de communication du médecin déjà établis) comportait deux étapes servant à examiner les associations suivantes : (1) le rapport qu'ont fait les patients sur l'efficacité de la communication des pharmaciens conformément à la théorie de l'accommodation de la communication (TAC) et la satisfaction du patient et (2) le rapport qu'ont fait les patients sur la communication des pharmaciens ainsi que leur satisfaction et la prise de médicaments des par les patients.

Résultats : Douze pharmaciens et 48 patients ont participé à l'étude. Concernant la première étape, presque tous les patients ont rapporté que les comportements de communication des pharmaciens étaient positivement corrélés aux énoncés de satisfaction des patients. Les fortes associations entre les comportements de communication liés à la TAC du pharmacien et la satisfaction des patients mettaient en exergue les comportements des pharmaciens qui sont importants pour les patients et nécessaires pour accroître l'efficacité des conversations. Concernant la deuxième étape, les corrélations étaient moindres entre les indices de comportement liés à la prise de médicaments et les comportements de communication du pharmacien ainsi que la satisfaction du patient.

Keywords: communication-outcome pathway, hospital pharmacist communication, patient satisfaction, medication adherence, Communication Accommodation Theory (CAT)

Can J Hosp Pharm. 2019;72(4):271-81

Conclusions : Cette étude a démontré comment un parcours de communication préliminaire entre le pharmacien et le patient peut être adapté avec succès à partir des résultats tirés des parcours de communication existants destinés au médecin. De tels parcours fournissent une plateforme initiale sur laquelle peuvent se développer les recherches futures servant à démontrer les résultats sur les patients de la communication du pharmacien.

Mots-clés : voie communication-résultat, communication des pharmaciens d'hôpitaux, satisfaction des patients, respect de la médication, théorie de l'accommodation de la communication (TAC)

INTRODUCTION

Nonadherence to medications results in poor health outcomes for patients and increased costs to health care systems.[1,2] Patients' nonadherence to medications varies considerably depending on the condition being treated. For example, nonadherence rates range from 35% to 69% for patients with type 2 diabetes mellitus, from 40% to 70% for those with asthma, and from 25% to 65% for those with hypertension.[3-5] The multiple determinants of nonadherence include socioeconomic factors, factors related to the health care team or the health system, condition-related factors, treatment-related factors, and patient-related factors.[4] Determinants attributed to health care providers, such as good relationships and effective communication with patients, have been found to facilitate medication adherence for the management of pain, diabetes, epilepsy, HIV/AIDS, tuberculosis, and hypertension, and for tobacco cessation.[4]

Pharmacists have been identified as key health care professionals in identifying and addressing nonadherence issues.[6,7] While much has been published about the pharmacist's role in improving medication adherence,[4,8-11] there is scant information about how and why effective pharmacist-patient communication might affect patients' medication adherence. This is a substantial gap in understanding the role that pharmacists play in patients' adherence to their medications, particularly over time and once a patient leaves the inpatient setting.

Conversely, numerous empirical studies have investigated the effect of good physician-patient relationships and effective communication on clinical outcomes, with such studies showing a positive relationship between effective physician communication skills and patients' adherence to treatment.[12-15] For example, a meta-analysis of 106 studies correlated physician-patient communication with patient adherence and also considered 21 experimental intervention studies evaluating the effect of physician communication training on patient adherence.[13] The researchers reported that the odds of a patient being adherent to treatment were 2.16 times better if the physician communicated well and 1.62 times better if the physician had received communication training, relative to those patients whose physicians had not had communication skills training.[13]

However, there are inconsistent findings within the medical literature, whereby attributes of effective physician communication have not always been associated with treatment adherence and other patient outcomes.[16] Research in this area has been criticized as not being clear about which aspects of physician-patient communication contribute to which health outcomes.[17] Furthermore, research into communication between health care providers and patients has failed to suggest pathways and processes to explain how effective communication could be associated with positive patient outcomes. Street and others[17] posited that the links between the effectiveness of physician-patient communication and patient outcomes are often complex. Although positive communication exchanges may directly result in desirable health outcomes for patients, these interactions often follow indirect paths leading first to proximal outcomes (e.g., rapport-building, patient satisfaction) and then to intermediate outcomes (e.g., self-care skills, treatment adherence), before achieving health outcomes (e.g., cure, emotional well-being) (Figure 1).[17]

Pharmacist communication – patient outcome research is relatively new and consequently understudied in comparison to the work completed by physician-patient communication researchers. Given the complexity of communication – health outcome research, it is important to use the lessons learned from physician communication studies and to develop "pharmacist communication to patient outcome" processes that allow the clear delineation of which measured communication behaviours are linked to which patient outcomes.

This research study intends to demonstrate how such a preliminary pathway could be adapted from the physician communication processes described by Street and others.[17] Relationships are explored, in multiple steps, among effective pharmacist-patient exchanges, patient satisfaction, and patients' medication-taking behaviour. To begin, relational aspects between communication and medication adherence are studied through a pathway adapted from previous research[17] (as depicted in Figure 1) to fit the pharmacist-patient context. Relationships between proximal outcomes, such as effectively used communication strategies and patient satisfaction, are studied. Then possible associations between these proximal outcomes and the intermediate outcome of adherence to treatment are explored (Figure 2).

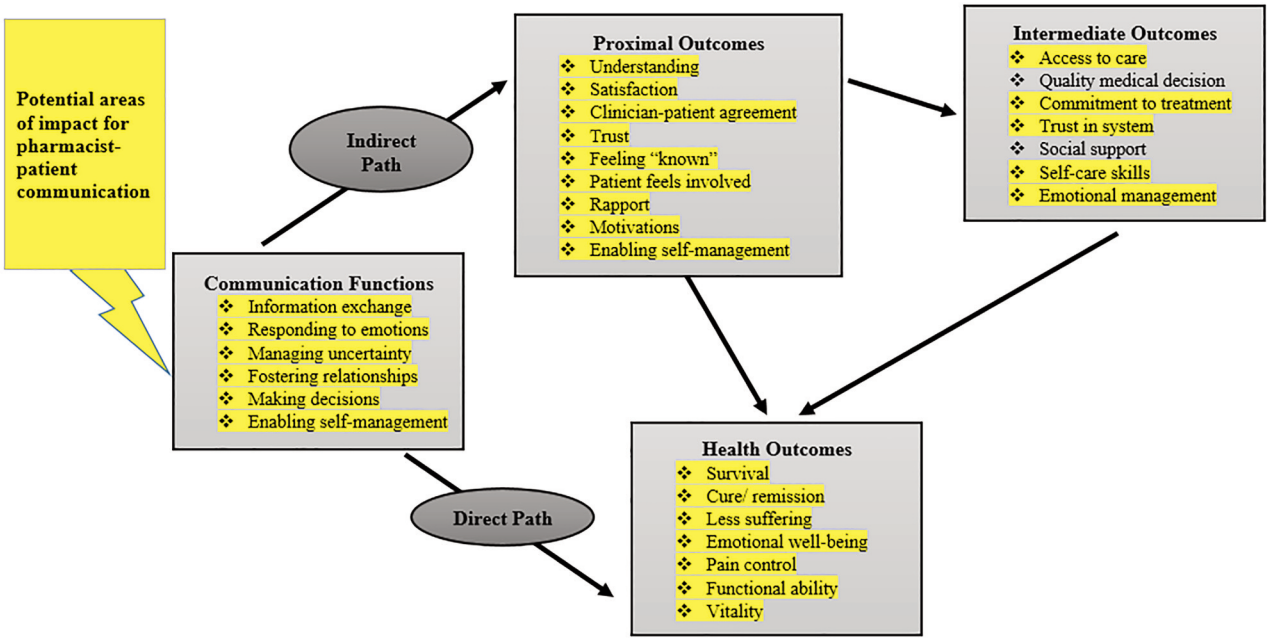

Figure 1. Pathways from pharmacist-patient communication to health outcomes. Potential areas for pharmacist-patient communication are shown in yellow. Adapted from *Patient Education and Counseling*, volume 75, no. 3, Street RL Jr, Makoul G, Arora NK, Epstein RM. "How does communication heal? Pathways linking clinician–patient communication to health outcomes", pages 295-301, © 2009, with permission from Elsevier.

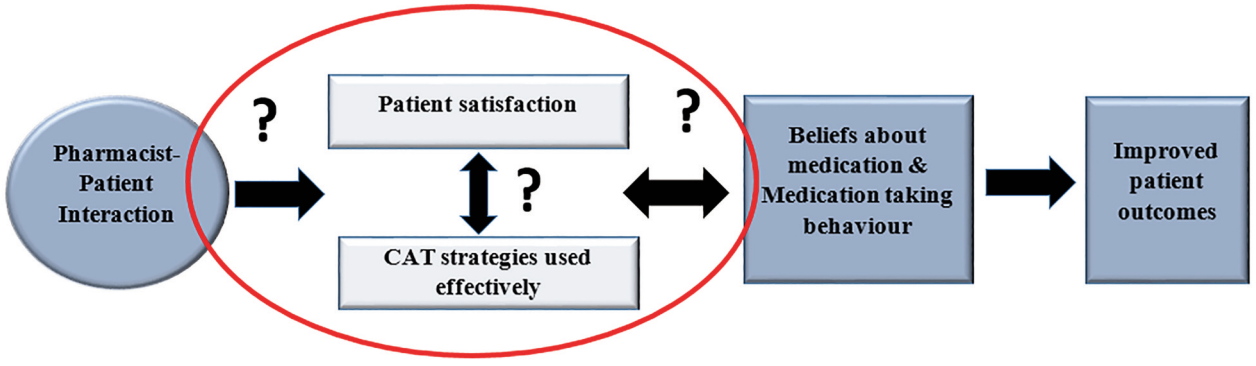

Figure 2. Relationships among effective communication, patient satisfaction, and medication-taking behaviour. CAT = Communication Accommodation Theory.

This study invoked the Communication Accommodation Theory (CAT) as the theoretical framework for all aspects of the research (i.e., design, data collection, analysis, and presentation of results and discussion). CAT is a widely used framework in health communication research[18-22] to help explain the emotional, behavioural, and motivational processes underlying communication exchanges.[23] The "CAT strategies used effectively" (as shown within Figure 2) are 5 strategies that are measured to establish the presence or lack of effective communication in interactions between patients and health professionals.[24-26] These strategies are approximation (matching another speaker's speech rate, volume, accent/dialect),[27] interpretability (using easily understood language and terms),[24] emotional expression (appropriately responding to the other speaker's emotional needs),[26] discourse management (engaging and maintaining conversations),[28] and interpersonal control (empowering/promoting equality between speakers).[25,29,30] CAT describes communication as being either accommodative (i.e., adjustments are made to bring speakers closer linguistically)

or non-accommodative (i.e., involving behaviour that creates barriers or linguistic distance between speakers).[24] In the pharmacist-patient communication context, accommodation takes place when pharmacists slow down their speech to match that of the patients, use medical terms understood by patients, and ask open-ended questions to enage patients in conversations about their medications. Conversely, non-accommodation occurs when pharmacists do not meet patients' conversational needs. For example, this might happen when pharmacists relay information in a one-way direction or frequently interupt patients, not allowing them to ask questions about their medications.

This research was intended to be exploratory. Data were collected as part of earlier research that focused on a qualitative investigation of communication effectiveness between hospital pharmacists and patients during medication counselling.[31] Therefore, this study was not designed or powered to detect differences in medication-taking behaviours over time. Rather, with this novel study, we sought to lay the foundation for the development of preliminary pharmacist communication – patient outcome pathways that could direct future research. Importantly, this study was longitudinal, with patients being followed over a 1-month period after discharge from hospital.

The study objective was to develop preliminary steps in a pharmacist communication – patient outcome pathway by adapting a physician communication pathway to the pharmacist-patient communication context. To achieve this objective, we undertook steps to show

- how effective pharmacist communication (using CAT) and patient satisfaction are associated (step 1)
- how patients' medication-taking behaviour is associated with patient-reported effective communication and satisfaction (step 2)

METHODS

Ethics Approval

Research ethics approval was received from the Royal Brisbane and Women's Hospital Human Research Ethics Committee (HREC/15/QRBW/433) and from the School of Pharmacy, The University of Queensland Ethics Committee (2015/13). All participants provided written informed consent.

Study Design

This descriptive study used quantitative methods to address the study's objective, involving 2 steps: (1) measuring the relationship between CAT-related pharmacist communication behaviours and patient satisfaction statements determined through semistructured interviews; (2) correlating pharmacist communication behaviours and patient satisfaction with the results of questionnaires on medication-taking behaviour. Step 2 also included investigating changes in patients' beliefs about their medications and their medication adherence over time.

Recruitment and Data Collection

Data were collected between November 2015 and April 2016 in a 1000-bed teaching hospital as part of doctoral research that focused on a qualitative investigation of communication effectiveness between hospital pharmacists and patients during medication counselling. Details about the methods used and results reporting communication effectiveness have been published elsewhere.[31] The current study focused on the data related to patients' assessment of pharmacist communication, patients' satisfaction, and patients' medication-taking behaviour. Two medication-taking behaviour questionnaires, the Beliefs about Medicines Questionnaire (BMQ)[32] and the 8-point Morisky Medication Adherence Scale (MMAS-8),[33,34] were administered to patients who consented to participate. Then, each patient underwent a medication consultation with a pharmacist (with audio-recording), which was immediately followed by semistructured interviews held separately with the pharmacist and the patient, to gain each participant's perspective. During these interviews, participants were asked to indicate their opinions about the consultation in terms of their level of agreement (on a 7-point Likert scale) with a series of statements, based on CAT strategies, with one of the statements being worded in reverse. The principal investigator (B.C.) conducted the interviews and answered any questions that participants had about any of the statements.

Four weeks after each patient left the hospital, the BMQ and MMAS-8 were administered again by telephone. This time frame was chosen to allow patients sufficient time to settle in at home and connect with their family physicians and community pharmacists after the initial pharmacist-patient interaction, without being so excessive that patients found it difficult to recall their experience.

Development of Semistructured Interview Guide

The interview guide consisted of 10 statements based on CAT strategies, reflecting aspects of pharmacist-patient communication, and 3 statements about participants' overall satisfaction. The face and content validity of the statements was assessed by the 3 pharmacists on the research team (B.C., M.A.B., W.N.C.), while the relevance of the statements to the CAT strategies was verified by the psychologist (B.M.W.) on the team. Cronbach α reliability testing was conducted to provide assurance of internal consistency within the 10 CAT-based statements.[35] The Cronbach α value calculated for the unidimensional scale for the 10 CAT-based statements was 0.75 for patients, above the acceptable 0.7 value.[35] A Cronbach α of 0.68 was calculated for the 3 patient satisfaction statements. This lower value was not surprising, given that only 3 items were included in the scale.[36] However, the mean inter-item correlation, which also analyzes internal consistency, was calculated as 0.4 for these patient satisfaction statements and was within the acceptable range (0.2–0.4).[36]

Medication-Taking Behaviour Questionnaires

The BMQ is a validated instrument that assesses patients' beliefs about the necessity of prescribed medications and their concerns about the potential dangers or disruptive effects of their medications.[32] Patients with strong beliefs about the value of their medications and few concerns about their medicines are more likely to be adherent to their medications.[32]

The MMAS-8 medication adherence tool, which is composed of 8 questions, requires patients to reflect on their medication-taking behaviours. A score of 8 indicates high adherence, scores of 6 to <8 reflect moderate adherence, and scores less than 6 are considered to represent low adherence.[33,34] The MMAS-8 was chosen because it is a convenient, easy-to-use, validated research tool that has been applied worldwide in a variety of health conditions.[34,37-41]

Data Analysis

The responses to the BMQ, the MMAS-8 tool, and the semistructured interview statements were recorded in a Microsoft Excel database (Microsoft Corporation, Redmond, Washington). All data were analyzed using SPSS Statistics for Windows, version 25.0 (IBM Corporation, Armonk, New York). A p value of less than 0.05 was considered statistically significant. Because the data were not normally distributed, nonparametric tests were used to analyze the data.

The Spearman correlation was used to test both the relationship between CAT behavioural statements and patient satisfaction statements, and the associations of the CAT and patient satisfaction statements with the 4-week BMQ and MMAS-8 results. For this part of the study, the 4-week postdischarge scores were used, rather than the baseline scores, because this assessment occurred after the pharmacist-patient conversation and would better reflect any effects of the exchange.

BMQ and MMAS-8 scores for questionnaires administered to patients before the pharmacist-patient conversation were compared with the 4-week postdischarge scores using the Wilcoxon signed-rank test to detect changes in scores over time. The effect size (r) for any significant difference was calculated by dividing the test statistic (Z) by the square root of the number of observations.[36] Based on the criteria provided by Cohen,[42] $r = 0.1$ indicates a small effect size, $r = 0.3$ indicates a medium effect size, and $r = 0.5$ indicates a large effect size.

RESULTS

Twelve pharmacists engaged 4 separate patients each for a total of 48 medication counselling interactions; however, not all 48 patients who consented to be in the study completed all parts of the study (Figure 3). The majority (10 [83%]) of the pharmacists who took part in the study were women, with about half being under 30 years of age and having less than 10 years' experience as a pharmacist. Participating patients were mostly men (27 [56%]) and over 60 years of age. Patients from both inpatient areas (cardiology, emergency, geriatrics, general medicine, nephrology, neurology, oncology, surgery) and outpatient clinics (heart failure, infectious diseases, renal disease) were included.

Step 1: Relationship between Patients' Assessment of Pharmacists' Communication Behaviours and Patients' Satisfaction

Overall, high proportions of patients (> 80%) indicated agreement or strong agreement that pharmacists demonstrated the communication behaviour described in each of the 10 statements. Patients' level of agreement on the 10 statements assessing pharmacists' communication behaviours and their association with the 3 patient satisfaction statements are displayed in Table 1.

Step 2: Relationship of Patients' Assessment of Pharmacists' Communication Behaviours and Level of Satisfaction with Medication-Taking Behaviour Indices

Almost all correlations with statistical significance involved the BMQ postdischarge necessity score, for which 5 of the pharmacists' communication behaviours and 2 of the patient satisfaction statements were positively correlated (Table 2).

Changes in BMQ and MMAS-8 Scores over Time

Differences between patients' BMQ and MMAS-8 scores measured before their respective conversations with a pharmacist about their medications and again 4 weeks after the patients had left the hospital are shown in Table 3. No statistically significant differences for any of the BMQ indices were found. Differences in MMAS-8 scores between the 2 time points were significant (median 6.75 versus 7.00; $p = 0.022$), although the calculated effect size was small ($r = 0.248$).

The distribution of MMAS-8 scores for the first and second questionnaires is shown in Table 4. Most patients had moderate or high adherence scores for both the first questionnaire (27/45 [60%]) and the second questionnaire (39/46 [85%]).

DISCUSSION

This novel longitudinal, exploratory study has shown how the theoretical communication – patient outcome pathways developed for physicians could be adapted to the pharmacist-patient communication context. This study focused on 2 preliminary steps within the original pathway (Figure 1) to demonstrate how effective communication (using CAT) and patient satisfaction are associated (step 1) and how patients' medication-taking behaviour is associated with patient-reported effective communication and satisfaction (step 2). The most impressive results were the high number of positive correlations between patient-reported

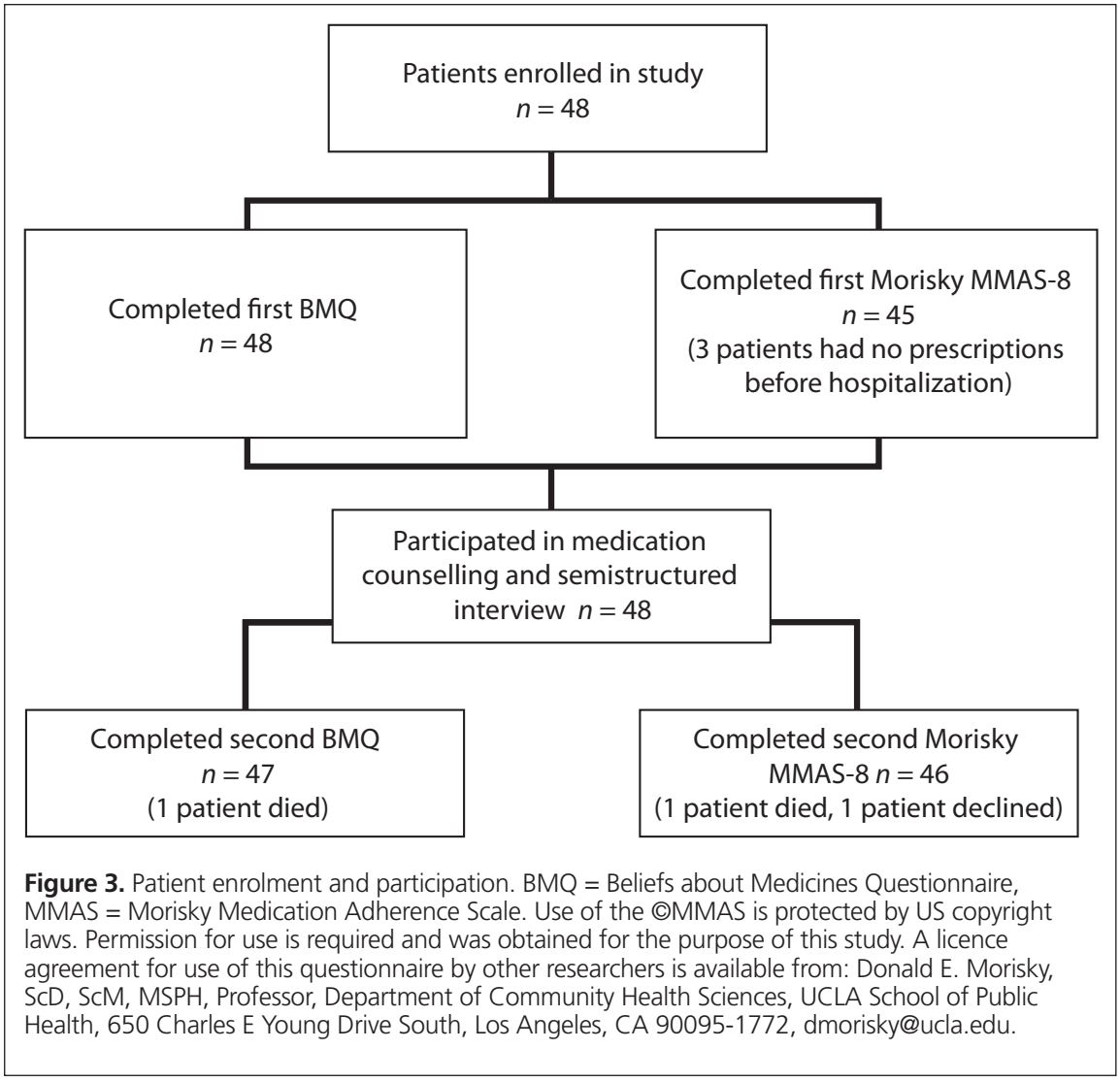

Figure 3. Patient enrolment and participation. BMQ = Beliefs about Medicines Questionnaire, MMAS = Morisky Medication Adherence Scale. Use of the ©MMAS is protected by US copyright laws. Permission for use is required and was obtained for the purpose of this study. A licence agreement for use of this questionnaire by other researchers is available from: Donald E. Morisky, ScD, ScM, MSPH, Professor, Department of Community Health Sciences, UCLA School of Public Health, 650 Charles E Young Drive South, Los Angeles, CA 90095-1772, dmorisky@ucla.edu.

pharmacist communication behaviours and patients' level of satisfaction. These results highlight the pharmacist communication behaviours that are of particular importance to patients and therefore necessary for effective conversations. In addition, some promising trends were observed in terms of correlations between medication-taking behaviours and pharmacist communication behaviours/patient satisfaction. The most important strength of this study is that it has mapped pathways for conducting future research that link pharmacist-patient communication to patient outcomes. This is an important step to facilitate rigorous pharmacist communication research that indicates how and where associations between communication and patient outcomes occur, and to avoid the pitfalls encountered by earlier physician communication researchers, who did not clearly delineate these relationships.[17]

This process of adapting a physician communication pathway for pharmacist communication research revealed some important and interesting findings. Step 1 of this investigation mirrored the relationships between "communication functions" and "proximal outcomes", as well as the interplay of communication behaviours and patient satisfaction found within "proximal outcomes" of Figure 1.[17] The first step showed that nearly all patient-assessed pharmacist communication behaviours were positively correlated with all 3 patient satisfaction statements. This finding implied that the more patients experienced these pharmacist communication behaviours, the higher their reported levels of satisfaction with the pharmacist-patient exchanges. However, 2 exceptions were noted for the communication behaviour statements. Statement 2 of Table 1, "The pharmacist used medical terms I could understand", was the only statement that was reverse-worded in the semistructured interview for patients. It is possible that the use of reverse wording may have been confusing to some patients, resulting in incorrect interpretation and scoring of the pharmacist's behaviour. Only one patient

Table 1. Relationship between Patients' Assessment of Pharmacists' Communication Behaviours and Patients' Satisfaction

Pharmacist Communication Behaviour Statement	Associated CAT Strategy	% of Patients Agreeing with Pharmacist Behaviour (*n* = 48)*	Patient Satisfaction Statement; Spearman Rank Correlation with Statement		
			The pharmacist did a good job helping me understand my medicines	I was satisfied with my experience I had with the pharmacist	This was an effective conversation with the pharmacist (I got what I needed)
1. The pharmacist spoke clearly, so I could understand what they were saying.	Approximation	100	0.361†	0.371‡	0.388‡
2. The pharmacist used medical terms I could understand.	Interpretability	88	–0.131	0.049	–0.031
3. The pharmacist explained how my medication works in a way I could easily understand.	Interpretability	100	0.369†	0.333†	0.601‡
4. The pharmacist gave me enough time to think about the medication information given to me so that I could ask any questions I had.	Discourse management	96	0.196	0.306†	0.498‡
5. The pharmacist paid attention and listened to my concerns about my medications.	Discourse management	100	0.501‡	0.328†	0.431‡
6. The pharmacist allowed me to interrupt to ask questions.	Interpersonal control	98	0.357†	0.334†	0.457‡
7. I felt like the pharmacist thought my worries and questions about my medicines were important.	Emotional expression	98	0.597‡	0.443‡	0.383‡
8. The pharmacist spoke to me in a respectful and courteous manner.	Emotional expression	100	0.432‡	0.592‡	0.395‡
9. The pharmacist encouraged me to talk to my doctor and/or community pharmacist about different medication options available to me.	Interpersonal control	87	0.383†	0.389‡	0.318†
10. The pharmacist encouraged me to take responsibility for managing my health.	Interpersonal control	87	0.143	0.117	0.303†

CAT = Communication Accommodation Theory.
*"Agreement" consists of the sum of "agree" plus "strongly agree" responses or, in the case of reverse-worded statements, "disagree" plus "strongly disagree" responses.
†Correlation significant at the $p < 0.05$ level (2-tailed).
‡Correlation significant at the $p < 0.01$ level (2-tailed).

satisfaction statement, "This was an effective conversation with the pharmacist", was positively correlated with statement 10, which described the pharmacist as encouraging the patient to take responsibility for managing his or her own health. It is unclear why a positive correlation was not observed between this pharmacist behaviour statement and the 2 other patient satisfaction statements. However, patients' assignment of lower scores to pharmacists' communication behaviour statements did not necessarily mean that pharmacists were non-accommodative to patients' conversational needs. Instead, it sometimes meant that the pharmacists' behaviour was not observed by the patients in their particular interactions.

