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The Canadian Journal of Hospital Pharmacy
Vol. 76, No. 4 Fall 2023
Pages 261–347

Le Journal canadien de la pharmacie hospitalière
Vol. 76, nº 4 Automne 2023
Pages 261–347

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Official Journal of the / Revue officielle de la

Canadian Society of Hospital Pharmacists / Société canadienne des pharmaciens d'hôpitaux

THE CANADIAN JOURNAL OF HOSPITAL PHARMACY
Published 4 times yearly, by the Canadian Society of Hospital Pharmacists, an organization pledged to further the progress of hospital pharmacy.

LE JOURNAL CANADIEN DE LA PHARMACIE HOSPITALIÈRE
Publié quatre fois par année par la Société canadienne des pharmaciens d'hôpitaux, une organisation vouée à l'avancement de la pharmacie hospitalière.

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Multimed Inc.
Tel: 519.578.9897
email: publishing_services@multi-med.com

Date of issue: October 2023
Date d'émission : octobre 2023

ISSN 1920-2903

WEBSITE / SITE WEB
cjhp.ca

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The Future of Hospital Pharmacy Practice: Pathways to Independent Clinical Pharmacy Practice

Jonathan Penm

https://doi.org/10.4212/cjhp.3527

The COVID-19 pandemic has stretched health care systems and exacerbated problems in areas that were already under pressure. To relieve this pressure, health care systems are looking for ways to expand pharmacists' scope of practice. One approach would be to increase both the utilization of pharmacist prescribing and the number of independent clinical pharmacist practitioners. Although pharmacist prescribing has been commonplace in some provinces for more than a decade,[1] only recently has it been implemented in others, such as Ontario.[2] Internationally, Australia has also recently adopted pharmacist prescribing for minor ailments (e.g., urinary tract infections).[3] Utilizing these skills is more common among pharmacists in community and outpatient settings. However, such roles have had less uptake in the hospital pharmacy setting. Correspondingly, expansion of the scope of pharmacist practice appears less clear in the inpatient hospital setting than in the community or outpatient setting.[4]

In this issue, Almawed and others[5] report on the proportion of patients for whom inpatient pharmacists with additional prescribing authorization (APA) prescribe at discharge. Prescribing at discharge by hospital pharmacists is a fairly novel concept. A recent randomized trial in an Australian geriatric medical ward showed that pharmacists who prescribed using handwritten prescriptions had fewer patients experiencing at least one medication error at discharge relative to conventional handwritten discharge prescribing (29% versus 95%, $p < 0.0002$).[6] A similar though smaller benefit was seen with digital prescriptions (62% versus 100%, $p = 0.005$).[6] Given these benefits, Almawed and others conducted a cross-sectional web-based survey of APA inpatient pharmacists, specifically asking about their activities at discharge. The authors found that fewer than half of APA pharmacists prescribed at discharge. They also identified the top three enabling factors for pharmacists who did prescribe at discharge: a supportive care team (71.4%), competence in the particular area of practice (54.9%), and desire to deliver more efficient care (51.6%).[5] From these results, it appears that the external environment, including availability of support, is perceived as having a greater influence on pharmacist prescribing at discharge than internal motivators.

Pharmacists' comfort with prescribing and the pathway to becoming independent clinical pharmacist practitioners are also explored in this issue by Parmar and others.[7] These authors define a clinical pharmacist practitioner as "a pharmacotherapy expert who practises independently at their full scope, conducts thorough patient assessments, responds to consultations, monitors and adjusts drug therapy, provides education to patients and colleagues, and may prescribe independently or in collaboration with other health care professionals." During 13 interviews with Canadian clinical pharmacist practitioners (mainly hospital pharmacists; $n = 8$), strong mentorship, internal motivation, and endorsement of diverse professional pathways were identified as important factors that led interview participants to become clinical pharmacist practitioners. In particular, they identified mentorship as a critical factor that helped shape their practice. Similar to the previously mentioned study,[5] the external environment and appropriate support were seen as the most crucial factors in the development of a clinical pharmacist practitioner.[7]

One possible way to develop supportive external environments is through a unified national credentialling system that signifies high-level pharmacy practice in Canada. Such a process has been explored in Australia and the United Kingdom, where frameworks for advanced pharmacy practice have been developed.[8,9] In Australia, such frameworks have been supported by the Society of Hospital Pharmacists of Australia's Advanced Training Residencies.[10] These residencies offer an accredited pathway for specialty development in a specific practice area or specialty in accordance with Stage 2 (the "Consolidation" level) of the National Competency Standards Framework for Pharmacists in Australia.[11] Such residencies have been available since 2020 and are ideal for practitioners with 3 to 7 years

of foundational hospital pharmacy experience.[10] Similar structured pathways could be considered for Canada to ensure that pharmacists wishing to develop as clinical pharmacist practitioners are supported on their journey.

Parmar and others[7] also identified role uncertainty within the pharmacy profession itself as a major barrier for the advancement of the profession. They highlighted that the future vision for pharmacists was unclear or even lacking in Canada.[7] This concern is not new and indeed has been expressed by pharmacists around the world for many years. For example, in response to this concern, the Hospital Pharmacy section of the International Pharmaceutical Federation (FIP) hosted the Global Conference on the Future of Hospital Pharmacy back in 2008 in Basel, Switzerland.[12] The FIP is the global body representing over 4 million pharmacists, pharmaceutical scientists, and pharmaceutical educators through its more than 150 national pharmacy organization members.[13] At the 2008 conference, the FIP's Hospital Pharmacy section developed the Basel Statements, a set of consensus statements reflecting a unified global vision of hospital pharmacy practice.[12] The statements have a strong focus on medication safety and describe hospital pharmacists' involvement in procurement; their influences on prescribing, preparation and delivery, administration, and monitoring of medicine use; and the role of human resources, training, and development.[12,14] The Basel Statements have been updated regularly to reflect current practice,[14] with the latest revision under discussion in September 2023 at the FIP Brisbane Congress.[15] I encourage all hospital pharmacists to contribute to these updates and to ensure that learnings from your country are heard and recognized around the world.[15] Although the Canadian Society of Hospital Pharmacists is not an organizational member of the FIP, it has already contributed toward revision of the Basel Statements. From this work, I believe pharmacists around the world have more commonalities than differences, and constant reflection on international practices will ensure that our patients receive the best care that pharmacists can provide.

References

1. Yuksel N, Eberhart G, Bungard TJ. Prescribing by pharmacists in Alberta. *Am J Health Syst Pharm.* 2008;65(22):2126-32.
2. Expanded scope of practice: Minor ailments 2023. Ontario College of Pharmacists; [cited 2023 Aug 4]. Available from: https://www.ocpinfo.com/practice-education/expanded-scope-of-practice/minor-ailment/
3. UTI program now permanent in Qld [news release]. Pharmacy Guild of Australia; 2022 Oct 12 [cited 2023 Jul 1]. Available from: https://www.guild.org.au/news-events/news/forefront/v12n10/uti-program-now-permanent-in-qld
4. Poh EW, McArthur A, Stephenson M, Roughead EE. Effects of pharmacist prescribing on patient outcomes in the hospital setting: a systematic review. *JBI Database System Rev Implement Rep.* 2018;16(9):1823-73.
5. Almawed R, Shiu J, Bungard T, Charrois T, Gill P. Pharmacist prescribing at inpatient discharge in Alberta. *Can J Hosp Pharm.* 2023;76(4):275-81.
6. Finn S, D'arcy E, Donovan P, Kanagarajah S, Barras M. A randomised trial of pharmacist-led discharge prescribing in an Australian geriatric evaluation and management service. *Int J Clin Pharm.* 2021;43(4):847-57.
7. Parmar R, Legal M, Dahri K, Wilbur K, Shalansky S, Partovi N. Pathways to developing clinical pharmacist practitioners: is there a better way forward? (Path-CPP). *Can J Hosp Pharm.* 2023;76(4):302-8.
8. *The RPS advanced pharmacy framework (APF).* Royal Pharmaceutical Society; 2013 [cited 2023 Aug 4]. Available from: https://www.rpharms.com/resources/frameworks/advanced-pharmacy-framework-apf
9. Jackson S, Martin G, Bergin J, Clark B, Stupans I, Yeates G, et al. An advanced pharmacy practice framework for Australia. *Pharmacy (Basel)* 2015;3(2):13-26.
10. Advanced training residencies. Society of Hospital Pharmacists of Australia; 2023 [cited 2023 Aug 4]. Available from: https://www.shpa.org.au/workforce-research/residency/advanced-training
11. *National competency standards framework for pharmacists in Australia.* Pharmaceutical Society of Australia Ltd; 2016 [cited 2023 Aug 4]. Available from: https://www.psa.org.au/wp-content/uploads/2018/06/National-Competency-Standards-Framework-for-Pharmacists-in-Australia-2016-PDF-2mb.pdf
12. International Pharmaceutical Federation. The Basel Statements on the future of hospital pharmacy. *Am J Health Syst Pharm.* 2009;66(5 Suppl 3):S61-6.
13. Who we are [webpage]. International Pharmaceutical Federation; 2023 [cited 2023 Jul 1]. Available from: https://www.fip.org/about
14. Vermeulen LC, Moles RJ, Collins JC, Gray A, Sheikh AL, Surugue J, et al. Revision of the International Pharmaceutical Federation's Basel Statements on the future of hospital pharmacy: from Basel to Bangkok. *Am J Health Syst Pharm.* 2016;73(14):1077-86.
15. Basel Statements: the future of hospital pharmacy practice. International Pharmaceutical Federation; 2023 [cited 2023 Jul 1]. Available from: https://www.fip.org/basel-statements

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Competing interests: For activities unrelated to this editorial, Jonathan Penm has received a grant from the Medical Research Future Fund (Australian Government). He has also received consulting fees (paid to the University of Sydney) from the Hospital Pharmacy Section of the International Pharmaceutical Federation. No other competing interests were declared.

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L'avenir de la pratique de la pharmacie hospitalière : Voies vers la pratique indépendante de la pharmacie clinique

par Jonathan Penm

https://doi.org/10.4212/cjhp.3539

La COVID-19 a mis à rude épreuve les systèmes de santé et a exacerbé les problèmes dans des domaines déjà sous pression. Pour soulager cette pression, les systèmes de santé cherchent des moyens d'élargir le champ de pratique des pharmaciens. Une approche possible consisterait à augmenter à la fois l'utilisation de la prescription par les pharmaciens et le nombre de pharmaciens cliniciens indépendants. Bien que la prescription par les pharmaciens soit courante dans certaines provinces depuis plus d'une décennie[1], ce n'est que récemment qu'elle a été mise en œuvre ailleurs au pays, comme en Ontario[2]. À l'échelle internationale, l'Australie a également récemment adopté la prescription de médicaments par les pharmaciens pour des affections mineures (p. ex., les infections des voies urinaires)[3]. L'utilisation de ces compétences est plus courante chez les pharmaciens en milieu communautaire et ambulatoire et ces rôles ont été moins adoptés dans le cadre de la pharmacie hospitalière. En conséquence, l'élargissement du champ d'exercice de la profession de pharmacien semble moins évident en milieu hospitalier qu'en milieu communautaire ou ambulatoire[4].

Dans ce numéro, Almawed *et al.*[5] rendent compte de la proportion de patients pour lesquels les pharmaciens hospitaliers titulaires d'une autorisation supplémentaire de prescrire prescrivent au moment du congé. La prescription au moment du congé de l'hôpital par les pharmaciens hospitaliers est un concept assez nouveau. Selon un récent essai randomisé dans un service de médecine gériatrique australien, le nombre de patients ayant subi au moins une erreur de médication au moment du congé était moins élevé lorsque les pharmaciens prescrivaient les médicaments que lorsque ceux-ci étaient prescrits par des médecins, dans les deux cas à l'aide d'ordonnances manuscrites (29 % contre 95 %, $p < 0{,}0002$)[6]. Un avantage similaire quoique plus faible a été observé avec les prescriptions numériques (62 % contre 100 %, $p = 0{,}005$)[6]. Compte tenu de ces avantages, Almawed *et al.* ont mené une enquête transversale en ligne auprès de pharmaciens hospitaliers titulaires d'une autorisation supplémentaire de prescrire en se penchant tout particulièrement sur leurs activités au moment du congé. Les auteurs ont constaté que moins de la moitié de ces pharmaciens prescrivaient au moment du congé. Ils ont également identifié les trois principaux facteurs propices pour que les pharmaciens prescrivent au moment du congé : le soutien de l'équipe de soins (71,4 %), la compétence dans le domaine de pratique particulier (54,9 %) et le souhait de fournir des soins plus efficaces (51,6 %)[5]. D'après ces résultats, il semble que l'environnement externe, y compris la disponibilité du soutien, soit perçu comme ayant une plus grande influence sur la prescription de médicaments par les pharmaciens au moment du congé que les facteurs de motivation internes.

Dans ce numéro également, Parmar *et al.*[7] se penchent sur le degré de confort des pharmaciens en matière de prescription ainsi que la voie à suivre pour devenir pharmacien clinicien indépendant. Ces auteurs définissent le pharmacien clinicien comme un expert en pharmacothérapie qui exerce de manière indépendante dans l'ensemble de ses compétences, mène des évaluations approfondies des patients, répond aux consultations, surveille et adapte la pharmacothérapie, donne des conseils aux patients et aux collègues et peut prescrire de manière indépendante ou en collaboration avec d'autres professionnels de la santé. Au cours de 13 entrevues menées avec des pharmaciens cliniciens canadiens (principalement des pharmaciens hospitaliers; $n = 8$), un solide mentorat, une motivation interne et un choix parmi divers cheminements professionnels approuvés ont été recensés comme des facteurs importants qui ont amené les participants aux entrevues à devenir des pharmaciens cliniciens. En particulier, ils ont noté le mentorat comme un facteur critique ayant contribué à façonner leur pratique. À l'instar de l'étude mentionnée précédemment[5], l'environnement externe et un soutien approprié sont considérés comme les facteurs les plus importants dans le développement d'un pharmacien clinicien[7].

Une façon possible de mettre au point des environnements externes favorables consiste à mettre en place un système national unifié d'accréditation qui indique une pratique pharmaceutique de haut niveau au Canada. Un tel processus a été étudié en Australie et au Royaume-Uni, où

des cadres pour la pratique pharmaceutique avancée ont été définis[8,9]. En Australie, de tels cadres ont été soutenus par la *Society of Hospital Pharmacists of Australia's Advanced Training Residencies*[10]. Les stages offerts par cette société proposent une voie d'accréditation pour le développement de la spécialité dans un domaine de pratique ou une spécialité précise conformément à l'étape 2 (le niveau de « consolidation ») du Cadre national de normes de compétence pour les pharmaciens en Australie (*National Competency Standards Framework for Pharmacists in Australia*)[11]. De tels stages sont offerts depuis 2020 et sont idéals pour les praticiens avec 3 à 7 ans d'expérience fondamentale en pharmacie hospitalière[10]. Des parcours structurés similaires pourraient être envisagés au Canada afin de s'assurer que les pharmaciens souhaitant se perfectionner en tant que pharmaciens cliniciens sont soutenus dans leur parcours.

Parmar *et al.*[7] ont également identifié l'incertitude liée au rôle au sein de la profession elle-même comme un obstacle majeur à l'avancement de la profession. Ils soulignent que la vision d'avenir pour les pharmaciens était incertaine, voire absente, au Canada[7]. Cette préoccupation n'est pas nouvelle et est d'ailleurs soulevée par des pharmaciens du monde entier depuis de nombreuses années. Par exemple, en réponse à cette préoccupation, la section Pharmacie hospitalière de la Fédération internationale pharmaceutique (FIP) a organisé la Conférence mondiale sur l'avenir de la pharmacie hospitalière en 2008 à Bâle, en Suisse[12]. La FIP est l'organisme mondial qui représente plus de 4 millions de pharmaciens, de scientifiques pharmaceutiques et d'éducateurs pharmaceutiques par l'intermédiaire de ses plus de 150 organisations pharmaceutiques nationales membres[13]. Lors de la conférence de 2008, la section Pharmacie hospitalière de la FIP a élaboré les Déclarations de Bâle : un ensemble de déclarations consensuelles reflétant une vision globale unifiée de la pratique de la pharmacie hospitalière[12]. Les déclarations mettent fortement l'accent sur l'innocuité des médicaments et décrivent la participation des pharmaciens hospitaliers à l'approvisionnement; leurs influences sur la prescription, la préparation et la livraison, l'administration et le suivi de l'utilisation des médicaments; ainsi que le rôle des ressources humaines, de la formation et du perfectionnement[12,14]. Les Déclarations de Bâle ont été régulièrement actualisées pour refléter les pratiques actuelles[14], la dernière révision étant à l'ordre du jour du Congrès FIP de Brisbane en septembre 2023[15]. J'encourage tous les pharmaciens hospitaliers à contribuer à ces mises à jour et à s'assurer que les apprentissages de leur pays soient entendus et reconnus dans le monde entier[15]. Bien que la Société canadienne des pharmaciens d'hôpitaux ne soit pas un membre organisationnel de la FIP, elle a déjà contribué à la révision des Déclarations de Bâle. D'après ce travail, je crois que les pharmaciens du monde entier partagent plus de points communs que de différences, et une réflexion constante sur les pratiques internationales garantira à nos patients de recevoir les meilleurs soins pouvant être fournis par les pharmaciens.