Several pharmacist communication behaviours were strongly correlated with patient satisfaction statements. Of note, pharmacist behaviour statements 1 and 3 to 9 (Table 1) were strongly correlated with all 3 patient satisfaction statements. Other researchers have found positive associations between similar communication behaviours and patient satisfaction. For example, in a study by White,[43] UK pharmacists who were trained in a cognitive behavioural therapy framework provided medication consults to patients on an inpatient mental health ward. Patients expressed high levels of satisfaction with having their questions answered in a way they could understand and being treated with respect and dignity.[43] Patients surveyed at a US immunization clinic after receipt of counselling and vaccination by a pharmacist expressed satisfaction in having the "pharmacist explain things to me in a way that I can understand" and having the "pharmacist [spend] as much time as is needed with me".[44] Australian researchers eliciting patients' assessment of their experience and level of satisfaction with prescribing pharmacists in a surgical preadmission clinic reported relationships between a number of assessment statements and patient satisfaction similar to those

Table 2. Relationship of Patients' Assessment of Pharmacists' Communication Behaviours and Satisfaction with BMQ and MMAS-8 Scores

Statement	% of Patients Agreeing with Statement (*n* = 48)	Score; Spearman Rank Correlation		
		Postdischarge Necessity Score (BMQ) (*n* = 47)	Postdischarge Concern Score (BMQ) (*n* = 47)	Postdischarge MMAS-8 Score (*n* = 46)
Pharmacist communication behaviour				
1. The pharmacist spoke clearly, so I could understand what they were saying.	100	0.272	0.008	–0.071
2. The pharmacist used medical terms I could understand.	88	0.226	–0.360†	0.042
3. The pharmacist explained how my medication works in a way I could easily understand	100	0.332†	–0.028	–0.185
4. The pharmacist gave me enough time to think about the medication information given to me so that I could ask any questions I had.	96	0.427‡	–0.042	–0.062
5. The pharmacist paid attention and listened to my concerns about my medications.	100	0.251	0.010	–0.065
6. The pharmacist allowed me to interrupt to ask questions.	98	0.143	–0.052	–0.103
7. I felt like the pharmacist thought my worries and questions about my medicines were important.	98	0.296†	0.087	–0.116
8. The pharmacist spoke to me in a respectful and courteous manner.	100	0.328†	–0.055	–0.082
9. The pharmacist encouraged me to talk to my doctor and/or community pharmacist about different medication options available to me.	87	0.388‡	0.117	–0.225
10. The pharmacist encouraged me to take responsibility for managing my health.	87	0.271	–0.53	–0.036
Patient satisfaction statement				
11. The pharmacist did a good job helping me understand my medicines.	98	0.326†	0.134	–0.072
12. I was satisfied with my experience I had with the pharmacist.	100	0.381‡	–0.002	–0.062
13. This was an effective conversation with the pharmacist.	98	0.167	–0.039	–0.059

BMQ = Beliefs about Medicines Questionnaire, MMAS-8 = 8-point Morisky Medication Adherence Scale. Use of the ©MMAS is protected by US copyright laws. Permission for use is required and was obtained for the purpose of this study. A licence agreement for use of this questionnaire by other researchers is available from: Donald E Morisky, ScD, ScM, MSPH, Professor, Department of Community Health Sciences, UCLA School of Public Health, 650 Charles E Young Drive South, Los Angeles, CA 90095-1772, dmorisky@ucla.edu.
*"Agreement" consists of the sum of "agree" plus "strongly agree" responses or, in the case of reverse-worded statements, "disagree" plus "strongly disagree" responses.
†Correlation significant at the $p < 0.05$ level (2-tailed).
‡Correlation significant at the $p < 0.01$ level (2-tailed).

Table 3. BMQ and MMAS-8 Scores at 2 Points in Time

Test	Timing of Questionnaire*; Median Score† (Range)		Wilcoxon Signed-Rank Test
	First Questionnaire	Second Questionnaire	
BMQ	*n* = 48	*n* = 47	
Necessity domain	21 (11–25)	21 (12–25)	$Z = 0$, $p > 0.99$
Concern domain	12 (5–22)	13 (5–22)	$Z = 1.690$, $p = 0.091$
MMAS-8	*n* = 45 6.75 (0.5–8)	*n* = 46 7.00 (1–8)	$Z = 2.298$, $p = 0.022$; $r = 0.248$

BMQ = Beliefs about Medicines Questionnaire, MMAS-8 = 8-point Morisky Medication Adherence Scale. Use of the ©MMAS is protected by US copyright laws. Permission for use is required and was obtained for the purpose of this study. A licence agreement for use of this questionnaire by other researchers is available from: Donald E Morisky, ScD, ScM, MSPH, Professor, Department of Community Health Sciences, UCLA School of Public Health, 650 Charles E Young Drive South, Los Angeles, CA 90095-1772, dmorisky@ucla.edu
*First questionnaire was administered before patient's conversation with pharmacist, and second questionnaire took place 4 weeks after patient left hospital.
†Possible BMQ scores range from 5 to 25 for each of 2 domains (necessity and concern); higher scores indicate a stronger belief in that domain. MMAS-8 scores range from 0 to 8; score < 6 indicates low adherence, score from 6 to <8 indicates moderate adherence, and score of 8 indicates high adherence.

Table 4. Distribution of MMAS-8 Scores at 2 Points in Time

Adherence level by MMAS-8	Timing of Questionnaire*; No. (%) of Patients	
	First Questionnaire (*n* = 45)	Second Questionnaire (*n* = 46)
Low (MMAS-8 score < 6)	18 (40)	7 (15)
Moderate (MMAS-8 score 6 to <8)	18 (40)	20 (44)
High (MMAS-8 score = 8)	9 (20)	19 (41)

MMAS-8 = 8-point Morisky Medication Adherence Scale. Use of the ©MMAS is protected by US copyright laws. Permission for use is required and was obtained for the purpose of this study. A licence agreement for use of this questionnaire by other researchers is available from: Donald E Morisky, ScD, ScM, MSPH, Professor, Department of Community Health Sciences, UCLA School of Public Health, 650 Charles E Young Drive South, Los Angeles, CA 90095-1772, dmorisky@ucla.edu.
*First questionnaire was administered before patient's conversation with pharmacist, and second questionnaire took place 4 weeks after patient left hospital.

observed in the current study. These assessments included "explained clearly", "provided relevant information", "listened", "answered questions in a way easily understood", and "understood medication concerns expressed".[45]

Step 2 of this study explored the link between "proximal" and "intermediate" outcomes (as shown in Figure 1) by investigating whether a relationship between pharmacists' communication behaviour or patients' level of satisfaction exists with patients' medication-taking behaviours.[17] The positive and statistically significant correlations between pharmacist communication behaviours and patients' satisfaction occurred mainly with the BMQ postdischarge necessity score. This positive correlation is understandable, because patients who have experienced a pharmacist-patient interaction in which the pharmacist provided well-explained information, at a pace that allowed patients enough time to ask questions, and addressed medication issues would likely appreciate the need for their medication and its benefits to their health and well-being. Patients who felt that the pharmacist was empathetic and provided reassurance in response to their concerns about their medications may have stronger beliefs that their medications are beneficial. Therefore, the strong positive correlations between 2 of the overall satisfaction statements ("I was satisfied with my experience I had with the pharmacist" and "The pharmacist did a good job helping me understand my medicines") and the necessity score were not surprising. However, it is unknown why the same associations were not observed for the satisfaction statement "This was an effective conversation with the pharmacist."

There was only one negative statistically significant correlation, which occurred between statement 2 ("The pharmacist used medical terms I could understand") and the postdischarge concern score. This indicates that the more patients experienced pharmacists using laypersons' terms rather than medical terminology, the less patients expressed concerns about the harmful effects of their medications.

No statistically significant associations were observed for any pharmacist behaviour statements, patient satisfaction, and postdischarge medication adherence (MMAS-8) scores. In addition, a significant difference in medication adherence indices measured at 2 time points was observed only for the MMAS-8 scores. For all other medication adherence indices, differences between the first and second time points were small. In this study population, many patients had been identified as moderately and highly adherent; therefore, there was little or no room for a change in adherence scores to occur. Other researchers have reported that initial scores reflecting higher levels of medication adherence make it difficult to see any significant changes in medication-taking behaviour.[34,46]

This study had potential limitations. Patients may have provided socially desirable responses when they assessed pharmacists' communication behaviours and indicated their levels of satisfaction. Although patient interviews were held immediately after their conversations with the pharmacist, it is possible that the patients did not recall specific details about these interactions. These biases may have also occurred at the 4-week follow-up. This research was conducted at a single public hospital, and therefore the results may not be transferable to all specialty areas at other hospitals or to rural or private hospitals. Patient outcomes such as medication adherence are influenced by multiple factors in addition to effective health professional – patient relationships and communication.[4] Therefore, the pharmacist communication – patient outcome pathway explored in this study helps to explain how different aspects of communication may be associated with a patient outcome such as medication adherence, but the links do not imply causality. Although the medication-taking behaviour questionnaires used in this study have been validated in a range of medical conditions and cultural contexts,[34,37-41] using additional measures of medication adherence, such as prescription fills, could have strengthened the methodology of this study. Future research will address these issues.

CONCLUSION

In this study, a physician communication – patient outcome pathway was adapted to the pharmacist-patient communication

context. This research has introduced a valuable foundation for future work by providing some preliminary process mapping of how effects of the pharmacist-patient communication exchange are linked to proximal and intermediate clinical outcomes.[17] For example, next steps in this research might include a randomized controlled trial with sufficient baseline numbers of patients with low adherence, subjected to multiple communication interventions and followed over time, to allow firm conclusions to be drawn.

By adapting an outcome pathway from the literature, a framework has been created for conducting exploratory research to investigate the relationship between effective pharmacist-patient exchanges and patients' medication-taking behaviour. This research represents an important preliminary step in establishing links between pharmacist-patient communication and patient outcomes.

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Competing interests: None declared.

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Funding: No external funding was received.

Acknowledgement: The authors gratefully acknowledge support provided by Metro North Hospital and Health Services in the conduct of this research. This study was conducted as part of Bernadette Chevalier's PhD research at The University of Queensland.

ORIGINAL RESEARCH

Medication Use by Alternate Level of Care Patients: A Descriptive Analysis

Mehrdad Azimi, Lisa Burry, Christinne Duclos, Jordan Pelc, Jason X Nie, and Ross Upshur

ABSTRACT

Background: The population of patients designated as alternate level of care (ALC) consists predominantly of frail older adults who are medically stable and awaiting discharge from hospital. They have complex medication regimens, often including potentially inappropriate medications (PIMs). There has been increasing emphasis on managing the burden that ALC patients place on the health care system, but little is known about their health care needs.

Objective: To characterize the medication regimens, including use of PIMs, of ALC patients at the study institution.

Methods: A cross-sectional chart audit of ALC patients was conducted between May and July 2017. For all patients in the sample, each medication was categorized by therapeutic class, and PIMs were categorized according to the Beers criteria, the STOPP/START criteria, and an established list of high-alert medications.

Results: A total of 82 patients met the audit criteria, for whom the mean number of chronic conditions was 6.4 (standard deviation [SD] 3.3) and the mean number of prescribed medications was 12.8 (SD 6.9). Twenty-four (29%) of the patients were receiving at least 1 drug from 7 different drug classes. All but one of the patients had PIMs in their regimen; the frequency of PIMs was highest according to the Beers criteria (mean 3.9 [SD 2.6] medications per patient).

Conclusions: At the study institution, ALC patients had on average more than 6 chronic conditions managed with at least 12 medications, of which one-quarter were PIMs. These data will be used to inform next steps in making recommendations to simplify, reduce, or discontinue medications for which there is an unclear indication, lack of effectiveness, or evidence of potential harm.

Keywords: alternate level of care, polypharmacy, potentially inappropriate medications, older adults

Can J Hosp Pharm. 2019;72(4):282-7

RÉSUMÉ

Contexte : La population de patients désignés comme « niveaux de soins alternatifs » (NSA) se compose majoritairement d'aînés faibles, médicalement stables et en attente de leur congé hospitalier. Ils suivent des traitements médicamenteux complexes qui comprennent souvent des médicaments potentiellement contre-indiqués (MPCI). L'accent a été progressivement mis sur la gestion du fardeau que les patients NSA font peser sur le système de soins de santé, mais on connait peu de choses sur leurs besoins en matière de soins de santé.

Objectif : Décrire les traitements médicamenteux, y compris l'utilisation des MPCI, des patients NSA dans l'institution où s'est déroulée l'étude.

Méthodes : Une vérification transversale des dossiers de patients NSA a été menée entre mai et juillet 2017. Chaque médicament pris par les patients de l'échantillon a été classé selon sa catégorie thérapeutique, et les MPCI ont été catégorisés selon les critères de Beers, les critères STOPP/START ainsi qu'une liste établie de médicaments dont le niveau d'alerte est élevé.

Résultats : Au total, 82 patients remplissaient les critères de l'audit, car le nombre moyen de maladies chroniques était de 6,4 (écart type [ET] 3,3) et le nombre moyen de médicaments prescrits se montait à 12,8 (ET 6,9). Vingt-quatre (29 %) patients recevaient au moins un médicament de sept classes médicamenteuses différentes. Tous les patients sauf un avaient des MPCI dans leur programme. La fréquence des MPCI était plus élevée selon les critères de Beers (moyenne de MPCI par patient de 3,9 [ET 2,6]).

Conclusions : Sur le lieu de l'étude, les patients NSA avaient en moyenne plus de six maladies chroniques gérées à l'aide d'au moins 12 médicaments, dont un quart était des MPCI. Ces données seront utilisées pour informer les cliniciens sur les étapes suivantes et formuler des recommandations afin de simplifier, de réduire ou d'arrêter les médicaments pour lesquels l'indication n'est pas claire, dont l'efficacité est insuffisante ou sur lesquels il existe des données probantes faisant état de dangers potentiels.

Mots-clés : autres niveaux de soins, polypharmacie, médicaments potentiellement contre-indiqués, ainés

INTRODUCTION

Research indicates that older adults are taking increasingly more medications.[1] Although there is disagreement about the best definition, polypharmacy is often defined as 5 or more medications for the same patient.[2] Polypharmacy is known to increase the risk of adverse drug events, drug–drug and drug–disease interactions, nonadherence, inappropriate prescribing, falls, hospitalization, and death.[3] In addition, polypharmacy may lead to medication wastage and a burden to society in terms of health care spending.[4]

Over the past 2 decades, methods have been developed to standardize the assessment of medication appropriateness for older adults, with the goal of reducing inappropriate prescribing and thus improving patients' outcomes.[5] These established methods include the Beers Criteria for Potentially Inappropriate Medication (PIM) Use in Older Adults,[6] the STOPP/START criteria,[7] and high-alert medications as identified by the Institute for Safe Medication Practices (US).[8] Nonetheless, inappropriate medication use is common, especially in the setting of multimorbidity and polypharmacy.[9,10]

One population that may be particularly at risk for polypharmacy and exposure to PIMs consists of hospitalized patients who are medically appropriate for discharge from hospital, but who remain in hospital awaiting discharge disposition. Prolonged stay in hospital for disposition reasons, rather than clinical need, is known as alternate level of care (ALC).[11] These patients are at risk of polypharmacy because of their advanced age, multiple chronic conditions, and the prolonged hospital stay. The ALC burden on Canadian health care is large and growing, representing 5% of all hospitalizations and contributing 14% of hospital days in acute care settings across Canada (data from 2009).[11] ALC patients are mainly older adults (≥ 65 years of age) with frailty and cognitive or behavioural problems.[12-14] Although the ALC population is growing, to date there have been few studies examining the medication regimens of these patients, and only one has investigated the potential appropriateness of medications.[15] The objective of the current study was to present a descriptive analysis of medication regimens used by ALC patients in a large tertiary care centre and to characterize the potential inappropriateness of medications prescribed for this patient population.

METHODS

Study Design

Between May and July 2017, we conducted a cross-sectional audit of patients who were designated ALC at 2 of our institutional sites, Mount Sinai Hospital and Bridgepoint Active Healthcare, in Toronto, Ontario. This quality improvement study was intended to gain a baseline understanding of medication use in this population and to help design future intervention work. Ethics approval was not required for the purpose of this quality improvement study.

Study Population

Patients designated as ALC in the hospital's computer system between May and July 2017 were considered for inclusion in this study. Patients with incomplete data and those missing one or more health-related reports from the electronic database (e.g., preadmission medications, ongoing chronic conditions) were excluded from the study. Patients who were discharged before assessment or for whom medication data were no longer available in the electronic database were also excluded.

Data Collection

Data were extracted from electronic records. For each individual patient, complete records were collected within a single day, providing a synopsis of their health status parameters. The research team designed an electronic case report based on previous work by the team. For each patient, the following data were extracted from the chart: demographic characteristics, reason for admission, expected postdischarge destination, length of stay in acute care hospital (calculated from admission date to audit date), length of ALC stay (calculated from date of ALC designation to audit date), history of falls, most current Morse fall risk,[16] and preadmission health status (based on admission notes, including number of chronic conditions). For each patient, we calculated the complexity score (sum of number of chronic conditions and number of medications).[17] We also extracted details of the medications in use at the time of admission to hospital from the best possible medication history and details of all medications given during the hospital stay (e.g., drug name, dose and frequency, and pill burden) from the medication administration record on the day of the audit. Pill burden was defined as the cumulative number of all solid oral dosage formulations prescribed per patient, which is a measure of the burden placed on a patient to take a specified number of solid oral medications (e.g., tablets, capsules). Data were entered into an Excel spreadsheet (Microsoft Corporation, Redmond, Washington), with standardized data entry using categorization by searchable drop-down menus.

Data Processing and Analysis

The medications were coded in terms of specific drug classes generated by the team (based on general use rather than an official classification). The following specific drug classes were used: psychotropic, cardiovascular, hematologic, endocrine, analgesic/anti-inflammatory, anti-infective, genital/urinary, respiratory, musculoskeletal, topical, supplements/natural health products, gastrointestinal (including bowel routines), and "other". An exhaustive list of these medication classes, as well as the specific drugs belonging to each class, is provided in Appendix 1 (available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/191/showToc). Medication appropriateness was assessed according

to the following criteria for inappropriate medications: Beers criteria,[6] STOPP/START criteria,[7] and high-alert medications.[8] The medications identified by these criteria may not be appropriate for certain patient populations (e.g., older adults with multimorbid conditions). Any medication used by a patient in the study sample that appeared on any of these lists was flagged as a PIM and was included in the analysis. This process was not intended to assess the clinical relevance of the prescribed medications, but rather to collect information on medications that might be deemed inappropriate according to the inappropriate medication references.[6-8] In addition, flagged PIMs were not based on the wrong classes of medications being prescribed for specific conditions or a lack of prescribing. The proportion of each patient's regimen represented by PIMs was calculated using each of the Beers criteria, the STOPP/START criteria, and the list of high-alert medications separately, and also using a combination of all 3 lists. Descriptive statistics, such as mean and standard deviation (SD) or median and interquartile range (IQR), were calculated as appropriate.

RESULTS

Of 93 patients with an ALC designation in the computer system, 82 patients (14 at Mount Sinai Hospital, 68 at Bridgepoint) met the inclusion criteria (Figure 1). The remaining 11 patients were excluded because health status information was incomplete upon audit. Forty-three (52%) of the patients were women, and the overall mean age was 75.6 (SD 15.1) years (Table 1). The mean number of chronic conditions before admission to hospital was 6.4 (SD 3.3) per patient, for which a mean of 12.8 (SD 6.9) distinct medications had been prescribed. A history of falls in the past 3 months was common (78% [64/81]), and 73% (59/81) of the patients were still considered to be at high risk of falling.

Data about prescriptions for these ALC patients are presented in Table 2. The mean number of medications per patient at the time of the audit was 17.6 (SD 5.2), and 64.7% of the prescriptions (943/1458) were scheduled orders (i.e., not for as-needed administration). The overall mean daily pill burden, which represented solid oral dosage formulations for all standing and PRN prescriptions, was 18.5 (SD 9.5) per patient, whereas the mean daily pill burden for standing orders alone was 10.1 (SD 6.3) per patient.

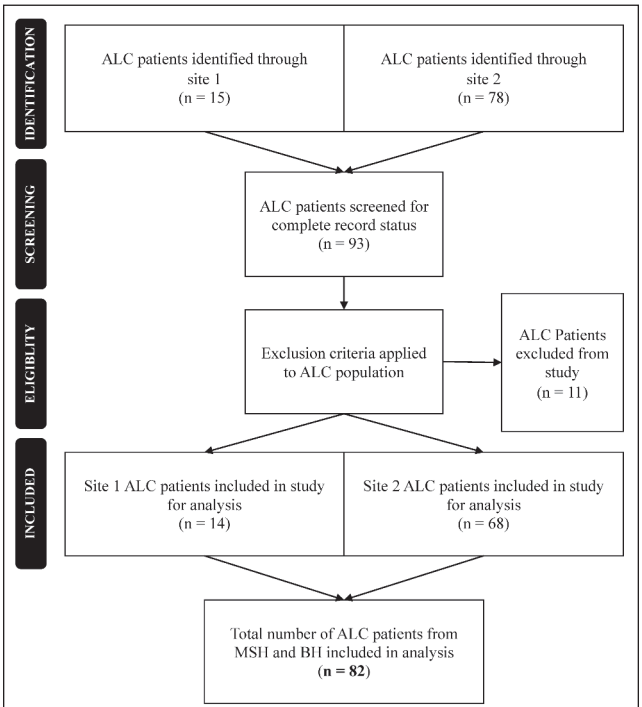

Figure 1. Flow chart of inclusion and exclusion criteria for study participants. ALC = alternate level of care, BP = Bridgepoint Active Healthcare, MSH = Mount Sinai Hospital.

Table 1. Demographic Characteristics of Participants

Characteristic	No. (%) of Patients* (*n* = 82)
Age (years) (mean ± SD)	75.6 ± 15.1
Sex (female)	43 (52)
ALC discharge destination	
Long-term care bed	67 (82)
Supportive housing	4 (5)
Geriatric rehabilitation	1 (1)
Home with CCAC	4 (5)
Unknown	6 (7)
Morse fall risk	
High	60 (73)
Moderate	14 (17)
Low	8 (10)
Length of stay (days) (median and IQR)	281 (107.8–596.3)
Length of ALC (days) (median and IQR)	182 (54.3–379.8)

ALC = alternate level of care, CCAC = Community Care Access Centre.
*Except where indicated otherwise.

Table 2. Characteristics of Prescriptions

Characteristic	Per-Patient Mean ± SD*
Hospital data (*n* = 82 patients)	
Total no. of prescriptions	1458
No. of standing *and* PRN† orders per patient	17.6 ± 5.2
No. of standing orders only per patient‡	11.4 ± 4.1
Pill burden§ (*n* = 78 patients)	
For standing *and* PRN† orders	18.5 ± 9.5
For standing orders only	10.1 ± 6.3

PRN = administration on as-needed basis, standing orders = scheduled orders.
*Except where indicated otherwise.
†Maximum PRN frequency.
‡Of the 1458 prescriptions, 943 (64.7%) were standing orders.
§Number of solid oral dosage formulations prescribed to the patient for daily administration.

The most frequently prescribed medication class was gastrointestinal drugs (mean 4.8 [SD 1.8] drugs per patient). Laxatives used for routine bowel preparation accounted for most of this class (mean 3.83 laxatives prescribed per patient; see Appendix 2, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/191/showToc). Supplements, cardiovascular drugs, and psychotropic agents were the next most frequently prescribed classes, with means of 2.8 (SD 1.6), 2.7 (SD 1.7), and 2.5 (SD 1.5) medications per patient, respectively (Table 3). Most psychotropics used by these patients were antipsychotics (36 patients) or antidepressants (31 patients). Figure 2 shows the proportion of patients by number of medication classes in their individual regimens. For 24 (29%) of the 82 patients, at least 1 drug from 7 different classes of medications was prescribed for concurrent use, and some patients had medications from 8 or 9 different classes (14/82 [17%] in each case). None of the patients were receiving drugs from fewer than 3 medication classes.

Depending on the particular list used to analyze PIMs, between 68 (83%) and 80 (98%) of the patients studied were receiving at least 1 PIM. Only 1 (1%) of the 82 patients in this study did not have a single medication on any of the 3 lists used here to identify PIMs (Figure 3). The number of PIMs ranged from 0 to 12 according to the Beers criteria (mean 3.9, SD 2.6), from 0 to 7 according to the STOPP/START criteria (mean 2.4, SD 1.9), and from 0 to 6 according to the ISMP list of high-alert medications (mean 1.4, SD 1.2) (Figure 4). Most prescribed PIMs belonged to the psychotropics, including antipsychotics, of which quetiapine accounted for 33 (2.26%) of

Table 3. Medications by Class

Medication Class	No. of Patients with ≥ 1 Drug in Class	No. of Drugs in Class per Patient (Mean ± SD)
Gastrointestinal	81	4.8 ± 1.8
Supplement/NHP	75	2.8 ± 1.6
Cardiovascular	62	2.7 ± 1.7
Psychotropic	62	2.5 ± 1.5
Analgesic/ anti-inflammatory	80	1.9 ± 1
Topical	49	1.9 ± 1
Respiratory	25	1.8 ± 1.2
Endocrine	31	1.5 ± 0.7
Genital/urinary	10	1.4 ± 0.5
Hematologic	59	1.3 ± 0.5
Musculoskeletal	13	1.2 ± 0.4
Anti-infective	17	1.1 ± 0.2
Other	8	1 ± 0

NHP = natural health product, SD = standard deviation.

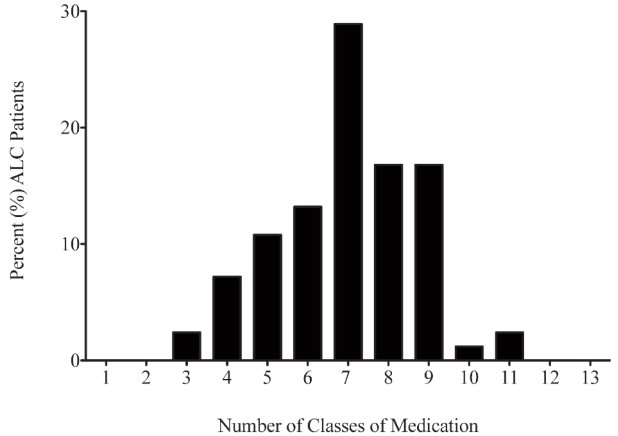

Figure 2. Frequency of concurrent medication classes used for alternate level of care patients.

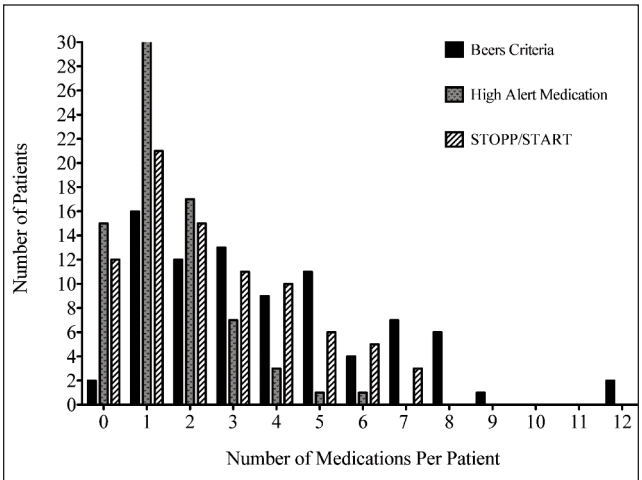

Figure 3. Distribution of patients with potentially inappropriate medications (*n* = 82 patients).

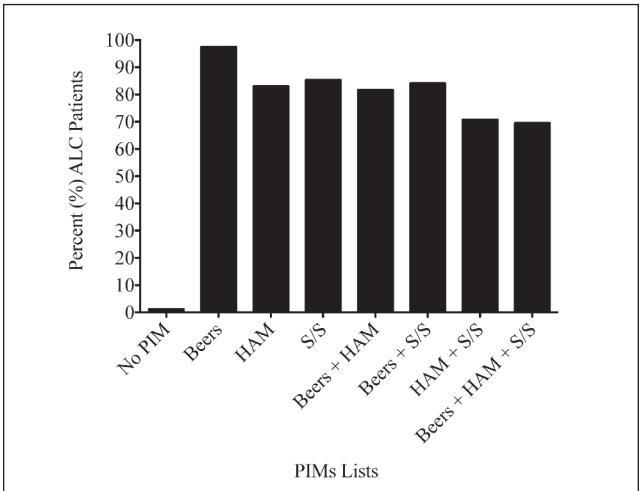

Figure 4. Proportion of patients with potentially inappropriate medications (PIMs), according to various criteria (*n* = 82 patients). Beers = Beers Criteria,[6] HAM = high-alert medications,[8] S/S = STOPP/START criteria.[7]

the 1458 medications prescribed for the 82 patients. Appendix 3 (available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/191/showToc) lists the most commonly prescribed medications in our ALC cohort. A breakdown by medication class for the psychotropic and gastrointestinal medication classes is also provided in Appendix 2.

DISCUSSION

This study was an audit of medication use by ALC patients admitted to the study institution between May and July 2017, with the aim of describing medication use and PIM exposure. Polypharmacy was common and exposure to PIMs was high in this cohort of ALC patients; these factors are known to put patients at high risk of adverse drug events, falls, medical complications, potential future repeat hospitalization, and death.[18,19] The typical characteristics of ALC patients, such as age, frailty status, and relatively high cognitive impairment, suggests that many of these patients will need assistance with their medications. High pill burden, with or without PRN orders, also contributes to the need for ALC patients to have assistance in order to take their medications accurately. As members of our team have previously suggested, one solution might be consolidation of the medication regimen and reduction of regimen complexity.[20]

In the context of older adults with multimorbidity, application of clinical guidelines often results in polypharmacy, fostering complications and adverse reactions.[21] We cross-referenced the medication regimens of these ALC patients with 3 lists that are frequently used to assess for PIMs in older adults. In the medication regimens of these ALC patients, PIMs were most frequent according to the Beers criteria, possibly because of the comprehensiveness of those criteria. At least 1 PIM from the Beers list was included in the medication regimen of 98% of the cohort, and only 1 patient had no PIMs in the medication regimen; these findings indicate a potential opportunity to improve prescribing in the ALC cohort at our institution. Although this work did not consider the clinical relevance of PIMs, our overview of the ALC medication regimen suggests that a more thorough review is needed to ensure appropriate prescribing.