Références

1. Yuksel N, Eberhart G, Bungard TJ. Prescribing by pharmacists in Alberta. *Am J Health Syst Pharm.* 2008;65(22):2126-32.
2. Expanded scope of practice: Minor ailments 2023. Ontario College of Pharmacists; [consulté le 4 août 2023]. Disponible à : https://www.ocpinfo.com/practice-education/expanded-scope-of-practice/minor-ailment/
3. UTI program now permanent in Qld [communiqué de nouvelles]. Pharmacy Guild of Australia; 2022 Oct 12 [consulté le 1er juillet 2023]. Disponible à : https://www.guild.org.au/news-events/news/forefront/v12n10/uti-program-now-permanent-in-qld
4. Poh EW, McArthur A, Stephenson M, Roughead EE. Effects of pharmacist prescribing on patient outcomes in the hospital setting: a systematic review. *JBI Database System Rev Implement Rep.* 2018;16(9):1823-73.
5. Almawed R, Shiu J, Bungard T, Charrois T, Gill P. Pharmacist prescribing at inpatient discharge in Alberta. *Can J Hosp Pharm.* 2023;76(4):275-81.
6. Finn S, D'arcy E, Donovan P, Kanagarajah S, Barras M. A randomised trial of pharmacist-led discharge prescribing in an Australian geriatric evaluation and management service. *Int J Clin Pharm.* 2021;43(4):847-57.
7. Parmar R, Legal M, Dahri K, Wilbur K, Shalansky S, Partovi N. Pathways to developing clinical pharmacist practitioners: is there a better way forward? (Path-CPP). *Can J Hosp Pharm.* 2023;76(4):302-8.
8. *The RPS advanced pharmacy framework (APF).* Royal Pharmaceutical Society; 2013 [consulté le 4 août 2023]. Disponible à : https://www.rpharms.com/resources/frameworks/advanced-pharmacy-framework-apf
9. Jackson S, Martin G, Bergin J, Clark B, Stupans I, Yeates G, et al. An advanced pharmacy practice framework for Australia. *Pharmacy (Basel)* 2015;3(2):13-26.
10. Advanced training residencies. Society of Hospital Pharmacists of Australia; 2023 [consulté le 4 août 2023]. Disponible à : https://www.shpa.org.au/workforce-research/residency/advanced-training
11. *National competency standards framework for pharmacists in Australia*. Pharmaceutical Society of Australia Ltd; 2016 [consulté le 4 août 2023]. Disponible à : https://www.psa.org.au/wp-content/uploads/2018/06/National-Competency-Standards-Framework-for-Pharmacists-in-Australia-2016-PDF-2mb.pdf
12. International Pharmaceutical Federation. The Basel Statements on the future of hospital pharmacy. *Am J Health Syst Pharm.* 2009;66(5 Suppl 3):S61-6.
13. Qui sommes-nous? [page Web]. Fédération internationale pharmaceutique; 2023 [consulté le 1er juillet 2023]. Disponible à : https://www.fip.org/about
14. Vermeulen LC, Moles RJ, Collins JC, Gray A, Sheikh AL, Surugue J, et al. Revision of the International Pharmaceutical Federation's Basel Statements on the future of hospital pharmacy: from Basel to Bangkok. *Am J Health Syst Pharm.* 2016;73(14):1077-86.
15. Basel Statements: the future of hospital pharmacy practice. Fédération internationale pharmaceutique; 2023 [consulté le 1er juillet 2023]. Disponible à : https://www.fip.org/basel-statements

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Conflits d'intérêts : Pour des activités non liées à cet éditorial, Jonathan Penm a reçu une subvention du Medical Research Future Fund (gouvernement australien). Il a également reçu des honoraires de consultation (payés à l'Université de Sydney) de la Fédération internationale pharmaceutique (section Pharmacie hospitalière). Aucun autre conflit d'intérêts n'a été déclaré.

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

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Can J Hosp Pharm. 2023;76(4):267-74 https://doi.org/10.4212/cjhp.3401

ABSTRACT

Background: Patient safety incidents are the third leading cause of death in Canada. These occurrences have negative effects on patients and on the well-being of health care professionals. They also lead to financial burdens on the health care system. Several organizations focus on minimizing patient safety incidents; however, an area requiring additional research is evaluating the emotional impact of medication-related patient safety incidents (MRPSIs) on Canadian hospital pharmacists. An MRPSI is a preventable, unintended outcome resulting from medication management rather than an underlying disease. The consequences may be no harm, temporary harm, prolonged hospital stay, disability, or death.

Objectives: To describe the psychological burden on pharmacists after occurrence of an MRPSI and to identify supportive strategies.

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

Results: Of the 128 pharmacists who had experienced an MRPSI and submitted a complete survey response, 105 (82%) had a score above 8 on the IES, indicating that the MRPSI had an important impact. Commonly reported factors contributing to MRPSIs were heavy workload, interruptions, and inexperience. The most desired support strategies included talking to a colleague, compassionate notification of the event through management, and involvement in team debriefs.

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

Keywords: emotional impact, trauma, error, mistake, safety incident

RÉSUMÉ

Contexte : Les incidents liés à la sécurité des patients sont la troisième cause de décès au Canada. Ces événements ont des effets négatifs sur les patients et sur le bien-être des professionnels de la santé. Ils entraînent en outre des charges financières pour le système de santé. Plusieurs organismes se concentrent sur la réduction de ces incidents; cependant, l'évaluation de l'effet émotionnel des incidents liés à la sécurité des patients découlant des médicaments (ci-après « les incidents ») sur les pharmaciens hospitaliers canadiens est un domaine qui nécessite des recherches supplémentaires. Un incident est un résultat évitable et imprévu résultant de la gestion des médicaments plutôt que d'une maladie sous-jacente. Les conséquences peuvent être l'absence de préjudice, un préjudice temporaire, un séjour prolongé à l'hôpital, une invalidité ou la mort.

Objectifs : Décrire le fardeau psychologique des pharmaciens dans un contexte où un incident s'est produit et identifier des stratégies d'accompagnement.

Méthodes : Cette étude à méthodes mixtes comportait une enquête volontaire auprès des pharmaciens hospitaliers et des entretiens individuels structurés. Les répondants au sondage ont noté leur détresse émotionnelle sur l'échelle de l'effet des événements (IES [*Impact of Event Scale*]), un outil d'auto-déclaration validé utilisé pour évaluer l'impact des événements traumatisants de la vie. Les réponses des personnes interrogées ont été analysées qualitativement.

Résultats : Sur les 128 pharmaciens qui avaient fait l'expérience d'un incident et qui avaient soumis une réponse complète à l'enquête, 105 (82 %) avaient un score supérieur à 8 sur l'IES. Ce score indique que l'incident avait eu un impact important. Les facteurs couramment signalés contribuant aux incidents étaient la lourde charge de travail, les interruptions et l'inexpérience. Les stratégies de soutien les plus recherchées comprenaient : la discussion avec un collègue; la notification compatissante de l'événement par l'intermédiaire de la direction; et la participation aux comptes rendus de l'équipe.

Conclusions : L'impact émotionnel des incidents, tel que rapporté par les pharmaciens hospitaliers canadiens, est important. La plupart des participants ont estimé qu'un soutien accru est nécessaire pour surmonter le fardeau émotionnel associé.

Mots-clés : effet émotionnel, traumatisme, erreur, incident de sécurité

INTRODUCTION

Patient safety incidents, an unfortunately common occurrence in Canada, have significant impacts on patients and on the health care system.[1] Patient safety incidents are the third leading cause of death, after cancer and heart disease.[1] It is estimated that over the next 30 years, up to 400 000 patient safety incidents will occur each year in Canada, generating more than $2.75 billion in treatment costs annually.[1] In the literature, medication-related events are reported to account for between 0.02% and 2.27% of patient safety incidents, but these rates may be an under-representation, given that medication-related events are often reported under different incident categories; for example, a fall secondary to a medication may be classified as a trauma.[1] As a result, medication-related patient safety incidents (MRPSIs) are a point of focus for many national organizations, such as the Institute for Safe Medication Practices Canada (ISMP Canada), the Canadian Patient Safety Institute (now incorporated within Healthcare Excellence Canada), the Canadian Institute for Health Information, and the Canadian Society of Hospital Pharmacists (CSHP).[1-3] An MRPSI is a preventable, unintended outcome resulting from medication management rather than an underlying disease.[1] The consequences may be no harm, temporary harm, prolonged hospital stay, disability, or death.[1] Increased reporting through avenues such as the Canadian Medication Incident Reporting and Prevention System have allowed various organizations to perform research and create reports with recommendations to improve patient safety.[1-3] However, one area of research that has not been evaluated is the emotional impact of MRPSIs on Canadian health care professionals, specifically hospital pharmacists.

Several factors can lead to MRPSIs, including human error by health care professionals (which can be due to underlying problems such as lack of training, being overworked, poor communication), patient-related factors (e.g., health literacy, polypharmacy), work environment (e.g., workload, distractions, lack of standardization), medication-related factors (e.g., packaging, medication names), and issues relating to computerized information systems (e.g., inaccuracies in patient records, design that allows for human error).[4] Therefore, it is common for an MRPSI to be the result of a complex combination of factors.[5] This phenomenon is often described as the Swiss cheese model, whereby a combination of holes in the system leads to a safety incident.[1]

Following an incident report, organizations often complete a root cause analysis, a systematic process to investigate factors contributing to the event.[5] Such an analysis tends to focus on identifying conditions contributing to the error, rather than the actions of a particular individual, with the goal of guiding future improvements.[5] The detrimental consequences of MRPSIs on health care providers are not considered in such analyses. Although patients and their families experience the most obvious toll of MRPSIs, the health care professionals involved can also face a great deal of distress. The notion of caregivers as second victims (the patient and their family being the first victims) in MRPSIs is well accepted.[6] One systematic review found that physicians involved in medical errors expressed emotional distress that seemed to increase their risk for burnout and depression, potentially leading to an increase in future errors.[7] Substance use, depression, suicide, quitting the medical field, and litigation stress have also been reported as sequalae of MRPSIs affecting health care professionals.[8-10]

Previous researchers have surveyed Canadian health care workers to determine the supports needed following medical errors and to identify the means to implement these supports.[11] Overall, there is consensus in the literature that support from colleagues and supervisors is key when coping with error-related stress.[7] Assistance from the institution of work is also cited as a main source of support, but a survey of practising physicians in the United States and Canada revealed that only 10% of respondents felt adequately supported by their organization following an MRPSI.[11] These results are in line with a survey of 390 health care professionals completed by the Canadian Patient Safety Institute, including responses from 32 pharmacists, which found that over half of participants (54.3%) were fearful of future errors and 35% were not satisfied with the support they received.[12] This dissatisfaction highlights that more research is needed to inform organizations on how they can support medical professionals following patient safety incidents.[11] For these reasons, the current study aimed to not only describe the emotional impact of patient safety incidents on hospital pharmacists, but also to identify strategies to help hospital pharmacists cope effectively with such events.

The primary objective of this study was to determine the emotional impact of MRPSIs on Canadian hospital pharmacists. The secondary objectives were to identify factors influencing pharmacists' emotional burden following MRPSIs and the support strategies currently in place to assist Canadian hospital pharmacists with their emotional burden following MRPSIs, as well as to determine the support strategies that Canadian hospital pharmacists desire to assist them in overcoming these emotional burdens.

METHODS

This mixed-methods study received ethics approval from the Montfort Research Ethics Board. Participants provided written informed consent. Research was conducted in accordance with the principles of the Helsinki Declaration.

Participants

Those eligible to participate included current or retired Canadian hospital pharmacists or pharmacy residents

who consented to participate and had been involved in an MRPSI. Potential participants were invited via email bulletins distributed through the CSHP, the Association des pharmaciens en établissement de santé du Québec, and the Canadian Association of Pharmacy in Oncology. Social media platforms and email messages sent directly to eligible pharmacists were also used. The survey was disseminated to pharmacists in all 13 Canadian provinces and territories. A consent letter was included, with a link to the voluntary survey, which was open from March 26 to April 26, 2021. The survey, available in French and English, used the web-based program Microsoft Forms. At the end of the survey, respondents were invited to participate in an interview.

Study Tool

The Impact of Event Scale (IES) was chosen to quantify the emotional burden of hospital pharmacists. This validated, self-reported measure was originally created to assess the impact of traumatic life events.[13] This instrument has shown good psychometric properties, supporting its use as a measure of stress reactions, and is often considered the gold standard in screening for post-traumatic stress disorder (PTSD).[13] Participants are asked to respond on a Likert scale ranging from "not at all" (scored as 0) to "often" (scored as 5). This tool has established thresholds, whereby a score of 9 represents the lower limit for a mild level of clinically concerning event-related distress.[14] A cut-off score of 27 on the IES was found to have a sensitivity of 0.91, specificity of 0.72, and overall correct classification of 0.80 when used as a PTSD screening tool for motor vehicle accident survivors.[15] Furthermore, a score of 35 produced sensitivity of 0.89, specificity of 0.94, and overall agreement of 0.94.[15] However, as noted by Beck and others,[16] IES scores are not diagnostic, and the original 15-item IES does not include the hyperarousal symptoms that appear in the most recent criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (fifth edition). The revised version of the scale includes additional items, but these were deemed less appropriate for the aims of the current study. Furthermore, diagnosis of PTSD was not within the scope of this research project; rather, the goal was to quantify the trauma experienced. Therefore, the original version of the IES was chosen. It was also selected for its brevity and applicability to MRPSIs.[16]

Procedure

The target sample size for the survey was 370 hospital pharmacists, which would represent more than 5% of the 6560 Canadian hospital pharmacists practising at the time.[17] Predefined subgroups for analysis were pharmacy residents, interviewees, pediatric pharmacists, oncology pharmacists, distribution pharmacists, and pharmacists working in the intensive care unit (ICU). In addition to the survey, we conducted web-based individual interviews to allow survey participants to anonymously share additional in-depth qualitative information. The questions (see Appendix 1, available from https://www.cjhp-online.ca/index.php/cjhp/issue/view/216) explored respondents' emotions resulting from the MRPSI, their interactions with others following the event, and how they could be better supported. In addition to the predetermined questions, the interviewer used prompting questions to maintain the conversation or ask for elaboration. Sessions were no longer than 20 minutes each and were conducted by a single interviewer (M.N.). The interviews were set up with respondents who volunteered in response to a question at the end of the survey. Interviews were conducted in English or French on the Microsoft Teams platform from April 19 to May 7, 2021. Instructions were provided for participants to anonymize their call settings, if they chose to remain anonymous. All interviews were audio-recorded for analysis by the research team. Given that the survey and the interviews could elicit emotional responses, contact information for a psychologist was offered in the consent portion of both the survey and the interview information package, and this offer was repeated at the beginning of each interview.

Data Analysis

Survey responses were analyzed quantitatively in total and by subgroup. Subgroups were assessed by 1-way analysis of variance (ANOVA) to determine whether the IES scores varied among types of errors (near miss and errors with unknown harm, no harm, reversible harm, or irreversible harm). Mann–Whitney *U* tests were also performed to compare the IES scores of population subgroups (pharmacy residents, ICU pharmacists, oncology pharmacists, pediatric pharmacists, distribution pharmacists, and study interviewees).

Responses from interviewees were transcribed and reviewed for thematic analysis, including categorization into codes by 2 independent reviewers (M.N., C.C.).

RESULTS

Quantitative Analysis

Responses were received from 179 hospital pharmacists across Canada. This corresponds to 2.73% of the target population.[17] Responses came from all provinces and the Yukon (Table 1). In total, 123 (69%) of the participants completed the survey in English and 56 (31%) in French. The majority (82%) of respondents were women, which was expected given the gender imbalance in the pharmacy profession.[18] Fifty-one participants were excluded from further analysis, 2 because they did not consent to participate and 49 because they had not been involved in an MRPSI. The data summarized below represent responses from the remaining 128 pharmacists, who answered all of the survey questions.

In terms of negative consequences following the incident, most participants noted stress (n = 124, 97%) and

TABLE 1 (Part 1 of 2). Demographic and Other Relevant Information

Characteristic	No. (%) of Respondents
Survey language	*n* = 179
English	123 (69)
French	56 (31)
Consent to participate	*n* = 179
Consented	177 (99)
Did not consent	2 (1)
Region of practice	*n* = 177
Western region (Yukon, British Columbia)	10 (6)
Prairie region (Alberta, Saskatchewan, Manitoba)	37 (21)
Ontario	63 (36)
Quebec	55 (31)
Atlantic region (New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador)	12 (7)
Gender	*n* = 177
Female	145 (82)
Male	29 (16)
Gender variant/nonconforming	1 (1)
Prefer not to answer	2 (1)
Pharmacist practice	*n* = 177
Hospital pharmacist (including managers and retirees)	168 (95)
Hospital pharmacy resident or candidate for master in pharmaceutical sciences (Quebec)	9 (5)
Residency status	*n* = 177
Completed a residency	111 (63)
Did not complete a residency	59 (33)
Currently completing a residency	7 (4)
Area of practice	*n* = 177
Inpatient hospital pharmacy	154 (87)
Outpatient hospital pharmacy	22 (12)
Pharmacy manager	1 (1)
Involvement in MRPSI	*n* = 177
Yes	128 (72)
No	49 (28)
Duration of practice (years)	*n* = 128
≤ 2	32 (25)
> 2 and < 5	36 (28)
5–10	27 (21)
11–20	22 (17)
> 20	11 (9)
Age (years)	*n* = 128
< 25	12 (9)
25–35	81 (63)
36–45	27 (21)
46–55	5 (4)
> 55	3 (2)

TABLE 1 (Part 2 of 2). Demographic and Other Relevant Information

Characteristic	No. (%) of Respondents
Time since the event (years)	*n* = 128
≤ 2	52 (41)
> 2 and < 5	24 (19)
5–10	27 (21)
11–20	22 (17)
> 20	3 (2)
Unit of practice	*n* = 128
General medicine	25 (20)
Oncology	23 (18)
Other (dispensary shift, management, sterile preparation)	18 (14)
Pediatrics	16 (13)
Intensive care unit	15 (12)
Emergency	7 (5)
Surgical specialties	7 (5)
Palliative care	6 (5)
Other medical specialties (cardiology, geriatrics, infectious disease, nephrology, neurology, psychiatry, pulmonary)	11 (9)
Did the pharmacist report the MRPSI to the patient?	*n* = 128
Yes	20 (16)
No	108 (84)
Was the incident reported in the workplace?	*n* = 128
Yes	120 (94)
No	8 (6)
Does your workplace culture support incident reporting?	*n* = 128
Strongly agree	27 (21)
Agree	52 (41)
Neutral	32 (25)
Disagree	15 (12)
Strongly disagree	2 (2)

MRPSI = medication-related patient safety incident.

anxiety (*n* = 119, 93%), with few experiencing new or worsened substance use disorder or suicidal ideation as a result of the MRPSI. Participants were generally earlier in their careers, with most (63%) being between the ages of 25 and 35 years at the time of the event. Most events (59%) were relatively recent, having occurred within the past 5 years, but some participants (20%) referred to events that occurred more than 10 years ago. Respondents' area of practice varied, but commonly reported areas were general medicine, dispensary work, oncology, pediatrics, and the ICU. There was also a wide range in the types of errors reported, from near misses to incidents resulting in irreversible harm. The 3 most frequently reported factors contributing to MRPSIs were heavy workload, interruptions, and cognitive overload.

The original 15-item IES has a maximum score of 75. On the IES, 12% of participants scored between 44 and 75 (severe impact), 34% scored between 26 and 43 (powerful impact), 36% scored between 9 and 25 ("impact event" that might have some effect), and 18% scored 8 or below (no meaningful impact) (Figure 1). In terms of subgroup analysis among the types of errors, mean IES scores were similar across the subgroups, ranging from 20.0 to 28.6. The 1-way ANOVA revealed no significant effect of the type of error on the IES score: $F(4,123) = 1.2$, $p = 0.3$. Mann–Whitney U tests between population subgroups showed that ICU pharmacists scored significantly lower on the IES (mean score 13.7) than all other pharmacists (mean score 26.1) ($p = 0.004$). A Bonferroni correction was applied to account for the increased risk of a type I error when completing multiple statistical tests; with this correction, the significance level of 0.05 was divided by the number of tests (6), yielding an adjusted significance level of 0.008. Even with this adjustment, the p value for the comparison between ICU pharmacists and all other pharmacists (0.004) remained statistically significant. Overall, ICU pharmacists tended to have more clinical experience at the time of the event and reported increased satisfaction with support received compared to other participants.

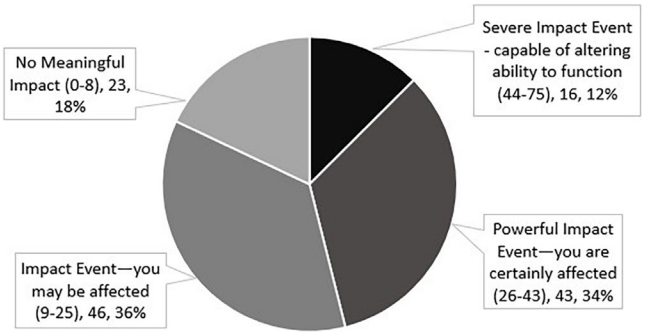

FIGURE 1. Scores on the Impact of Event Scale for the 128 participants who submitted complete responses.

Lastly, 78 (61%) of the participants agreed or strongly agreed that they needed support following the incident, whereas 51 (40%) agreed or strongly agreed that they were satisfied with the support they received. Desired support strategies are summarized in Figure 2. The most popular method of support that respondents had actually pursued was talking to a colleague ($n = 100$, 78%) and the least popular method was support through an employee assistance program ($n = 2$, 2%).

Qualitative Analysis

Twenty-two participants volunteered for an interview. Eighteen interviews were conducted, 1 in French and 17 in English; the other 4 participants did not respond to email invitations to schedule an interview. Thematic analysis exposed the following recurrent themes: factors contributing to the error, impact on the pharmacist, and strategies for overcoming emotions. All of the interviewees discussed factors contributing to the error, both systemic (such as staffing levels, technology-related deficiencies, and inefficient workflows) and personal (such as inexperience, making assumptions, and cognitive overload). All interview participants spoke of negative emotions pertaining to the event, and 16 (89%) also outlined positive emotions. All interview participants revealed strategies (coded as personal, peer, and institutional methods) for overcoming incident-related emotions. The various themes, codes with examples, and interview quotes are summarized in Table 2.

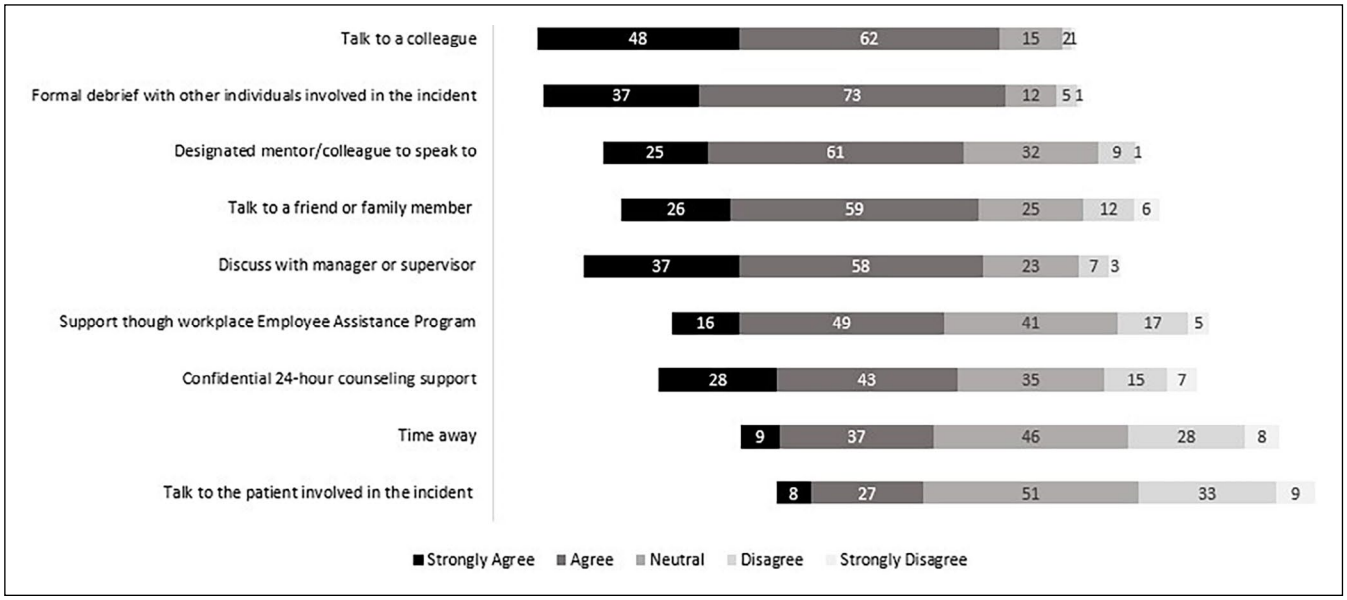

FIGURE 2. Desired forms of support following medication-related patient safety incidents for the 128 participants who submitted complete responses. In the graph, bars are aligned on "neutral" responses, to show skewing toward agree or disagree for each item.

TABLE 2. Summary of Qualitative Interview Findings

Overarching Theme and Related Codes	Frequency of Code (%)[a]	Supporting Quotes
Theme: Factors contributing to the error		
Code: Systemic (e.g., workload, lack of standardization, insufficient resources, computerized information systems [designs that allow for human error])	100	"It got through so many steps of checks and balances of something that was weird that multiple people did say yeah that's weird but then it never really was actioned or resolved." (Interviewee 1) "It's not like you did something bad on purpose. There were flaws in the system. There's holes in the Swiss cheese model. There's lots of places you know that this could happen to someone else." (Interviewee 3)
Code: Personal (e.g., lack of training, inadequate knowledge, being overworked, poor communication, making an assumption)	100	"I think I was also a little bit on autopilot, just trying to finish the orders." (Interviewee 13) "As a new practitioner, you don't necessarily have that experience, so you are relying more on those resources. And in that moment having to make a decision that you know seems clinically sound and obviously in the end it really wasn't." (Interviewee 8)
Theme: Impact on the pharmacist		
Code: Negative emotions (e.g., shame, guilt, shock, surprise, expecting perfection from oneself, hurt, fear, blame from others, feeling incompetent)	100	"Her child is dead because of me so that was really hard to kind of I guess have that image in my mind." (Interviewee 3) "Can I go back to work? Can I still be a pharmacist? Am I competent to be a pharmacist?" (Interviewee 3) "I think that perfectionism contributed to the negative emotions because we're never trained to not be perfect." (Interviewee 15) "It was just completely overwhelming. I was just absolutely devastated. I felt obviously extreme sadness, guilt, the guilt was weighed very heavily, you know replaying it back in your mind." (Interviewee 12) "Definitely there was scared, you know, fear for myself as well in definitely the fear of like oh my gosh am I going to lose my job? Am I going to lose my license? Am I going to be financially, you know like, oh am I going to be sued for this incident you know?" (Interviewee 10)
Code: Positive emotions (e.g., pride in preventing future errors)	89	"So it did give me an opportunity to make some suggestions for change, which I thought was really good." (Interviewee 16)
Theme: Strategies for overcoming emotions		
Code: Personal (e.g., time off from work, faith, counselling, resiliency in accepting errors as human)	100	"Every mistake is a learning opportunity." (Interviewee 15) "I was sent home because obviously I was not in a condition to continue working that day." (Interviewee 3) "Making one mistake doesn't automatically invalidate everything else that I do." (Interviewee 10) "I am human and I made a human error." (Interviewee 6)
Code: Peer (e.g., showing empathy for others, support from colleagues/family/ friends, understanding that others experience similar feelings after MRPSIs)	100	"Even competent and thorough people, who take their work to heart, will make mistakes." (Interviewee 6) "To hear from people afterwards, I think was reassuring when they tell you, you know, similar stories or just show empathy." (Interviewee 12) "The greatest support is the team around us." (Interviewee 6) "So it was really important to know that I wasn't alone I think was probably one of the biggest things." (Interviewee 12)
Code: Institutional (e.g., disclosure training, formal support being offered, improving processes, improving error culture)	100	"If errors happen and they're not shared and we don't share the solutions, I feel like we're wasting the opportunity to make changes that are needed to prevent them." (Interviewee 2) "The lack of support from the manager led me to blame myself even more." (Interviewee 9) "If we don't have a culture of safety in our organization, what happens is errors are hidden, and when errors are hidden, change can't be made to improve them." (Interviewee 2)

MRPSI = medication-related patient safety incident.
[a]Percentage of interviews with this code.

DISCUSSION

Previous research has evaluated the emotional impact of errors on health care professionals, but to our knowledge, this study is the first to focus specifically on hospital pharmacists. Overall, hospital pharmacists participating in our study reported significant emotional impacts following MRPSIs. More specifically, the survey results suggest that anxiety (93%) and stress (97%) are the most frequent reactions following MRPSIs, but the qualitative analysis revealed that guilt, shame, fear of repeating the error, blame from others, and a tendency to be hard on oneself are also repercussions of MRPSIs in which pharmacists have been involved. Research interviews highlighted and expanded upon the participants' feelings, and these findings reinforced the survey outcomes. Participants expressed these emotions both in cases of near misses and in cases of irreversible harm to the patient. Of concern, the majority of participants also expressed feeling a lack of competence or questioning their abilities after the incident. Many questioned whether they could continue working or whether they should continue in the profession. Many also expressed litigation-related stress or fears (Table 2).

Interestingly, positive emotions, such as pride in preventing future errors, were also reported. The interviews revealed that participants felt that, following these events, they increased their level of vigilance or contributed to the implementation of systemic changes to prevent similar errors from occurring in the future.

Among the predefined subgroups, specifically pharmacy residents, interviewees, and pharmacists working in pediatrics, oncology, distribution, and the ICU, the only subgroup for which the IES result differed from that of the other survey respondents were the ICU pharmacists. A possible explanation for this finding is that the ICU pharmacists reported a higher degree of satisfaction with the support they received following MRPSIs. Additionally, although not specifically evaluated in this research project, ICU pharmacists may have extra opportunities for support within their workplace through their integration within the medical team. They may also have more time to come to fully informed decisions about patient care compared with pharmacists working distribution shifts. The ICU pharmacists also had more years in practice and more clinical experience than the other pharmacists who responded to the survey.

Although the average IES score for the 18 interviewees (29.8) was not significantly higher than that of other participants, it did trend higher than the overall average (24.6). This is reasonable, given that participants who carry emotional burden from an MRPSI would likely be biased toward participating in an interview. Interestingly, the subgroup with the highest mean IES score was pharmacists working distribution shifts (32.4). One hypothesis to explain this value is that pharmacists must make numerous quick decisions during distribution shifts, often involving patients who are unfamiliar to them. There is less time to establish an informed decision, which may lead to increased emotional burden in the event of an MRPSI.

Strategies for managing emotions could be stratified into 3 main codes: personal strategies, peer support, and institutional strategies. Methods for supporting oneself included faith, self-acceptance, letting go of perfectionism, and professional counselling. Peer support methods were the most commonly sought out strategy and focused on accepting that everyone makes mistakes. Sharing incidents with colleagues and gathering reassurance of a thought process or reassurance that the mistake could happen to anyone were comforting to participants. Finally, methods for institutional support focused on conveying errors in a compassionate way, offering disclosure training, including all members of the team in debriefs, following up with pharmacists after the event, making improvements to error culture and perfectionism culture, and changing processes to prevent errors. Notably, 63% of participants were early in their careers (under the age of 35 at the time of the event), and many attributed the incident to a lack of experience or training, particularly when working in an area of decreased familiarity. Workplaces can better support employees by providing adequate training opportunities, particularly in new areas of work.

Limitations

The limitations of this research project include the sample size, language offerings for interviews, and recall bias. The target sample size for the survey was 370 hospital pharmacists, with the aim of reaching over 5% of the 6560 Canadian hospital pharmacists practising at the time.[17] This value was not achieved, as there were only 179 survey responses. One reason for lower-than-desired participation may have been the ongoing pandemic, when pharmacists were facing increased workplace demands and therefore had less time available for research participation. However, the research team was able to recruit sufficient volunteers for the qualitative portion of the study. Another limitation was the restricted advertising to recruit French interviewees. As a result, only 1 French interview was completed. Recall bias was also evident, given that 59% of events described by participants had happened in the past 5 years. Pharmacists were more likely to think of a recent incident because the emotional effects were probably more easily recalled. Conversely, for events that occurred more than 10 years prior, we speculate that the emotional effects on the pharmacist were likely significant, given that they continued to recall the event even after such a long time. Recall bias may lead to memory amplification, resulting in vivid memories of highly emotional events. Contrariwise, an individual may unconsciously suppress memories of traumatic events, which may lead to decreased recall. These forms of recall bias may have affected participants' responses in this project.