Of particular interest, we found that psychotropic drugs were the third most commonly prescribed drug class, with about three-quarters of the ALC patients in our sample receiving at least one psychotropic drug. Antipsychotic use increases the risk of stroke, cognitive decline, and death among older persons with dementia.[6] In addition, antipsychotic use by older adults may increase the risk of ventricular arrhythmia and cerebrovascular events, leading to a higher risk of death.[22]

Most of the patients in this study were at high risk of falling, and the association between psychotropic drugs and increased risk of falls among older adults has been well described.[23-25] Furthermore, it has been shown that deprescribing medications associated with an increased risk of falls significantly lowers the incidence of falls,[24] which suggests an opportunity for intervention in our institution.

Strengths and Limitations

We examined patients' drug therapy regimens in detail and categorized exposure to PIMs using all of the commonly used scoring systems available. Our work was limited by the lack of a control group for comparison, by the retrospective study design, and by having a nonrandomized convenience sample, whereby individuals were predetermined for analysis. In addition, the indications for each medication were rarely documented, which limited our ability to discern clinical appropriateness.

CONCLUSION

ALC patients face many chronic conditions, which contribute to the complexity of their health status and for which large numbers of medications are prescribed. In this setting, prescribing often results in polypharmacy. The concerning presence of PIMs in the medication regimens of ALC patients warrants further attention. Psychotropics were the most commonly prescribed PIMs in the ALC cohort described here, and next steps for the study institution include developing and implementing initiatives to minimize their inappropriate use in this population, such as the introduction of deprescribing algorithms. More generally, the ALC population is only expected to grow, as life expectancy increases over the next couple of decades, along with new treatments for an array of chronic conditions; further work is needed to optimize prescribing safety for this population. Given that ALC patients have a high medication burden, which may include PIMs, there is an opportunity for pharmacists to become involved in deprescribing and optimizing medication use.

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Competing interests: None declared.

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Funding: None received.

Acknowledgements: The authors are grateful for the support of Janice Takata-Shewchuk and Kori Bilben, Department of Pharmacy, Bridgepoint Active Healthcare.

ORIGINAL RESEARCH

Hospital Pharmacists' Perceptions and Decision-Making Related to Drug-Drug Interactions

Harkaryn Bagri, Karen Dahri, and Michael Legal

ABSTRACT

Background: Pharmacists often overlook drug interaction alerts because of limitations in clinical decision support (CDS) software systems intended to detect evidence-based, clinically significant drug-drug interactions (DDIs). Alert fatigue, which occurs when pharmacists become desensitized to an overload of DDIs, may also contribute.

Objectives: To gain a better understanding of how pharmacists assess common DDIs and the extent to which computerized drug alerts affect their decision-making, as background for initiatives to overcome alert fatigue and improve detection of DDIs.

Methods: This qualitative study used focus group methodology. A structured focus group was planned at each of 3 large tertiary hospitals. Pharmacists were invited to participate if their jobs included patient care and/or dispensary responsibilities. The focus group discussions were audio-recorded and subsequently transcribed, analyzed, and coded into themes using NVivo software. Four main categories of themes were identified: perceived challenges, pharmacists' assessment of DDIs, barriers to responding to alerts, and proposed solutions.

Results: The participants (n = 24) described a large discrepancy among CDS software systems in terms of the severity of specific DDIs, which made it difficult to view these systems as reliable sources. The participants agreed that alert fatigue is present and contributes to DDIs being overlooked. However, lack of patient information to make an initial assessment, as well as the constant need for multitasking, prevents pharmacists from focusing on the evaluation of DDIs.

Conclusions: Although alert fatigue was reported to be a common factor responsible for pharmacists missing DDIs, other barriers also exist. Participants suggested ways to limit DDI alerts to those that are clinically relevant. Having a collaborative team of pharmacists periodically review the DDIs embedded in the CDS system, incorporating a colour-code system, and removing duplicate entries were discussed as ways to improve system efficiency.

Keywords: alert fatigue, drug-drug interactions, pharmacists

RÉSUMÉ

Contexte : Les pharmaciens ignorent souvent les alertes d'interactions médicamenteuses à cause des limites des logiciels d'aide à la décision clinique (ADC) conçus pour détecter les interactions médicamenteuses (IM) factuelles et significatives d'un point de vue clinique. La fatigue liée aux alarmes (alert fatigue), qui survient lorsque les pharmaciens sont désensibilisés à cause d'une surcharge d'IM, peut aussi contribuer à cette situation.

Objectifs : Mieux comprendre comment les pharmaciens évaluent les IM courantes et dans quelle mesure les alertes médicamenteuses affectent leur prise de décision, dans le cadre de la mise en œuvre d'initiatives visant à surmonter la fatigue liée aux alarmes et à mieux détecter les IM.

Méthodes : La méthodologie de cette étude qualitative se basait sur les groupes de discussion. Un groupe de discussion structuré était prévu dans chacun des trois grands hôpitaux tertiaires. Les pharmaciens étaient invités à participer si leur travail comprenait des soins offerts aux patients ou des responsabilités dans la distribution de médicaments. Les discussions dans les groupes ont fait l'objet d'un enregistrement audio avant d'être retranscrites, analysées et codées selon les thèmes à l'aide du logiciel NVivo. Quatre catégories de thèmes principaux ont été établies : les défis perçus, l'évaluation des IM par les pharmaciens, les obstacles à lever pour répondre aux alertes et les solutions proposées.

Résultats : Les participants (n = 24) ont mentionné un écart important dans les définitions de la gravité [severity] d'IM spécifiques données par les logiciels d'ADC, de sorte qu'il était difficile de se fier à ces systèmes. Les participants ont indiqué que la fatigue liée aux alarmes existait bel et bien et qu'elle contribuait au manque de prise en compte des IM. Cependant, le manque d'information sur les patients pour faire l'évaluation initiale, ainsi que le besoin constant d'effectuer plusieurs tâches à la fois, empêche les pharmaciens de se concentrer sur l'évaluation des IM.

Conclusions : Bien que la fatigue liée aux alarmes empêche fréquemment les pharmaciens de remarquer les IM, il existe d'autres obstacles. Les participants ont proposé de limiter les alertes d'IM à celles pertinentes d'un point de vue clinique. Les solutions examinées pour améliorer l'efficacité du système ont porté sur la formation d'une équipe collaborative de pharmaciens qui examine périodiquement les IM intégrés dans le système ADC, l'incorporation d'un système de codes de couleur et l'élimination des entrées dupliquées.

Mots clés : fatigue liée aux alarmes interactions médicamenteuses, pharmaciens

Can J Hosp Pharm. 2019;72(4):288-94

INTRODUCTION

A drug-drug interaction (DDI) occurs when one drug affects the pharmacokinetics or pharmacodynamics of another drug, resulting in a qualitative or quantitative change in action.[1,2] An adverse DDI is one that leads to increased drug toxicity.[2] DDIs are preventable occurrences that can result in adverse drug events (ADEs), causing serious harm to patients or reducing the therapeutic efficacy of one or more medications.[1] Up to 11% of patients experience adverse effects due to DDIs, with 2%–3% of these adverse effects being responsible for hospital admission.[3]

Pharmacists are in a unique position to identify DDIs and intervene when necessary to prevent ADEs.[1] When pharmacists review drug regimens manually, 66% of DDIs in 2-drug regimens are correctly detected, with the proportion decreasing as the number of drugs increases.[4] Within hospitals and in the community, clinical decision support (CDS) software systems are available to assist pharmacists in identifying DDIs of clinical importance.[1] However, these drug information software programs can cause pharmacists to become desensitized to an overload of DDI alerts; as a result, they may not spend an appropriate amount of time evaluating each DDI.[1] Evaluating DDIs can be mentally exhausting and time-consuming when there are too many alerts, which may lead pharmacists to ignore both relevant and irrelevant warnings, a phenomenon known as alert fatigue.[1,4] It is reported that pharmacists' override rates can be as high as 71.9% during daily practice.[5] Furthermore, DDI screening software programs are limited in their ability to detect evidence-based, clinically significant DDIs, and they sometimes fail to alert pharmacists about DDIs of real concern.[5,6]

In general, all CDS software systems function in a similar manner; however, in British Columbia, different health authorities work with different CDS software companies. All of the systems are intended to display DDI alerts according to the severity of the interaction; however, severity may be presented in the form of numbers (1, 2, 3) or letters (A, B, C), with the designation 1/A being most severe and 3/C being least severe. It is important to note, however, that not all health authorities were included in this study; therefore, there may be other designations for indicating severity levels.

Studies performed to date have mainly focused on evaluating the performance of DDI screening software programs in identifying select clinically significant DDIs in the hospital setting.[6-9] Many of these studies have concluded that a high number of pharmacy CDS systems perform suboptimally.[6] In addition, customization of drug alerts at various hospital sites allows pharmacists to miss DDIs of higher severity.[10] Software customization involves turning certain interactions on or off at the discretion of pharmacy staff.[7] Such customization can create variation in the system's performance, which can in turn compromise patient care.[7]

The purpose of this study was to investigate how hospital pharmacists assess common DDIs and to evaluate the extent to which computer alerts affect pharmacists' decision-making (in terms of determining which DDIs are clinically significant). Our assessment of how pharmacists deal with DDIs in their daily practice, as well as which information sources they use and wish to have on hand, will help inform initiatives to overcome alert fatigue and improve interaction detection rates. Improving a pharmacist's ability to detect DDIs could reduce the chance of ADEs, preserve patient safety, and prevent medical and legal problems.[4]

METHODS

A qualitative study was conducted using focus group methodology. Three structured focus groups, consisting of 6 to 8 pharmacists each at 3 different sites (Surrey Memorial Hospital, St Paul's Hospital, and Vancouver General Hospital), were planned. An invitation to participate in the focus groups was sent via e-mail by site-specific hospital clerical staff to group e-mail lists for pharmacists. Those interested in participating were asked to contact one of the co-investigators (H.B.). Potential participants were included if they worked in an institutional setting and had dispensary or patient-care responsibilities. Community pharmacists and pharmacy technicians were excluded, because the study's focus was primarily on hospital software systems. However, hospital pharmacists who participated in the study might have been working concurrently or have had past experience in the community. We did not ask participants to report their community experience, and the focus group questions pertained to pharmacists' experiences with CDS software systems in the hospital setting. All participants gave written informed consent. Ethics approval to conduct the study was obtained from the University of British Columbia Behavioural Research Ethics Board.

The target sample size for each focus group was 6 to 8 participants. If an insufficient number of pharmacists responded to the initial e-mail invitation, the investigators approached individual pharmacists from a cross-section of positions. The focus groups were planned to last about 1 hour and were scheduled during the participants' lunch hour, with lunch being provided by the unrestricted start-up research fund of one of the coauthors. No other honorarium or incentive was offered to participants, and no other funding was involved in any other aspect of the study.

One of the co-investigators (H.B.) conducted all of the focus groups, with a designated research assistant also present to observe and take notes. The sessions were audio-recorded for subsequent transcription and analysis.

A comprehensive literature search was performed to determine the questions that would be used in the focus groups. A panel of pharmacists reviewed the preliminary questions with a view to further improvement. The focus group questions could be categorized as seeking the resources that pharmacists use when reviewing DDIs and their thought processes when assessing DDIs

of potential concern (see Appendix 1, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/191/ showToc).

The audio-recordings were transcribed by the research assistants and reviewed for accuracy by the focus group moderator. One of the investigators (H.B.) then coded the transcripts and organized the content into common themes using NVivo software (https://www.qsrinternational.com/nvivo/what-is-nvivo).

This was a qualitative study, so there was no primary outcome. The 2 primary objectives of this qualitative evaluation were to learn more about how pharmacists perceive DDI alerts and to determine the extent to which computer alerts affect pharmacists' decision-making when dispensing a medication.

RESULTS

A total of 24 participants were recruited: 9 from Surrey Memorial Hospital, 8 from St Paul's Hospital, and 7 from Vancouver General Hospital. Fifteen (62%) of the participants had been working at their respective hospital sites for no more than 5 years, and 15 (62%) had both clinical and dispensary duties (Table 1). Only 1 pharmacist had dispensary duties only.

The qualitative analysis revealed themes, which were organized into the following 4 main categories: perceived challenges, pharmacists' assessment of DDIs, barriers to responding to alerts, and proposed solutions.

Perceived Challenges

One theme mentioned frequently in the focus groups was that the CDS systems can be overwhelming in terms of the information they provide about DDIs (Box 1). Furthermore, some pharmacists felt that the CDS systems were not a reliable source when it came to assessing more severe or unusual DDIs. As a result, they found themselves referring to other resources to determine whether a particular DDI was clinically significant.

Many pharmacists agreed that there is a large discrepancy in the severity of specific DDIs among the various CDS software systems.

> "It feels like 95% of the interactions are maybe completely useless … I wouldn't do anything about them."
> —Participant

For example, a DDI flagged in the CDS software system as having severity 1 or severity X, meaning that the drug combination should be avoided, might not be categorized as having the same severity by the pharmacist reviewing the DDI, who might consider it as having severity 3 or severity C, meaning that the drug therapy should be monitored. Furthermore, participants in all 3 focus groups frequently cited interactions embedded in the CDS systems that were irrelevant or for which they felt they did not have enough information to do an adequate assessment. For example, QT prolongation was commonly mentioned (in all 3 focus groups) as irrelevant or useless, and many participants stated that this is something they would watch out for but not act upon (Box 1). Another interaction mentioned as irrelevant was "same drug, multiple routes". This concern typically referred to opioids,

Box 1. Participants' Opinions Concerning Challenges Associated with CDS Software Systems, Presented as Common Themes*

Challenges

- Current CDS systems are not a reliable source to assess drug interaction alerts (*n* = 24)
- The information provided by CDS systems can be overwhelming (*n* = 7)
- More severe or unusual interactions will prompt pharmacists to look to other resources to determine if the interaction is clinically relevant (*n* = 5)
- A discrepancy in severity exists among the different CDS systems (*n* = 4)
- The CDS systems are outdated (*n* = 2)

Interactions perceived as irrelevant or "useless"†

- QT prolongation (*n* = 3)
- Insulin and β-blockers (*n* = 2)
- Same drug, multiple routes (*n* = 2)
- Bleeding risk (*n* = 2)
- PRN opioid sedation (*n* = 2)
- Dimenhydrinate interactions (*n* = 1)

CDS = clinical decision support, PRN = administration as needed.

*The common themes presented here were mentioned during some or all of the focus groups. The *n* value for each theme represents the total number of times the theme was mentioned over the course of the 3 focus groups

†Refers to interactions embedded in the CDS software system that pharmacists perceived as irrelevant or for which they would not have the necessary information to act.

Table 1. Demographic Characteristics of Participants (*n* = 24)

Characteristic	Hospital Site; No. of Participants		
	Surrey Memorial Hospital (*n* = 9)	St Paul's Hospital (*n* = 8)	Vancouver General Hospital (*n* = 7)
Years at hospital site			
≤ 5	7	4	4
> 5	2	4	3
Primary work area			
Dispensary only	0	1	0
Clinical only	3	2	3
Clinical + dispensary	6	5	4

which can be administered by different routes (e.g., hydromorphone oral or IV). The possibility of multiple routes for a single drug can also contribute to alert fatigue, which can result in pharmacists missing both irrelevant and relevant DDIs.

Pharmacists' Assessment of DDI

When participants were asked how they assessed whether a potential DDI is of concern, they commonly reported asking themselves, "What are the ramifications of dispensing the medications that could cause the DDI?" (Box 2). Only those with the potential for an immediate effect would be considered clinically significant.

> "The first step I would think is what is the extreme things that could happen if I don't act on this. Are we either going to compromise therapy or reduce efficacy of something? Are we going to cause patient harm?" —Participant

Participants also described a series of questions they often ask themselves before acting upon a DDI alert: Is the consequence of the DDI reversible or irreversible? What is the indication for the medication? What are the patient's own risk factors for experiencing this DDI? What is the reported incidence of the interaction? How likely is the DDI to occur in my patient?

An additional theme was that a pharmacist's familiarity with the particular DDI plays a role in determining whether it is deemed to be clinically relevant. Recent pharmacy graduates often flagged a DDI because they lacked of experience and did not want to cause patient harm. Participants indicated that although they frequently turned to the Lexicomp database as their initial resource for assessing the clinical significance of a DDI, they often had to use other references, including Micromedex and the *Compendium of Pharmaceuticals and Specialties* (Box 3).

Barriers to Detecting DDIs

Most participants agreed that alert fatigue is a common contributor to the underdetection of DDIs (Box 4). However, other barriers may also impede pharmacists' optimal workflow. Participants felt that there was a lack of resources, such as patient-specific information, rather than a lack of time. Participants reported that, in the dispensary, they were often presented with a DDI alert that they would never act upon, because they do not have enough information about the patient to assess the DDI in the first place. Moreover, participants felt that they had multiple competing duties to which they had to attend throughout the day and thus might not be entirely focused on the orders in front of them, as illustrated by the following quotation:

> "We're dealing with phone calls at the same time, questions are being asked by other pharmacists, by technicians, we may be dealing with shortages, we are not 100% as focused as we can be on the order at any given time of the day …" —Participant

Box 2. Factors Leading Pharmacists to Assess DDIs as Clinically Significant*

DDIs with immediate, severe ramifications are considered clinically significant (*n* = 9)
Recent pharmacy graduates are more likely to flag a DDI because of lack of experience (*n* = 2)

DDI = drug-drug interaction.

*The *n* value for each factor represents the total number of times the factor was mentioned over the course of the 3 focus groups

Box 3. Drug Information Resources* Preferred by Pharmacists†

University of Liverpool HIV Drug Interaction Checker (*n* = 3)
Natural Medicine (*n* = 3)
Case reports (*n* = 2)
Compendium of Pharmaceuticals and Specialties (*n* = 2)
Micromedex (*n* = 1)
Credible Meds QT (*n* = 1)

*Tertiary drug information resources used by pharmacists when clinical significance of a drug-drug interaction could not be determined from the Lexicomp database.

†The *n* value for each resource represents the total number of times the resource was mentioned over the course of the 3 focus groups.

Box 4. Barriers to Responding to Alerts about DDIs, Presented as Common Themes*

Alert fatigue is a common factor in missing potential DDIs (*n* = 16)
Pharmacists lack the clinical context to assess a DDI in the dispensary (*n* = 5)
Heavy workload and multitasking can contribute to pharmacists not identifying clinically important DDIs (*n* = 4)
Pharmacists working clinical shifts feel they are limited by time available to assess DDIs (*n* = 2)

DDI = drug-drug interaction.

*The *n* value for each theme represents the total number of times the theme was mentioned over the course of the 3 focus groups.

In contrast to pharmacists working in the dispensary, pharmacists working clinical shifts felt limited by time, as opposed to resources, when assessing DDIs. They often have 20 to 40 patients to look after, and it is not possible to spend hours determining whether a DDI is clinically important and requires immediate action.

Proposed Solutions

Throughout the focus groups, participants suggested various ways to improve drug alert detection rates (Box 5). Common suggestions included a periodic review of the DDIs embedded in the hospital's computer systems by a collaborative team of pharmacists, who would decide which of those being flagged were clinically relevant. The purpose would be to limit the alerts to those that are clinically important, in an effort to reduce alert fatigue. Furthermore, the implementation of a colour-coding scheme to differentiate the various severity levels might also help to improve drug alert detection rates. For example, information presented in red would stand out more and be harder to miss; this

Box 5. Participants' Ideas for Overcoming Alert Fatigue, Presented as Common Themes*

Annual review of DDIs in CDS software systems, performed by team of pharmacists (*n* = 8)
Allow colour-coding to differentiate severity levels (*n* = 6)
Limit duplication (*n* = 2)
Customize severities (*n* = 2)

CDS = clinical decision support, DDI = drug-drug interaction.

*The *n* value for each theme represents the total number of times the theme was mentioned over the course of the 3 focus groups.

colour could be implemented for the highest severity of interaction (i.e., the combination of medications should be avoided). Conversely, the colour green could be used to indicate less severe interactions, for which the clinical decision would be to simply monitor therapy.

Another interesting suggestion was to have a way of documenting that a specific DDI had been reviewed by a specific person, who would be different from the person who verified the entire order. For example, the pharmacist would be prompted to enter his or her initials once the DDI had been verified. Limiting duplication (e.g., for cases of the same drug by multiple routes) would also substantially reduce alert fatigue. Finally, customization of severities was commonly mentioned throughout the focus groups. Customization is a feature of the software that allows hospital sites to select certain DDIs to be turned on or off, depending on their frequency of occurrence at the specific hospital site. In contrast to the identification of clinically relevant DDIs by a team of pharmacists, customization may be carried out by nonpharmacist staff members.

DISCUSSION

The findings of this study indicate that pharmacists believe the CDS software systems perform suboptimally when it comes to detecting clinically important DDIs. Discrepancies among the hospital CDS software systems in terms of severity assigned to specific DDIs cause pharmacists to utilize other resources (e.g., Lexicomp database) to thoroughly assess the DDIs, leaving less time to care for their patients. When it came to actually assessing a DDI, participants explained that they often went through a series of questions before they could confidently act upon the DDI. An important question they often ask themselves is "What are the ramifications of dispensing the medications involved in this DDI?" Alert fatigue was determined to be a major contributor to pharmacists missing DDI alerts; however, other barriers, such as lack of resources in the dispensary and lack of time when performing clinical duties, can also prevent pharmacists from fully assessing DDIs. In addition, because pharmacists have multiple duties throughout the day, they may not be entirely focused on the job at hand, with the distractions causing them to miss DDIs. Many of the focus group participants proposed potential solutions to improve drug alert detection rates. Periodic review of the DDIs embedded in the CDS systems was the most common recommendation.

Four main categories of themes were identified in the focus group data: perceived challenges, pharmacists' assessment of DDIs, barriers to responding to alerts, and proposed solutions. Although alert fatigue was identified as a major contributor to the underdetection of DDIs, several other barriers also impeded the optimal workflow of pharmacists.

This study aimed to gain a better understanding of how pharmacists assess common DDIs and the extent to which computer drug alerts affect their decision-making. Similar to previous studies, we found that a discrepancy in severity exists among the DDIs identified by the CDS software systems. In a review of 30 million prescriptions dispensed in a community pharmacy, the pharmacists considered only 5.7% of initially detected DDIs to be clinically relevant.[11] This may be partially due to the absence of a universal policy for organizing the severity of DDIs.[5] The severity rating associated with individual DDIs comes primarily from in vitro studies, case reports, and retrospective reviews, there being no studies that have specifically evaluated the clinical effects of DDIs.[5] Furthermore, the CDS systems do not take into consideration an individual patient's characteristics or the dosing modifications and precautions already taken by health care professionals, leading to the frequent reporting of DDIs that are irrelevant.[11] As a result, health care professionals may not find the CDS software systems to be an accurate source for detecting DDIs. Additionally, there may be differences in the perceptions of hospital versus community pharmacists, dependent upon the practice setting. In the hospital setting, there is more capability to monitor the patient, so a hospital pharmacist may be less likely than a community pharmacist to act upon a DDI. As in previous studies, our study also found that pharmacists were more likely to act upon a DDI that could have an immediate effect resulting in patient harm or the inefficacy of one or more medications.[5]

During initial assessment of a DDI's clinical relevance, pharmacists reported that they most often considered the immediate effects of the interactions if the medications were to be dispensed by them. They might then consider other clinical questions to help determine whether they should act upon the DDI alert. Although pharmacists are typically more concerned with the immediate effects of a DDI, delayed effects are just as important and may be missed if they are not considered with the same priority as immediate effects. In addition, because of the unreliability of the CDS systems, pharmacists often have to utilize additional resources to complete their clinical assessment of a DDI. The process illustrates the thorough job that pharmacists do in assessing DDIs but also alludes to the increased workload and pressures on their time that may result. It was also found that the pharmacists' level of experience affected their decision-making

regarding DDIs, with more recent pharmacy graduates flagging most of the DDIs identified by the system. These practitioners may lack the clinical experience of a pharmacist who has been working for many years and has had the opportunity to witness the clinical result of the interaction in question. Newer pharmacists also expressed concern about liability and did not want to do anything that might jeopardize their newly started career. Given these findings, we suggest that an algorithm be developed as a universal tool for all pharmacists to use in assessing DDIs. Such a tool would alleviate the fears of newly practising pharmacists.

This study revealed that, in addition to alert fatigue, pharmacists felt they were too busy to address all of the DDI alerts. The medicolegal implication of this perception is that a pharmacist would become liable if they dispensed the medications involved in a DDI that resulted in potential harm or inefficacy. Nonetheless, the heavy workload contributes to pharmacists not identifying clinically significant DDIs. As is the case for community pharmacists, hospital pharmacists are often multitasking, and the chances of completing any given task without interruption are low. As a result of interruptions, pharmacists may lose their concentration on the task at hand, which may lead to medical errors and patient harm.[1] Furthermore, interruptions in the thought process may impair a pharmacist's memory to follow up on DDI alerts that were flagged. Alternatively, unexplored reasons for not resolving DDIs may be clinical inertia, lack of knowledge, or lack of skills concerning which DDIs are clinically significant.

Several suggestions for improvement have been described to overcome alert fatigue. The findings in our study were similar to those of Australian research, which evaluated the design of CDS alerts, to increase the effectiveness of DDI alerts.[12,13] However, those studies focused on computerized physician order entry, whereas our research focused on pharmacists. Periodic review of the DDIs embedded in the CDS systems by a team of pharmacists might help to identify which DDIs are clinically relevant. Having at least one member of the review panel with a pharmacy background would be vital to help ensure that only those DDIs that are relevant pop up, to reduce alert fatigue. Having someone who is familiar with the issue of duplication (e.g., same drug by multiple routes) would also help to decrease the number of alerts. In addition, customization has the advantage of allowing a focus on those alerts that are clinically significant at the particular hospital site.[10] Although customization would solve some of the issues associated with alert fatigue, there are also concerns. For example, turning certain DDI alerts on or off at the discretion of any pharmacy staff member might cause interactions of higher severity to be missed, as different pharmacists will have different perceptions of what DDIs are irrelevant. The practicality of determining which DDIs should be allowed and which should be blocked may have medicolegal implications. The tailoring of DDI alerts to be turned off according to the preference of individual hospital sites may result in the manufacturer of the CDS system being absolved of liability, should adverse events occur. Site-specific customization may also cause variability in the performance of the CDS systems. One disadvantage of removing DDI alerts pertaining to "same drug, multiple routes" would be that patients who receive 2 similar medications may be at increased risk of harm. For example, if a patient had prescriptions for 2 different nonsteroidal anti-inflammatory medications and the DDI alert was overlooked, the patient might experience serious consequences from the duplication of therapy, such as acute renal failure. Although a colour-coding scheme might help to differentiate the various severity levels, this idea has limitations. Pharmacists might interpret "green" to mean that no action is required and might not implement an appropriate monitoring plan for the patient. Yellow alerts might be considered less critical and thus might be overlooked, but in fact this designation might reflect a potential delayed interaction that does require action. Also, alert fatigue can occur with any system that has multiple flags (such as a system of colour coding), and difficulties may be encountered in assigning the appropriate colour to each DDI.

This study had several limitations. The focus groups were held at 3 large tertiary hospitals. Pharmacists working at smaller sites or in different settings may use different computer systems and may have different experiences. Only 1 dispensary-only pharmacist was able to participate in the study. Pharmacists whose duties are limited to the dispensary may have different perceptions of DDIs than pharmacists with dual job duties (dispensary and clinical). One of the major limitations in developing a system that alerts the most clinically relevant DDIs is its subjectivity, as there is little evidence to guide practice and variability in terms of how pharmacists would act upon DDIs, depending on level of experience and prior knowledge. To overcome this limitation, higher-quality overall monitoring of the clinical effects of the DDIs themselves are needed, to guide what should be done in practice. At some sites, the study investigators had to independently encourage pharmacist participation to reach the target size of the focus groups, which might have introduced selection bias. Because this was a qualitative study using focus group methodology, the analysis and interpretation of the results were subjective. Lastly, the number of times that a theme was mentioned may not necessarily depict the "truth" and may not indicate the strength of agreement among participants. Rather, the intent of qualitative research is to explain the underlying reasons for certain observations.

CONCLUSION

The pharmacists who participated in this study believed that definitions of interaction severity differed among the various CDS software systems, which meant they had to look to secondary and tertiary resources to determine whether a DDI was clinically significant. When assessing DDIs, the pharmacists' first step was to assess whether the DDI would have an immediate effect and

what the implications of that effect would be for patients. Alert fatigue was a major problem in DDI alerts being overlooked; however, other barriers do exist, which result in pharmacists being unable to completely focus on evaluating the DDIs. This study did not specifically reveal the benefits of CDS systems; however, there are apparent benefits to having a more efficient CDS system. In addition, a more reliable CDS software system, which detects only those DDIs with clinical relevance, would allow pharmacists to improve their drug alert detection rates, thus reducing the amount of time spent consulting secondary references and increasing the time allocated to patient care. Future research should explore whether the DDIs that pharmacists prioritize and those that the CDS software system flags are in agreement and of clinical importance.

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Competing interests: None declared.

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Funding: None received.

Acknowledgements: The authors thank Ilena Djuana and Kevin Hong, research assistants, for their help in taking notes during the focus group sessions and transcribing the audio-recordings.