Future Directions

Future research could investigate why ICU pharmacists experienced less emotional burden or could expand the pool of respondents to include additional pharmacy populations, such as technicians and community pharmacists. Such research could describe additional approaches for supporting individuals in a variety of settings. Additionally, future studies could survey the curriculums of Canadian pharmacy schools to identify opportunities for content related to managing emotional distress.

CONCLUSION

Hospital pharmacists responding to our survey experienced significant emotional impacts following MRPSIs, and only 40% reported satisfaction in the support they received. Institutions can support their pharmacists by improving error culture, specifically by fostering an environment in which staff members learn from mistakes, by informing staff of errors compassionately, by including all those affected in debriefs or investigations, and by training pharmacists on how to disclose errors. Future projects could include development of pharmacist support campaigns, for example, mentorship experiences or training related to managing errors and the associated emotional distress.

References

1. *The case for investing in patient safety in Canada*. RiskAnalytica; 2017 Aug [cited 2022 Sep 12]. Available from: https://www.patientsafetyinstitute.ca/en/About/Documents/The%20Case%20for%20Investing%20in%20Patient%20Safety.pdf
2. Medication safety and drug use management enhanced by drug distribution. Canadian Society of Hospital Pharmacists; 2008 [cited 2021 Jan 10]. Available from: https://cshp.ca/sites/default/files/files/Advocacy/Drug%20Distribution/DrugDistributionSystBackgroundPaperJune5'08%20FINAL.pdf
3. *Evaluation of the Institute for Safe Medication Practices Canada (ISMP Canada) activities for the Canadian Medication Incident Reporting and Prevention System (CMIRPS): final report executive summary.* Prairie Research Associates; 2012 Dec 18 [cited 2022 Sep 12]. Available from: https://www.ismp-canada.org/download/cmirps/rptISMPC_CMIRPS_Final_Report_2012.pdf
4. *Technical series on safer primary care: medication errors*. World Health Organization; 2016 [cited 2022 Sep 12]. Available from: https://apps.who.int/iris/bitstream/handle/10665/252274/9789241511643-eng.pdf;jsessionid=0818EAD0F9C0076ACD9E57A10A8007D3?sequence=1
5. Davies JM, Hébert P, Hoffman C. *The Canadian patient safety dictionary*. Self-published; 2003 Oct [cited 2022 Sep 12]. Available from: https://www.ottawahospital.on.ca/en/documents/2017/01/patient_safety_dictionary_e.pdf/
6. Denham CR. TRUST: the 5 rights of the second victim. *J Patient Saf*. 2007;3(2):107-19.
7. Schwappach DL, Boluarte TA. The emotional impact of medical error involvement on physicians: a call for leadership and organisational accountability. *Swiss Med Wkly.* 2009;139(1-2):9-15.
8. Oreskovich MR, Shanafelt T, Dyrbye LN, Tan L, Sotile W, Satele D, et al. The prevalence of substance use disorders in American physicians. *Am J Addict*. 2015;24(1):30-8.
9. Stehman C, Testo Z, Gershaw R, Kellogg A. Burnout, drop out, suicide: physician loss in emergency medicine, part I. *West J Emerg Med*. 2019;20(3):485-94.
10. Grissinger M. Too many abandon the "second victims" of medical errors. *P T*. 2014;39(9):591-2.
11. Waterman AD, Garbutt J, Hazel E, Dunagan WC, Levinson W, Fraser VJ, et al. The emotional impact of medical errors on practicing physicians in the United States and Canada. *Jt Comm J Qual Patient Saf*. 2007;33(8):467-76.
12. *Creating a safe space. Section 1: Survey of healthcare providers' perceptions related to the second victim phenomenon*. Canadian Patient Safety Institute; 2019 [cited 2022 Sep 12]. Available from: https://www.patientsafetyinstitute.ca/en/toolsResources/Creating-a-Safe-Space-Psychological-Safety-of-Healthcare-Workers/Documents/Manuscript%20Documents/1_Survey%20of%20Healthcare%20Providers%20Perceptions.pdf
13. Sundin EC, Horowitz MJ. Impact of Event Scale: psychometric properties. *Br J Psychiatry*. 2002;180(3):205-9.
14. Reed SB. Measuring the emotional impact of an event: how to use an effective PTSD test. Self-published; 2007 [cited 2022 Aug 2]. Available from: https://psychotherapy-center.com/counseling-issues/trauma-and-stressors/ptsd-post-traumatic-stress-disorder-therapy/measuring-the-emotional-impact-of-an-event/
15. Coffey SF, Gudmundsdottir B, Beck JG, Palyo SA, Miller L. Screening for PTSD in motor vehicle accident survivors using the PSS-SR and IES. *J Trauma Stress*. 2006;19(1):119-28.
16. Beck JG, Grant DM, Read JP, Clapp JD, Coffey SF, Miller LM, et al. The Impact of Event Scale-Revised: psychometric properties in a sample of motor vehicle accident survivors. *J Anxiety Disord.* 2008;22(2):187-98.
17. *National statistics*. National Association of Pharmacy Regulatory Authorities; 2020 Jan 1 [cited 2022 Sep 12]. Available from: https://napra.ca/national-statistics
18. *Women in pharmacy: the current landscape*. Canadian Pharmacists Association [cited 2022 Aug 2]. Available from: https://www.pharmacists.ca/cpha-ca/assets/File/cpha-on-the-issues/WomeninPharmacyReport_final.pdf

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Competing interests: Melanie Trinacty has received speaker's honoraria from Teva Pharmaceutical Industries and support for travel and/or meeting attendance from Jazz Pharmaceuticals and Gilead; she has also served on an advisory board for Teva Pharmaceutical Industries. Mélanie Joanisse has received research grants from the Institut du Savoir Montfort and the Consortium national de formation en santé – Université d'Ottawa; book royalties from Momentum Press; consulting fees for emotion-focused therapy from the Department of National Defence, Ottawa Heart Institute, and private clients; and speaker's fees from Sick Kids, Flemingdon Health Centre, and Colloque des médecins francophones; she is also co-owner of a psychological clinic (Orleans Psychological Health Team). No other competing interests were declared.

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Funding: None received.

Pharmacist Prescribing at Inpatient Discharge in Alberta

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Can J Hosp Pharm. 2023;76(4):275-81 https://doi.org/10.4212/cjhp.3346

ABSTRACT

Background: Pharmacists in the province of Alberta may apply for additional prescribing authorization (APA), which allows them to independently prescribe medications. Currently, no literature exists about pharmacist prescribing for inpatients at the time of discharge.

Objectives: The primary objective was to report the proportion of patients for whom inpatient pharmacists with APA prescribed at discharge across Alberta, Canada. Secondary objectives were to describe discharge interventions other than prescribing that were provided, enablers of and barriers to discharge prescribing, and differences in discharge prescribing by facility or population type, clinical area, and health care charting system.

Methods: A descriptive, cross-sectional web-based survey of inpatient pharmacists with APA across Alberta was conducted over a 6-week period in early 2022.

Results: A total of 104 respondents met the inclusion criteria. Under half (45/102, 44.1%) of the participants reported prescribing at discharge. Those that reported prescribing at discharge did so for only a median 14.5% of their patients. The most common enabler of discharge prescribing was a supportive care team, and the most common barrier was the presence of other prescribers. Pharmacists who did not report prescribing at discharge selected "discomfort with being responsible for the prescription" and "fear of professional liability" as barriers more often than those who did report discharge prescribing (51.0% [26/51] vs 33.3% [13/39] and 43.1% [22/51] vs 25.6% [10/39], respectively). The proportion of pharmacists who reported prescribing at discharge was greater with increasing population/facility size (30% [6/20] of pharmacists in settings that served small populations vs 50% [29/58] of those in settings that served large populations).

Conclusions: Inpatient pharmacists who use APA at discharge reported prescribing for only a minority of patients, and discharge prescribing practices varied widely across the province. Future areas of research include how pharmacists can overcome barriers to prescribing at discharge.

Keywords: discharge, inpatient pharmacy, prescribing, additional prescribing authorization

RÉSUMÉ

Contexte : Les pharmaciens de la province de l'Alberta peuvent demander une autorisation supplémentaire de prescrire des médicaments de manière indépendante. À l'heure actuelle, aucune documentation n'existe sur la prescription de médicaments destinés aux patients hospitalisés au moment de leur congé par les pharmaciens.

Objectifs : L'objectif principal visait à rendre compte de la proportion de patients à qui les pharmaciens en milieu hospitalier titulaires d'une autorisation supplémentaire de prescrire prescrivaient des médicaments au moment du congé en Alberta, au Canada. Les objectifs secondaires visaient quant à eux à décrire : les interventions au moment du congé, autres que la prescription; les obstacles et les facilitateurs de la prescription au moment du congé; et les différences en matière de prescription au moment du congé par type d'établissement ou de population, domaine clinique et système de dossiers de soins de santé.

Méthode : Une enquête en ligne descriptive et transversale a été menée auprès de pharmaciens en milieu hospitalier titulaires d'une autorisation supplémentaire de prescrire en Alberta, sur un intervalle de 6 semaines au début de 2022.

Résultats : Au total, 104 répondants satisfaisaient aux critères d'inclusion. Moins de la moitié (45/102, 44,1 %) des participants ont déclaré prescrire au moment du congé. Ceux-ci le faisaient pour seulement une médiane de 14,5 % de leurs patients. Le facteur le plus courant favorisant la prescription au moment du congé était une équipe de soins de soutien; l'obstacle le plus courant était la présence d'autres prescripteurs. Les pharmaciens ayant déclaré ne pas prescrire au moment du congé ont plus fréquemment indiqué comme obstacle le fait d'être « mal à l'aise à l'idée d'être responsable de la prescription » et la « crainte de la responsabilité professionnelle » que les pharmaciens ayant indiqué prescrire au moment du congé (51,0 % [26/51] contre 33,3 % [13/39] et 43,1 % [22/51] contre 25,6 % [10/39], respectivement). La proportion de pharmaciens ayant déclaré prescrire au moment du congé était plus élevée lorsque la taille de la population/de l'établissement était plus importante (30% [6/20] des pharmaciens dans des milieux desservant de petites populations contre 50 % [29/58] de ceux dans des milieux desservant de grandes populations).

Conclusions : Les pharmaciens en milieu hospitalier titulaires d'une autorisation supplémentaire de prescrire ont déclaré prescrire pour seulement une minorité de patients au moment du congé, et les pratiques en la matière variaient largement dans la province. Les futurs domaines de recherche comprennent la manière dont les pharmaciens peuvent surmonter les obstacles les empêchant de prescrire au moment du congé.

Mots-clés : congé, pharmacie en milieu hospitalier, prescription, autorisation supplémentaire de prescrire

INTRODUCTION

Since the inception of additional prescribing authorization (APA) for pharmacists in Alberta in 2007, pharmacists have shifted their practice to include prescribing for patients.[1,2] Existing literature demonstrates various benefits of pharmacist-managed drug therapy, including fewer medication errors,[3,4] as well as clinical benefits such as reduced cardiovascular risk and improved glycemic control.[5-7] Most available studies have involved pharmacists in community or outpatient settings,[5-11] with only selected articles exploring prescribing within inpatient settings.[1,12-14] Some pertinent studies have explored discharge interventions other than prescribing provided by pharmacists[15-17]; however, the literature regarding prescribing practices at discharge from an inpatient setting is limited.

Alberta is currently the only province in Canada where any pharmacist on the provincial college register may apply to receive authorization to prescribe Schedule 1 medications (except drugs defined in the *Controlled Drugs and Substances Act*).[18,19] Those who submit an application and who meet the minimum standard set by the Alberta College of Pharmacy are granted authorization to prescribe according to an assessment of the patient and creation of a monitoring and follow-up plan that is communicated to other relevant health care providers. As of December 31, 2020, a total of 3339 (56.7%) of the 5892 registered pharmacists regulated under the Alberta College of Pharmacy had been granted APA.[20]

Medication errors are more likely to occur at points of transition, particularly at discharge from acute care.[15] Although all clinical pharmacists within Alberta Health Services (AHS) and Covenant Health (the provincial Catholic hospital system) are expected to have APA, typically within a year after clinical deployment, the utilization of APA is not mandated, and pharmacists prescribe at their own discretion. As such, prescribing at the point of discharge is likely diverse and inconsistent, and, to our knowledge, this practice diversity has not yet been explored. The purposes of this study were to gain insight into current practices for pharmacist prescribing at inpatient discharge and to describe enablers, barriers, and other factors that may be associated with prescribing at discharge.

More specifically, the primary objective of this survey study was to report the proportion of patients for whom acute care inpatient APA pharmacists within AHS and Covenant Health prescribed at discharge within their most recent 2 weeks of clinical service before completing the survey. The secondary objectives were to describe nonprescribing discharge interventions provided by APA pharmacists; identify perceived enablers of and barriers to prescribing at discharge; explore differences between pharmacists who do and do not prescribe at discharge; and determine differences in discharge prescribing by facility type, population size, clinical practice area, and health record charting system used.

METHODS

Study Design and Ethics Approval

A descriptive study using an anonymous cross-sectional web-based survey was conducted during a 6-week period from January to February 2022. The study was approved by the University of Alberta health research ethics board (Pro00114597).

Participants and Survey

APA pharmacists, who were self-identified, were eligible to participate in this study if they were clinically deployed in an inpatient program (excluding critical care) within AHS and/or Covenant Health, were actively involved in the discharge process within their practice, and met these criteria for at least 2 weeks. The survey invitation was sent by email to an estimated 1200 pharmacists (intended to capture all AHS and Covenant pharmacists). Given the provincial proportion of 56.7% of pharmacists having APA at the end of 2020, we estimated that 680 of those invited would have APA. We further estimated that 80% of pharmacists with APA would meet the other eligibility criteria, which yielded a potential total of 544 eligible participants.

Using the existing literature and consultation with practising inpatient pharmacists, we developed a web-based questionnaire through the electronic surveying platform Qualtrics (Supplementary Material 1, available from https://www.cjhp-online.ca/index.php/cjhp/issue/view/216). We invited 3 pharmacists to trial and provide feedback on the survey before it was distributed by pharmacy administrators using a province-wide email distribution list. The survey remained open for 6 weeks, and potential participants received 2 reminders before the survey was closed. Consent to participate was implied by completion of the survey. Of note, not all participants provided responses to all questions; the only mandatory survey questions were those pertaining to the study's inclusion criteria.

Data Analysis

Descriptive statistics were used to report proportions, percentages, and medians and interquartile ranges derived from the survey responses. These values were calculated in Microsoft Excel (2016). Likert-type scale responses were assessed for patterns, and responses to free-text questions were analyzed for themes independently by 2 of the authors (R.A. and P.G.), who then compared and discussed discrepancies to achieve consensus.

RESULTS

The survey was sent via email to more than 1200 AHS and Covenant Health pharmacists. The number of pharmacists who are clinically deployed or who participate in the discharge process within these organizations could not be

specifically defined; as such, respondents were asked to self-assess their eligibility for the survey. A total of 121 pharmacists responded, for an approximate survey response rate of 22% (based on the estimated 544 eligible participants). Of these, 17 were excluded because they did not meet the inclusion criteria (Supplementary Figure 1, available from https://www.cjhp-online.ca/index.php/cjhp/issue/view/216). Of the included pharmacists, most were women (73.6%), most were from a large urban population centre (66.7%), and 42.5% indicated completion of education beyond the entry-level requirements to be a pharmacist (Table 1). The respondents represented diverse clinical backgrounds, and most had been practising with APA for at least 3 years.

Of the 102 respondents who answered questions about their prescribing activities at discharge, 45 (44.1%) reported using their APA to prescribe at discharge. These pharmacists reported prescribing for a median of 14.5% (interquartile range [IQR] 9.5%–50.0%) of their patients (Table 2). These respondents reported caring for a median of 20 (IQR 15.8–25.0) patients daily, whereas pharmacists who reported not prescribing at discharge cared for a median of 22.5 (IQR 18.0–28.3) patients daily. The 2 groups of pharmacists (those who did and did not prescribe at discharge) offered nonprescribing interventions to a median of 82.0% (IQR 35.0–100.0%) and 80.0% (IQR 35.0–93.0%) of their patients, respectively. The 3 most common nonprescribing interventions (based on 93 respondents) were coordinating with community pharmacy/other outpatient providers to ensure continuity of care (95.7%), coordination of outpatient coverage (84.9%), and comprehensive discharge counselling (83.9%) (Supplementary Table 1, available from https://www.cjhp-online.ca/index.php/cjhp/issue/view/216). The order of most commonly provided interventions was almost identical between the 2 groups, except that preparing discharge prescriptions to be signed by another prescriber was the second most frequently selected option among pharmacists who did not prescribe at discharge, but the sixth most frequently selected among those who did prescribe at discharge. Telephone follow-up with patients was selected by almost triple the number of pharmacists who prescribed at discharge relative to those who did not prescribe at discharge (11 vs 4).