Analysis of Real-World Experiences with the Ontario MedsCheck Program

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ABSTRACT

Background: The Ontario MedsCheck program was introduced in April 2007, with enhancements to strengthen the program made in October 2016. Previous literature has characterized patients who received the service before the enhancements and described the experiences of community pharmacists and physicians, but the experiences of participants in the enhanced MedsCheck program and those of hospital pharmacists and pharmacy technicians have not been explored.

Objectives: This study was designed to describe and compare the demographic and clinical characteristics of patients admitted to Sunnybrook Health Sciences Centre (SHSC) who had received a MedsCheck before and after the program enhancements of 2016. The study also aimed to describe the experiences of patients, hospital pharmacists, and pharmacy technicians with the MedsCheck program.

Methods: Chart reviews were completed to identify and characterize patients who had received a MedsCheck and were admitted to SHSC between March and May 2016 (retrospective cohort) and between March and May 2017 (prospective cohort). Patients were interviewed and focus groups were conducted with pharmacy staff to explore their experiences with the MedsCheck program.

Results: MedsChecks had been performed for 321 (14.5%) of 2216 patients in the retrospective cohort and 172 (6.8%) of 2547 patients in the prospective cohort, an absolute decline of 7.7% after the 2016 enhancements. Patient characteristics were similar between the 2 cohorts. Patients' experiences were varied, but because of low enrolment in the interview process (n = 3), it was difficult to identify and summarize common themes. The analysis of focus groups involving pharmacy staff (n = 27 participants) revealed that the benefits of MedsChecks depended on quality and access, and also identified common barriers and opportunities for future enhancements.

Conclusions: Patient interviews revealed the features of the program that patients valued. Pharmacy staff identified several benefits and barriers encountered when using MedsChecks. These findings can guide clinicians in optimal application of the current MedsCheck program and can inform subsequent program revisions.

Keywords: patient preference, hospital pharmaceutical services, community pharmacy services, MedsCheck, medication review

RÉSUMÉ

Contexte : En avril 2007, l'Ontario a introduit le programme MedsCheck assorti d'améliorations visant à renforcer le programme élaboré en octobre 2016. La documentation antérieure décrivait l'expérience des patients recevant le service ainsi que celle des pharmaciens et des médecins communautaires avant les améliorations, mais les expériences des participants au programme MedsCheck amélioré ainsi que celles des techniciens en pharmacie et des pharmaciens d'hôpitaux n'avaient toutefois pas été étudiées.

Objectifs : Cette étude a été conçue pour décrire et comparer les caractéristiques démographiques et cliniques des patients admis au Sunnybrook Health Sciences Centre (SHSC) qui ont reçu un MedsCheck avant et après les améliorations apportées au programme de 2016. L'étude vise également à décrire les expériences qu'ont faites les patients, les pharmaciens d'hôpitaux et les techniciens en pharmacie avec le programme MedsCheck amélioré.

Méthodes : Des examens de graphiques ont permis d'identifier et de caractériser les patients admis au SHSC entre mars et mai 2016 (cohorte rétrospective) et entre mars et mai 2017 (cohorte prospective), ayant reçu un MedsCheck. Les patients ont été interrogés et des groupes de discussion avec le personnel de pharmacie ont été organisés pour étudier les expériences qu'ils ont faites avec le programme MedsCheck.

Résultats : Des MedsChecks ont été effectués auprès de 321 patients (14,5 %) sur les 2216 dans la cohorte rétrospective, et de 172 patients (6,8 %) sur les 2547 dans la cohorte prospective : une diminution de 7,7 % après les améliorations apportées en 2016. Les caractéristiques des patients étaient similaires dans les deux cohortes. Les expériences des patients étaient variées, mais la faible inscription au processus d'entretien (n = 3) n'a pas permis de déterminer et de résumer les thèmes communs. L'analyse des groupes de discussion comprenant des membres du personnel de pharmacie (n = 27 participants) a révélé que les avantages du programme MedsChecks dépendaient de la qualité de l'information fournie par le programme et de l'accès à cette information, et elle a aussi permis de cibler les obstacles courants et des possibilités d'améliorations futures.

Conclusions : Les entretiens avec les patients ont révélé les caractéristiques du programme que les patients appréciaient. Le personnel de pharmacie a relevé plusieurs avantages et quelques obstacles liés à l'utilisation du programme MedsChecks. Ces résultats peuvent faciliter l'application optimale du programme MedsCheck actuel par les cliniciens et orienter les révisions ultérieures.

Mots-clés : préférences des patients, services pharmaceutiques en hôpital, services des pharmacies communautaires, MedsCheck, examen des médicaments

Can J Hosp Pharm. 2019;72(4):295-300

INTRODUCTION

The Ontario MedsCheck program aims to improve patients' medication knowledge, to optimize the safety and effectiveness of medication therapy, and to facilitate communication of patient information to the interdisciplinary team.[1] It also aims to promote adherence, healthier patient outcomes, and disease self-management.[1] MedsChecks provide an opportunity for pharmacists to review patients' prescription and nonprescription medications, as well as their medication-taking behaviour.[1]

The program began in 2007 with the MedsCheck Annual and has since been expanded to include MedsCheck Follow-Up, MedsCheck at Home, MedsCheck for Diabetes, and MedsCheck Long-Term Care.[1] On October 1, 2016, the Ontario government launched enhancements to strengthen the program. The changes included introduction of a MedsCheck brochure for patients, a standardized patient acknowledgement form, a pharmacist worksheet for professional notes, a standardized MedsCheck personal medication record, a take-home summary for the patient, and a standardized notification template for the health care provider.[1] These changes represented a significant increase in workload and documentation over previous versions.

About 1 in 9 Ontarians have received a MedsCheck,[2] and patients who receive MedsChecks are taking an average of 8 to 11 medications,[2-5] have multiple comorbidities,[2] and are more likely (relative to those not receiving the service) to be taking a high-risk medication.[6] It is important to consider that comorbidities, number of medications, and complexity of the medical situation may not indicate how well patients understand their medications or their desire to receive education about their medications.

Previous studies of medication review programs have explored the experiences of community pharmacists and physicians. In a study at an ambulatory internal medicine clinic, medical residents agreed that having access to MedsCheck records saved time when gathering a medication history, that they consulted medication lists when making treatment decisions, and that having an up-to-date medication list allowed them to provide better care.[5] Community pharmacists reported a beneficial effect on job satisfaction, improved interprofessional communication, and improved patient-pharmacist relationships, and they appreciated the opportunity to provide patient education and create more accurate and complete patient profiles.[7]

Hospital pharmacists and pharmacy technicians use MedsChecks to assist in gathering a medication history. However, the MedsCheck experiences of these health care professionals have not yet been explored. In addition, little is known about patients' experiences with the MedsCheck program. Several researchers have conducted surveys to determine patients' attitudes regarding the role of the pharmacist and interest in expanded pharmacy services,[5,8-10] and the types of patients who receive the MedsCheck service have been well documented.[2,3] However, few studies have explored the patient experience in depth. The objectives of this study were to quantify and characterize patients who received a MedsCheck and were admitted to Sunnybrook Health Sciences Centre (SHSC) in 2017 (after enhancements to the program), for comparison with a cohort of patients admitted in the same period of the previous year (before enhancements). The study also aimed to describe the experiences of patients, hospital pharmacists, and pharmacy technicians with the MedsCheck program.

METHODS

This study was approved by the Research Ethics Board at SHSC. The study had 2 components: a retrospective chart review and a prospective data collection phase. Both quantitative and qualitative data were collected.

The retrospective period was defined as March 1 to May 31, 2016, and the prospective period as March 1 to May 31, 2017. The study periods were selected for convenience, given the time constraints of a residency project.

Identification and Consent of Participants

At the study institution, every patient admitted to the emergency department is flagged by the hospital's electronic patient management system and is subsequently seen by one of the institution's pharmacy technicians for completion of the admission best possible medication history (BPMH). For purposes of this study, the charts of all patients identified by this method (in both cohorts) were reviewed, and community pharmacy dispensing records were used to identify those patients for whom a MedsCheck had been completed before the admission. In addition, during the prospective data collection period, patients eligible for interviews were identified by pharmacy technicians when they were completing the admission BPMH. Pharmacy technicians obtained written informed consent from those who agreed to participate.

Eligible pharmacy staff were invited by email to participate in a focus group. One researcher (A.G.) obtained written informed consent from those who agreed to participate.

Inclusion Criteria

All patients admitted to the emergency department or an inpatient ward of SHSC and who were identified as needing a BPMH during the prospective study period were screened for this study. To be eligible for the interview, patients had to be able to provide informed consent and to participate in a telephone interview after discharge.

All hospital pharmacy staff (pharmacists and pharmacy technicians) who were responsible for gathering a BPMH for newly admitted patients were invited to participate in a focus group.

Data Collection

For both the retrospective and prospective cohorts, the charts of patients admitted to inpatient units or the emergency department were reviewed to obtain clinical characteristics and demographic data (age, sex, number of medications, number of prescribers, number of pharmacies, pharmacy type, and place of residence).

Patients who were identified as having had a MedsCheck before the admission and who agreed to participate were interviewed using a semistructured telephone interview (Appendix 1, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/191/showToc). The interview questions were reviewed in advance with a patient volunteer to verify understandability and use of patient-friendly language. The postdischarge telephone interview format was chosen to reduce the influence of stressors due to hospital stay, to minimize distractions in the hospital environment, and to increase convenience for the patient.

The experiences of pharmacy staff were gathered by means of focus groups (Appendix 2, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/191/showToc). This mode of data collection was chosen to utilize group dynamics to generate ideas, gather a broad range of ideas in a limited amount of time, and minimize workflow disruption for staff.

The interviews and focus groups were recorded and transcribed by one researcher (A.G.).

Data Analysis

Descriptive statistics (means, standard deviations [SDs], medians, frequencies, and percentages) were used to describe patients' demographic and clinical characteristics.

Transcriptions of the interviews and focus groups underwent content analysis to identify, code, and categorize emergent themes. The themes were reviewed and categorized to create a set of codes. Finally, the transcripts were read again to facilitate application of the codes and to highlight associated passages. Two reviewers (A.G., A.D.) reviewed the transcripts independently and met to reach consensus on the final themes.

RESULTS

A total of 4763 patients were screened: 2216 patients in the retrospective cohort and 2547 in the prospective cohort. The number of patients with a prior MedsCheck was 321 (14.5%) in the retrospective cohort and 172 (6.8%) in the prospective cohort. This represents a 7.7% absolute reduction in the proportion of patients with a MedsCheck admitted to SHSC after the 2016 enhancements to the program.

The demographic and clinical characteristics of the retrospective and prospective cohorts were compared (Table 1). No major differences between the cohorts were identified.

The pharmacy staff involved in the study consisted of 22 clinical pharmacists from various practice areas across the hospital and 5 registered pharmacy technicians, who were responsible for conducting BPMHs.

Review of the interview and focus group transcriptions revealed 4 major themes: quality, benefits, barriers, and collaboration (see Box 1 and Box 2). There was limited enrolment of patients for interviews (n = 3), so the themes and quotations presented here are derived from focus groups involving pharmacy staff, unless otherwise noted.

Quality of MedsChecks

Most of the comments relating to the quality of MedsChecks identified inconsistent or poor quality. Factors relating to poor quality included missing or inconsistent information, illegibility of information recorded on forms, variation between individual pharmacists and between types of pharmacies, hasty completion of MedsChecks, and completion of MedsChecks by someone other than a licensed pharmacist. The focus group participants reflected that some of these quality issues are linked to barriers experienced by community pharmacists.

Benefits

The second major theme was benefits. Focus group participants noted that MedsChecks can serve as a good source of information for physicians, allied health professionals, and caregivers and that they provide a representation of the patient in a non–acute care setting. Pharmacy staff believed that MedsChecks can increase patients' knowledge about medications; however, this perception was not supported by findings from patient interviews. Nevertheless, a MedsCheck generates an up-to-date medication list that the patient can refer to and share with various health care providers, which focus group participants characterized as an important benefit.

Additionally, both patients (in interviews) and pharmacy professionals (in focus groups) discussed several benefits of the clinical analysis that occurs during a MedsCheck, including the identification and prevention of medication errors. The pharmacy professionals also identified the MedsCheck as an opportunity to generate suggestions for medication changes (which could then be communicated to the patient's primary physician).

Finally, focus group participants believed that MedsChecks can help to establish the role of pharmacists and to facilitate the development of patient-pharmacist rapport. Hospital pharmacy staff noted that this understanding of the role of a pharmacist can facilitate BPMH interviews while the patient is in hospital.

Barriers

Patients and focus group participants identified many barriers to optimal MedsChecks, including inadequate time spent completing the MedsChecks and lack of preparation on the part of patients (because the service is often not appointment-based). Inappropriate patient selection was identified as a barrier by both patients and hospital pharmacy staff, which suggests that

community pharmacists may not be offering MedsChecks to patients with the most complex medication regimens or those who are struggling to understand their medications. Finally, even when MedsChecks have been completed, they are not being utilized to their full potential, because pharmacy staff prefer to rely on other information sources, and patients do not carry their MedsCheck documents or share them with health care providers.

Collaboration

The final major theme was collaboration. Pharmacy staff reported that they encountered resistance when requesting MedsChecks from community pharmacies and were frustrated with the lack of access; this was such a common problem that some participants reported that they had stopped asking for MedsChecks documents altogether. Others believed that MedsChecks are nearly useless if the findings cannot be shared with other health care providers. Pharmacy staff felt that the program would benefit from increased collaboration between health care providers, and some cited examples of times when they had tried to engage patients so as to involve other health care providers.

Opportunities for Improvement

Future directions to improve the MedsCheck program for patients and hospital pharmacy staff were identified, which included increasing collaboration among health care providers, allowing community pharmacies to share MedsChecks via the Ontario government's eHealth Portal, updating the forms to include information that is valuable to hospital staff (e.g., medication-taking behaviours and caregiver names), and introducing accreditation or quality standards to improve quality and increase access. Other suggestions from focus group participants included integrating patient-level technology, such as medication management apps, to help patients record and use their medication lists or providing updates to the patient's current list of medications to make it more user friendly (e.g., use of wallet-sized cards, inclusion of information such as indication and pertinent warnings/cautions). Finally, participants in the focus groups identified the potential role of pharmacy technicians in the technical task of gathering information for MedsChecks in the community setting (similar to how some hospitals use pharmacy technicians to gather the BPMH) while still involving the pharmacist in the clinical review.

Table 1. Demographic and Clinical Characteristics of Patients

Characteristic	Cohort; No. (%) of Patients*	
	Retrospective Cohort (*n* = 321)	Prospective Cohort (*n* = 172)
Sex		
Male	161 (50.2)	92 (53.5)
Female	160 (49.8)	80 (46.5)
Age (years) (mean ± SD)	75.3 ± 13.3	76.4 ± 12.9
No. of medications (mean ± SD)	9.8 ± 4.5	9.8 ± 4.6
Pharmacy type performing MedsCheck		
Chain	187 (58.3)	114 (66.3)
Independent	134 (41.7)	58 (33.7)
Place of residence		
Home	301 (93.8)	152 (88.4)
Long-term care facility	20 (6.2)	20 (11.6)
No. of prescribers per patient (mean ± SD)	4 ± 2.3 (*n* = 316)	3.9 ± 2.4
No. of pharmacies per patient (mean ± SD)	1.7 ± 1 (*n* = 319)	1.8 ± 1
Medications		
Antidepressants	74 (23.1)	51 (29.7)
Antihyperglycemics	78 (24.3)	52 (30.2)
Antihypertensives	263 (81.9)	136 (79.1)
Antilipidemics	203 (63.2)	105 (61.0)
Benzodiazepines	51 (15.9)	25 (14.5)
Gastroprotective agents	155 (48.3)	89 (51.7)
Insulin	32 (10.0)	22 (12.8)
Narcotics	77 (24.0)	46 (26.7)
Osteoporosis medications	32 (10.0)	19 (11.0)
High-risk medications†	268 (83.5)	141 (82.0)

*Except where indicated otherwise.
†High-risk medications are listed in Appendix 3 (available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/191/showToc).

Box 1. Sample Views of Pharmacy Staff (Focus Groups)

Quality of MedsChecks

"I think we see a huge difference in good quality versus poor quality, so it's hard to say. When we do see the good quality ones […] we can't say that's not valuable because it's clearly valuable."

"We've all been disappointed with some of the quality."

"The quality is hit and miss."

"I find it variable. I think it depends on the one you get and who's doing it."

"The potential is there but it's not done well."

Benefits of MedsChecks

"I think it's important because it's another source, another piece of information."

"The good quality lists usually come from the patient, so it's a MedsCheck that they have, that they recognize is accurate and they keep in their wallet or purse with them."

"I think it's a great platform for the community pharmacist. Especially in terms of re-establishing the communities' understanding of what the potential role of the community pharmacist is."

Barriers to using MedsChecks

"I have to admit, I don't really use it. I start from scratch."

"I've never […] seen a patient have a MedsCheck with them."

"I've never found them to be useful personally."

Collaboration related to MedsChecks

"Getting them is the hardest part."

"Majority of the time I haven't even bothered to chase after it."

"So, I kind of stopped asking them anymore because of the resistance that I see."

"There is no point in gathering that information if it's just going to be stored in the corner somewhere."

"I just think as a whole, the medical field, all of us, need to work closer with each other. I mean as a whole, if we have information it's good to give to them and then vice versa."

Box 2. Sample Views of of Patients (Interviews)

Benefits of MedsChecks

"They helped me clear my mind about my medications and I wasn't nervous that I was taking the wrong thing."

"There were some [medications] that she didn't think were quite necessary and she spoke about those and she crossed them out and I took them to my doctor and my doctor did the rest."

"[They] went through all my medications with me, made sure that I was taking what I was supposed to be taking, that everything was up to date."

Barriers to using MedsChecks

"I would have appreciated if they had taken just a little bit more time."

"It could be important for *somebody* who does not know [about their medications]."

"I think it would certainly be beneficial for *other patients* that ... might not be as knowledgeable about the medications."

DISCUSSION

In this study, we have described the patients who received a MedsCheck and were admitted to an acute care hospital before and after the introduction of program enhancements in 2016. Changes in the MedsCheck program may have reduced the proportion of patients admitted to SHSC with a MedsCheck completed; however, the characteristics of patients who received this service remained the same. Additionally, we have described the experiences of patients, hospital pharmacists, and pharmacy technicians with the MedsCheck program. Pharmacy staff clearly identified benefits and barriers that were largely dependent on quality and access. Opportunities for improvement were also identified, such as the need for increased collaboration and communication, including ease of access to MedsChecks documentation to improve seamless care.

Given the time constraints of a residency project, we restricted our data-gathering to a period of 3 months in each calendar year, and we did not achieve saturation of themes during the patient interviews because of the low sample size. Our results may not be generalizable across Ontario, because they do not represent individuals from rural areas or those admitted to smaller hospitals. Finally, we did not collect outcome data, so we cannot comment on whether undergoing a MedsCheck was associated with changes in outcomes (such as likelihood of being admitted to hospital for adverse effects caused by multiple medications or likelihood of taking an inappropriate medication).

Despite these limitations, we were able to characterize patients who received a MedsCheck before and after the 2016 program enhancements and to describe experiences with the program. To our knowledge, this was the first study to examine the experiences of hospital pharmacists and pharmacy technicians with the MedsCheck program; however, given the lack of previous literature, our findings for hospital pharmacy staff cannot be compared with data for other health professionals. Perceived benefits of the program, such as generating a medication list and establishing the role of the pharmacist, indicate aspects of the program that are currently working well for patients and pharmacy staff. Opportunities for future program enhancements relate to barriers identified by the focus group participants, such as poor quality, illegibility, inability to locate or share MedsChecks findings, inappropriate patient selection, and lack of collaboration. These opportunities could be addressed in various ways, such as standardized education, peer-to-peer education (between hospital and community pharmacists), electronic forms (ideally uploaded to a web-based portal, such as the ConnectingOntario Clinical-Viewer, to allow multiple providers to view the information), and perhaps a review of patient eligibility criteria.

CONCLUSION

These findings can guide community pharmacists in the optimal use of the current MedsCheck program, and the opportunities for improvement identified can inform subsequent program revisions. Future studies could further explore the patient perspective and examine the association between MedsChecks findings and patient outcomes.

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Competing interests: None declared.

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Funding: None received.

Pediatric Pharmacy Services in Canadian Adult Hospitals: An Inventory and Prioritization of Services

Amanda Burns, Leslie Manuel, Andrew Dickie, and Jennifer Bessey

ABSTRACT

Background: The rate of potential adverse drug events is reported to be 3 times higher among pediatric inpatients than among their adult counterparts. Various methods have been suggested to reduce medication errors in pediatric patients. One of the most influential of these strategies is inclusion of a clinical pharmacist on the multidisciplinary care team. However, there is currently no literature describing the inventory of pharmacy services provided to pediatric patients in Canadian adult hospitals.

Objectives: The primary objective of this study was to describe pediatric and neonatal pharmacy services provided in adult hospitals in Canada. The secondary objective was to determine whether the services provided correspond to services that pharmacists working in Canadian pediatric hospitals identified as important for adult hospitals that provide pediatric services.

Methods: Two web-based surveys were created, focusing on 35 pharmacy services. The first survey was intended for adult hospitals, and the second for pediatric hospitals. The surveys were distributed by e-mail and were completed in January and February 2018.

Results: A total of 55 and 43 valid responses were received from respondents in adult hospitals and pediatric hospitals, respectively. An inventory of pharmacy services provided by adult hospitals to their pediatric and neonatal patients was obtained. Of the adult hospitals that responded, 61% (33/54) had pharmacists assigned to pediatric or neonatal units. The frequency with which most pharmacy services were provided was comparable to the importance identified by pharmacists working in pediatric hospitals. However, for the provision of education during admission and at discharge and for the provision of medication reconciliation at discharge, frequency and importance were not comparable.

Conclusions: Adult hospitals with a pharmacist assigned to an inpatient pediatric or neonatal clinical area met most expectations of pharmacists working in pediatric hospitals in terms of pharmacy services provided. However, some services require optimization for this patient population.

Keywords: pediatric patients, neonate/neonatal, pediatric pharmacy services, pharmacists, Canada, adult hospitals, pediatric hospitals

RÉSUMÉ

Contexte : On rapporte que le taux de réactions indésirables potentielles aux médicaments est trois fois plus élevé chez les enfants hospitalisés que chez les adultes. Diverses méthodes ont été proposées pour réduire les erreurs de médication chez les patients pédiatriques. L'une des stratégies les plus influentes consiste à inclure un pharmacien clinique au sein de l'équipe de soins pluridisciplinaire. Cependant, il n'existe actuellement aucun document dressant l'inventaire des services de pharmacie offerts aux patients pédiatriques dans les hôpitaux canadiens pour adultes.

Objectifs : L'objectif principal de cette étude consistait à décrire les services de pharmacie pédiatriques et néonataux offerts dans les hôpitaux pour adultes au Canada. L'objectif secondaire consistait quant à lui à déterminer si les services offerts à la population pédiatrique dans les hôpitaux pour adultes correspondaient à ceux que les pharmaciens travaillant dans les hôpitaux pédiatriques canadiens reconnaissaient comme étant importants.

Méthodes : Deux sondages en ligne se focalisant sur 35 services de pharmacie ont été créés. Le premier était destiné aux hôpitaux pour adultes et le deuxième aux hôpitaux pédiatriques. Les sondages ont été distribués par courriel et effectués en janvier et février 2018.

Résultats : Cinquante-cinq (55) répondants des hôpitaux pour adultes et 43 des hôpitaux pédiatriques y ont répondu en bonne et due forme. Les investigateurs ont obtenu en outre la liste des services de pharmacie offerts par les hôpitaux pour adultes à leurs patients pédiatriques et néonataux. Soixante et un pour cent (61 %), soit 33 sur 54, des répondants provenant des hôpitaux pour adultes à étaient des pharmaciens affectés aux unités pédiatriques ou néonatales. La fréquence de l'offre de la majorité des services de pharmacie était d'importance comparable à ce que les pharmaciens travaillant dans les hôpitaux pédiatriques ont relevé. Toutefois, pour ce qui est des instructions données au patient à l'admission et au congé et de la prestation du bilan des médicaments au congé, la fréquence et l'importance de ces services n'étaient pas comparables.

Conclusions : Les hôpitaux pour adultes disposant d'un pharmacien affecté à un domaine clinique pédiatrique ou néonatal répondaient à la plupart des attentes des pharmaciens travaillant dans les hôpitaux pédiatriques en termes d'offre de services de pharmacie. Cependant, certains services demandent à être optimisés pour cette population de patients.

Mots-clés : patients pédiatriques, nouveau-nés / néonatal, services de pharmacie pédiatrique, pharmaciens, Canada, hôpitaux pour adultes, hôpitaux pédiatriques

Can J Hosp Pharm. 2019;72(4):301-10

INTRODUCTION

The pediatric population is a vulnerable group, especially when receiving medications, with multiple contributing factors. As a child develops, there are ongoing changes to body composition and physiology, which can affect pharmacokinetic parameters, such as absorption, distribution, metabolism, and excretion. In addition, most dosing is based on patient-specific calculations using weight, age, or body surface area.[1] Numerous medications are unavailable in suitable child-friendly formulations and strengths, which results in the need to manipulate dosage forms. These factors contribute to an increased risk of pediatric patients being exposed to a 10-fold or greater medication error.[1]

Kaushal and others[2] found that the rate of medication errors, adverse drug events (ADEs), and preventable ADEs in pediatric inpatients was similar to that reported for adult inpatients. However, the rate of potential ADEs—defined as medication errors with a significant potential to injure the patient—is reportedly 3 times higher in the pediatric population than in adults, and is substantially higher in neonates than in other age groups.[2] Furthermore, neonates in the neonatal intensive care unit (NICU) are subject to a higher rate of medication errors and potential ADEs than neonates in other wards.[2]

The Joint Commission[3] and the American Academy of Pediatrics[4] have released guiding documents regarding the prevention of medication errors in pediatric inpatients. Among these risk-reduction recommendations is an emphasis on including a clinical pharmacist on the multidisciplinary care team.

Various methods have been suggested to assist in the reduction of medication errors. Fortescue and others[5] analyzed 10 medication error-prevention strategies for pediatric inpatients. They determined that the presence of ward-based clinical pharmacists could have resulted in an 81.3% reduction in the rate of medication errors and could have prevented 88.3% of potentially harmful errors.[5] In another study with similar results, physician reviewers judged that 94% of the potential ADEs and 4 of the 5 preventable ADEs could have been prevented by ward-based clinical pharmacists.[2]

Published studies have identified numerous benefits of pharmacist-led interventions for pediatric inpatients. For example, the presence of a clinical pharmacist in the pediatric intensive care unit can reduce the rate of serious medication errors by 79%.[6] The most common intervention implemented by ward-based clinical pharmacists has consisted of changing drug dose regimens,[7-9] given that most intercepted errors occurred at the physician ordering stage.[6] Furthermore, increased presence of a clinical pharmacist in the pediatric intensive care unit was positively correlated with an increase in the number of interventions.[8]

The 2016/2017 *Hospital Pharmacy in Canada Report* published data on pediatric pharmacy services. The report provided information for both adult hospitals and pediatric hospitals. Among the adult hospitals with pediatric and/or neonatal critical care units that responded to the survey, 76% reported having an inpatient pharmacist assigned to these areas.[10] However, this report did not capture details regarding the amount of pharmacist coverage or the type of services offered. Currently, there is no literature describing the inventory of pharmacy services provided to pediatric or neonatal patients within adult hospitals in Canada.

The primary objective of this study was to describe pediatric and neonatal pharmacy services provided in adult hospitals in Canada. The secondary objective was to determine whether the services provided correspond to services that pharmacists working in Canadian pediatric hospitals identified as important for adult hospitals that provide pediatric services.

We hypothesized that in adult hospitals with an assigned pediatric pharmacist, the services that are frequently provided would correspond to those with greater importance, as identified by pharmacists working in pediatric hospitals.

METHODS

Participants

Canadian adult hospitals were identified through the websites of provincial and territorial health authorities. In addition, internet searches were performed to identify hospitals not affiliated with a provincial or territorial health authority. Each health authority or hospital was reached by telephone to obtain contact information for the pharmacy director, pharmacy manager, or an alternate contact, as appropriate. Adult hospitals were included in this study if their facilities had an inpatient pediatric unit or NICU. Within this population, pharmacy managers, designates of the pharmacy manager, or pharmacists in pediatric or neonatal clinical roles were invited to participate. Canadian pediatric hospitals were identified through the Canadian Association of Paediatric Health Centres[11] and were reached by telephone to obtain contact information for their respective pharmacy managers. Within this population, pharmacists in a clinical role were invited to participate. This population was chosen as the reference, because these clinical pharmacists specialize in pediatrics and experience greater patient volume and acuity than pharmacists who care for pediatric patients in adult hospitals. Including their perspective may allow for greater understanding of the needs of this patient population.