The top 3 enabling factors reported by all respondents were a supportive care team (71.4% of respondents), competence in area of practice (54.9%), and desire to deliver more efficient care (51.6%) (Figure 1). Conversely, the top 3 barriers to prescribing at discharge were the presence of other prescribers on the team (74.4%), overwhelming patient workload (i.e., unable to allocate time for prescribing) (52.2%), and being unable to prescribe medications commonly used in participants' practice for legal or insurance reasons (50.0%) (Figure 1). "Motivation to practise to full scope" was a much more common enabler among those who prescribed than among those who did not prescribe (57.5% vs 25.5%), whereas larger proportions of pharmacists who did not prescribe at discharge selected "discomfort with being responsible for the prescription" and "fear of professional liability" relative to pharmacists who did prescribe at discharge (51.0% vs 33.3% and 43.1% vs 25.6%, respectively).

With regard to population size, pharmacists from centres with small populations (fewer than 30 000 people)

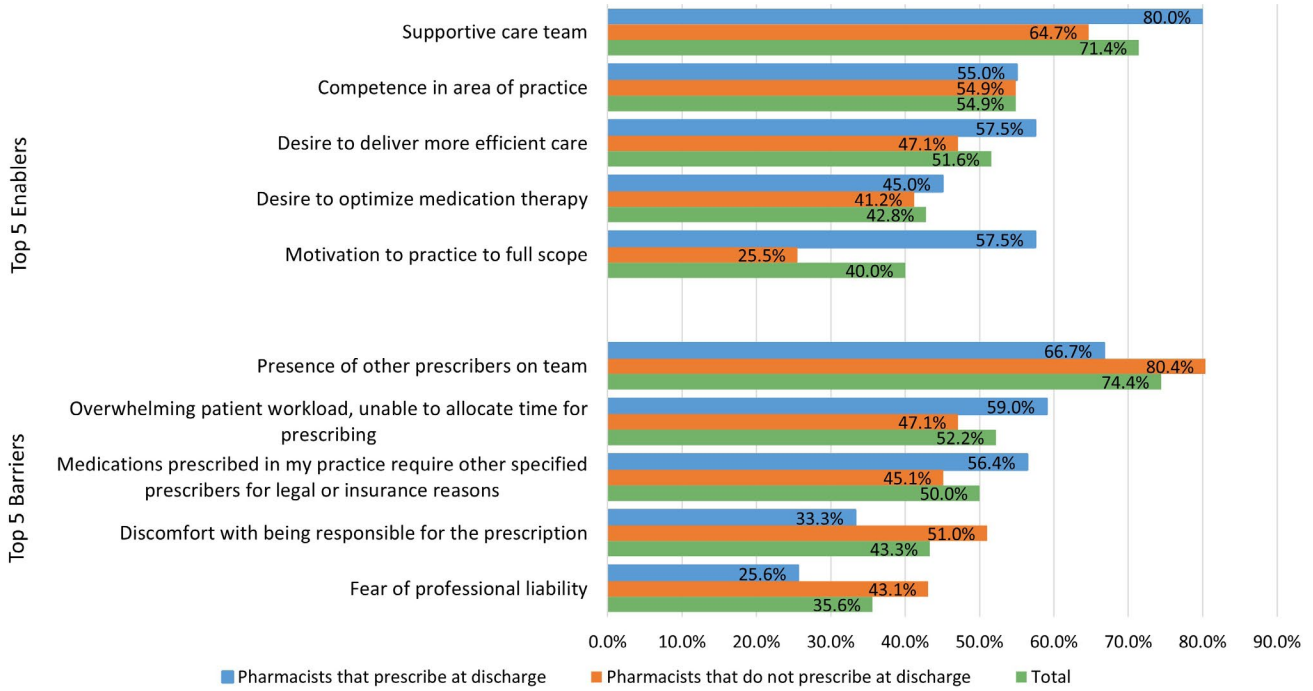

FIGURE 1. Top 5 enablers and barriers to prescribing at discharge (n = 91 respondents: 40 who reported discharge prescribing [one of whom did not indicate any barriers] and 51 who reported no discharge prescribing).

TABLE 1. Characteristics of Study Population

Characteristic	No. (%) of Respondents (n = 87)[a]
Gender	
Women	64 (73.6)
Men	22 (25.3)
Prefer not to say	1 (1.1)
Level of education[b]	
Bachelor of Science in pharmacy	73 (83.9)
Entry-level PharmD	7 (8.0)
Postgraduate PharmD	9 (10.3)
Master's degree	9 (10.3)
Accredited Canadian Pharmacy Residency	24 (27.6)
Current student in postgraduate program	1 (1.1)
Completion of one or more education programs beyond entry-level requirements	37 (42.5)
Primary clinical practice area	
Internal medicine	22 (25.3)
Family medicine	16 (18.4)
Surgery	8 (9.2)
Rural	7 (8.0)
Cardiology	7 (8.0)
Pediatric non-ICU	6 (6.9)
Nephrology	4 (4.6)
Palliative care	3 (3.4)
Infectious diseases	2 (2.3)
Other	12 (13.8)
Duration of experience as pharmacist in primary clinical area (years)	
< 3	17 (19.5)
3–6	22 (25.3)
> 6	48 (55.2)
Experience with APA (years)	
< 3	12 (13.8)
3–6	50 (57.5)
> 6	25 (28.7)
Population of centre where facility is located	
Small (< 30 000)	20 (23.0)
Medium (30 000–100 000)	9 (10.3)
Large urban (> 100 000)	58 (66.7)
Facility size (no. of beds)	
< 100	20 (23.0)
100–500	31 (35.6)
> 500	36 (41.4)

APA = additional prescribing authorization, ICU = intensive care unit, PharmD = Doctor of Pharmacy.

[a]Not all participants provided responses to all questions (the only mandatory questions in the survey were those pertaining to inclusion criteria for this study). Percentages for a given characteristic may not sum to exactly 100% because of rounding.

[b]Percentages sum to more than 100%, because respondents were allowed to select multiple responses.

prescribed at discharge for a median of 10.5% (IQR 0.3%–20.0%) of their patients, and those in centres with medium populations (30 000 to 100 000 people) prescribed at discharge for a median of 30.0% (IQR 17.5–45.0%) of their patients (Supplementary Table 2, available from https://www.cjhp-online.ca/index.php/cjhp/issue/view/216). For centres with large populations (more than 100 000 people), pharmacists prescribing at discharge could be stratified into 2 groups: those working in facilities with 100–500 beds prescribed at discharge for 10.0% (IQR 10.0%-41.5%) of patients, and those working in facilities with more than 500 beds prescribed for 22.0% (IQR 10.0%–57.5%) of patients. According to responses categorized by practice area, larger proportions of pharmacists reported prescribing at discharge in areas such as palliative care (100%), pediatric non–intensive care units (67%), and nephrology (50%); however, this does not mean that they prescribed for all patients under their care. In fact, there was high variability in the proportions of patients for whom they prescribed: 5.0% (IQR 3.8%–7.5%), 52.5% (IQR 10.0%–96.3%), and 52.0% (IQR 28.5%–76.0%), respectively (Table 3).

The majority of respondents (54/88, 61.4%) generated discharge prescriptions using a process not directly linked with the rest of the patient chart, whereas a smaller proportion (34/88, 38.6%) used electronic health systems with medication reconciliation functions linked with the patient chart (Supplementary Table 3, available from https://www.cjhp-online.ca/index.php/cjhp/issue/view/216). Themes identified from open-text responses about the impact of clinical charting systems on prescribing were no impact, impediment to prescribing (because systems were tedious or error-prone), or facilitation of prescribing (through ease of use and accessibility to health information). There was no apparent association between the type of system used and the theme of the response. Most respondents were either neutral or in disagreement with survey statements about the impact of the clinical system on prescribing, the provision of nonprescribing interventions, and collaboration with other providers at discharge (Supplementary Figure 2, available from https://www.cjhp-online.ca/index.php/cjhp/issue/view/216).

DISCUSSION

Although some prior studies have endeavoured to quantify pharmacists who prescribe in an inpatient setting within Alberta,[1,13] our study is the first that attempts to quantify prescribing at discharge and to describe potential barriers and enablers at this point of care. Our results show that fewer than half of surveyed pharmacists reported prescribing at discharge, and they did so for a median of only 14.5% of the patients under their care, with wide variability demonstrated by the IQR of 9.5% to 50.0%. "Fear of professional liability" and "discomfort with being responsible for the prescription" were barriers that had a stronger effect among pharmacists

TABLE 2. Discharge Activities of Inpatient APA Pharmacists

Pharmacist Group	Outcome; Median (IQR)		
	No. of Patients Cared for Daily	% of Patients for Whom Pharmacists Provided Nonprescribing Interventions	% of Patients for Whom Pharmacists Prescribed at Discharge
Reported prescribing at discharge (n = 45)	20.0 (15.8–25.0) (n = 44 respondents)	82.0 (35.0–100.0) (n = 39 respondents)	14.5 (9.5–50.0) (n = 38 respondents)
Reported not prescribing at discharge (n = 57)	22.5 (18.0–28.3) (n = 56 respondents)	80.0 (35.0–93.0) (n = 53 respondents)	NA

APA = additional prescribing authorization, IQR = interquartile range, NA = not applicable.

who did not prescribe at discharge. There was an apparent increase in the proportion of pharmacists prescribing at discharge with increases in population and facility size; however, the clinical area and clinical charting system did not appear to have a clear association with prescribing patterns.

In our study, pharmacists who prescribed at discharge did so for a minority of their patients, whereas in at least 1 study looking at overall inpatient prescribing, pharmacists used their APA to create orders for about half their patients.[1] It is difficult to directly compare our results with the existing literature because the studies differed in terms of research questions, inclusion criteria, and measurements of prescribing frequency. In our study, we found that between the 2 groups (i.e., pharmacists who did and did not prescribe at discharge) there were only small differences when it came to parameters such as patient caseload and the proportion of patients for whom they provided nonprescribing interventions. These findings suggest that other contextual factors in the pharmacist's practice setting may play a role in their willingness to prescribe at discharge, which brings to attention the prescribing differences related to size of the population or facility and the clinical practice area. For example, the increase in proportion of pharmacists prescribing at discharge with increased size of population or facility could be due to pharmacists in rural areas often being responsible for both dispensing and rounding. In urban areas, where staff levels are higher, there are designated pharmacists for the dispensary, which allows clinical pharmacists to allocate their full attention to direct patient care. This finding is comparable to a past survey, in which the frequency of prescribing was greater in tertiary care centres than in community hospitals.[1]

Of particular interest were the differences in enablers and barriers between the 2 groups; for example, "fear of professional liability" was selected much more commonly by pharmacists who did not prescribe at discharge (43.1% vs 25.6%, relative to pharmacists who prescribed at discharge). In contrast, only 9.9% (9/91) of all participants selected "understanding of professional liability" as an enabler to prescribing. Although the risk of liability is certainly a serious factor to consider when prescribing, a 2018 review of Canadian disciplinary reports for pharmacists showed that licence revocation was a rare result of unintentional, isolated clinical errors made by pharmacists.[21] We hypothesized that more recent graduates of pharmacy programs might have greater confidence in prescribing, given that this

TABLE 3. Prescribing by Clinical Area

Clinical Area	No. (%) of Pharmacists Prescribing at Discharge	% of Patients for Whom Pharmacists Prescribed at Discharge (Median and IQR)
Internal medicine (n = 22)	9 (41)	10.0 (8.5–30.0)
Family medicine (n = 16)	5 (31)	19.0 (3.4–20.0)
Surgery (n = 8)	2 (25)	52.5 (36.1–76.3)
Rural (n = 7)	1 (14)	0
Cardiology (n = 7)	2 (29)	10.0 (5.0–10.0)
Pediatric non-ICU (n = 6)	4 (67)	52.5 (10.0–96.3)
Nephrology (n = 4)	2 (50)	52.0 (28.5–76.0)
Palliative care (n = 3)	3 (100)	5.0 (3.8–7.5)
Other (n = 13)	9 (69)	41.5 (21.3–57.5)

ICU = intensive care unit, IQR = interquartile range.

activity has now been incorporated into practice labs and lectures within these programs; however, most respondents to our survey had been in practice for at least 3 years, and no participants selected "recent completion of schooling" as an enabler for prescribing. These findings suggest that despite the 15-year existence of APA and its incorporation into pharmacy education, many pharmacists are still hesitant to prescribe at discharge because of possible overestimation of the risk of disciplinary repercussions.

A greater proportion of pharmacists who reported not prescribing at discharge also selected "discomfort with being responsible for the prescription" relative to those who did report discharge prescribing. In past surveys examining overall pharmacist prescribing in the hospital setting (not only at discharge), respondents reported prescribing more frequently in scenarios where the medication had already been initiated by other prescribers, such as discontinuations, medication reconciliation, and dosage adjustment based on organ function.[1,13] As expected on the basis of this observation, Heck and others[1] showed an increase in prescribing by APA pharmacists after a team discussion, relative to situations in which pharmacists prescribed without a team discussion. Our finding of greater telephone follow-up by pharmacists who prescribed at discharge could not be confirmed in the previous literature, but it appears to corroborate an increased feeling of responsibility when prescribing. Given that a follow-up plan is a requirement for prescribing, this could represent yet another obligation that pharmacists who did not prescribe at discharge might wish to avoid. Overall, it appears that inpatient APA pharmacists may prefer to prescribe in collaborative settings where the responsibility for prescribing decisions can be shared, as reported in the existing literature.[1,13,22] It could be argued that discharge prescribing of medications that have been initiated by other inpatient prescribers is another example of prescribing with shared responsibility. Even so, pharmacists who do not prescribe at discharge are uncomfortable with taking on this responsibility, and thus it is understandable that the presence of other prescribers was the top barrier to discharge prescribing in our study. Nonetheless, it is important to recognize that prescribing at discharge is distinct from prescribing at other points along the inpatient timeline, and although we may speculate that inpatient pharmacists likely prescribe more at other points of care, we did not ask our participants about their frequency of prescribing or associated enablers/barriers for points of care other than discharge.

In terms of differences related to clinical practice areas, it was interesting that all of the palliative care pharmacists who responded to the survey (n = 3) reported prescribing at discharge but only for a median of 5.0% of their patients. All of these pharmacists indicated a supportive care team and significant prescribing experience (at least 5 years with APA) as their top 2 enablers, and each selected "medications prescribed in my practice require other specified prescribers for legal reasons" among their top 5 barriers. These findings may indicate that these individuals feel well supported and are willing to prescribe at discharge, but given the nature of their practice—where many patients rely on opioids for palliation—they are unable to prescribe, in accordance with the *Controlled Drugs and Substances Act*. Aside from this group of pharmacists, however, there appeared to be wide variability in prescribing at discharge in other practice areas (that is, much wider IQRs for the proportion of patients for whom pharmacists prescribed), and it was difficult to discern any patterns. For example, we expected surgical pharmacists to do more discharge prescribing, because they work in a unique field where other prescribers are not always available, and indeed this group reported prescribing for the highest proportion of patients (52.5%) relative to other areas. However, only 2 of the 8 surgical pharmacists reported prescribing at discharge. There did not appear to be an association between surgical pharmacists' experience with APA (i.e., time in years) and whether they engaged in discharge prescribing, and all surgical pharmacists worked in medium or large facilities in large urban centres. Overall, we received a diverse range of responses that resulted in wide variation in our results, whereas the few responses from palliative care pharmacists seemed relatively consistent.

This study had limitations that should be considered when interpreting its results. First, there is a possibility of response bias, whereby pharmacists with more experience using their APA or those who feel strongly about not prescribing at discharge might have been more likely to respond to the survey. To mitigate this risk, the inclusion criterion relating to APA experience was liberal (minimum of 2 weeks' experience), to encourage newer pharmacists to respond; in addition, those who did not prescribe at discharge were included in the survey to allow us to compare outcomes such as nonprescribing interventions and enablers of and barriers to prescribing between the 2 groups. Second, although an estimated response rate of 22% was calculated, the definitive response rate could not be determined. The email distribution list that we used contains all pharmacists employed by AHS and Covenant Health, regardless of whether or not they have APA, and we also did not take into account individuals employed by the University of Alberta who may have been eligible but were not included on this distribution list. Although we considered 104 participants to be a reasonable sample size, and it was comparable to those reported in past similar surveys, our results may not reflect current prescribing practices and perspectives across the province of Alberta. Furthermore, differences among clinical practice areas discussed in this study were based on very small sample sizes, and valid conclusions cannot be drawn from these results. The methods used to quantify prescribing in this study led to potential difficulties in interpretation of the data. Finally, there was a missed

opportunity to ask participants to report their prescribing frequency at points other than discharge; such data would have made comparisons with the existing literature easier.