Materials

An initial set of questions was developed to obtain an inventory of pharmacy services provided to pediatric and neonatal patients in adult hospitals. A second set of a similar number of questions was created to determine the importance rating of these pharmacy services according to pharmacists working in pediatric hospitals. Several aspects of the questions surrounding pharmacy services were adapted from relevant publications[12,13] and from studies that

investigated pharmacist-led interventions in pediatric inpatient units.[7-9,14,15]

Preliminary questions addressed information about the hospital respondents (e.g., type of hospital, total number of beds, total number of pharmacist full-time equivalents [FTEs], types of pediatric inpatient areas and corresponding number of beds, types of pediatric ambulatory care clinics, clinical pharmacist assignment and corresponding number of FTEs, and clinical pharmacy assistant/technician coverage and corresponding number of FTEs). The main section of each survey focused on 28 direct and 7 indirect patient care pharmacy services. In the survey of Canadian adult hospitals, participants were asked to identify how often the specified direct and indirect patient care pharmacy services were provided to pediatric and neonatal patients, according to a 5-point Likert scale, where the available options ranged from "never/not applicable" to "> once per day". In the survey of pharmacists working in Canadian pediatric hospitals, participants were asked to rank the same specified direct and indirect patient care pharmacy services in terms of their importance to be provided by adult hospitals to their pediatric and neonatal populations, according to a 5-point Likert scale, where the available options ranged from "not important/never" to "very important".

The surveys were initially distributed to a group of 5 pharmacists within Horizon Health Network, who assessed the appropriateness, comprehensiveness, clarity, and face validity of each survey. These 5 pharmacists were not excluded from participating in the survey, but they were not involved in survey administration or analysis of responses.

Procedure

The web-based surveys were available in English and French through the online research survey platform LimeSurvey, version 2.73.1 (2017; https://www.limesurvey.org/). A signed consent form was not required, because the survey was anonymous. However, each survey contained an informed consent page that detailed the purpose of and participation in the research study. Completion of the survey was deemed to imply that the participant had given consent.

Each web-based survey was distributed by e-mail to the corresponding population of interest, through pharmacy directors and pharmacy managers, the Canadian Society of Hospital Pharmacists (CSHP), and the Association des pharmaciens des établissements de santé du Québec. Each survey was available for a 5-week period in January and February 2018. One reminder was sent by e-mail to each potential participant at the halfway point. This study was reviewed and approved by the Horizon Health Network Research Ethics Board on December 1, 2017.

Statistical Analyses

Calculation of descriptive statistics, including means, standard deviations, and percentages, was the primary data analysis method. These measures were used to summarize hospital-related information, to describe the frequency with which pharmacy services were being provided by Canadian adult hospitals to their pediatric and neonatal populations, and to describe the importance ranking that pharmacists working in Canadian pediatric hospitals attributed to each given pharmacy service.

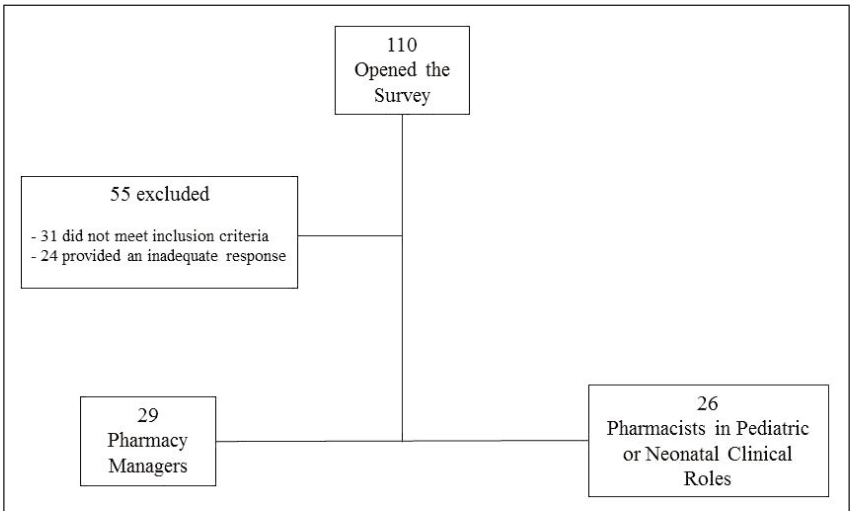

Figure 1. Responses to a web-based survey of pharmacy staff in Canadian adult hospitals. Responses that were excluded from further analysis did not meet the inclusion criteria or were inadequate for analysis.

The unit of analysis for the survey of Canadian adult hospitals was the hospital itself. If more than one response was received from the same facility, the primary investigator determined which response was most relevant and merged the data when appropriate. The unit of analysis for the survey of Canadian pediatric hospitals was the individual clinical pharmacist.

RESULTS

Survey of Canadian Adult Hospitals

A total of 55 valid responses were received from Canadian adult hospitals, which consisted of responses from 29 pharmacy managers and 26 pharmacists in pediatric or neonatal clinical roles (Figure 1). Representation from 9 provinces was achieved. The characteristics of these hospitals are presented in Table 1. Of the adult hospitals represented, 84% (46/55) were reported to have a general pediatric unit, and 69% (37/54) were reported to have a NICU. In terms of pharmacist assignment, 39% (21/54) of the adult hospitals were reported to have no pharmacist assigned to an inpatient pediatric or neonatal clinical area. The remaining 33 adult hospitals did have a pharmacist assigned to a pediatric or neonatal area: 50% (27/54) of all hospitals had pharmacists assigned to the NICU and 44% (24/54) had pharmacists assigned to the general pediatric unit. Among the 31 hospitals with pharmacists assigned to an inpatient pediatric unit that provided information about direct patient care, 11 (35%) reported that the pharmacists spent less than 25% of their day providing direct patient care, with 8 (26%) reporting that they spent more than 75% of their day providing direct patient care. This survey also collected information about the assignment of pharmacists to pediatric ambulatory care clinics. The majority (19/29 [66%]) of respondents from adult hospitals reported that no pharmacists were assigned to these areas. The remaining 10 adult hospitals did have a pharmacist assigned to pediatric ambulatory care clinics; the largest proportion of all respondents (7/29 [24%]) had a pharmacist assigned to a pediatric oncology clinic.

Overall, 33 (60%) of respondents from adult hospitals reported that no pharmacy learners completed experiential rotations in their pediatric or neonatal clinical areas. Of the 22 adult hospitals with pharmacy learners in these areas, 19 (86%) and 12 (55%) had pharmacist students and pharmacy residents, respectively. Other types of pharmacy learners identified included pharmacy technician students.

Table 1. Characteristics of Canadian Adult Hospitals*

Characteristic	No. (%) of Respondents†
Hospital type (*n* = 54)	
Teaching	38 (70)
Nonteaching	16 (30)
No. of beds in facility (*n* = 54)	
< 50	3 (6)
50–200	14 (26)
201–500	28 (52)
> 500	9 (17)
No. of pharmacist FTEs in facility (mean ± SD) (*n* = 52)	23.7 ± 35.0
Inpatient pediatric areas	
General pediatric unit (*n* = 55)	46 (84)
NICU (*n* = 54)	37 (69)
PICU (*n* = 54)	9 (17)
Pediatric mental health (*n* = 55)	15 (27)
Assignment of inpatient pediatric pharmacist (*n* = 54)	
None	21 (39)
General pediatric unit	24 (44)
NICU	27 (50)
PICU	5 (9)
Pediatric mental health	6 (11)
Assignment of inpatient pediatric clinical pharmacy assistant or technician (*n* = 52)	
None	44 (85)
General pediatric unit	3 (6)
NICU	7 (13)
Pediatric ambulatory care clinics (*n* = 53)	
None	24 (45)
Oncology clinic	13 (25)
Cardiology clinic	5 (9)
Respiratory clinic	10 (19)
Diabetes clinic	11 (21)
Assignment of pharmacist to pediatric ambulatory care clinic (*n* = 29)	
None	19 (66)
Oncology clinic	7 (24)
Cardiology clinic	1 (3)
Respiratory clinic	1 (3)
Assignment of clinical pharmacy assistant or technician to pediatric ambulatory care clinic (*n* = 30)	
None	28 (93)
Oncology clinic	2 (7)
Direct patient care/day provided by pharmacists assigned to inpatient pediatric unit (*n* = 31)	
< 25%	11 (35)
25%–50%	6 (19)
51%–75%	6 (19)
> 75%	8 (26)

FTE = full-time equivalent, NICU = neonatal intensive care unit, PICU = pediatric intensive care unit, SD = standard deviation.
*A total of 55 respondents provided data adequate for inclusion in the analysis; however, not all respondents answered every question on the survey. For each characteristic, the *n* value is shown.
†Except where indicated otherwise.

Survey of Pharmacists in Canadian Pediatric Hospitals

A total of 43 valid responses were received from pharmacists working in Canadian pediatric hospitals (Figure 2). Of the 7 provinces with pediatric hospitals, representation from 5 provinces was achieved. The practice characteristics of these pharmacists, including information about their hospital setting, are presented in Table 2. Overall, the majority of pharmacists working in a pediatric hospital reported practising in either the NICU, the pediatric intensive care unit, or a pediatric medical unit (12 [28%] each). In terms of direct patient care, nearly half (18 [42%]) reported spending 51%–75% of their day providing direct patient care.

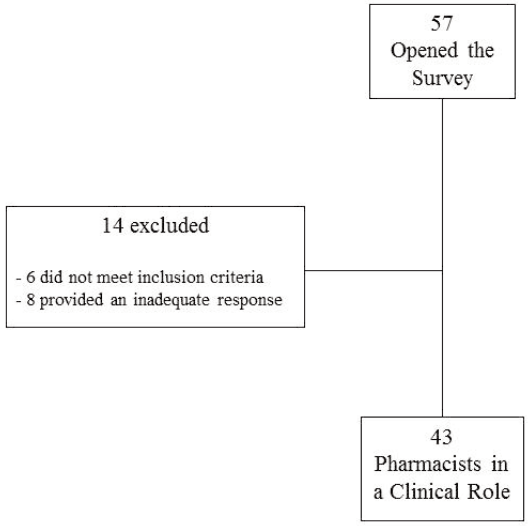

Figure 2. Responses to a web-based survey of pharmacists working in Canadian pediatric hospitals. Responses that were excluded from further analysis did not meet the inclusion criteria or were inadequate for analysis.

Nearly all pharmacists working in pediatric hospitals (42 [98%]) reported that pharmacy learners completed experiential rotations in their practice area. The majority reported the presence of pharmacist students and pharmacy residents (34 [79%] and 29 [67%], respectively). Other types of pharmacy learners identified included pharmacy technician students, PharmD students, and international students.

Pharmacy Services

The Canadian adult hospitals with survey responses were further subdivided into the following 2 categories: adult hospitals with a pharmacist assigned to one or more inpatient pediatric or neonatal clinical areas and adult hospitals without any pharmacists assigned to such areas. The frequencies with which adult hospitals with and without assigned pharmacists provided direct and indirect patient care pharmacy services to their pediatric and neonatal patients are presented in Table 3.

The importance ratings for direct and indirect patient care pharmacy services provided to pediatric and neonatal patients in adult hospitals, as ranked by pharmacists working in pediatric hospitals, are presented in Table 4.

Clinical Pharmacy Services

In adult hospitals with pharmacists assigned to an inpatient pediatric unit, respondents reported that certain pharmacy services, such as "drug interaction assessment" and "identify and resolve drug therapy problems", were provided to their pediatric and neonatal populations more than once per day, whereas

Table 2. Practice Characteristics of Pharmacists Working in Canadian Pediatric Hospitals*

Characteristic	No. (%) of Respondents†
No. of beds in facility (*n* = 42)	
< 50	1 (2)
50–200	26 (62)
201–500	9 (21)
> 500	6 (14)
No. of pharmacist FTEs in facility (mean ± SD) (*n* = 34)	22.6 ± 12.0
Inpatient practice area(s) where respondent works (*n* = 43)	
Emergency medicine	2 (5)
Hematology/oncology	8 (19)
NICU	12 (28)
PICU	12 (28)
Pediatric medical unit	12 (28)
Gastroenterology	1 (2)
Mental health	1 (2)
Infectious disease	2 (5)
Cardiology	1 (2)
Ambulatory care practice area(s) where respondent works (*n* = 8)	
Oncology	2 (25)
Respiratory	1 (13)
Clinical pharmacy assistant or technician assigned (*n* = 43)	11 (26)
Respondent's provision of direct patient care/day (*n* = 43)	
< 25%	3 (7)
25%–50%	13 (30)
51%–75%	18 (42)
> 75%	9 (21)

FTE = full-time equivalent, NICU = neonatal intensive care unit, PICU = pediatric intensive care unit, SD = standard deviation.
*A total of 43 respondents provided data adequate for inclusion in the analysis; however, not all respondents answered every question on the survey. For each characteristic, the n value is shown.
†Except where indicated otherwise.

other pharmacy services, such as "medication reconciliation on admission", "physician-led patient care rounds", "therapeutic drug monitoring", "laboratory monitoring", and "IV-to-oral conversion", were provided to their pediatric and neonatal populations daily. Interestingly, large proportions (nearly half) of these respondents reported that educational pharmacy services (such as patient/caregiver education during admission and at discharge) were provided to their pediatric and neonatal populations only monthly. Furthermore, equal percentages of these respondents reported that "medication reconciliation at discharge" was never provided or not applicable or was provided only on a monthly basis.

The majority of pharmacists working in pediatric hospitals reported that certain pharmacy services, such as "medication reconciliation on admission", "identify and resolve drug therapy problems", "physician-led patient care rounds", "therapeutic drug monitoring", "medication reconciliation at discharge", and "patient/caregiver education at discharge", were very important services for adult hospitals to provide to their pediatric and neonatal populations.

Table 3 (Part 1 of 2). Frequency of Direct and Indirect Patient Care Pharmacy Services Provided by Canadian Adult Hospitals, with (*n* = 31) and without (*n* = 24) an Assigned Pharmacist, to Pediatric and Neonatal Patients

	Frequency; % of Respondents				
Activity	**Never/NA**	**Monthly**	**Weekly**	**Daily**	**> Once per Day**
Direct Patient Care Pharmacy Services					
Allergy assessment					
Assigned pharmacist*	20	30	3	30	17
No assigned pharmacist	29	21	21	12	17
Antimicrobial stewardship					
Assigned pharmacist†	3	21	10	48	17
No assigned pharmacist	25	25	8	25	17
BPMH or medication reconciliation on admission					
Assigned pharmacist*	20	17	17	27	20
No assigned pharmacist	38	29	4	25	4
Centralized intravenous additive services					
Assigned pharmacist†	28	10	7	31	24
No assigned pharmacist	29	12	4	17	38
Collaborative prescribing					
Assigned pharmacist‡	14	32	11	25	18
No assigned pharmacist	50	17	17	17	0
Drug coverage requests					
Assigned pharmacist†	14	52	14	17	3
No assigned pharmacist	58	38	4	0	0
Drug interaction assessment					
Assigned pharmacist*	0	10	7	33	50
No assigned pharmacist	8	8	12	17	54
External drug information requests					
Assigned pharmacist*	7	67	20	7	0
No assigned pharmacist	25	50	17	4	4
Identify and resolve drug therapy problems					
Assigned pharmacist*	0	7	13	40	40
No assigned pharmacist	8	17	17	21	38
Immunizations					
Assigned pharmacist†	17	45	10	21	7
No assigned pharmacist	75	12	8	0	4
Interdisciplinary patient care rounds (no physician present)					
Assigned pharmacist†	59	17	7	17	0
No assigned pharmacist	83	8	4	4	0
Internal drug information requests					
Assigned pharmacist†	0	10	38	31	21
No assigned pharmacist	8	38	29	8	17
Investigational drug access					
Assigned pharmacist*	67	27	0	7	0
No assigned pharmacist§	78	17	0	4	0
IV-to-oral conversion					
Assigned pharmacist†	7	24	14	38	17
No assigned pharmacist	25	25	17	17	17
Laboratory monitoring					
Assigned pharmacist†	7	17	3	48	24
No assigned pharmacist	12	21	12	25	29
Medication error or adverse drug event reporting					
Assigned pharmacist*	7	67	20	7	0
No assigned pharmacist	38	58	0	4	0
Medication preparation					
Assigned pharmacist†	17	10	3	38	31
No assigned pharmacist	4	17	8	8	62
Medication reconciliation at discharge					
Assigned pharmacist*	33	33	10	13	10
No assigned pharmacist	50	29	8	8	4
Medication reconciliation on transfer					
Assigned pharmacist*	33	27	17	13	10
No assigned pharmacist	54	29	8	4	4

continued on page 307

Table 3 (Part 2 of 2). Frequency of Direct and Indirect Patient Care Pharmacy Services Provided by Canadian Adult Hospitals, with (*n* = 31) and without (*n* = 24) an Assigned Pharmacist, to Pediatric and Neonatal Patients

	Frequency; % of Respondents				
Activity	**Never/NA**	**Monthly**	**Weekly**	**Daily**	**> Once per Day**
Order clarification with prescriber					
Assigned pharmacist*	0	7	13	43	37
No assigned pharmacist	4	12	29	8	46
Order verification as part of order entry/review					
Assigned pharmacist*	7	0	3	27	63
No assigned pharmacist	4	8	4	17	67
Pain management					
Assigned pharmacist†	14	34	17	28	7
No assigned pharmacist	62	25	8	0	4
Patient/caregiver education at discharge					
Assigned pharmacist†	14	45	21	14	7
No assigned pharmacist	38	50	8	4	0
Patient/caregiver education during admission					
Assigned pharmacist*	7	40	27	17	10
No assigned pharmacist	33	50	17	0	0
Pharmaceutical care plans					
Assigned pharmacist*	27	27	3	30	13
No assigned pharmacist	46	38	8	8	0
Physician-led patient care rounds					
Assigned pharmacist*	23	13	20	33	10
No assigned pharmacist	79	8	4	8	0
Special Access Programme requests					
Assigned pharmacist†	7	76	7	7	3
No assigned pharmacist	38	54	8	0	0
Therapeutic drug monitoring					
Assigned pharmacist*	0	27	17	40	17
No assigned pharmacist	25	17	12	33	12
Indirect patient care pharmacy services					
Committee work**					
Assigned pharmacist*	20	57	23	0	0
No assigned pharmacist	33	42	21	4	0
Drug-use evaluation					
Assigned pharmacist†	45	52	3	0	0
No assigned pharmacist	54	38	8	0	0
Investigational drug services or clinical trials					
Assigned pharmacist*	67	27	7	0	0
No assigned pharmacist	75	25	0	0	0
Pharmacy practice–based research					
Assigned pharmacist*	63	27	10	0	0
No assigned pharmacist	83	12	0	4	0
Protocol development					
Assigned pharmacist*	7	70	20	3	0
No assigned pharmacist	29	54	12	4	0
Smart pump library development and review					
Assigned pharmacist*	27	57	13	3	0
No assigned pharmacist	50	38	8	0	4
Staff education (e.g., pharmacy, nursing)					
Assigned pharmacist*	17	63	20	0	0
No assigned pharmacist	29	62	8	0	0

BPMH = best possible medication history, NA = not applicable.
*For this activity, *n* = 30.
†For this activity, *n* = 29.
‡For this activity, *n* = 28.
§ For this activity, *n* = 23.
**For example, continuous quality improvement committee, drug-use evaluation committee, or pharmacy and therapeutics committee.

Table 4. Importance Ratings among Pharmacists Working in Canadian Pediatric Hospitals (*n* = 43) for Direct and Indirect Patient Care Pharmacy Services Provided to Pediatric and Neonatal Patients in Canadian Adult Hospitals

Activity	Importance; % of Respondents				
	Not Important/ Never	Slightly Important	Fairly Important	Important	Very Important
Direct patient care pharmacy services					
Allergy assessment*	3	3	5	18	72
Antimicrobial stewardship†	0	3	8	30	60
BPMH or medication reconciliation on admission*	0	0	10	23	67
Centralized intravenous additive services†	3	0	24	40	32
Collaborative prescribing*	0	5	20	44	31
Drug coverage requests*	5	10	23	28	33
Drug interaction assessment*	0	0	5	20	74
External drug information requests‡	3	24	29	29	16
Identify and resolve drug therapy problems*	0	0	0	18	82
Immunizations*	0	10	20	38	31
Interdisciplinary patient care rounds (no physician present)†	19	11	22	32	16
Internal drug information requests‡	0	5	18	47	29
Investigational drug access*	0	15	20	36	28
IV-to-oral conversion†	0	3	27	38	32
Laboratory monitoring†	0	3	16	30	51
Medication error or adverse drug event reporting†	0	11	16	38	35
Medication preparation*	3	3	13	26	56
Medication reconciliation at discharge†	0	3	11	22	65
Medication reconciliation on transfer‡	0	3	13	34	50
Order clarification with prescriber*	0	0	5	20	74
Order verification as part of order entry/review*	3	0	3	26	69
Pain management*	0	0	18	49	33
Patient/caregiver education at discharge†	0	3	11	30	57
Patient/caregiver education during admission†	0	3	14	46	38
Pharmaceutical care plans‡	0	5	18	32	45
Physician-led patient care rounds‡	0	3	3	45	50
Special Access Programme requests*	0	8	23	31	38
Therapeutic drug monitoring‡	0	0	5	24	71
Indirect patient care pharmacy services					
Committee work*§	0	13	41	31	15
Drug-use evaluation*	5	13	41	36	5
Investigational drug services or clinical trials*	0	26	44	23	8
Pharmacy practice-based research‡	3	16	34	37	10
Protocol development*	0	5	23	46	26
Smart pump library development and review*	3	3	28	46	20
Staff education (e.g., pharmacy, nursing)*	0	3	13	51	33

BPMH = best possible medication history.
*For this activity, *n* = 39.
†For this activity, *n* = 37.
‡For this activity, *n* = 38.
§For example, continuous quality improvement committee, drug-use evaluation committee, or pharmacy and therapeutics committee.

Task-Based Pharmacy Services

Substantial proportions of respondents from adult hospitals with pharmacists assigned to an inpatient pediatric unit reported that some pharmacy services, such as "order clarification with prescriber", "medication preparation", and "centralized intravenous additive services", were provided to their pediatric and neonatal populations daily; for other pharmacy services, such as "medication error or adverse drug event reporting" and "drug coverage requests", the majority of respondents reported provision to their pediatric and neonatal populations monthly.

Substantial proportions of pharmacists working in pediatric hospitals reported that certain pharmacy services, such as "order clarification with prescriber", "medication preparation", and "drug coverage requests", were very important services for adult hospitals to provide to their pediatric and neonatal populations, whereas other pharmacy services, such as "medication error or adverse drugevent reporting" and "centralized intravenous additive services", were deemed to be important services to provide.

Indirect Pharmacy Services

The majority of respondents from adult hospitals with pharmacists assigned to an inpatient pediatric unit reported that certain indirect patient care pharmacy services, such as "smart pump library development and review", "protocol development", and "staff education", were completed monthly. Pharmacists

working in pediatric hospitals identified these services as important for adult hospitals to provide to their pediatric and neonatal populations.

DISCUSSION

The proportion of adult hospitals with a pharmacist assigned to an inpatient pediatric or neonatal clinical area was comparable to that reported in the 2016/2017 *Hospital Pharmacy in Canada Report*[10] (61% and 76%, respectively). The latter survey achieved a higher response rate, which may explain the discrepancy. This finding emphasizes that a number of adult hospitals remain without a pharmacist assigned to their pediatric and/or neonatal clinical areas. Therefore, patients in these areas are at greater risk of adverse drug events. The guidelines of the American Society of Health-System Pharmacists and the Pediatric Pharmacy Advocacy Group (ASHP-PPAG) recommend that clinical pharmacy services be prioritized to provide care to the highest-risk populations.[16] In the context of resource limitations, the pharmacy department should aim to allocate a clinical pharmacist to areas such as critical care, neonatology, and the emergency department.

To the authors' knowledge, this is the first study to establish an inventory of pharmacy services provided to pediatric and neonatal patients in Canadian adult hospitals. The frequency with which most pharmacy services were being provided by adult hospitals with an assigned pediatric pharmacist was comparable to the importance identified by pharmacists working in pediatric hospitals. Because our 2 surveys used different Likert scales (based on frequency versus importance), we are unable to draw any conclusions regarding correlation. However, when comparing the data reported for these pharmacy services, it is evident that adult hospitals providing clinical pediatric services met the expectations of pharmacists working in pediatric hospitals for the majority of direct patient care pharmacy services investigated (i.e., 25 of 28).

For 3 clinical pharmacy services, the frequency of provision in adult hospitals did not correspond to the importance identified by pharmacists working in pediatric hospitals: patient/caregiver education during admission and at discharge and medication reconciliation at discharge. The majority of pharmacists working in pediatric hospitals identified these pharmacy services as being important or very important for adult hospitals to provide to their pediatric and neonatal populations, but they were provided by adult hospitals with an assigned pediatric pharmacist at a reduced frequency relative to the identified importance. For these services, adult hospitals with an assigned pediatric pharmacist were not meeting the expectations of pharmacists working in pediatric hospitals.

The CSHP Excellence in Hospital Pharmacy survey recently reported similar findings for the general population.[17] Of the patients surveyed, only 26% reported that they always received education from a hospital pharmacist before starting a new medication. Of the pharmacists surveyed, only 28% reported that more than 50% of their patients were receiving education during admission and at discharge. In addition, only 32% reported that medication reconciliation at discharge was provided to more than 50% of their patients.[17]

Interestingly, the provision of these pharmacy services is supported and promoted by various national organizations.[13,16,18] For instance, the ASHP-PPAG guidelines state that "counseling of pediatric patients and their caregivers is an important role for the pharmacist."[16] The findings presented in this study further emphasize that these pharmacy services in particular need to be optimized for pediatric and neonatal populations receiving care within the adult hospital setting. An important point to consider when interpreting the above results is that these pharmacy services can be provided by other health care providers (i.e., non-pharmacists). It is plausible that provision of these pharmacy services was under-reported in the current study, as we did not ask participants to identify other health care providers who might have performed these tasks, if they themselves were not the ones primarily doing so.

An important area for consideration within the adult hospital setting is the fact that all pharmacists generally take call, which may include questions relating to pediatric patients. The ASHP-PPAG guidelines recommend that "the pharmacy department should provide adequate training for all staff members who may be called on to provide care to pediatric patients."[16] A pharmacist assigned to an inpatient pediatric or neonatal clinical area could play a significant role in achieving this recommendation. These pharmacists have invaluable experience and knowledge that could assist in educating other pharmacists to help ensure they are able to provide care to this patient population.

Several task-based pharmacy services were provided in adult hospitals with an assigned pediatric pharmacist at a frequency greater than expected, including "medication preparation" and "centralized intravenous additive services." This may be suggestive of an additional role for the pharmacist in these patient care areas or may reflect an incorporated centralized role.

In this study, the majority (60%) of adult hospitals did not have pharmacy learners completing experiential rotations in their pediatric or neonatal clinical areas. This may, in part, be attributed to the fact that 39% of the adult hospitals did not have a pharmacist assigned to these areas. Pediatric hospitals are not accessible to all pharmacy learners because of their geographic distribution. Therefore, adult hospitals with inpatient pediatric or neonatal clinical areas could offer opportunities for pharmacy learners to gain experience with this patient population. The American College of Clinical Pharmacy and the Pediatric Pharmacy Advocacy Group have published recommendations supporting experiential education in the pediatric patient care setting.[19] These organizations emphasized that this opportunity should be offered by all schools of pharmacy to promote the development of future pediatric pharmacists.

This study had several limitations. Unfortunately, we were unable to reach all eligible hospital pharmacy staff, and among

those that we did reach, not all provided a response. For example, we did not receive any responses from children's hospitals in British Columbia or Quebec. It is possible that pharmacy practice at these locations is significantly different from practice at sites for which responses were received. Therefore, the absence of responses from these provinces may have influenced the results. For the 3 pharmacy services for which importance and frequency of provision in adult hospitals did not correspond, it is important to recognize that the services could be provided by other health care professionals. Therefore, it is possible that these pharmacy services were under-reported in the current study. Finally, as with any survey, response bias may have influenced the results.

Several factors contribute to the strength of this study. It was a multisite study conducted across Canada, with a well-distributed survey response. The authors surveyed both adult hospitals and pediatric hospitals, which allowed for additional comparisons. Finally, this study contributes to closing the gap in knowledge surrounding pharmacy services that are currently being provided by adult hospitals to their pediatric and neonatal populations by generating an inventory of these services.

CONCLUSION

Adult hospitals with a pharmacist assigned to an inpatient pediatric or neonatal clinical area met most expectations of pharmacists working in pediatric hospitals in terms of provision of pharmacy services. This study identified 3 major pharmacy services—patient/caregiver education during admission and at discharge and medication reconciliation at discharge—that need to be optimized for pediatric and neonatal patients who are receiving care in adult hospitals in Canada. It is the authors' hope that this study will increase awareness of the identified deficiencies and contribute to improved pharmaceutical care for this vulnerable population.

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Competing interests: None declared.

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Funding: None received.

Acknowledgements: The authors thank Stacey MacAulay for presubmission editing assistance and Donaldo Canales for performing the statistical analysis.

Evaluation of Rasburicase Use in the Fraser Health Authority: A Retrospective Review

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ABSTRACT

Background: Rasburicase, a recombinant urate oxidase, is restricted in the Fraser Health Authority (FHA) to the "treatment of acute or at high risk of tumour lysis syndrome [TLS], when other therapeutic options are not suitable". The manufacturer's recommended dosage is 0.2 mg/kg daily for up to 7 days. Given the high cost of this drug, several studies have investigated other strategies and found that a single dose, repeated as needed, is effective in reducing serum uric acid. However, there are currently no guidelines in FHA for the use of rasburicase, which may result in different prescribing practices within the health authority.