CONCLUSION

Overall, 55.9% of survey respondents faced barriers that prevented them from prescribing at discharge, while 44.1% reported prescribing at discharge but only for a minority of patients. There was wide variation among respondents regarding the proportion of patients for whom they would prescribe at discharge and no clear association between prescribing and clinical practice area or charting system. Differences in the top enablers and barriers identified by the 2 groups revealed that those who do not prescribe at discharge may have a greater fear of professional liability and are uncomfortable with being responsible for prescriptions at this point of care. Future research could investigate how pharmacists can be empowered to overcome barriers that prevent them from practising to their full scope.

References

1. Heck T, Gunther M, Bresee L, Mysak T, Mcmillan C, Koshman S. Independent prescribing by hospital pharmacists: patterns and practices in a Canadian province. *Am J Health Syst Pharm*. 2015;72(24):2166-75.
2. Guirguis LM, Hughes CA, Makowsky MJ, Sadowski CA, Schindel TJ, Yuksel N. Survey of pharmacist prescribing practices in Alberta. *Am J Health Syst Pharm*. 2017;74(2):62-9.
3. Baqir W, Crehan O, Murray R, Campbell D, Copeland R. Pharmacist prescribing within a UK NHS hospital trust: nature and extent of prescribing, and prevalence of errors. *Eur J Hosp Pharm*. 2015;22(2):79-82.
4. Biggs MJ, Biggs TC. Independent prescribing pharmacists supporting the early discharge of patients through completion of medical discharge summaries. *J Pharm Pract*. 2020;33(2):1735.
5. Tsuyuki RT, Al Hamarneh YN, Jones CA, Hemmelgarn BR. The effectiveness of pharmacist interventions on cardiovascular risk: the multicenter randomized controlled RxEACH trial. *J Am Coll Cardiol*. 2016;67(24):2846-54.
6. Al Hamarneh YN, Charrois T, Lewanczuk R, Tsuyuki RT. Pharmacist intervention for glycaemic control in the community (the RxING study). *BMJ Open*. 2013;3(9):e003154.
7. Tsuyuki RT, Houle SKD, Charrois TL, Kolber MR, Rosenthal MM, Lewanczuk R, et al. Randomized trial of the effect of pharmacist prescribing on improving blood pressure in the community: the Alberta clinical trial in optimizing hypertension (RxACTION). *Circulation*. 2015;132(2):93-100.
8. Law MR, Ma T, Fisher J, Sketris IS. Independent pharmacist prescribing in Canada. *Can Pharm J (Ott)*. 2012;145(1):17-23.e1.
9. Mansell K, Bootsman N, Kuntz A, Taylor J. Evaluating pharmacist prescribing for minor ailments. *Int J Pharm Pract*. 2015;23(2):95-101.
10. Wu JHC, Khalid F, Langford BJ, Beahm NP, McIntyre M, Schwartz KL, et al. Community pharmacist prescribing of antimicrobials: a systematic review from an antimicrobial stewardship perspective. *Can Pharm J (Ott)*. 2021;154(3):179-92.
11. Navarrete J, Yuksel N, Schindel TJ, Hughes CA. Sexual and reproductive health services provided by community pharmacists: a scoping review. *BMJ Open*. 2021;11:e047034.
12. Poh EW, McArthur A, Stephenson M, Roughead EE. Effects of pharmacist prescribing on patient outcomes in the hospital setting: a systematic review. *JBI Database System Rev Implement Rep*. 2018;16(9):1823-73.
13. Saunders S, Dersch-Mills D, Mysak T, Romonko-Slack L, Chernick A, Lazarenko G, et al. CAPABLE: Calgary zone usage of Additional Prescribing Authorization By pharmacists in an inpatient setting: review of the prescribing Landscape and Environment. *Res Soc Adm Pharm*. 2020;16(3):342-348.
14. Zhou M, Desborough J, Parkinson A, Douglas K, McDonald D, Boom K. Barriers to pharmacist prescribing: a scoping review comparing the UK, New Zealand, Canadian and Australian experiences. *Int J Pharm Pract*. 2019;27(6):479-89.
15. Abdel-Qader DH, Harper L, Cantrill JA, Tully MP. Pharmacists' interventions in prescribing errors at hospital discharge. *Drug Saf*. 2010; 33(11):1027-44.
16. Tran T, Hardidge A, Heland M, Taylor SE, Garrett K, Mitri E, et al. Slick scripts: impact on patient flow targets of pharmacists preparing discharge prescriptions in a hospital with an electronic prescribing system. *J Eval Clin Pract*. 2017;23(2):333-9.
17. Basger BJ, Moles RJ, Chen TF. Impact of an enhanced pharmacy discharge service on prescribing appropriateness criteria: a randomised controlled trial. *Int J Clin Pharm*. 2015;37(6):1194-205.
18. *Scope of practice.* Canadian Pharmacists Association; 2022 [cited 2022 May 29]. Available from: https://www.pharmacists.ca/advocacy/scope-of-practice/
19. *Guide to receiving additional prescribing authorization.* 6th ed. Alberta College of Pharmacy; 2022 [cited 2022 May 29]. Available from: https://abpharmacy.ca/sites/default/files/APAGuide_Electronic.pdf
20. *Alberta College of Pharmacy annual report 2020. Adapting through crisis: meeting Albertans' needs in a pandemic.* Alberta College of Pharmacy; 2021 [cited 2023 Aug 22]. Available from: https://abpharmacy.ca/sites/default/files/2020_Annual_Report_Web.pdf
21. Foong EAL, Grindrod KA, Houle SKD. Will I lose my license for that? A closer look at Canadian disciplinary hearings and what it means for pharmacists' practice to full scope. *Can Pharm J (Ott)*. 2018;151(5):332-44.
22. Cope LC, Tully MP, Hall J. An exploration of the perceptions of non-medical prescribers, regarding their self-efficacy when prescribing, and their willingness to take responsibility for prescribing decisions. *Res Soc Adm Pharm*. 2020;16(2):249-56.

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Competing interests: For activities unrelated to the case reported here, Jennifer Shiu has served as Co-chair of the CSHP Pharmacy Practice Vision Committee (unpaid role); Tammy Bungard has received an unrestricted quality improvement grant from Pfizer, has served (on a voluntary basis) as cochair of the Patient & Family Committee of Thrombosis Canada, and has received Fragmin, Lovenox, and Innohep cards (allowing drugs to be supplied to patients unable to afford their medications); Theresa Charrois has received speaker's fees from CSHP and the Alberta Pharmacists Association; and Pawandeep Gill has served as chair of the CSHP Pharmacy Appreciation Month Committee, Alberta Branch (unpaid role). No other competing interests were declared.

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Funding: None received.

Acknowledgements: Educational materials and guidance in support of this project, including project building and writing the manuscript, was provided by the Alberta Pharmacy Practice Residency Program within AHS Pharmacy Services. The authors thank Darlene Korn, Lynnea Schultz, and Maria Anwar for their aid in trialling the survey and Connie Jones for her assistance in distributing the survey.

Association between Pharmacists' Country of Qualifying Education and Practising in a Hospital Setting: A Cross-Sectional Ontario Study

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Can J Hosp Pharm. 2023;76(4):282-9 https://doi.org/10.4212/cjhp.3440

ABSTRACT

Background: It is hypothesized that international pharmacy graduates (IPGs) are underrepresented in more clinically challenging work.

Objective: To examine the association between country of qualifying education for pharmacists in Ontario and the likelihood of practising in a hospital setting.

Methods: This study was based on publicly available data from the Ontario College of Pharmacists website, specifically records for all Ontario pharmacists with authorization to provide patient care and for whom country of qualifying education and an accredited pharmacy as a place of practice were reported. Pharmacists who met the inclusion criteria were categorized as Canadian graduates or IPGs. The odds ratio (OR) and 95% confidence interval (CI) for reporting hospital pharmacy as a place of practice were estimated by fitting a logistic regression, with adjustment for gender and years since graduation.

Results: A total of 14 689 pharmacists were included in the study: 7403 (50.4%) Canadian graduates and 7286 (49.6%) IPGs. These pharmacists worked in a total of 5028 accredited pharmacies (243 hospital pharmacies [4.8%] and 4785 community pharmacies [95.2%]). Among Canadian graduates, 2458 (33.2%) reported at least 1 hospital pharmacy practice site, whereas the proportion was much smaller among IPGs (427, 5.9%). Canadian graduates represented 85.2% (2458/2885) of all pharmacists who reported hospital practice. The estimated crude OR for practice in a hospital pharmacy was 7.98 (95% CI 7.16–8.91), and the adjusted OR was 7.12 (95% CI 6.39–7.98).

Conclusions: IPGs may face barriers impeding their ability to practise in a hospital setting. Providing opportunities such as structured clinical training and experiential placements may facilitate integration of IPGs in institutional settings.

Keywords: international pharmacy graduates, hospital practice, institutional setting, integration, experiential training, bridging, equity, diversity, inclusion

RÉSUMÉ

Contexte : On émet l'hypothèse que les diplômés internationaux en pharmacie (DIP) sont sous-représentés dans des tâches plus cliniquement exigeantes.

Objectif : Étudier l'association entre le pays de formation qualifiante des pharmaciens en Ontario et la probabilité de pratiquer dans un environnement hospitalier.

Méthodes : Cette étude se fondait sur des données accessibles au public sur le site Web de l'Ordre des pharmaciens de l'Ontario, plus précisément les dossiers de tous les pharmaciens de l'Ontario autorisés à prodiguer des soins aux patients et pour lesquels le pays de formation qualifiante ainsi qu'une pharmacie accréditée en tant que lieu de pratique étaient signalés. Les pharmaciens répondant aux critères d'inclusion ont été catégorisés en tant que diplômés canadiens ou DIP. Le rapport de cotes (RC) et l'intervalle de confiance (IC) à 95 % pour le signalement de la pharmacie pratiquée en milieu hospitalier ont été estimés en utilisant une régression logistique, tenant compte du sexe et du nombre d'années depuis l'obtention du diplôme.

Résultats : Un total de 14 689 pharmaciens ont été inclus dans l'étude : 7403 (50,4 %) diplômés canadiens et 7286 (49,6 %) DIP. Ces pharmaciens travaillaient dans 5028 pharmacies accréditées au total (243 pharmacies en milieu hospitalier [4,8 %] et 4785 pharmacies communautaires [95,2 %]). Parmi les diplômés canadiens, 2458 (33,2 %) ont signalé au moins un site de pratique en pharmacie hospitalière, tandis que la proportion était beaucoup plus faible parmi les DIP (427, 5,9 %). Les diplômés canadiens représentaient 85,2 % (2458/2885) de tous les pharmaciens ayant signalé une pratique de la pharmacie en milieu hospitalier. Le rapport de cotes (RC) brut estimé pour la pratique en pharmacie en milieu hospitalier était de 7,98 (IC à 95 % 7,16-8,91), et le RC ajusté était de 7,12 (IC à 95 % 6,39-7,98).

Conclusions : Les DIP peuvent être confrontés à des obstacles qui entravent leur capacité à exercer dans un environnement hospitalier. Offrir des occasions, comme des formations cliniques structurées et des stages expérientiels, pourrait faciliter leur intégration dans des milieux institutionnels.

Mots-clés : diplômés internationaux en pharmacie, pratique hospitalière, milieu institutionnel, intégration, formation expérientielle, transition, équité, diversité, inclusion

INTRODUCTION

Future planning of Canada's health care labour force relies on initiatives to increase its diversity to mirror the nation's changing demographics, as well as to achieve health equity and improve patients' access to quality care.[1-6] One such initiative includes the recruitment of internationally educated health care professionals as a pathway to diversify professions and meet the needs of underserved minority populations.[1,7,8] The 2016 census of Canada reported that approximately one-third of the health care labour force was internationally trained[9]; however, this level of diversity has not resulted in equity and inclusion for those trained outside of Canada. Reports from nursing and medical professions suggest that international nursing and medical graduates face structural disadvantages that limit their career options.[10-14] This situation points to a hierarchical or "pyramidal" structure within the health care labour force, with domestic graduates occupying higher-status clinical positions, while internationally educated workers are overrepresented in lower-status front-line work.[10-15]

Although there are no data regarding the ethno-racial make-up of pharmacists in Canada, available information indicates that international pharmacy graduates (IPGs) contribute greatly to the diversity of the Canadian pharmacy labour force. For example, approximately 50% of newly registered pharmacists in Ontario are IPGs,[16] most of whom have immigrated from the Middle East, Africa, and Asia.[17] Additionally, in 2020, in Ontario, there were equal numbers of international and domestically (i.e., Ontario) educated pharmacists, at 42% for each cohort, with the remaining being from other Canadian provinces or the United States.[18,19] IPGs represent a significant proportion of the pharmacist labour force in Canada; however, their level of integration into all areas of practice is unknown, nor is it known if there exists a pyramidal structure within the pharmacy labour force whereby IPGs are overrepresented in community practice. Conversely, for domestically educated pharmacists, access to entry-level hospital pharmacist positions is facilitated through their participation in residency programs. Institutional pharmacists require greater involvement in clinical decision-making and medication-therapy management for a more vulnerable and complex patient population, and residency programs address this need.[20] The response of IPGs to these structural barriers is not known, and few studies have examined their workplace satisfaction.[21] However, in a recent study on IPG identity,[22] it was noted that while many IPGs enjoy community pharmacy, with its greater scope of practice, some preferred careers as hospital pharmacists but faced structural barriers to gaining access to these positions, despite having hospital experience similar to that of Canadian graduates.

Pharmacy is striving to support equity, diversity, and inclusion (EDI) in the profession,[23-25] but there is very limited information available to assess the success of these efforts.[26] Understanding how IPGs are integrated within the pharmacy profession is essential to optimizing patient care for underserved populations and the populations of Ontario and Canada in general, and to realize the profession's efforts to remove structural barriers at all levels,[24] including in institutional settings such as hospitals. As such, the objective of this study was to examine the association between a pharmacist's country of qualifying education and practise in a hospital setting.

METHODS

Study Design and Data Source

This was a cross-sectional quantitative observational study based on data from a single province.

We used publicly available data from the Ontario College of Pharmacists (OCP) website to identify all pharmacy professionals and accredited pharmacies in Ontario (as of January 20, 2022).[27] We obtained data pertaining to all practising pharmacists in Ontario with regard to their educational background and declared workplaces, with a focus on the community and hospital settings. Data from other institutional and clinical practice settings (e.g., long-term care, family health teams, or community health centres) were not included in the study because such practice settings are not accredited by the OCP.

We collected the following data on all OCP registrants: licence number, member type (pharmacist, pharmacist emeritus, intern, student, or pharmacy technician), institution and country of qualifying education, year and month of graduation, gender, and member status (can provide patient care, can provide patient care – with conditions, does not provide patient care, not entitled to practice [specifically, cancelled due to non-payment, expired, interim suspension, rescinded, resigned, revoked, suspended for discipline, or deceased]). We collected the following data for all accredited pharmacies: accreditation number, status (active, closed, relocated, sold), type (community pharmacy, hospital pharmacy, drug preparation premises, remote dispensing location), address, and licence numbers of pharmacists who declared this pharmacy as their place of practice.

This research was conducted using publicly available data; therefore, ethics board approval was not required.[28]

Study Sample

From among all OCP registrants, members were included in our analysis if they were pharmacists, had member status "can provide patient care", and reported both a country of qualifying education and at least 1 place of practice. From among all accredited pharmacies, those included in our study were active pharmacies with unique accreditation numbers and a reported pharmacy type.

Data Analysis

We used Python 2.7.8 (Python Software Foundation) and Beautiful Soup library software to extract the data from the OCP website and SAS version 9.4 (SAS Institute Inc) to perform the analysis. After extracting the data, we changed the format from Unicode to text base and then transferred the data to the statistical software for analysis.

Pharmacists were categorized according to their declared site of practice either as hospital pharmacists (if they reported at least 1 hospital practice site) or as community pharmacists (if they reported other sites of practice, but not hospitals).

Drug preparation premises and remote dispensing locations[29] are sites where pharmacists engage in drug compounding activities, including the compounding of sterile medications, such as chemotherapy drugs for hospitals and clinics. As such, because pharmacists who work in these settings are expected to have hospital product–related knowledge and compounding skills, these settings were grouped with hospital pharmacies. The mean, median, and range of the number of pharmacists declaring these pharmacies as their place of practice were calculated. Depending on the reported country of qualifying education, pharmacists were categorized as Canadian graduates or IPGs. The frequency of each country of qualifying education was determined, and the most frequent country of qualifying education was identified.

The following characteristics of Canadian graduates and IPGs were compared: reporting of at least 1 hospital practice site, years since graduation, gender, and number of declared sites of practice. In addition, the frequency of location of qualifying education (Canadian graduates versus IPGs) in each practice setting (hospital versus community) was identified. Statistical significance was tested by the χ^2 test (for categorical variables) and the *t* test (for continuous variables).

Thereafter, we fitted a logistic regression with the outcome of reporting at least 1 hospital pharmacy as a place of practice; the independent variable was the location of qualifying education (Canadian graduates versus IPGs). Data were analyzed with both a crude model (where only the independent variable was included in the model) and an adjusted model (where variables for gender and years since graduation were included in the model). Odds ratios (ORs) and 95% Wald confidence intervals (CIs) were calculated for both crude and adjusted models.

We conducted a sensitivity analysis in which pharmacists were categorized, on the basis of country of qualifying education, as North American graduates or IPGs. In this sensitivity analysis, pharmacy graduates from the United States were combined with Canadian graduates to create a North American pool for comparison with other IPGs. The United States was chosen not only for its close geographic location but also because of similarities with Canada in terms of educational curriculums, experiential rotations, clinical guidelines, and residency programs. In a second sensitivity analysis, we tested if our assumption of drug preparation premises and remote dispensing locations as hospital practice sites was reasonable by removing them from the hospital pharmacy category and adding them to the community pharmacy category of practice setting.

RESULTS

Study Sample

From a total of 5946 extracted pharmacy records, we included 5028 accredited pharmacy sites in our analysis (Figure 1). Of these, 4785 (95.2%) were community pharmacies, and 243 (4.8%) were hospital pharmacies. Most of the pharmacies (n = 5018, 99.8%) had at least 1 pharmacist (range 0 to 248) who reported the pharmacy as their place of practice. Of the 10 pharmacies without any associated pharmacists, 9 were hospital pharmacies and 1 was a community pharmacy. The mean number of pharmacists per accredited pharmacy was 6.2 (median 4.0).

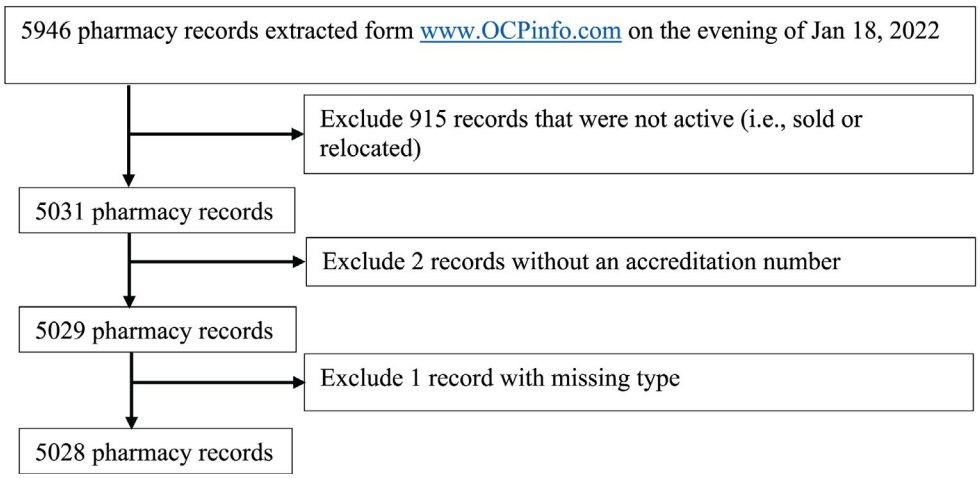

FIGURE 1. Selection of accredited pharmacies (sites).

From a total of 26 614 extracted OCP member records, we included 14 689 pharmacists in our analysis (Figure 2). When categorized by country of qualifying pharmacy education, 7403 (50.4%) were Canadian graduates, and 7286 (49.6%) were IPGs. Egypt, India, the United States, and England were the most frequent countries of qualifying education, and these countries accounted for 66.4% of all IPGs (or 32.9% of the entire sample). The frequencies for all qualifying countries are listed in Appendix 1 (available from https://www.cjhp-online.ca/index.php/cjhp/issue/view/216).

Table 1 shows the characteristics of pharmacists in our sample by location of qualifying education. Overall, more of the Canadian graduates than IPGs were women (63.2% versus 52.3%, $p < 0.01$), and graduation had occurred more recently (17.4 versus 22.1 years since graduation, $p < 0.01$). The mean number of practice sites was only slightly higher

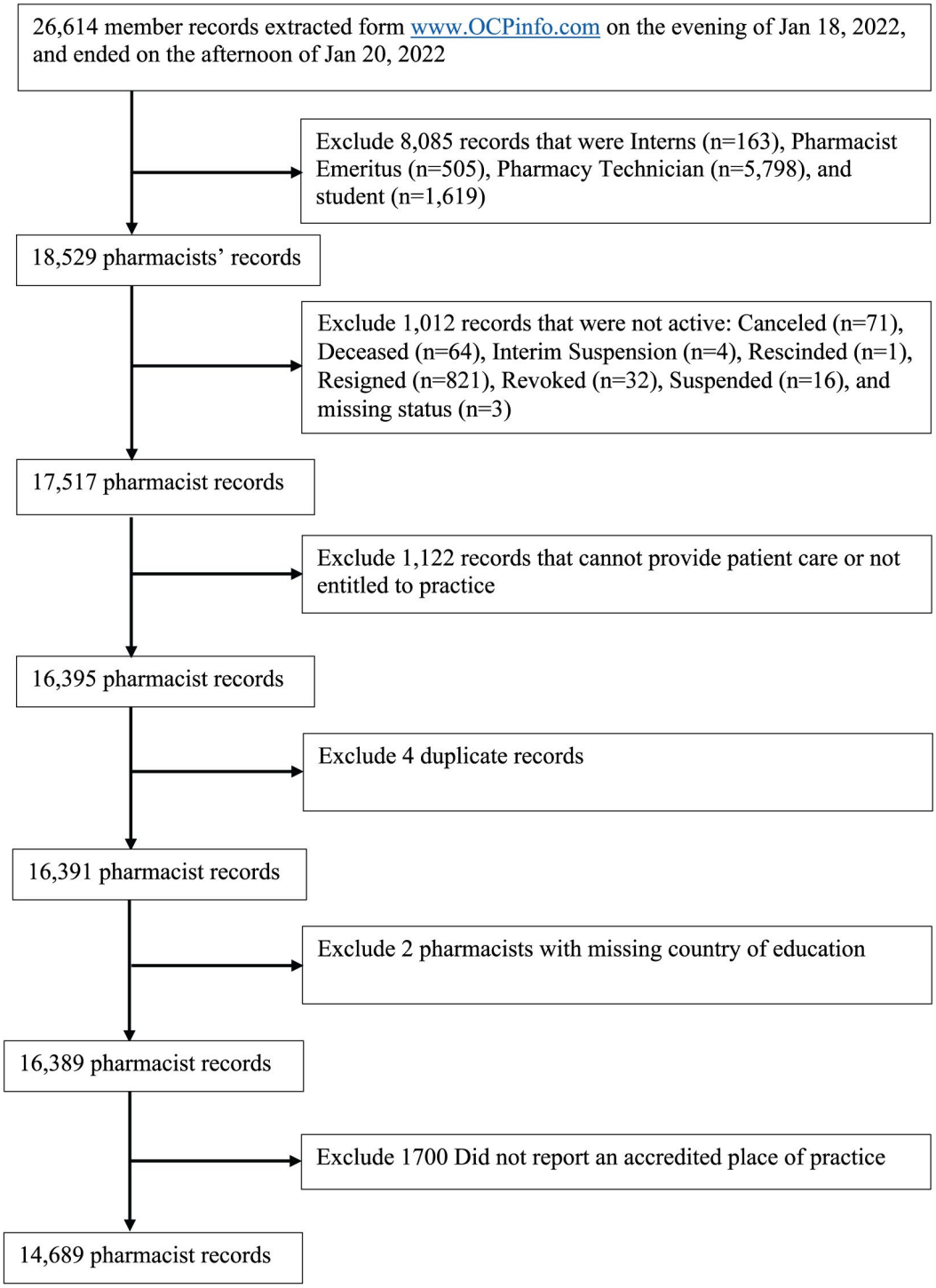

FIGURE 2. Selection of Ontario College of Pharmacist members.

in numeric terms (1.6 versus 1.5), but this difference was statistically significant ($p = 0.02$).

Canadian versus IPGs in hospital practice

Among all pharmacists in our sample, 2885 (19.6%) reported at least 1 hospital pharmacy as a place of practice. Most of these ($n = 2458$, 85.2%) were Canadian graduates. Furthermore, the proportion of pharmacists in each group who reported practising in least 1 hospital pharmacy differed significantly between Canadian graduates ($n = 2458/7403$, 33.2%) and IPGs ($n = 427/7286$, 5.9%) ($p < 0.01$).

Graduating from Canada was associated with higher odds of practising in a hospital pharmacy. In the crude model, the OR for Canadian graduates reporting at least 1 hospital pharmacy as a place of practice was 7.98 (95% CI 7.16–8.91). This association between location of qualifying education and hospital practice was similar in the adjusted model (OR 7.12, 95% CI 6.39–7.98). Men had lower odds of practising in a hospital pharmacy (OR 0.40, 95% CI 0.36–0.44). Similarly, every additional year since graduation was associated with lower odds of practising in a hospital pharmacy (OR 0.98, 95% CI 0.98–0.99).

Sensitivity Analyses

In the first sensitivity analysis, pharmacists graduating from institutions in the United States were combined with Canadian graduates to create a category of North American graduates, which totalled 8279 pharmacists (56.4%), leaving 6410 (43.6%) in the IPG category. With this configuration, North American graduates formed 91.3% ($n = 2634$) of the hospital pharmacist workforce, relative to only 8.7% ($n = 251$) who were IPGs (Table 2). The association between location of qualifying education and hospital practice was more pronounced: crude OR 11.45 (95% CI 10.01–13.09) and adjusted OR 10.32 (95% CI 9.00–11.82). Gender and years since graduation had a similar association with hospital practice in the comparison of North American graduates and IPGs.

In the second sensitivity analysis, drug preparation premises were combined with community pharmacies (instead of being classified as hospital pharmacies). With this change, there was a total of 237 hospital pharmacies, but the overall distribution of pharmacists in the hospital practice setting was similar to what was observed in the main analysis (see Appendix 2, available from https://www.cjhp-online.ca/index.php/cjhp/issue/view/216), with a crude OR of 8.19 (95% CI 7.33–9.14) and adjusted OR of 7.33 (95% CI 6.55–8.20).

DISCUSSION

Using publicly available data from the OCP website, we examined whether the location of qualifying education of pharmacists in Ontario was associated with practice in a

TABLE 1. Characteristics of Pharmacists by Location of Qualifying Education: Canadian versus IPG

Characteristic	Location of Qualifying Education: Canadian Graduates ($n = 7403$)	IPGs ($n = 7286$)	All ($n = 14\,689$)	p Value[a]
No. (%) with at least 1 hospital practice site	2458 (33.2)	427 (5.9)	2885 (19.6)	< 0.01
No. (%) females	4679 (63.2)	3807 (52.3)	8486 (57.8)	< 0.01
Time since graduation (years) (mean ± SD)	17.4 ± 13.2	22.1 ± 11.0	19.7 ± 12.4	< 0.01
No. of declared sites of practice (mean ± SD)	1.6 ± 2.4	1.5 ± 1.5	1.6 ± 2.0	0.02

IPG = international pharmacy graduate, SD = standard deviation.
[a]Based on χ^2 or t test.

TABLE 2. Characteristics of Pharmacists by Location of Qualifying Education: North American versus IPG

Characteristic	Location of Qualifying Education: North American Graduates ($n = 8279$)	IPGs ($n = 6410$)	All ($n = 14\,689$)	p Value[a]
No. (%) with at least 1 hospital practice site	2634 (31.8)	251 (3.9)	2885 (19.6)	< 0.01
No. (%) females	5152 (62.2)	3334 (52.0)	8486 (57.8)	< 0.01
Time since graduation (years) (mean ± SD)	17.6 ± 13.0	22.4 ± 11.0	19.7 ± 12.4	< 0.01
No. of declared sites of practice (mean ± SD)	1.6 ± 2.3	1.5 ± 1.6	1.6 ± 2.0	< 0.01

IPG = international pharmacy graduate, SD = standard deviation.
[a]Based on χ^2 or t test.

hospital setting. We found that among Canadian graduates, approximately 1 in 3 pharmacists (33.2%) reported practising at 1 or more hospital sites. In contrast, among the IPGs, just over 1 in every 20 pharmacists (5.9%) reported practising at a hospital site. Based on adjusted ORs, Canadian pharmacy graduates had 7.12 times higher odds of working in a hospital setting relative to IPGs. When North American pharmacy graduates were analyzed collectively, the effect was even larger, with US and Canadian graduates having 10.32 times higher odds of working in a hospital setting relative to IPGs.

This research provides empirical data regarding the distribution of IPGs and domestic graduates at pharmacy practice sites in Ontario and fills a significant gap in the literature regarding the integration of IPGs at all levels of the profession. Our data revealed that IPGs are underrepresented in higher-status clinical work within hospital settings, which mirrors the pyramidal structure existing in other health care professions.[10-15] Principles of EDI have been widely adopted as institutional practice by the pharmacy profession.[23-25] However, our data suggest that although the pharmacy labour force may be diverse in terms of its members' ethno-racial profile, there is a lack of equity and inclusion in some of its institutions, as indicated by pharmacists' country of graduation.

The lack of integration of IPGs into hospital settings may stem from structural barriers that exist within the licensing process. Compared with Canadian graduates, IPGs do not have the same access to structured practical and clinical training and co-op placements, which are favoured by employers when filling hospital residency positions.[30] Pharmacy programs in Canada have transitioned to the Doctor of Pharmacy (PharmD) degree, which has become the standard for entry to practice. In the PharmD curriculum, there is an added emphasis on experiential clinical placements, relative to the previous baccalaureate degree programs. For example, the PharmD program at the University of Toronto provides all students in their final year with 44 weeks of hands-on clinical training.[31] Beyond these initial clinical placements, graduates who are interested in hospital-based practice seek out hospital residency training,[32-34] which is the expectation for most entry-level institutional positions across Canada.[20] Conversely, IPGs' pathway to licensure lacks such opportunities.[35] For example, the bridging program for IPGs at the University of Toronto does not offer students structured clinical placements, which arguably deprives IPGs of key networking opportunities that would improve their chances of matching in a pharmacy residency program.[36] A similar situation exists for IPGs in the United States, who lack the exposure to advanced clinical training opportunities that their domestic counterparts enjoy.[30] IPGs' participation in the Canadian residency matching process is not known, and the OCP database does not provide information on additional training/education. As such, future research could seek empirical evidence to show the extent to which IPGs are underrepresented in this process, to examine potential facilitators and barriers that could affect IPGs' ability to secure advanced training opportunities, and to gauge the impact of these barriers on IPGs' workplace satisfaction.

Although the methods and data in our study do not support the claim that IPGs face implicit or unconscious bias in the hiring process, the data demonstrate that US graduates have a greater chance of getting hired in Ontario hospitals, possibly because of similarities in education and training to the Canadian graduates, making them a better institutional "fit". Future research could investigate how employers can better assess and value the unique contributions of IPGs, particularly at a time when institutions are interested in promoting equitable and inclusive workplaces. However, this may require changes to an institutional culture that views Canadian education and training as the norm against which other knowledge and experience are compared.[37] Integration of IPGs into hospital pharmacy practice may require initiatives similar to those used for international nurses, including a longer orientation period, a mentorship program, and the creation of networks through formal education such as bridging programs embedded with experiential training.[38-40] Initiatives could also include diversity training for managers and staff, with the goal of creating supportive and inclusive work environments[40] and a greater range of networking opportunities supported by national and provincial pharmacy organizations.

It has been suggested that a more diverse health care workforce, one that mirrors Canada's evolving demographics, could improve health disparities for underrepresented and vulnerable patient populations.[1-5] In keeping with initiatives from other health care professions,[1,7,8] the integration of more IPGs into hospital pharmacy practice may improve patients' access to culturally competent care; however, the extent to which IPGs can fulfill this mandate in Ontario hospitals or how it is being addressed currently by domestic graduates is unknown and would be an area for future study.[41] Culturally competent care is promoted within the profession of pharmacy,[42,43] and IPGs arguably possess knowledge that can facilitate this agenda. However, it must be stressed that serving a diverse population is the responsibility of all pharmacists; the burden of expectation should not rest solely on IPGs, as doing so could potentially limit their practice to a smaller segment of the patient population.[44] In addition, evidence has shown that some IPGs prefer to serve patients beyond their own diaspora.[22] The main impetus for IPG integration into hospital practice should be in keeping with the principles of EDI, whereby the profession advocates for breaking down barriers at all levels of the profession,[24] including structural barriers for those trained outside of Canada.