Objectives: To describe the prescribing of rasburicase in FHA, including indications and doses, and to report the uric acid–lowering effects of rasburicase and any clinical outcomes, such as dialysis or death.

Methods: This retrospective descriptive chart review included adult patients receiving care in FHA for whom rasburicase was prescribed between June 1, 2010, and November 30, 2016. Descriptive statistics were used to summarize patient characteristics and results.

Results: The prescribing practices for rasburicase in this health authority were largely inconsistent, but the most common dose administered was 3 mg (8/12 [67%] among those receiving rasburicase for prophylaxis and 9/32 [28%] among those receiving rasburicase for treatment; combined total 17/44 or 39%). Regardless of dose, rasburicase reduced serum uric acid levels to less than 476 µmol/L and decreased the risk of TLS.

Conclusions: Having a uniform approach—involving a single dose that can be repeated as needed—for prevention and treatment of elevated serum uric acid levels could result in sufficient reduction of uric acid levels with fewer doses and lower cost. The results of this study support the need for a resource in FHA to guide and standardize the use of rasburicase.

Keywords: rasburicase, tumour lysis syndrome, uric acid, hyperuricemia

RÉSUMÉ

Contexte : La Fraser Health Authorty limite l'usage de la rasburicase, une urate oxydase recombinée, au « traitement du syndrome de lyse tumorale (SLT) aigu ou comportant un risque élevé, lorsque les autres options thérapeutiques ne conviennent pas ». Le fabricant recommande une dose quotidienne de 0,2 mg/kg pendant une durée allant jusqu'à sept jours. Étant donné le coût élevé de ce médicament, plusieurs études ont exploré d'autres stratégies et ont permis de conclure qu'une dose unique, répétée au besoin, était efficace pour réduire le taux sérique d'acide urique. Cependant, il n'existe actuellement aucune ligne directrice provenant du Fraser Health relative à l'utilisation de la rasburicase, ce qui pourrait entraîner des pratiques différentes en matière de prescription au sein de l'institution.

Objectifs : Décrire la prescription de rasburicase au Fraser Health, y compris les indications et les doses, et rapporter les effets réducteurs de l'acide urique de la rasburicase et tout autre résultat clinique, comme la dialyse ou la mort.

Méthodes : Cet examen rétrospectif et descriptif des dossiers comprenait des patients adultes soignés au Fraser Health, qui avaient reçu une prescription de rasburicase entre le 1er juin 2010 et le 30 novembre 2016. Le résumé des caractéristiques des patients et des résultats de l'étude a été obtenu à l'aide de statistiques descriptives.

Résultats : Les pratiques en matière de prescription de la rasburicase au Fraser Health étaient largement incohérentes, mais la dose la plus communément administrée aux personnes recevant de la rasburicase en prophylaxie était de 3 mg (8/12 [67 %] alors que 9/32 [28 %] des personnes recevaient la même dose comme traitement, donc un total combiné de 17/44 ou 39 %). Quelle que soit la dose, la rasburicase réduisait le taux sérique d'acide urique à moins de 476 µmol/L et diminuait le risque de SLT.

Conclusions : L'adoption d'une approche uniforme—impliquant une dose unique pouvant être répétée au besoin—pour la prévention et le traitement du taux sérique élevé d'acide urique pourrait entraîner une réduction suffisante du taux d'acide urique avec une durée de traitement plus courte et des coûts moins importants. Les résultats de cette étude soutiennent le besoin d'une ressource au Fraser Health pour guider et standardiser l'utilisation de la rasburicase.

Mots-clés : rasburicase, syndrome de lyse tumorale, acide urique, hyperuricémie

Can J Hosp Pharm. 2019;72(4):311-9

INTRODUCTION

Tumour lysis syndrome (TLS) is an oncologic metabolic emergency, whereby lysis of malignant tumour cells and the rapid release of nucleic acid, potassium, and phosphate can lead to severe neuromuscular and cardiovascular complications and death.[1] Hyperuricemia from the catabolism of nucleic acids is a key instigator for the laboratory abnormalities and clinical complications seen in this condition.[2] The accumulation and precipitation of uric acid in the kidneys can cause acute uric acid nephropathy. The resulting renal dysfunction can create a vicious circle, whereby further increases in the build-up and crystallization of uric acid worsen electrolyte abnormalities, ultimately leading to further renal injury.

The likelihood of TLS depends on age, stage of malignancy, tumour burden, tumour grade and turnover rate, white blood cell (WBC) count, lactate dehydrogenase (LDH) level, pre-existing renal impairment, renal involvement by the tumour, intensity of cancer treatment, sensitivity of the tumour to cytotoxic therapy, patient's sex, baseline uric acid levels, and use of drugs that increase uric acid.[1-4] Malignancies with rapid cell proliferation or large tumour burden are considered to carry high risk for TLS, as it is theorized that high nucleoprotein turnover increases serum uric acid.[5] Box 1 lists conditions that are considered to be associated with high and intermediate risk for TLS.[3,6] Although TLS is more commonly observed with rapidly dividing hematologic malignancies and after cytotoxic chemotherapy,[1,4] it has been reported with nearly all malignancies, either spontaneously or after radiation therapy, cytolytic antibiotic therapy, intrathecal chemotherapy, dexamethasone, and newer chemotherapeutic agents.[2,4,7-12]

Hyperuricemia can develop rapidly, so it is important to identify and prevent TLS in high-risk patients and to treat appropriately if TLS does occur.[2] The consequence of renal injury was highlighted in a prospective study by Canet and others,[13] who showed that acute kidney injury in patients with high-grade hematological malignancies, including those caused by TLS, was associated with a higher mortality rate and lower 6-month complete remission rate.

Strategies for prophylaxis include aggressive hydration, urinary alkalinization, and, depending on the risk of TLS, administration of allopurinol or rasburicase.[6] Allopurinol works by inhibiting xanthine oxidase, thereby decreasing the formation of uric acid.[14] Its maximum effect for hyperuricemia associated with chemotherapy occurs 27 h after administration,[4,14] and this drug could therefore be considered for patients at low and moderate risk.[1,3,6] Rasburicase, a highly potent recombinant urate oxidase, metabolizes uric acid into a more soluble, inactive metabolite called allantoin.[6,15] Unlike allopurinol, rasburicase affects the existing uric acid and has a faster onset, decreasing uric acid level within 4 h of administration.[15,16] Thus, it is generally reserved for patients at high risk of TLS and those for whom allopurinol is contraindicated.[1,4,6,16,17] A review by Dinnel and others[18] showed that rasburicase reduced TLS, acute kidney injury, and need for renal replacement therapy, and was superior to allopurinol in the reduction of uric acid levels.

Treatment of TLS generally includes aggressive hydration with or without a loop diuretic, correction of electrolyte abnormalities, and administration of rasburicase and renal replacement therapy, if appropriate.[1] Allopurinol, which only reduces the formation of uric acid, is not considered an effective treatment option because of its slow onset.[1,14] The manufacturer's recom-

Box 1. Conditions with High and Intermediate Risk for Tumour Lysis Syndrome[3,6]

High risk

- Advanced-stage Burkitt lymphoma/leukemia
- Advanced-stage lymphoblastic leukemia
- Acute lymphoblastic leukemia with white blood cells ≥ 100 × 10^9/L and/or lactate dehydrogenase ≥ 2× upper limit of normal
- Acute myeloid leukemia with white blood cells ≥ 100 × 10^9/L
- Adult T-cell lymphoma with lactate dehydrogenase > upper limit of normal and bulky tumour disease
- B-cell acute lymphoblastic leukemia (L3-ALL)
- Diffuse large B-cell lymphoma with lactate dehydrogenase > upper limit of normal and bulky tumour disease
- Mantle cell lymphoma (blastoid variants) with lactate dehydrogenase > upper limit of normal and bulky tumour disease
- Peripheral T-cell lymphoma with lactate dehydrogenase > upper limit of normal and bulky tumour disease
- Transformed lymphoma with lactate dehydrogenase > upper limit of normal and bulky tumour disease
- Intermediate risk with renal dysfunction and/or renal involvement*
- Intermediate risk with uric acid, potassium, or phosphate > upper limit of normal

Intermediate risk

- Acute lymphoblastic leukemia with white blood cells < 100 × 10^9/L and lactate dehydrogenase < 2× upper limit of normal
- Acute myeloid leukemia with white blood cells 25–100 × 10^9/L
- Acute myeloid leukemia with white blood cells < 25 × 10^9/L and lactate dehydrogenase ≥ 2× upper limit of normal
- Adult T-cell lymphoma with lactate dehydrogenase > upper limit of normal and non-bulky tumour disease
- Adult intermediate grade non-Hodgkin lymphoma and lactate dehydrogenase ≥ 2× upper limit of normal
- Diffuse large B-cell lymphoma with lactate dehydrogenase > upper limit of normal and non-bulky tumour disease
- Early-stage Burkitt lymphoma/leukemia and lactate dehydrogenase < 2× upper limit of normal
- Early-stage lymphoblastic leukemia and lactate dehydrogenase < 2× upper limit of normal
- Mantle cell lymphoma (blastoid variants) with lactate dehydrogenase > upper limit of normal and non-bulky tumour disease
- Peripheral T-cell lymphoma with lactate dehydrogenase > upper limit of normal and non-bulky tumour disease
- Transformed lymphoma with lactate dehydrogenase > upper limit of normal and non-bulky tumour disease

*Renal conditions that may increase risk of tumour lysis syndrome include pre-existing hyperuricemia, reduced urinary flow, acidic urine, oliguria, anuria, renal insufficiency, and renal failure.

mended dosage for rasburicase is 0.2 mg/kg IV once daily for up to 7 days,[15,19] with a maximum single dose of 0.2 mg/kg. This dose regimen has been found to rapidly decrease uric acid levels in 95% to 99% of patients.[20] However, rasburicase is expensive, costing about $130 per 1.5-mg vial in the Fraser Health Authority (FHA). Therefore, for a 70-kg person, each dose costs about $1200. Because of this high cost, numerous investigators have trialled other strategies in attempts to lower costs while maintaining efficacy. Possible strategies include a single low, fixed dose ranging from 3 to 7.5 mg[21-30] and a single weight-based dose ranging from 0.05 to 0.20 mg/kg,[23,27,31-36] with subsequent doses given daily as needed. Although most of the cited studies were relatively small and retrospective, with uric acid levels used as a surrogate marker for TLS management, their results suggested that a single reduced dose of rasburicase, with subsequent doses given as needed, is sufficient to reduce and normalize uric acid levels. In their retrospective study, McBride and others[25] reviewed patients who received rasburicase 3 mg, 6 mg, or 7.5 mg or a weight-based dose for prevention or treatment of TLS. They observed no statistically significant differences in uric acid normalization within 24 h (92.9% with 3-mg dose, 97.6% with 6-mg dose, 100.0% with 7.5-mg dose, 98.0% with weight-based dosing [mean 0.16 mg/kg]; p = 0.1238). In their meta-analysis, Feng and others[37] found that a single dose ranging from 3 to 7.5 mg (fixed) or from 0.05 to 0.2 mg/kg (weight-based) effectively maintained the uric acid level below 267 µmol/L at 24 to 72 h. Although some patients needed more than one dose, implementing these dosing strategies generally resulted in management of TLS at a lower dose and with shorter treatment duration. In other studies, Coutsouvelis and others[30] and Liu and others[32] also showed that a single dose of rasburicase helped return renal function to within the normal range or creatinine level to baseline.

In terms of safety, rasburicase is considered to be well tolerated.[20,37] Currently, the FHA formulary restricts rasburicase to the "treatment of acute or at high risk of tumour lysis syndrome, when other therapeutic options are not suitable".[38] However, it does not provide any definitions of high risk, nor does it include guidelines to direct the prescribing and monitoring of rasburicase. Unlike FHA, another health authority in British Columbia has a monograph for rasburicase to guide its use, which recommends the off-label dose of 3 mg.[39]

The overall goal of this study was to investigate and characterize how rasburicase is being prescribed in FHA and to describe the outcomes of patients receiving rasburicase. The lack of standardized and evidence-based guidelines in this health authority may be resulting in inconsistent prescribing practices and may also be unnecessarily increasing expenses. This study was undertaken to help identify any discrepancies between current prescribing practices and current formulary restrictions, guidelines, and evidence. The results might also help justify the need for a standardized approach to rasburicase prescribing in FHA. The primary objective was to describe the prescribing of rasburicase in FHA, including indication and dose. The secondary objectives were to report the uric acid–lowering effects of this drug, the clinical outcomes (such as need for dialysis or death), and adverse events.

METHODS

Study Design and Population

This study was a retrospective descriptive chart review based on electronically scanned records from FHA. The data collected included demographic characteristics (age, sex, weight), indication for rasburicase, risk factors (underlying malignancy, baseline WBC count, baseline LDH level), characteristics of the patient's condition (signs and symptoms of clinical TLS, laboratory markers of TLS), outcomes of treatment for TLS (serum uric acid level, TLS markers, dialysis, death), outcomes of prophylaxis for TLS (serum uric acid level, TLS markers, presence of TLS), and adverse drug reactions. The TLS markers were serum uric acid, potassium, and phosphate. Data points for continuous variables, specifically age, weight, serum creatinine, and dose of rasburicase, were plotted graphically in Excel software (Microsoft Corporation, Redmond, Washington) for visual examination; those that did not follow a normal distribution curve are reported as medians and interquartile ranges (IQRs; presented as 25th percentile to 75th percentile). Categorical variables, such as type of malignancy and sex, are reported as proportions.

This study was approved by the Fraser Health Research Ethics Board. No identifying information appears in this article.

Inclusion and Exclusion Criteria

Eligible patients were those 19 years of age or older for whom rasburicase was prescribed in FHA from June 1, 2010, to November 30, 2016. Patients were excluded if they had contraindications to rasburicase, such as hypersensitivity to the drug or glucose-6-phosphate deficiency.

Definitions

The definitions used in this study were based on a widely used classification system developed by Cairo and Bishop.[1] Laboratory TLS was defined as 2 or more of the following within 3 days before or 7 days after administration of cytotoxic therapy: uric acid ≥ 476 µmol/L; potassium ≥ 6.0 mmol/L; phosphorus ≥ 1.45 µmol/L; calcium ≤ 1.75 mmol/L; 25% increase from baseline in uric acid, potassium, or phosphorus; or 25% decrease from baseline in calcium. Clinical TLS was defined as laboratory TLS plus at least one of the following complications: increase in serum creatinine ≥ 1.5 times the upper limit of normal, cardiac arrhythmia, seizures, or sudden death. Cases that did not meet either of these definitions were classified as spontaneous TLS or suspected TLS. In this study, TLS was classified as spontaneous if

it met the Cairo-Bishop criteria for laboratory or clinical TLS but did not occur within 3 days before or 7 days after cytotoxic therapy. TLS was classified as suspected if the Cairo-Bishop criteria for laboratory or clinical TLS were not met, but TLS was the documented indication for rasburicase. Rasburicase therapy was defined as prophylactic if the Cairo-Bishop criteria for laboratory and clinical TLS were not met and the patient was expected to receive chemotherapy; otherwise, rasburicase was deemed to have been ordered for treatment of TLS. For TLS prophylaxis, rasburicase is generally given 24 h before chemotherapy,[15] whereas for TLS treatment, rasburicase is given at any time that TLS has been identified.

RESULTS

There were 46 orders for rasburicase from June 1, 2010, to November 30, 2016. Of these, 32 (70%) were for treatment of TLS, 12 (26%) were for prophylaxis of TLS, and 2 (4%) were for treatment of hyperuricemia, in the absence of confirmed malignancy. Patient characteristics and baseline TLS markers for prophylaxis and treatment of TLS are presented in Table 1. No patients were documented as having glucose-6-phosphate dehydrogenase deficiency.

Overall, 30 (65%) of the orders were initially prescribed as single, one-time doses, whereas the other 16 (35%) were prescribed for daily administration. However, the duration of therapy for 9 of the daily orders was eventually reduced because of insufficient stock or upon liaison with pharmacy. For 6 (13%) of the orders, the dose was also reduced from the initial prescription for similar reasons. The results presented below refer to the first doses administered and exclude the 2 orders for treatment in absence of malignancy.

Because of the wide variation in doses administered, the first doses and results are presented relative to the 3-mg dose (the lowest effective dose studied), with other doses being presented in terms of ranges of weight-based doses (i.e., < 0.10 mg/kg, 0.10–0.14 mg/kg, 0.15–0.20 mg/kg, > 0.20 mg/kg) (Tables 2 and 3). Tables 4 and 5 show the administered first doses as prescribed (i.e., fixed dosing: 3, 6, or 7.5 mg and weight-based dosing).

Prophylaxis for TLS

Patients who received prophylaxis were mostly male (10/12 or 83%), with median age 62 years (IQR 52–68 years) and median weight 80 kg (IQR 64–84 kg) (Table 1). The median serum creatinine before administration of rasburicase was 70 µmol/L (IQR 63–85 µmol/L). The most common underlying malignancy was large B-cell lymphoma (8/12 or 67%), which at a high tumour burden has been associated with increased risk of TLS.[3] The doses for these patients ranged from 3 to 16 mg (median 3 mg, IQR 3–7.9 mg), and the most common dose was 3 mg (8/12 or 67%) (Tables 2 and 4). Before the first dose,

Table 1. Patient Characteristics

Characteristic	Study Group; No. (%) of Patients*			
	Treatment (*n* = 32)		Prophylaxis (*n* = 12)	
Sex				
Male	23	(72)	10	(83)
Female	9	(28)	2	(17)
Age (years) (median and IQR)	67	(61–77)	62	(52–68)
Weight (kg) (median and IQR)	78	(63–85)	80	(64–84)
Serum creatinine before first dose (median and IQR)	178	(142–329)	70	(63–85)
Type of malignancy				
Large B-cell lymphoma	9	(28)	8	(67)
Mantle cell lymphoma	5	(16)	0	(0)
Acute myeloid leukemia	3	(9)	0	(0)
Burkitt lymphoma†	1	(3)	0	(0)
Other	14	(44)‡	4	(33)§
Laboratory values before first dose				
Uric acid ≥ 476 µmol/L	31	(97)	5	(42)
Potassium ≥ 6.0 mmol/L	12	(38)	0	(0)
Phosphorus ≥ 1.45 mmol/L	24	(75)	3	(25)
LDH > 2× upper limit of normal	17	(53)	11	(92)

IQR = interquartile range, LDH = lactate dehydrogenase, TLS = tumour lysis syndrome.
*Except where indicated otherwise.
†Considered to be high risk for TLS.
‡The other malignancies were 4 cases of metastatic cancer (12%); 2 cases each (6%) of small-cell lung cancer, chronic myeloid leukemia, and suspected malignancy not yet diagnosed; and 1 case each (3%) of chronic lymphocytic leukemia, final myelodysplastic syndrome, neuroendocrine tumour, and lymphoma.
§The other malignancies were 1 case each of plasma blastic lymphoma, lymphoma with metastasis to lung and bones, metastatic small-cell lung cancer, and post-transplant lymphoproliferative disorder.

9 (75%) of the 12 patients did not have elevation of serum potassium and phosphate levels sufficient to meet the Cairo-Bishop criteria for TLS. Eleven (92%) of the patients had elevated LDH, indicating high tumour burden, and 5 (42%) of the patients had serum uric acid level above 476 µmol/L.

The use of allopurinol, an alternative for prophylaxis, was also documented. Of these 12 patients, 5 (42%) received allopurinol before the rasburicase was started. With the exception of one patient who had problems swallowing pills and another who received allopurinol while waiting for a supply of rasburicase, the reasons for either switching to rasburicase or using rasburicase in addition to allopurinol were not clearly documented. Two of these 5 patients had normalization of their elevated baseline serum uric acid level (to less than 476 µmol/L) with allopurinol, before administration of rasburicase. An additional 3 patients (25%) started allopurinol at the same time as rasburicase. For 5 of the 8 patients who received both rasburicase and allopurinol for prophylaxis, allopurinol was continued after initiation of rasburicase.

Of the 12 patients with rasburicase ordered for prophylaxis, one did not receive the dose that was ordered; as such, outcome data were available for 11 patients (Table 2). Only 3 patients, all of whom had an initial 3-mg dose, received more than 1 dose. For 1 of these 3 patients, the order was initially written for daily administration rather than a single dose; however, despite the patient's serum uric acid levels remaining below 476 µmol/L after the first dose, a second dose was given for rising potassium and phosphate levels, which were still below the criteria for laboratory TLS. For another patient, additional doses were given because the patient had received chemotherapy on multiple days during the hospital stay. For another patient, an additional dose was given before repeat testing of serum uric acid level, and the rationale for the additional dose was not documented. Therefore, it is likely that the administration of additional doses for the 3-mg dose is not a reflection of lack of efficacy in reducing serum uric acid levels. The additional doses may have been prescribed on the basis of the patients' overall clinical status or perceived risk of TLS, or due to not recognizing that the primary mechanism of action of rasburicase is to reduce serum uric acid levels. Regardless of the dose, no patients met the criteria for TLS. Three patients died for reasons unrelated to TLS.

Treatment of TLS

As in the group receiving rasburicase for prophylaxis, patients who received rasburicase for treatment of TLS were mostly male (23/32 or 72%), with median age 67 years (IQR 61–77 years) and median weight 78 kg (IQR 63–85 kg) (Table 1). The median serum creatinine before administration of rasburicase was 178 µmol/L (IQR 142–329 µmol/L), and 22 (69%) of the 32 patients had elevated serum creatinine level. The most common malignancy was also large B-cell lymphoma (9/32 or 28%), followed by mantle cell lymphoma (5/32 or 16%) and metastatic cancer (4/32 or 12%). The indications for treatment included clinical TLS (12 patients [38%]), laboratory TLS (1 patient [3%]), spontaneous clinical TLS (10 patients [31%]), and spontaneous laboratory TLS (2 patients [6%]). Seven (22%) of the orders did not fall within any of these indication categories, but TLS was suspected. The treatment doses ranged from 3 to 24 mg (median 9 mg, IQR 5.2–15 mg) (Table 5), and the most common doses were 0.15–0.20 mg/kg (12/32 or 38%) and 3 mg (9/32 or 28%) (Table 3). Six (19%) of the patients received more than 1 dose, including 4 patients in the 3-mg dosing category; however, only 2 of these patients received additional doses because the serum uric acid level remained above 476 µmol/L. One patient in the 0.10–0.14 mg/kg dosing category received an additional dose, but for this patient, no sample was drawn between doses for uric acid testing. Another patient, in the 0.15–0.20 mg/kg dosing category, received an additional dose because uric acid levels remained elevated.

Of the 32 patients with rasburicase ordered for treatment, outcome data were available for 28 (Table 6); outcomes are not reported for patients who did not receive the ordered dose or those for whom monitoring could not be performed in FHA. At base-

Table 2. Prophylaxis of TLS: Dose of Rasburicase, TLS Markers, Risk Factors, and Clinical Outcomes

		Marker; No. (%) of Patients (*n* = 12)							
Dose	**No. (%)**	**Uric acid ≥ 476 µmol/L**	**Baseline Renal Dysfunction†**	**Potassium ≥ 6.0 mmol/L**	**Phosphate ≥ 1.45 mmol/L**	**LDH > 2× ULN**	**WBC > 50 × 10^9/L**	**Occurrence of TLS**	**Death‡**
3 mg (mean 0.04 mg/kg)	8 (67)	3 (25)	1 (8)	0	2 (17)	7 (58)	0	0	3 (27)§
< 0.10 mg/kg*	1 (8)	1 (8)	0	0	1 (8)	1 (8)	0	0	0
0.10–0.14 mg/kg	1 (8)	0	0	0	0	1 (8)	0	0	0
0.15–0.20 mg/kg	2 (17)	1 (8)	1 (8)	0	0	2 (17)	0	0	0
All doses	12 (100)	5 (41)	2 (17)	0 (0)	3 (25)	11 (91)	0 (0)	0 (0)	3 (27)§

LDH = lactate dehydrogenase, TLS = tumour lysis syndrome, ULN = upper limit of normal, WBC = white blood cell.
*Excluding dose of 3 mg.
†History of renal dysfunction before admission was documented in patients' electronic records.
‡One 12-mg dose was excluded from death outcomes because the chemotherapy was prescribed but not given (with a decision to provide comfort care). Therefore, percentages for death outcomes are based on *n* = 11.
§Primary reasons for death were unrelated to TLS.

line, 1 of these 28 patients did not have elevation of serum uric acid level. Of the remaining 27 patients, 26 (96%) had normalization of serum uric acid level (≤ 476 μmol/L), which occurred within 24 h for 18 patients (67%). Despite normalization of serum uric acid levels in most patients, 9 (32%) of the 28 patients for whom outcomes are available required dialysis and 14 (50%) died during the hospital stay. Of the 14 deaths, 7 occurred when TLS was documented as ongoing or the acute kidney injury caused by TLS had not improved or had worsened. The initial dose administered to these 7 patients was 6 mg, 12 mg, 15 mg, 15 mg, 17 mg, 18 mg, and 24 mg, respectively. Although TLS may have contributed to the other deaths, there were other confounding factors as well, such as severity of the malignancy, which make it challenging to attribute death primarily to TLS.

Safety of Rasburicase

There were no adverse drug reactions reported with rasburicase.

DISCUSSION

In this study, which examined the prescribing of and outcomes with rasburicase for prophylaxis and treatment of TLS, the doses prescribed were generally inconsistent. Additionally, for reasons such as insufficient stock, the doses administered were not completely reflective of prescribing practices in FHA. No clear trends were observed, in terms of baseline serum uric acid levels or creatinine levels, that would explain the use of different doses. However, patients treated with the higher doses (0.15 to 0.20 mg/kg) might have had a poorer prognosis, given that a greater proportion of patients in that group died. In addition, prescribers might have been more inclined to use higher doses for treatment, given that the median dose was higher for treatment than for prophylaxis. The differences in doses could also be partly explained by the fact that a wide range of rasburicase doses have been studied in the setting of TLS. For most patients, monitoring of electrolytes, serum uric acid levels, and renal function was performed at least every 24 h after administration of rasburicase. However, for 3 orders, testing of serum uric acid level was not repeated before the subsequent dose(s), even though such testing would typically be used to help justify an additional dose. These inconsistencies in prescribing and monitoring support the need for a resource to guide the proper monitoring and rational use of rasburicase.

The Cairo-Bishop definitions are commonly used in the literature, but they exclude spontaneous TLS occurring in the absence of cytotoxic therapy. Another issue with these criteria is

Table 3. Dose of Rasburicase for Treatment of Tumour Lysis Syndrome

	No. (%) of Patients	
Dose	**With Prescribed Dose**	**Received > 1 Dose**
3 mg (mean 0.04 mg/kg)	9 (28)	4 (13)
< 0.10 mg/kg (excluding 3 mg)	3 (9)	0 (0)
0.10–0.14 mg/kg	7 (22)	1 (3)
0.15–0.20 mg/kg	12 (38)	1 (3)
> 0.20 mg/kg	1 (3)	0 (0)
All doses	32 (100)	6 (19)

Table 4. Dose of Rasburicase as Prescribed for Prophylaxis of Tumour Lysis Syndrome

Dose as Prescribed*	No. (%) of Patients
Fixed	
3 mg	8 (67)
7.5 mg	1 (8)
Weight-based	
0.1 mg/kg	1 (8)†
0.15 mg/kg	1 (8)‡
0.20 mg/kg	1 (8)§
All doses	12 (100)

*Dose was considered fixed if ordered as 3, 6, or 7.5 mg. Dose was considered weight-based if ordered in terms of milligrams per kilogram or if more than 7.5 mg.
†Dose was 9 mg.
‡Dose was 12 mg.
§Dose was 16 mg.

Table 5. Dose of Rasburicase as Prescribed for Treatment of Tumour Lysis Syndrome

Dose as Prescribed*	No. (%) of Patients
Fixed	
3 mg	9 (28)
6 mg	2 (6)
7.5 mg	4 (12)
Weight-based	
0.10–0.14 mg/kg	4 (12)†
0.15–0.19 mg/kg	4 (12)‡
0.20 mg/kg	8 (25)§
> 0.20 mg/kg	1 (3)**
All doses	32 (100)

*Dose was considered fixed if ordered as 3, 6, or 7.5 mg. Dose was considered weight-based if ordered in terms of milligrams per kilogram or if more than 7.5 mg.
†Doses were 7.5 mg, 9 mg, 9 mg, and 13.5 mg, respectively.
‡Doses were 15 mg, 15 mg, 18 mg, and 19 mg, respectively.
§Doses were 12 mg, 12 mg, 13.5 mg, 15 mg, 15 mg, 16 mg, 16 mg, and 17 mg, respectively.
**Dose was 24 mg.

Table 6. Normalization of Serum Uric Acid Level with Rasburicase for Treatment of TLS and Clinical Outcomes

		Baseline Uric Acid		Time to Attain Uric Acid ≤ 476 μmol/L°			Outcome	
Dose	No.	Median (IQR)	< 476 μmol/L	≤ 24 h	> 24 h	Did Not Normalize	Dialysis	Death*
3 mg (mean 0.04 mg/kg)	9	781 (739–858)	1	3	5	0	3	3
< 0.10 mg/kg (excl. 3 mg)	2	1158 (1027–1288)	0	1	0	1	1	1
0.10–0.14 mg/kg	5	848 (731–1014)	0	4	1	0	0	1
0.15–0.20 mg/kg	11	1092 (839–1179)	0	9	2	0	5	8
> 0.20 mg/kg	1	771	0	1	0	0	0	1
All doses	28	873 (752–1060)	1 (4%)	18 (64%)	8 (29%)	1 (4%)	9 (32%)	14 (50%)

IQR = interquartile range, TLS = tumour lysis syndrome
*Seven of the deaths occurred when (according to documentation) TLS was still ongoing or the acute kidney injury caused by TLS had not improved or had worsened. For these patients, the initial dose administered was 6 mg, 12 mg, 15 mg, 15 mg, 17 mg, 18 mg, and 24 mg, respectively.

that their definition of acute kidney injury (serum creatinine level more than 1.5 times the upper limit of normal) could include patients with baseline chronic kidney disease.[2] Of the 32 patients with a diagnosis of TLS, 97% had elevated serum uric acid levels, 75% had elevated serum phosphate levels, 68% had elevated serum creatinine levels, and 38% had elevated serum potassium levels. Therefore, in practice, these definitions and criteria guiding the use of rasburicase may not be appropriate for every patient.

For prophylaxis, rasburicase has been recommended for high-risk patients requiring immediate chemotherapy.[1,3] In this review, 75% patients had high risk of TLS and 92% had chemotherapy planned within 72 h. Therefore, this group included patients who could have been received allopurinol instead of rasburicase for prophylaxis. Although there are insufficient data to make strong recommendations on how rasburicase should be prescribed, this review highlights the importance of having a reference (e.g., a monograph) to guide the prescribing and monitoring of rasburicase. Given that prompt recognition and management of TLS is imperative to prevent acute kidney injury (a strong predictor of death among patients with TLS[2]), it is critical that any restrictions or guidelines created for rasburicase do not inadvertently prevent its use in patients who could benefit from it. Aside from uric acid nephropathy, there are other possible mechanisms of acute kidney injury in TLS, such as acute phosphate nephropathy and precipitation of calcium phosphate within the renal parenchyma.[40,41] Therefore, although rasburicase was observed to normalize serum uric acid levels, its efficacy in reducing the risk of and reversing acute kidney injury, as well as preventing death, is less clear. Even though the majority of patients had normalization of serum uric acid, some patients required dialysis and others died. Larger studies would be required to fully evaluate the clinical efficacy and safety of the various doses of rasburicase. Despite this need for additional study, this review does suggest that implementing a strategy whereby a single dose is prescribed and subsequent doses are given daily, as needed, could conserve stock and minimize unnecessary expenditure, without compromising the efficacy of rasburicase in normalizing serum uric acid levels.

This study had several limitations. Because of the retrospective design, it was challenging to assess the appropriateness and safety of each order, and potential confounding factors made it impossible to compare different doses. Some factors, such as kidney involvement due to malignancy or renal dysfunction due to other acute conditions (e.g., infection), might not have been consistently documented yet could have affected the clinical outcomes. In addition, the small sample size did not allow sufficient power to compare the different doses and detect a significance difference in outcomes, had such a difference been present. Furthermore, the doses evaluated were the first doses administered, not the total doses, which made it challenging to compare efficacy and safety. This study was also dependent on the documentation accessible from FHA; however, not all charts were completely scanned. The rationale for each particular dose and for the decision to use rasburicase instead of allopurinol for prophylaxis was often poorly documented. For 21 patients, allopurinol was prescribed for treatment, and for another 7 patients, allopurinol was prescribed for prophylaxis, at the clinician's discretion. However, given the slower onset of allopurinol, the addition of this drug is unlikely to have significantly affected the efficacy of rasburicase. Moreover, it was unclear whether serum samples for determination of uric acid levels after the rasburicase dose were properly collected (in prechilled tubes containing heparin) and analyzed within 4 h. At room temperature, rasburicase causes ex vivo enzymatic degradation of uric acid, resulting in falsely low levels.

CONCLUSION

Overall, this study showed that prescribing practices and monitoring of rasburicase in FHA were not standardized. These results indicate the need for a resource in this health authority to help guide the prescribing and monitoring of rasburicase. Creating an institution-specific monograph that recommends a uniform approach—involving a single dose, to be repeated as needed—for treatment of elevated serum uric acid levels could result in appropriate management with shorter treatment duration and lower cost.

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Competing interests: None declared.

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Funding: None received.

ON THE FRONT COVER

Cherry Hill Beach, Nova Scotia

The cover photograph was taken along Nova Scotia's stunning southern shoreline at Cherry Hill Beach, as some stratus clouds threatened an impending shower after a particularly hot summer day. Lucas Thorne-Humphrey captured this scene using a FujiFilm Z33WP waterproof digital camera. Lucas works as a Clinical Pharmacist at Valley Regional Hospital in Kentville, Nova Scotia.

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

Pharmacy Informatics: Where Medication Use and Technology Meet

Daniel Cortes, Jodie Leung, Andrea Ryl, and Jenny Lieu

INTRODUCTION

As technology and innovation continue to rapidly shape health care and medication management, the need for specialized roles to support and optimize clinical workflows, system usage, and data capture is ever more important.[1] Health informatics is an established field that bridges health care with information technology as a means to improve clinical care, ensure patient safety, and increase the efficiency and effectiveness of organizational processes.[2] Pharmacy informatics, a subset of health informatics, leverages both clinical expertise and knowledge about information technology to improve medication management processes and drug administration safety.[3] Pharmacy informaticists are pharmacists with a solid background in clinical pharmacy practice, knowledge of pharmacotherapy, and extensive working knowledge of clinical information systems and drug distribution systems.

EVOLUTION OF PHARMACY INFORMATICS

Hospital pharmacies are well known to embrace technology and automation to support drug distribution. Between the 1980s and the 1990s, information systems were primarily used to manage pharmacy inventory and produce financial reports; then, in the early 2000s, hospitals adopted computerized practitioner order entry (CPOE) and other computerized systems with **clinical decision support*** (CDS) software.[4] Clinicians were required to oversee and tailor these systems to actualize their utility, yet the early experience and research of these investigators described only general benefits, and they could not report or measure the systems' effectiveness or value.[5,6] During this period of rapid technological growth, hospital pharmacy departments were challenged to manage and maintain new hardware and software, employing technical analysts to support the devices and applications, while pharmacy staff optimized system use to meet clinical and dispensing needs. By the late 2000s, the health informatics field was emerging, with specialization in pharmacy practice ultimately defining the pharmacy informatics role. Pharmacy informaticists became a natural fit to engage health technology advancements, evaluate system limitations and risk, educate pharmacy end-users, and investigate system issues related to medication safety, while supporting pharmacy practice. The American Society of Health-System Pharmacists (ASHP) first described the pharmacist's role, responsibilities, and competencies in informatics in 2006, with a recent statement update in 2016.[7]

*Bold indicates terms that are defined in Appendix 1.

ENABLING GROWTH: COMPETENCIES OF PHARMACY INFORMATICISTS

The diversity in skills and pathways of those who work in pharmacy informatics has prompted the definition of core competencies that promote a technologically optimized medication-use process that is safe, effective, efficient, and timely. The ASHP defined 5 major competencies critical for pharmacy informaticists to successfully contribute to any health care organization: data, information, and knowledge management; information and knowledge delivery; practice analytics; applied clinical informatics; and leadership and management of change[7] (Table 1).

In the remainder of this article, we discuss the advanced practice of a pharmacy informaticist within our own Canadian hospital network by highlighting past work completed and projects currently underway within our hospital organization. Using these interrelated core competencies, as outlined below, we describe how pharmacy informatics aligns people, processes, and technologies with medication management.

Data, Information, and Knowledge Management

Pharmacy informaticists support the medication-use process through best practice management of data, information, and knowledge. Health care data, such as patients' birthdates,

Table 1. Core Competencies for Pharmacy Informaticists[8]*

Competency	Definition	Example of Roles and Responsibilities

Data, information, and knowledge management	The management of medication-related information while promoting integration, **interoperability**, and information exchange	• Data governance and stewardship
		• Control terminology, standards, and reference data
		• Ensure data accuracy
		• Audit and evaluate
		• Ensure data are easily understood
		• Maintenance
		  ○ Corrective
		  ○ Customized
		  ○ Enhancement
		  ○ Preventive

Information and knowledge delivery	The delivery of medication-related information and knowledge through the clinical knowledge life cycle:
	• Information and knowledge delivery
	• Knowledge application and delivery
	• Knowledge asset management
		• Deliver clinical knowledge
		  ○ Proactively
		  ○ Interactively
		  ○ Passively
		• Analyze data to understand performance, reporting, evaluation, prediction, and harvesting of new information to improve outcomes
		• Optimize use of **clinical decision support** and tool development
		• Reduce information overload to provider
		• Manage, support, and govern medication information
		  ○ Cataloguing, encoding, versioning, updating, disseminating, and maintaining inventory of information

Practice analytics	The development of point-of-business analytic solutions to improve decision-making	• Ensure data are standardized, structured, and modelled to support **business intelligence** goals • Create effective tools that allow for multiple formats and layers of analysis • Develop, maintain, and ensure the quality of these tools to guide the achievement of treatment and strategic goals • Drive analytics to the front line by creating greater end-user accessibility • Monitor the effectiveness of tools and information to deploy or further develop point-of-care and analytical systems
Applied clinical informatics	The application of user experience, research, and theory of informatics to clinical practice and system usability	• Acquire professional perspective by understanding the profession's history and values and its relationship to other fields • Analyze problems • Produce solutions • Articulate rationale • Implement, evaluate, and refine • Innovate by creating new theories, frameworks, and processes to address informatics problems • Work collaboratively within and across all disciplines • Educate, share, and discuss with students and other disciplines
Leadership and management of change	The provision of leadership and management in the procurement, development, implementation, customization, evaluation, and continuous improvement of clinical information systems	• Lead local and external organizations to sound conclusions regarding use of technology in medication management • Lead and manage the risk/benefit evaluation and communication of a newly implemented technology • Translate user requirements into safe and effective designs • Implement project management best practices • Attain key leadership roles within the health care information technology industry and organizations, as well as pharmacy practice associations

*Bold indicates terms that are defined in Appendix 1.

laboratory test results, or drug doses, are represented by discrete numbers, descriptions, or measurements. Information is a collection of data that has been interpreted via relationships within and between separate data points, with knowledge transforming information into deliberate action.[8] For example, a single blood glucose reading cannot compare (in terms of usefulness for diagnosis and treatment) to an assessment of the patient's blood glucose trend, family history, oral glucose tolerance test result, and hemoglobin A1c (HbA1c) level. When considering these data points and information together, a clinician develops knowledge

about the patient's blood glucose control, which can be used to determine if the patient is diabetic. Related information is organized into records and files, which make up a database.

Pharmacy informaticists manage the databases that support the pharmacist's clinical and administrative role, which is guided by the pharmacist's practice setting and responsibilities. It is necessary that the databases, electronic medical records (EMRs), and drug distribution systems are built to promote the safe use of high-risk medications, to highlight therapeutic order sets or dosing guidelines for clinicians, and to deliver and document best practices in pharmaceutical care. The other core competencies (described in subsequent sections) are critically dependent on how data, information, and knowledge are managed, and the various examples we discuss later will relate back to this competency. The remainder of this section focuses on management of the drug database.

Developing standardized drug and order set nomenclature in the drug database is important, to provide a consistent description of a medication regardless of which system is being used. Standardized nomenclature avoids confusion within and between systems and ensures that a clinician who is ordering, validating, or administering a drug can safely identify the intended medication. In our organization, we faced numerous challenges in creating a safe medication-use system, such as identifying drugs despite character limits within our pharmacy and prescriber systems, using a US National Drug Code system for Canadian drug content, and integrating data between overlapping clinical information systems. As such, it was necessary to develop guiding principles and standard operating procedures that specified the use of generic names (versus brand names), an approval process for use of medication abbreviations, and truncation rules that prioritized the display of a drug's salt, formulation, extended-release modifier, or strength. For example, new drug additions to the medication databases must undergo an evaluation process to ensure alignment with the database conventions and to prevent selection errors by the end-user. In a recent review for subcutaneous (SC) rituximab (Rituxan SC 120 mg/mL), we mitigated the risk of erroneously selecting intravenous (IV) rituximab (10 mg/mL) by adding the concentration and route to the drug name. We also employed this strategy when new biosimilar drugs were recently added to the formulary. In the case of filgrastim, the brand names Grastofil and Neupogen were displayed and capitalized in all systems. The naming convention we chose also aligns with Health Canada's policy statement[9] on the naming of biologic drugs, which was released earlier this year.

In another example from our organization, pharmacy informaticists discovered a system limitation that led to a database improvement. In a case of a "wrong drug" administration error, a patient incorrectly received Humalog instead of the intended order Humalog Mix 25. A review highlighted that, because of a limit on the number of characters available, the "Mix 25" text wrapped to a second line in the medication administration software, which obscured the critical information required for the nurse to select the correct product right before medication administration. In response to this incident, a comprehensive risk reduction review was completed, which led to the renaming of multiple medications to ensure that key drug data needed for identification would always be visible to clinicians at the time of medication ordering, dispensing, and administration.

Information and Knowledge Delivery

The next core competency, information and knowledge delivery, involves how the databases are utilized. Pharmacy informaticists ensure that there is **interoperability** between the pharmacy information system and all other medication-related systems. With constant changes to clinical practice and complexities within health care, integrated systems are needed to support the delivery of accurate medication-related information to the end-user at the point of clinical decision-making. Pharmacy informaticists support best practices and apply knowledge of informatics principles, human factors, and systems design to the user interface, to ensure that there is no confusion or incorrect information at the point of care. This information delivery can be provided before decisions are made or passively as reference information. Pharmacy informaticists not only support and oversee the creation, application, delivery, and management of clinical information and knowledge, but they also inform how systems should be developed and why **interoperability** is essential to safe medication management.[7]

CDS software aids clinicians during the decision-making process by way of **event-driven alerts**, **forcing functions**, care plans, evidence-based order sets, documentation templates, and patient data summaries. With in-depth knowledge of EMR functionalities and limitations, pharmacy informaticists can translate clinical requirements and determine the best way to incorporate CDS to meet the needs of clinical workflows and patient safety. Considerations of national practice standards or locally created policies and procedures should also drive the selection of the types of CDS tools that are best suited to specific clinical scenarios, such as managing high-risk medications or guiding dose adjustments in special populations.

One such example involves using evidence-based research and clinical quality outcome data for thromboprophylaxis risk assessment to develop preprinted order sets or guideline-based risk assessment models[10] and thus to reduce the unnecessary use of pharmacologic thromboprophylaxis. One of the sites within our organization implemented a mandatory CPOE module for venous thromboembolism (VTE) prophylaxis within all admission order sets, whereby the prescriber is required to document if pharmacologic thromboprophylaxis is required or contraindicated. This mandatory module serves as a **forcing function** for assessment and documentation for VTE prophylaxis within 24 hours of admission.

At another site in our organization, the use of **medical logic modules** allows flexibility to develop and customize electronic CDS tools, such as custom pop-up alerts that prompt independent double checks to be completed by nursing staff for specific medications or automatic display of important patient-specific laboratory values (e.g., serum creatinine) or key findings (e.g., weight) on the order screen to aid with decision-making at the point of order entry. In our organization, pharmacy informaticists worked with the Antimicrobial Stewardship Program to create custom reports that consolidate unit-specific treatment courses and antibiotic information to trigger prompt reassessment on the basis of specified criteria, such as critical care patients presenting with sepsis.[11] CDS has also been developed to guide antibiotic prescribing based on indication, renal function, and clinical criteria for use.

Although the use of CDS systems is an asset to clinicians and their workflows, it is important to monitor and evaluate the effectiveness of these systems on the basis of ordering practices or user feedback, and adjust when required. Pharmacy informaticists play an integral role in reviewing medication safety incidents to determine whether the root cause is information system–based. They also identify opportunities to incorporate changes that will prevent potential medication incidents in the future. Given the quantity of **alerts** presented to clinicians, including drug interactions, allergy verification, and critical laboratory values, **alert fatigue** can develop. It has been reported that the override rate for medication alerts often exceeds 80%–90%, which can result in preventable adverse events leading to morbidity or mortality.[12] Guidelines exist on how to effectively use and monitor **alerts**, given that alerts with low effectiveness and ones upon which clinicians may not agree can lead to the creation of workaround solutions.[13] To mitigate these issues, it is necessary for pharmacy informaticists to take **alert fatigue** and data overload into account when designing CDS. At our organization, retrospective data are collected concerning alert use and overrides associated with medical incidents; these data are then reviewed by both a committee and the clinicians who commonly override alerts. It is necessary to continually perform system maintenance to ensure that CDS remains clinically appropriate, relevant, and effective for the end-user.[14]

Practice Analytics

The third core competency of pharmacy informaticists is to play a significant role in practice analytics with respect to medication management. Practice analytics refers to a **business intelligence** process that uses technology and database creation to study clinical and fiscal processes and to improve decision-making in these areas.[15] Pharmacy informaticists must understand the capabilities of their system, as well as the "big picture", to help drive pharmacy practice improvements and increase performance in the medication-use process.

As an opportunity to evaluate and measure pharmacy practice and services, one of the sites in our organization recently launched documentation of clinical pharmacy key performance indicators (cpKPIs)[16] within our EMR. The existing pharmacist assessment form was enhanced, piloted, and implemented. Our updated documentation tool allowed clinical pharmacists to document their initial patient assessment with follow-up notes, and now they can select which cpKPIs have been completed throughout a patient's admission. The data from this electronic form can be easily extracted and audited with the intention of improving clinical pharmacy services and achieving optimal patient care and safety.[17]

Another major undertaking at one of our sites involved the development of an **enterprise data warehouse**. Pharmacy informaticists were involved in this project as subject matter experts, collaborating with the decision support, project management, and research departments. The warehouse will provide clinicians with easier access to a large repository of business, operational, and clinical data that can be used for research, quality improvement initiatives, and predictive analytics. Data generated from the **enterprise data warehouse** are reviewed by the pharmacy informaticists to provide background understanding, to ensure queries are accurate, and to ensure that data are used in the correct context.

Applied Clinical Informatics

The next core competency of pharmacy informatics practice is applied clinical informatics, which improves clinical practice and the usability, efficiency, and safety of systems by applying "user experiences, research, and theoretical informatics principles".[7] Applied clinical informatics focuses on providing solutions that are advantageous to clinical workflows and improve every stage of medication use: ordering, processing, dispensing, and administration. Pharmacy informaticists leverage their clinical experiences to identify and evaluate the feasibility of technology-based solutions, identify gaps, and determine risks to support departmental and organizational initiatives related to medication use and electronic systems. At one of our sites, pharmacy informaticists recently led the implementation of **automated dispensing units** (ADUs) on inpatient and outpatient clinical units, collaborating with nursing leadership to develop key principles for system configuration and decisions surrounding emergency overrides and discrepancy management.

Although ADUs represent one of our latest improvements in stock management, our pharmacy informaticists continue to collaboratively manage back orders, nonformulary ordering, and the use of autosubstitution or therapeutic interchanges. With increased integration of technology in the drug procurement process, system changes have a broader impact, and careful consideration is required before such changes are implemented. Drug shortages and back orders have become increasingly difficult

to manage in the hospital setting and require that pharmacy informaticists work alongside pharmacy technical operations staff. The severity of each shortage is assessed by evaluating existing inventory, estimated usage patterns, and availability of alternative products, while considering the impact or degree of changes on order entry and medication administration. CDS may be added to CPOE or pharmacy order processing systems to alert system users to the shortage and offer alternative actions as appropriate. For example, one site in our organization followed best practices and customized various strategies during a recent shortage of IV levofloxacin that considerably affected multiple clinical areas and medical specialties. Depending on the clinical scenario, prescribers were instructed to change the order to oral levofloxacin, use a different IV antibiotic, or use some of the limited supply of IV levofloxacin if indicated. Pharmacy informaticists updated all systems to provide guidance and information to prescribers, and careful monitoring and ongoing collaboration with distribution team members enabled pharmacy informaticists to respond rapidly when the back order was lifted.

Leadership and Management of Change

The final core competency calls upon pharmacy informaticists to be engaged and to participate in impact analyses and change initiatives while also providing oversight of and leadership concerning the medication management systems.[7] Pharmacy informaticists can manage and lead change through their involvement in project work, engagement at any stage of the project life cycle (from initiation to closing), and participation in a variety of tasks such as building, testing, and optimizing a solution. A pharmacy informaticist's scope of practice includes clinical and policy knowledge, change management skills, project management, and also an understanding of systems technology enabling participation in or leadership of projects and initiatives within or across all sites.

Over the last few years within our organization, pharmacy informaticists have contributed their specialized knowledge and strong guidance to corporate projects such as the implementation of CPOE, IV smart pumps, ADUs, and electronic medication reconciliation. They continue to work with stakeholders in drug distribution, drug information and utilization, pharmacy clinical and technical operations, and corporate medication safety. To facilitate change management processes and knowledge transfer, one of the sites in our organization formed a committee to coordinate upcoming changes to clinical systems, determine potential impacts on end-users, support upcoming initiatives, and manage issues related to drug shortages or formulation changes. The committee includes staff members involved in medication management, such as pharmacists, pharmacy technicians, nurses, informatics specialists, and managers, and acts as a forum for continuous process improvement through biweekly meetings, which ensure that issues arising are addressed in a timely manner. A recent example of our pharmacy informaticists being leaders in change involved revision of IV bag labels to include diluent volume plus overfill. This labelling change was evaluated by the committee, and a clear communication plan was developed to address changes to the clinical systems, batch labelling, worksheets, and IV pumps to ensure that all parties involved were aware and on board.

Our pharmacy informatics team has also worked on national initiatives such as Choosing Wisely Canada. A recently implemented recommendation consisted of decreasing unnecessary blood work monitoring (e.g., international normalized ratio [INR], HbA1c, and thyroid-stimulating hormone [TSH]), improving formulary management, and revising order sets. Work efforts included decoupling the laboratory orders for INR and activated partial thromboplastin time, and the addition of CDS to affected admission order sets helped prescribers to select the suggested options. Also, routine orders for TSH and HbA1c were discouraged, both to educate prescribers about the utility of these tests and to disallow repeat ordering within specified time frames.

FUTURE DIRECTIONS

There are many more interesting areas within health and pharmacy informatics to learn about and further develop. We have described only some examples of a pharmacy informaticist's operational responsibilities and current initiatives, but we foresee that the future holds many exciting changes.

The health informatics curriculum is well established in medical and nursing training; however, in pharmacy, it has been slower to evolve.[18] A 2017 survey of pharmacy curriculums in the United States showed that only 36% included an informatics course, which was not much of an improvement from 10 years before.[19] Pharmacy or health informatics courses are now offered in most Canadian pharmacy faculties; however, many of those currently working in the field entered with little to no formal education or training. Rather, skills have been gained through on-the-job experience, by working alongside nonpharmacy clinical informatics colleagues, through education provided by information system vendors, by attending public interest conferences, or through continuing education. There is a recognized need for advanced training in the pharmacy informatics field to support systems innovation to "enable a shift to a more fully system-supported pharmacy practice".[20]

"Big data", a term referring to large and complex data sets from many data sources,[21] is being leveraged to improve clinical decision-making and pharmacy research.[22] Artificial intelligence and machine learning are becoming the future of health care, whereby computers are used to simulate learning, analysis, and prediction.[23] In terms of application to pharmacy and medication management, development is currently underway to assist in many areas, such as drug design,[24] formulary selection, choice of drug therapy,[25] treatment predictions and results, health care data

processing (e.g., diagnostic tests, wearable devices, and natural language processing[26]), potential drug interactions or adverse event alerts, and adherence monitoring.[27] In the coming years, pharmacy informaticists will be essential to the development and adoption of artificial intelligence tools to ensure that data currently captured and used for computation are meaningful and accurate.

The creation of larger hospital networks will prompt the work of understanding needs across various clinical and financial systems for the affected institutions. Challenges to harmonize the practices of multiple hospitals of different sizes, using different information systems and with different levels of patient acuity, must be anticipated, and it is important that pharmacy informatics is represented at all sites, with collaboration at all organizational levels.[28] Increased representation of pharmacy informatics would certainly create opportunities to encourage further growth of the field and to promote pharmacy informaticists' role as leaders at the place where information technology and medication management meet.

CONCLUSION

Although it is not new, the practice of pharmacy informatics is in a state of rapid growth. This diverse and evolving field leads the use of technology at multiple levels of pharmacy practice, from departmental projects to national collaboratives. Equipped with a strong understanding of medication management workflows and knowledge of clinical system functionalities, pharmacy informaticists are in a great position to collaborate with other health care providers to optimize information management, improve workflow, and reduce medication errors. By supporting and developing the pharmacy informaticist role, the profession of hospital pharmacy can optimize innovations to medication-related processes so that pharmacists can continue to improve patient care and outcomes.

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Competing interests: None declared.

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Acknowledgements: The authors are grateful to Linda Stoyanoff for her contributions to content research, writing assistance, technical editing, and proofreading in advance of submission.

Appendix 1. Definitions of key terms

Term	Definition
Alert, event-driven	An urgent, patient-specific notice generated by a CDS system and directed to clinicians at their decision-making point. Some alerts are prompted when an event or a series of events has occurred. Some require a response before the clinician can continue. Examples: • A warning regarding a documented action/decision (or lack thereof) • A notification of a new clinical condition, circumstance, or change in a patient, test, or drug status that requires immediate attention
Alert fatigue	A state of irritability, exhaustion, or bewilderment triggered in clinicians who have been exposed to too many alerts, or alerts with perceived irrelevance, causing the user to ignore some or all of the alerts. This situation reduces the safety benefit of the CDS system.
Automated dispensing unit (ADU)	A secure storage unit typically in a decentralized location in patient care units. An ADU is capable of maintaining medication inventory via an audit trail of activity, automating drug cost charging of medication products when dispensed for patient use, and reporting the need for inventory replacement according to usage and par levels.
Business intelligence	A term to describe the strategic integration of technology and process that enables organizations to leverage their data to make better decisions.
Clinical decision support (CDS)	The provision of basic clinical knowledge and appropriate patient-specific information to aid health care providers in making the appropriate or best possible clinical decision.
Enterprise data warehouse (EDW)	A large database containing data from numerous systems, designed to provide real-time information to support organizational decision-making.
Forcing function	A design that prevents the user from taking an action without consciously considering information relevant to that action. It forces the user's attention upon something and deliberately disrupts the efficient or automatic performance of a task.
Interoperability	The ability of different information technology systems and software applications to communicate; to exchange data accurately, effectively, and consistently; and to use the information that has been exchanged.
Medical logic module (MLM)	An encoded clinical rule that contains enough logic to make a single clinical decision. Examples: • Clinical alerts, recommendations, reminders, informational notices, interpretations, diagnoses, quality assurance functions, continuous quality improvement, biosurveillance, administrative support, and clinical research

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Should Melatonin Be Used as a Sleeping Aid for Elderly People?

THE "PRO" SIDE

Sales of exogenous melatonin, a hormone that regulates the circadian rhythm, have increased significantly over the past few years.[1] In the United States, the most recent National Health Interview Survey showed that the overall use of melatonin among adults more than doubled between 2007 and 2012, to an estimated 3.1 million users.[2] Research has shown that endogenous melatonin levels decline with age, thereby providing the rationale to use melatonin supplements for sleep.[1] However, before considering this treatment, it is critical to determine the situations in which it may be effective and safe. More importantly, pharmacists should be aware of the situations where it has not been proven effective and therefore should not be recommended.

For chronic insomnia, melatonin has a statistically significant but relatively small effect on sleep latency, with a mean reduction of 9 min relative to placebo (95% confidence interval [CI] 2–15 min).[3] The effect on total sleep time or sleep quality is generally considered small or nonsignificant.[3] The practice guideline of the American Academy of Sleep Medicine (AASM) suggests ramelteon (a melatonin receptor agonist that is not available in Canada) as a treatment for sleep-onset insomnia, since its benefits marginally outweigh its harms, with limited to no consistent evidence of adverse events in excess of placebo (mean difference on sleep latency relative to placebo 10 min, 95% CI 6–13 min).[3] The AASM guideline does not recommend melatonin for insomnia in adults, because the quality of the evidence is lower, but it does report mixed evidence suggesting a possible greater improvement in sleep latency in the subpopulation of older adults (mean difference in sleep latency relative to placebo 16 min, 95% CI 6–25 min).[3] Given the positive effect on sleep latency and a good tolerance profile in 2 large trials involving older adults,[4,5] the British Association for Psychopharmacology consensus statement recommends prolonged-release melatonin as a first-line option for older patients when a hypnotic is indicated.[6] However, more data are required for very elderly people, given that the mean age of patients in these studies was below 70 years.[4,5]

Although the effect of melatonin on typical insomnia is mild, it may be useful for other types of sleep disorders, including rapid eye movement sleep behaviour disorder, which is commonly associated with synucleinopathies such as Parkinson disease or Lewy body dementia. In these settings, melatonin is considered the preferred pharmacological option for elderly patients.[7] It is also an option for patients who are blind and suffer from non–24-hour sleep–wake rhythm disorder, given evidence supporting circadian entrainment.[8]

While melatonin may be useful in the aforementioned clinical settings, it is also worthwhile to highlight situations where its effectiveness has not been demonstrated. For example, melatonin should not be substituted for a proper tapering regimen for benzodiazepine cessation. A meta-analysis of 6 tapering trials found no significant effect of melatonin on the odds of successful benzodiazepine discontinuation (odds ratio 0.72, 95% CI 0.21–2.41).[9] However, there was significant heterogeneity among the included studies, with inconsistent effects, and the authors reiterated the need for larger and higher-quality trials.[9]

Caution should also be applied in the use of melatonin for patients with dementia. Although Wang and others,[10] in a meta-analysis published in 2017, reported that melatonin may improve nocturnal sleep time in patients with dementia, a Cochrane review published the previous year found no evidence that melatonin affected any major sleep outcomes in this population.[11] Reassuringly, no detrimental effect on cognition or activities of daily living was detected.[11]

Melatonin is generally well tolerated, and it has a low potential for abuse and no significant withdrawal effects.[12,13] However, side effects may include residual daytime sedation, irritability, restlessness, abnormal dreams, anxiety, nausea, and diarrhea.[12,13] Although melatonin is usually considered safer than benzodiazepines, an increased fracture risk has recently been reported with this drug, and caution should be advised for elderly patients at risk for falls.[14]

Melatonin is only one option in the armamentarium of sleep solutions for older adults. On the extremely harmful end of the spectrum are benzodiazepines, the so-called Z-drugs (nonbenzodiazepines), trazodone, quetiapine, and over-the-counter antihistamines, many of which are used off-label. Almost 17% of 85-year-olds take benzodiazepines, despite questionable clinical benefit.[15] Benzodiazepines reduce sleep-onset latency by 4.2 min and modestly increase total sleep duration, but the latter effect tends to wear off after 4 weeks.[16] Benzodiazepines are associated with significant adverse effects, such as cognitive decline, delirium, falls, fractures, and dependence.[17,18] The Z-drugs, including zopiclone and zolpidem, are not safer alternatives to benzodiazepines because they are also associated with a significant risk of adverse events, such as delirium, falls, and fractures, with minimal improvement in sleep latency and duration.[17] Among over-the-counter medications, antihistamines

such as diphenhydramine were identified as the most frequently used nonprescription products for sleep in a subset of older adults[19]; however, these drugs should be avoided for this purpose because tolerance develops when they are used as hypnotics, and they carry strong anticholinergic properties.[17]

Given the paucity of hypnotics that are safe for use by elderly patients, should melatonin be considered a legitimate alternative? Certainly the effect of melatonin on sleep, as demonstrated in clinical studies, remains of questionable clinical significance. However, when balancing the risks of insomnia itself, including impaired daytime functioning, cognitive impairment, falls, reduced quality of life, and increased mortality, and the known risks associated with benzodiazepines and Z-drugs, some may consider melatonin to be a reasonable alternative when nonpharmacological therapies have failed.[12] In Europe, Clay and others[20] reported that campaigns to reduce the use of benzodiazepines and derivatives were less successful when not associated with availability and sales uptake of melatonin.

Indeed, melatonin is already used by many patients as an over-the-counter product and, in this context, pharmacists should encourage appropriate use. For this purpose, identification of drug-induced insomnia is essential, to prevent medication cascades.[12] Sleep patterns should be assessed to differentiate pathological insomnia from normal age-related sleep changes and to establish realistic sleep expectations.[12] Patients should also be referred for appropriate medical assessment, because comorbidities contributing to insomnia (e.g., pain, heart failure, obstructive sleep apnea, restless leg syndrome) are frequent among elderly patients.[12] As first-line therapy for insomnia, cognitive behavioural therapy should be recommended,[12,16] and various online resources are available to pharmacists who wish to support patients in this area (e.g., the noncommercial Canadian websites https://mysleepwell.ca and https://deprescribing.org/).[16] Subsequently, education for patients about the documented marginal efficacy and potential adverse effects of melatonin (as well as other prescription and nonprescription sedatives) may help them in making an informed choice.

If a trial of melatonin is considered, experts recommend low doses (as low as 0.3 mg up to 2 mg) given 1 h before bedtime.[1,13] In fact, many of the large studies involving older patients with insomnia used a 2-mg dose.[3] Also, maximum concentrations reached with exogenous melatonin are higher in older than in younger adults, and higher doses increase the risk of prolonged supraphysiological blood levels and possible side effects on the following day.[1] Products licensed by Health Canada (identified by a Natural Product Number) should be selected. Appropriate monitoring should be instituted, and melatonin should be stopped if either significant adverse effects occur or lack of efficacy is noted, to avoid unnecessary polypharmacy.

Melatonin use is not a panacea for insomnia experienced by elderly patients. Efficacy remains marginal, and more data from very elderly and fragile patients are required to assess efficacy and safety at low doses. However, melatonin could be useful in specific clinical situations and might help to avoid the use of other hypnotic agents, given its comparatively favourable side effect profile.[13] Moreover, considering its widespread use, pharmacists are well placed to promote the rational and appropriate use of melatonin.

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Competing interests: None declared.

THE "CON" SIDE

Aging is associated with changes, both qualitative and quantitative, in relation to sleep pattern and distribution.[1] The definition of an "elderly person", as used in this article, is based on the chronological age of 65 years.[2] Elderly people have difficulty falling and staying asleep because of frequent awakenings. With aging, total sleep time decreases, sleep onset is delayed, and nap time increases, along with an increase in awakenings and arousals. The quality of sleep declines, and sleep becomes more fragmented with daytime naps.[3] A meta-analysis of 65 studies, representing 3577 healthy individuals aged 5 to 105 years, identified age-related changes by recording sleep patterns across the human lifespan. The authors reported that the total amount of sleep declined with age, with a loss of about 10 min per decade of life.[4]

Sleep architecture also changes with aging. Normal sleep is divided into rapid eye movement (REM) sleep and non–rapid eye movement (NREM) sleep, the latter consisting of 3 stages: N1 (formerly known as stage 1), N2 (stage 2), and N3 (stages 3 and 4).[3] With age, the proportion of total sleep that is REM sleep decreases; however, this decline appears subtle. An increase in N1 and N2 sleep, which results in waking up several times during the night, is described as sleep fragmentation. A decrease in N3 sleep with slow wave sleep is reported, and there are fewer sleep cycles throughout the night. Elderly people spend more time in the lighter phases of sleep (N1 and N2) than in the deep phase (N3).[1,3,4] Physiologic changes in circadian rhythm with aging help to explain why elderly patients often go to bed earlier and wake up earlier, which affects the quality and duration of their sleep.[3]

Sleep architecture may differ between men and women. Results from a meta-analysis suggested that men's sleep patterns are more affected by age than women's.[4] The same meta-analysis reported that men have less total sleep time, with a lower percentage in N3 and REM sleep and a higher percentage in N2 sleep, relative to women.[4] Conversely, women have more sleep latencies than men. These findings may be important, given that women frequently self-report shorter and lower-quality sleep than men.[5] This difference between men and women in the perception of sleep problems is often presented as a reason why hypnotics are prescribed more frequently for women than for men.[6] Overall, the sex-based difference in sleep architecture remains to be elucidated.

Melatonin (*N*-acetyl-5-methoxytryptamine), a hormone released by the pineal gland, binds to the MT1 and MT2 receptors and regulates circadian rhythm.[7] Its production is controlled by light, whereby levels of serum melatonin increase during the evening hours, reaching peak concentration between 0200 and 0400, and are suppressed by light, with low concentrations occurring during daytime.[1,3,4,7] Studies have shown that melatonin level declines with age, which may increase conditions related to circadian rhythm, such as sleep disorders.[1,3,4]

Melatonin is often prescribed to treat insomnia in older patients. It is absorbed rapidly, reaching peak plasma concentration 60 min after oral administration, with a half-life of 35 to 61 min.[8] Bioavailability is about 15% (range 9% to 33%), with extensive first-pass metabolism. A small amount (5%) is excreted unchanged by the kidney.[8] Melatonin is extensively metabolized primarily by the cytochrome P450 1A2 isoenzyme, with minimal contributions by CYP2C9 and CYP2C19 isozymes.[8] In a cohort study involving 5 male volunteers, coadministration of fluvoxamine 50 mg and melatonin 5 mg increased the maximum serum concentration of melatonin by a factor of 12 and the area under the concentration–time curve of melatonin by a factor of 17.[9]

Erland and Saxena[10] analyzed 31 commonly available melatonin supplements purchased from local grocery stores and pharmacies in Guelph, Ontario. The products consisted of 16 different brands in various formulations, such as liquid, tablet, and capsule. The authors found that the melatonin content ranged from –83% to +478% of the label claim. Furthermore, lot-to-lot variability within the same product varied by as much as 465%.[10] Sublingual and tablet products had the least variability, and liquid formulations had the greatest variability. Furthermore, 8 (26%) of the 31 supplements tested were contaminated with the indoleamine serotonin.[10]

Melatonin administered orally has been reported to imitate endogenous melatonin by shifting the circadian clock earlier, thus promoting sleep onset and morning awakening. Numerous studies of the effects of melatonin on sleep in elderly patients have been published,[11,12] but their results have been inconsistent because of a lack of high-quality randomized controlled trials. Results from these studies have shown no overall improvement in objective measures of sleep, with a lack of significant effect on sleep time, sleep latency, number of awakenings, and sleep efficiency.[11,12] Safety concerns, especially among elderly patients, are residual daytime drowsiness, tiredness upon rising, and increased sleep disruption.[11,12]

A 2016 Cochrane systematic review evaluated melatonin's

clinical effect on sleep and its side effects in persons with dementia.[13] Only randomized placebo-controlled trials, including crossover trials, were included in the review. Two studies (with a total of 184 patients) met the inclusion criteria. The primary outcomes were total nocturnal sleep time (mean difference 10.68 min, 95% CI –16.22 to 37.59) and ratio of daytime sleep to night-time sleep (mean difference –0.13, 95% CI –0.29 to 0.03). In this systematic review, the authors reported that a dose of up to 10 mg of melatonin did not improve sleep outcome measures over an 8- to 10-week period in patients with Alzheimer disease and sleep disturbance. They also reported no effect of melatonin on cognition or activities of daily living, and no serious side effects.[13]

In 2016, the Agence nationale de sécurité du médicament et des produits de santé (France) published a summary list of 200 side effects associated with the use of melatonin, reported between 1985 and 2016.[14] These reported side effects included neurological disorders (43%), such as syncope, headache, and convulsion; psychiatric disorders (24%), such as anxiety and depression; skin disorders (19%), such as rashes and maculopapular rashes; and digestive problems (19%), such as constipation, acute pancreatitis, and nausea.[14]

Factors causing insomnia in elderly patients should be ruled out. Treatment for chronic medical conditions, such as congestive heart failure, chronic obstructive pulmonary disease, Parkinson disease, depression, dementia, and pain, should be instituted and optimized. Numerous medications and other substances, such as caffeine, decongestants, corticosteroids, diuretics, nicotine, selective serotonin reuptake inhibitors, theophylline, thyroid hormone, and alcohol, can contribute to (or cause) insomnia.[15] Patients' use of these medications and substances should be carefully evaluated on a regular basis.

Cognitive behavioural therapy for insomnia is a nonpharmacological approach that has been shown to improve sleep hygiene. It is based on various elements of sleep hygiene and behaviour modification, such as restricting the amount of time in bed, reducing external stimuli, promoting relaxation through meditation, limiting caffeine and alcohol intake, and avoiding daytime napping and exercise close to bedtime. Randomized controlled trials involving older patients have found that these interventions can achieve long-term improvements in sleep and reductions in hypnotic use by older patients.[15]

In summary, the quality of the evidence for using melatonin to treat insomnia in elderly patients is weak. Furthermore, some clinically significant side effects have been reported with its use in this population. In Canada, melatonin can be obtained as an over-the-counter supplement and in health food stores; hence, adverse effects are likely under-reported. As alternatives to melatonin therapy, factors that may contribute to insomnia should be reduced and nonpharmacological treatments suggested to the patient, along with cognitive behavioural interventions. Patients should also be educated about changes in sleep pattern with aging. Pharmacists can play an important role in providing this information.

As a final comment, we perhaps need to reconsider the time at which elderly patients are put to bed in some nursing homes and other long-term care settings in Canada. Anecdotal information indicates that it is not uncommon for elderly patients to be in bed by 1900. If you were 85 years old and put to bed by early evening, wouldn't you be awake at midnight, asking for a hypnotic or sedative? Ultimately, we need to meet the needs of our patients, not those of the nursing home.

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Competing interests: None declared.

Duration of Antibiotic Therapy in Sepsis Secondary to Urinary Stones: A Retrospective Observational Study

Pharmacists are essential members of antimicrobial stewardship programs, which have been in place for several years in many institutions, in response to the urgent threat posed by antibiotic resistance. It is well established that prolonged antibiotic exposure is associated with an increased risk of antimicrobial resistance, infection with *Clostridioides difficile* (previously known as *Clostridium difficile*), and adverse events[1-3]; however, research to optimize the duration of antibiotic therapy is still needed for many infections. During weekly antimicrobial stewardship rounds at the authors' institution, it was noted that some patients presenting with an obstructive infected urinary stone were treated with a 2-week course of antibiotics, whereas others were treated with antibiotics until removal of the stone. Although guidelines recommend that removal of infected urinary stones not be undertaken until the infection has been adequately treated,[4,5] the appropriate duration of antibiotic therapy has not been defined.[4-8]

To help address this gap in knowledge, we conducted a retrospective observational study to compare effectiveness and safety outcomes for patients admitted with sepsis secondary to one or more obstructive urinary stones, who were treated with the 2 most common durations of antibiotic therapy. The study was approved by the Ottawa Health Science Network Research Ethics Board. Patients 18 years of age or older who were admitted with an obstructive infected stone, who had undergone decompression (typically via urinary stenting), and who had been treated with either a 10- to 14-day course of antibiotics (± 2 days) followed by an antibiotic-free period until stone removal (group 1) or a longer, continuous course of antibiotics until stone removal (group 2) were included. Records of patients with the discharge diagnosis keywords ("stone", "calculus", or "calculi") AND ("sepsis", "septic", "infected", "urosepsis", "UTI", or "pyelonephritis") from January 2014 to January 2017 inclusive were reviewed. The primary end point was recurrent infection (i.e., new antibiotic course or change in antibiotics prescribed for a urinary tract–related infection, on the basis of reported signs and symptoms, regardless of culture results) before stone removal. Secondary end points included recurrent infection between the time of stone and stent removal, stone- or stent-related complications, antibiotic-related adverse events and new microorganism resistance. The sample size needed was calculated as 49 patients per group, for a total of 98 patients. This sample size calculation was based on guidelines for chart audits.[9] We based our calculation on a desired power of 0.8, precision of 0.2, α of 0.05, and expected proportion within the population with recurrent infection as 0.15. There were no previous studies to draw upon for determining the expected proportion; therefore, the estimate of 15% was conservative and was based on expert clinical opinion. Chi-square and Fisher exact tests were used for statistical analysis of the primary and secondary end points.

Because we had difficulty identifying patients for inclusion in group 2, we had fewer patients than planned: 50 patients in group 1 and 27 in group 2. Group 2 had significantly more men, higher American Society of Anesthesiologists scores, higher risk of not receiving an appropriate empiric antibiotic regimen, more bloodstream infections, more infectious diseases consultations, and more frequent admission to the intensive care unit relative to group 1 (Table 1). Primary and select secondary outcomes are presented in Table 2. All 8 patients with recurrent urinary tract infection before stone removal had received appropriate initial antibiotic therapy. In addition, among those for whom culture results were available ($n = 5$), the microorganism identified at the time of recurrent infection was different from that identified at the time of initial presentation, except for 1 patient, who was found to have a perinephric abscess. Infection with *C. difficile* occurred in 1 patient in group 1. New microorganism resistance was found in 2 urine specimens in each group. Antibiotic adverse events occurred in 1 patient in group 1 (diarrhea) and 2 patients in group 2 (rash, diarrhea).

To the authors' knowledge, this is the first published study to assess different durations of antibiotic therapy in patients with an obstructive infected urinary stone. In this study, patients in group 1 had a more than 3-fold increased risk of recurrent infection before stone removal relative to patients in group 2. This difference, while not statistically significant, may be clinically relevant.

Patients treated with a prolonged, uninterrupted course of antibiotics (group 2) were more likely to be male, were more likely to receive an ineffective empiric antibiotic, and were more severely ill on admission relative to the patients with an initial 10- to 14-day course of antibiotics followed by an antibiotic-free period (group 1). Despite these differences, patients in group 2 had a lower risk of recurrent infection before stone removal. If a difference between the 2 groups truly exists, these results suggest that a prolonged, uninterrupted course of antibiotics may be preferable. Alternatively, we hypothesize that the duration of the antibiotic-free period before definitive stone

Table 1. Patient Characteristics

Characteristic	Group; No (%) of Patients*		*p* Value
	Group 1: Antibiotics for 10–14 Days, then Antibiotic-Free Period (*n* = 50)	Group 2: Antibiotics until Removal of Stone (*n* = 27)	
Mean duration of antibiotics (days) (range)	13 (8–16)	39 (17–103)	< 0.001
Mean age (years) (range)	59 (25–84)	66 (26–89)	0.055
Sex, male	19 (38)	17 (63)	0.036
Mean ASA score on admission (range)	2.98 (1–4)‡	3.48 (2–5)§	0.039
Altered urinary tract (anatomic or functional)	14 (28)	12 (44)	0.21
Immunocompromised	1 (2)	0 (0)	> 0.99
Diabetes mellitus	14 (28)	11 (41)	0.31
Admission to ICU	4 (8)	8 (30)	0.020
Bloodstream infection between admission and discharge†	9/29 (31)	20/22 (91)	< 0.001
Microbiologic results available	30 (60)	25 (93)	0.003
Concordance between empiric antimicrobial agent and microorganism susceptibility	30/30 (100)	16/25 (64)**	0.001
ID consultation for urosepsis	2 (4)	25 (93)	< 0.001
Clostridioides difficile infection in 12 months before admission	0	0	NA
Mean size of largest obstructing stone (mm) (range)	8.7 (2.5–30)	14.7 (4–100)	0.11
History of obstructive infected stone			0.23
First episode	47 (94)	22 (82)	
Second episode	2 (4)	3 (11)	
Third or more episode	1 (2)	2 (7)	
Location of obstructive stone			0.30
One ureter	30 (60)	18 (67)	
Both ureters	2 (4)	0 (0)	
One ureterovesical junction	3 (6)	0 (0)	
Both ureterovesical junctions	1 (2)	0 (0)	
Ureteropelvic junction	13 (26)	9 (33)	
Ureter and kidney	1 (2)	0 (0)	
Intervals (days)			
Between onset of symptoms and decompression	Mean 2.3, median 2 (range 0–10)	Mean 3.5, median 2 (range 0–20)	0.25
Between presentation and definitive stone removal	Mean 38, median 32 (range 13–109)	Mean 38, median 32 (range 17–103)	NA
Between definitive stone removal and stent removal	Mean 14, median 14 (range 0–35)	Mean 20, median 21 (range 0–76)	0.29
No. of antibiotic-free days (mean and range)	25 (3–95)	NA	

ASA = American Society of Anesthesiologists, ICU = intensive care unit, ID = infectious diseases, NA = not applicable.
*Except where indicated otherwise.
†All cases were attributed to the infected urinary stone(s).
‡Data were available for 49 of 50 patients.
§Data were available for 25 of 27 patients.
**All regimens were changed as soon as susceptibility results were available. None of these patients had a recurrent infection.

Table 2. Recurrent Infections and Stone- or Stent-Related Complications

Event	Group; No (%) of Patients		*p* Value
	Group 1: Antibiotics for 10–14 Days, then Antibiotic-Free Period	Group 2: Antibiotics until Removal of Stone	
Before removal of stone			
Recurrent infection	7/50 (14)	1/27 (4)	0.25
Stone- or stent-related complication*	8/50 (16)	8/27 (30)	0.24
Between removal of stone and removal of stent			
Recurrent infection	4/43 (9)	5/20 (25)	0.13
Stone- or stent-related complication*	10/43 (23)	5/21 (24)	> 0.99

*Examples: stent-related pain or discomfort, hematuria, encrustation of stent.

removal may have influenced the risk of recurrent infection, although this would need to be confirmed through further investigation. It is possible that a threshold of antibiotic-free days exists, beyond which the risk of recurrent infection increases. In both groups in our cohort, there was a wide range in the time to definitive stone treatment (Table 1), largely because of differences in access to operative time between surgeons.

Although there were no significant differences in the rate of new resistant microorganisms, *C. difficile* infections, and adverse drug events between groups 1 and 2, it is well established that the risk for these events increases with duration of antibiotic treatment.[1-3] Given the lower number of patients we were able to enroll in group 2, our study may not have had sufficient power to detect any difference, even if such differences had been present. Other limitations include the retrospective nature of the study and the possibility that unassessed variables (e.g., antibiotics prescribed for non-urinary-tract-related infections after discharge, hydration status, potential missed events) may have contributed to the complications reported.

Although the optimal duration of treatment remains unresolved, these data may signal a difference in favour of a continuous course of antibiotics until definitive stone management, and they certainly provide an impetus to conduct a larger trial. Stewardship teams are well positioned to share these findings, while weighing the risks and potential benefits of both approaches.

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Competing interests: None declared.

Funding: None received.

Acknowledgements: The authors sincerely thank Amanda Owen for her assistance in collecting data and Pierre Giguère for his general guidance.

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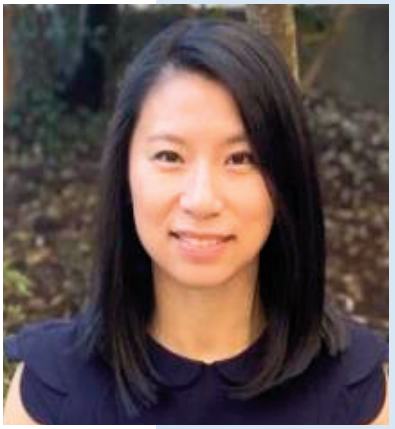

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Un pas en avant : la Stratégie de développement durable

par Patrick Fitch

Dans des commentaires précédents, j'ai décrit certains changements prévus pour la Société canadienne des pharmaciens d'hôpitaux (SCPH). Peut-être pendant l'été avez-vous également vu des annonces vidéo ou lu dans les médias sociaux au sujet de la Stratégie de développement durable de la SCPH. J'aimerais détailler ici la manière dont elle a été élaborée et ce qu'elle signifie pour les membres.

En janvier dernier, la direction de la SCPH a terminé son travail relatif à la Stratégie. Ensuite, le Conseil et les délégués des sections ont examiné attentivement la Stratégie et les hypothèses qui avaient pour objectif de transformer la SCPH en une association plus pertinente, mieux apte à réagir aux changements, davantage orientée vers les besoins de ses membres, et donc plus utile pour eux, et capable d'assurer une gestion financière responsable. Ces consultations ont entraîné un grand nombre de révisions, dont le résultat final est une stratégie pluriannuelle en vue d'un changement complexe et transformateur qui modifiera le mode de fonctionnement de la SCPH et entraînera sa viabilité financière.

La Stratégie repose sur cinq piliers : la croissance des adhésions par la valorisation des services, l'augmentation de la profitabilité des programmes, le renforcement de la gestion financière, l'exploration de grandes idées (comme l'adhésion des techniciens, le cannabis et l'assurance-médicaments) et le renforcement de l'infrastructure.

Pour mener à bien ce plan, la SCPH doit investir environ 950 000 $ sur quatre ans. Cet investissement proviendra des réserves de la SCPH, en d'autres termes, des provisions faites pour les « mauvais jours » qui maintenant sont arrivés! Voici la ventilation des contributions : 81 % proviendront de la réserve nationale, 16 % des réserves des sections et du séminaire de Banff et 3 % des fonds inutilisés accumulés par les conseils affiliés à la SCPH.

Après avoir approuvé la Stratégie au début du mois de mars, le Conseil s'est réuni en avril pour discuter des options visant à déterminer les contributions spécifiques des sections. Ces discussions ont laissé transparaître un véritable souci d'impartialité et d'équité entre toutes les sections. Les options ont été présentées aux présidents des sections pour qu'ils les examinent. Ensuite, ces derniers ont rencontré le Conseil pour décider de la formule des contributions.

Au moment de la rédaction de la description des cinq piliers (début de l'été), la mise en place de la Stratégie avait déjà commencé. Sous le pilier « Grandes Idées », la SCPH a constitué des groupes de travail consacrés aux techniciens de pharmacie et au cannabis ainsi qu'un conseil consultatif pour conseiller sur la mise en place des Appels à l'action de la Commission vérité et réconciliation. Sous le pilier « Renforcement de l'infrastructure », Clara Wicke s'est jointe au bureau de la SCPH et occupe le nouveau poste de directrice du marketing et des communications. Parmi ses nombreuses tâches, on notera la nécessité de rendre opérationnelle l'activité des groupes de travail consacrés au recrutement et à la rétention des membres ainsi que la préparation d'un plan marketing visant à accroître la profitabilité de la Conférence sur la pratique professionnelle (CPP). Une partie de ce plan consistera à organiser les CPP partout au Canada à partir de 2022. Restez à l'affût des annonces concernant le premier congrès itinérant!

La Stratégie aura également un impact important sur le prochain plan stratégique de la SCPH. Pour nous assurer d'effectuer un travail optimal en vue de renforcer l'expérience des membres, nous mènerons un sondage qui recueillera leur avis sur le travail de planification stratégique du Conseil lors de sa réunion de l'automne. Le sondage se déroulera de la mi-août à la mi-septembre.

C'est ici mon dernier commentaire en tant qu'agent présidentiel de la SCPH. J'ai hâte de voir l'évolution de la SCPH au cours des années à venir et je suis très heureux d'avoir pu jouer un certain rôle dans la pérennité de son succès.

[Traduction par l'éditeur]

Patrick Fitch, B. S. P., A. C. P. R., est président sortant et agent de liaison interne de la Société canadienne des pharmaciens d'hôpitaux.

A Path Forward: The Strategy Towards Sustainability

Patrick Fitch

In previous commentaries, I have written about some of the changes in store for the Canadian Society of Hospital Pharmacists (CSHP), and you may have seen social media and video announcements about CSHP's Strategy Towards Sustainability over the course of the summer. Here, I would like to share some details about how the strategy was developed and what it means for members.

The CSHP Executive completed work on the strategy in January. The Board and Branch Executives then provided robust scrutiny of the strategy and its assumptions, with the goals of transforming CSHP into a more relevant, responsive, member-centric, and thus valuable association, and ensuring responsible financial stewardship for the Society. These consultations led to further revisions, the net result being a multiyear strategy for complex, transformational change that will alter the way CSHP operates and lead to financial sustainability.

The strategy encompasses 5 pillars: growing membership by enhancing value; increasing profitability of programs; enhancing financial stewardship; exploring big ideas (such as technician membership, cannabis, and pharmacare); and strengthening infrastructure.

To accomplish the plan, CSHP will require an investment of about $950 000 over 4 years. The source of this investment will be CSHP's reserves—in other words, the "rainy day" for which we built those reserves has now arrived. The breakdown of contributions will be 81% from the national reserve, 16% from Branch and Banff Seminar reserves, and 3% from unused funds accumulated by CSHP's affiliated boards.

After approving the strategy in early March, the Board met in April to discuss options for determining specific Branch contributions. Foremost in these discussions was a remarkable concern for equity and fairness for all Branches. The options were presented to Branch presidents for consideration. The Branch presidents then met with the Board to decide upon the contribution formula.

At the time of writing (early summer), implementation of the strategy had begun. Under the "big ideas" pillar, CSHP has struck task forces on pharmacy technicians and cannabis, as well as an advisory circle to advise on implementing relevant Calls to Action from the Truth and Reconciliation Commission. Under the "strengthening infrastructure" pillar, Clara Wicke joined the CSHP office in the new role of Director of Marketing and Communication. Among her many tasks will be operationalizing the work of the membership recruitment and retention working groups and developing a marketing plan to help increase the profitability of the annual Professional Practice Conference (PPC). Part of that plan will see the PPC location circulate throughout Canada, beginning in 2022. Look for announcements about PPC's first road trip.

This strategy will also have a significant impact on the next CSHP Strategic Plan. To ensure we do the best job of enhancing the CSHP membership experience, we will be surveying members for input to the Board's strategic planning work at its fall meeting; the survey will be open from mid-August to mid-September.

This is my final commentary as a CSHP Presidential Officer. I look forward to watching the progress of CSHP in the coming years and feel grateful for having played a part in ensuring the ongoing success of our Society.

Patrick Fitch, BSP, ACPR, is Past President and Internal Liaison for the Canadian Society of Hospital Pharmacists.

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