For our study, we used a comprehensive database from the most populous province in Canada, where a significant

proportion of new immigrants settle. However, several limitations should be noted. First, we used self-declared place of practice as the outcome, but the information in the database may be outdated, and some pharmacists may not have declared all their current places of practice. Nonetheless, it is expected that all Ontario pharmacists accurately declare their place of practice upon annual license renewal. In addition, when pharmacists change their place of practice, they are required to report the new site to the OCP within 30 days.[45] We also considered that reporting at least 1 hospital practice site was a proxy for practising in a hospital; however, it is not known if pharmacists are practising at these sites on a full-time or casual basis. Nevertheless, reporting at least 1 hospital practice site is a valid indicator of practice in such a setting. Lastly, given the lack of data regarding the ethno-racial profile of pharmacists in Ontario, we considered the country of qualifying education as a proxy for diversity, keeping in mind that some Canadian students who are not visible minorities attend pharmacy schools abroad and are considered IPGs and also that many domestic graduates are from diverse backgrounds.

CONCLUSION

We found that the pharmacy profession in Ontario, despite being diverse, is "missing [its] other half".[19] In particular, IPGs have significantly lower odds of realizing their professional ambitions. We hypothesize that this is due to structural barriers impeding their ability to enter institutional practice and have thus identified a need for the pharmacy labour force to diversify into hospital settings. Indeed, our goal should be to enhance the integration of IPGs in all arenas of the profession, including hospitals, academia, advocacy, and regulatory organizations, to meet the needs of a changing Canadian population. Integrating minority professionals, including those with international training, can contribute greatly to the reduction of health disparities when they are represented in all areas of professional life. Future research should examine facilitators and interventions to enhance the integration of internationally educated health care professionals as a pathway to diversifying professions.

References

1. Baumann A, Crea-Arsenio M, Ross D, Blythe J. Diversifying the health workforce: a mixed methods analysis of an employment integration strategy. *Hum Resour Health*. 2021;19(1):62.
2. Phillips JM, Malone B. Increasing racial/ethnic diversity in nursing to reduce health disparities and achieve health equity. *Public Health Rep*. 2014;129(Suppl 2):45-50.
3. Williams SD, Hansen K, Smithey M, Burnley J, Koplitz K, Koyama K, et al. Using social determinants of health to link health workforce diversity, care quality and access, and health disparitieis to achieve health equity in nursing. *Public Health Rep*. 2014;129(Suppl 2):32-6.
4. Glazer G, Clark A, Bankston K. Legislative: From policy to practice: a case for holistic review diversifying the nursing workforce. *Online J Issues Nurs*. 2015;20(3). doi: 10.3912/OJIN.Vol20No03LegCol01
5. Smedley BD. Moving beyond access: achieving equity in state health care reform. *Health Aff (Millwood)*. 2008;27(2):447-55.
6. Effland KJ, Hays K, Ortiz FM, Blanco BA. Incorporating an equity agenda into health professions education and training to build a more representative workforce. *J Midwifery Womens Health*. 2020; 65(1):149-59.
7. Tyson H, Wilson-Mitchell K. Diversifying the midwifery workforce: inclusivity, culturally sensitive bridging, and innovation. *J Midwifery Womens Health*. 2016;61(6):752-8.
8. Zaidi Z, Dewan M, Norcini J. International medical graduates: promoting equity and belonging. *Acad Med*. 2020;95(12S):S82-S87.
9. *Immigration matters in health care* [webpage]. Immigration Refugees and Citizenship Canada; [cited 2022 Nov 22]. Available from: https://www.canada.ca/en/immigration-refugees-citizenship/campaigns/immigration-matters/growing-canada-future/health.html?utm_campaign=ircc-ircc-inclusivecommunities-21-22&utm_medium=smp&utm_source=fb&utm_content=static-facebooknationaldentisten-en&adv=21
10. Dicicco-Bloom B. The racial and gendered experiences of immigrant nurses from Kerala, India. *J Transcult Nurs*. 2004;15(1):26-33.
11. Premji S, Etowa JB. Workforce utilization of visible and linguistic minorities in Canadian nursing. *J Nurs Manag*. 2014;22(1):80-8.
12. Showers F. Being black, foreign and woman: African immigrant identities in the United States. *Ethn Racial Stud*. 2015;38(10):1815-30.
13. Shuval JT. The reconstruction of professional identity among immigrant physicians in three societies. *J Immigr Health*. 2000;2(4):191-202.
14. Jenkins TM, Franklyn G, Klugman J, Reddy ST. Separate but equal? The sorting of USMDs and non-USMDs in internal medicine residency programs. *J Gen Intern Med*. 2020;35(5):1458-64.
15. Working Group on Diversity and Systemic Racism. *Moving towards diversity, equity and inclusion*. Parole Board of Canada; 2022 [cited 2022 Nov 11]. Available from: https://www.canada.ca/en/parole-board/corporate/publications-and-forms/moving-towards-diversity-equity-inclusion.html#p9
16. *2019 annual report: Working together for patient safety. Advancing quality and accountability through collaboration*. Ontario College of Pharmacists; [cited 2022 Nov 22]. Available from: https://www.ocpinfo.com/wp-content/uploads/2020/04/ocp_annual_report_2019.pdf
17. *Pharmacists*. Canadian Institute for Health Information; 22 Nov 17 [cited 2022 Oct 3]. Available from: https://www.cihi.ca/en/pharmacists
18. *2020 annual report: Trusted to lead. Inspired to serve. Driven to protect*. Ontario College of Pharmacists; [cited 2022 Oct 3]. Available from: https://www.ocpinfo.com/wp-content/uploads/2021/04/ocp_annual_report_2020.pdf
19. Patel D. Missing the other half: considering institutional experiential training for international pharmacy graduates in Ontario. *Can Pharm J (Ott)*. 2019;152(5):288-90.
20. Mills A. Should a PGY-1 residency be mandatory for all hospital pharmacists in the era of entry-level Doctor of Pharmacy programs? The "pro" side. *Can J Hosp Pharm*. 2015;68(4):342-3.
21. Elbayoumi U. Identifying the perceived factors affecting career transition among international pharmacy graduates (IPGs) who are in the process of obtaining their license in Ontario [dissertation]. University of Toronto, Leslie Dan Faculty of Pharmacy; 2021 [cited 2023 Feb 7]. Available from: https://search.proquest.com/openview/2302269aa94e4ea6dcd769d41e294f15/1?pq-origsite=gscholar&cbl=18750&diss=y%0Ahttps://tspace.library.utoronto.ca/bitstream/1807/104956/1/Elbayoumi_Usama_202103_PhD_thesis.pdf
22. Mickleborough TO. A Foucauldian discourse analysis of the construction of Canadian international pharmacy graduate (IPG) professional identities and subjectivities [dissertation]. University of Toronto, Leadership, Adult and Higher Education; 2020 [cited 2022 Nov 21]. Available from: https://hdl.handle.net/1807/103378
23. *Resources for pharmacy professionals to support EDI*. Ontario College of Pharmacists; [cited 2022 Oct 12]. Available from: https://www.ocpinfo.com/about/equity-diversity-and-inclusion/resources-for-pharmacy-professionals-to-support-edi/

24. Diversity and inclusion [CPhA statement of commitment]. Canadian Pharmacists Association; [cited 2022 Nov 21]. Available from: https://www.pharmacists.ca/about-cpha/diversity-and-inclusion/
25. Equity, diversity and inclusion resources. University of Toronto, Leslie Dan Faculty of Pharmacy; [cited 2022 Nov 21]. Available from: https://www.pharmacy.utoronto.ca/about-leslie-dan-faculty-pharmacy/equity-diversity-and-inclusion-leslie-dan-faculty-pharmacy/equity-diversity-and-inclusion-resources
26. Swidrovich J. A Canadian perspective of pharmacy education for students belonging to diverse groups. *Curr Pharm Teach Learn*. 2021;13(7):895-902.
27. Ontario College of Pharmaicsts homepage. Ontario College of Pharmacists; [cited 2022 Nov 16]. Available from: https://www.ocpinfo.com/
28. TCPS 2 (2018) – Chapter 2: Scope and approach. In: *Tri-Council policy statement: ethical conduct for research involving humans*. Panel on Research Ethics; 2018 [cited 2022 Nov 16]. Available from: https://ethics.gc.ca/eng/tcps2-eptc2_2018_chapter2-chapitre2.html
29. Drug preparation premises. Ontario College of Pharmacists; [cited 2023 Feb 7]. Available from: https://www.ocpinfo.com/practice_resource/dpp/
30. Al-Azzawi A. The relationship between pharmacy licensing policies on clinical training (CT) and success rates for international pharmacists (IPs) within Canada, United Kingdom, and the United States: a comparative policy analysis. *Pharm Educ*. 2021;21:420-31.
31. PharmD experiential rotations. University of Toronto, Leslie Dan Faculty of Pharmacy; [cited 2022 Jan 30]. Available from: https://www.pharmacy.utoronto.ca/current-students/pharmd/oee/pharmd-experiential-rotations
32. Loewen P, Mills A, Harder C. Should the postgraduate year 2 (PGY-2) residency be focused on advanced pharmacy practice training? The "pro" side. *Can J Hosp Pharm*. 2015;68(6):485-6.
33. Zed PJ. Pharmacy practice residencies in Canada: opportunities and emerging challenges [editorial]. *Can J Hosp Pharm*. 2009;62(1):7-8.
34. Shannon SB, Bradley-Baker LR, Truong HA. Pharmacy residencies and dual degrees as complementary or competitive advanced training opportunities. *Am J Pharm Educ*. 2012;76(8):145.
35. *Pharmacists' gateway Canada for international pharmacists* [website]. National Association of Pharmacy Regulatory Authorities; [cited 2022 Nov 19]. Available from: https://www.pharmacistsgatewaycanada.ca/
36. Gregory P, Austin Z. Postgraduation employment experiences of new pharmacists in Ontario in 2012–2013. *Can Pharm J (Ott)*. 2014;147(5):290-9.
37. Neiterman E, Bourgeault IL. Professional integration as a process of professional resocialization: internationally educated health professionals in Canada. *Soc Sci Med*. 2015;131:74-81.
38. Blythe J, Baumann A, Rhéaume A, McIntosh K. Nurse migration to Canada: pathways and pitfalls of workforce integration. *J Transcult Nurs*. 2009;20(2):202-10.
39. Covell CL, Primeau MD, Kilpatrick K, St-Pierre I. Internationally educated nurses in Canada: predictors of workforce integration. *Hum Resour Health*. 2017;15(1):26.
40. Ramji Z, Etowa J. Current perspectives on the integration of internationally educated nurses into the healthcare workforce. *Humanit Soc Sci Rev*. 2014;3:225-33. Available from: https://www.university-publications.net/hssr/0303/pdf/T4N467.pdf
41. Nurkowski J, Rustad K, Fox K. Cultural competency education for health care providers: a literature review to guide Canadian pharmacy residency programs. *Can J Hosp Pharm*. 2023;76(1):71-5.
42. *AFPC educational outcomes for first professional degree programs in pharmacy in Canada 2017*. Association of Faculties of Pharmacy of Canada; 2017 [cited 2022 Nov 21]. Available from: https://www.afpc.info/system/files/public/AFPC-Educational Outcomes 2017_final Jun2017.pdf
43. *Cultural competence resources*. American Association of Colleges of Pharmacy; 2022 [cited 2022 Nov 21]. Available from: https://www.aacp.org/resource/cultural-competence
44. Michalec B, Martimianakis MAT, Tilburt JC, Hafferty FW. Why it's unjust to expect location-specific, language-specific, or population-specific service from students with underrepresented minority or low-income backgrounds. *AMA J Ethics*. 2017;19(3):238-44.
45. Regulations and standards. Ontario College of Pharmacists; [cited 2022 Nov 19]. Available from: https://www.ocpinfo.com/regulations-standards/

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Competing interests: None declared.

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Funding: None received.

Antibiotic Prescribing Practices for Urinary Tract Infection in a Pediatric Emergency Department: Is This a Problem Worth Cefix-ing?

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Can J Hosp Pharm. 2023;76(4):290-5 https://doi.org/10.4212/cjhp.3444

ABSTRACT

Background: Pediatric urinary tract infection (UTI) is associated with diagnostic and therapeutic challenges.

Objective: To determine the least-broad-spectrum oral antibiotic that would cover 80% of pathogens from lower (afebrile) and upper (febrile) UTIs in a Canadian pediatric emergency department (ED).

Methods: This retrospective case series involved children discharged from the ED between September 2020 and February 2021 with a diagnosis of UTI and collection of a sample for urinalysis that had growth on culture.

Results: Of 188 patients who met the inclusion criteria, 184 (97.9%) were discharged on antibiotics. Culture results indicated a UTI in 170 cases (92.4% of those discharged on antibiotics). The 95 urinary isolates from lower UTIs were susceptible to cephalexin (n = 81, 85.3%), cefixime (n = 78, 82.1%), nitrofurantoin (n = 76, 80.0%), trimethoprim–sulfamethoxazole (TMP–SMX) (n = 64, 67.4%), and amoxicillin (n = 55, 57.9%). The 75 urinary isolates from upper UTIs were susceptible to cefixime (n = 71, 94.7%), TMP–SMX (n = 57, 76.0%), and amoxicillin (n = 48, 64.0%). The mean prescribed duration of antibiotic therapy was 8.3 days for patients with a lower UTI and 9.1 days for those with an upper UTI (mean difference 0.80 days, 95% confidence interval 0.05–1.54).

Conclusions: Empiric treatment with cephalexin or nitrofurantoin would have been successful for almost all lower UTIs. More complete reporting of cephalexin minimal inhibitory concentrations might have allowed use of this drug for most upper UTIs. Although there was a trend toward shorter duration of therapy for lower versus upper UTI, lower UTIs were always treated for longer than recommended by current guidelines.

Keywords: pediatrics, urinary tract infection, emergency department, antimicrobial stewardship

RÉSUMÉ

Contexte : L'infection des voies urinaires (IVU) pédiatrique présente des défis diagnostiques et thérapeutiques.

Objectif : Déterminer l'antibiotique oral à large spectre le moins élevé qui couvrirait 80 % des pathogènes des IVU inférieures (sans fièvre) et des IVU supérieures (avec fièvre) dans un service d'urgences pédiatriques canadien.

Méthodes : Cette série de cas rétrospective impliquait des enfants sortis du service des urgences entre septembre 2020 et février 2021 avec un diagnostic d'IVU et la collecte d'un échantillon pour une analyse d'urine avec croissance dans la culture d'urine.

Résultats : Parmi les 188 patients répondant aux critères d'inclusion, 184 (97,9 %) ont reçu des antibiotiques au moment du congé. Les résultats de la culture ont indiqué une IVU dans 170 cas (92,4 % des patients ayant reçu des antibiotiques au moment du congé). Les 95 isolats urinaires des IVU inférieures étaient sensibles à la céphalexine (n = 81, 85,3 %), au céfixime (n = 78, 82,1 %), à la nitrofurantoïne (n = 76, 80,0 %), au triméthoprime-sulfaméthoxazole (TMP-SMX) (n = 64, 67,4 %) et à l'amoxicilline (n = 55, 57,9 %). Les 75 isolats urinaires des IVU supérieures étaient sensibles au céfixime (n = 71, 94,7 %), au TMP-SMX (n = 57, 76,0 %) et à l'amoxicilline (n = 48, 64,0 %). La durée moyenne de prescription d'antibiotiques était de 8,3 jours pour les patients atteints d'une IVU inférieure et de 9,1 jours pour ceux atteints d'une IVU supérieure (différence moyenne 0,80 jours, IC à 95 % 0,05-1,54).

Conclusions : Un traitement empirique avec la céphalexine ou la nitrofurantoïne aurait été efficace pour la grande majorité des infections urinaires inférieures. Un rapport plus complet des concentrations minimales inhibitrices de la céphalexine aurait peut-être permis d'utiliser ce médicament pour la plupart des infections urinaires supérieures. Bien qu'il y ait eu une tendance vers une durée de traitement plus courte pour les infections urinaires inférieures par rapport aux infections urinaires supérieures, les infections urinaires inférieures étaient toujours traitées plus longtemps que ce qui est recommandé par les lignes directrices actuelles.

Mots-clés : pédiatrie, infection des voies urinaires, service des urgences, gestion des antimicrobiens

INTRODUCTION

Urinary tract infection (UTI) is one of the most common infections seen in the pediatric emergency department (ED). Diagnosis is challenging, as symptoms cannot be elicited in preverbal children, urine is commonly contaminated with bowel flora upon collection, and urinalysis lacks diagnostic accuracy.[1] Almost all children with a UTI have 1 or more of the following signs: positive test result for nitrites, positive test result for leukocyte esterase, and presence of white blood cells or bacteria on microscopy. The specificity of these tests ranges from 78% for leukocyte esterase to 98% for nitrites.[2]

Empiric antimicrobial selection should be guided by local susceptibility patterns. The current guideline of the Canadian Paediatric Society (CPS) states that "Currently, cefixime is a good choice in most areas."[3] However, there is increasing recognition of the need for antimicrobial stewardship to prevent development of resistance, and cefixime may have a broader spectrum of activity than currently required.

The main objective of this study was to determine whether cefixime is still the optimal choice for pediatric UTI or whether less-broad-spectrum antibiotics could be used for empiric outpatient treatment of UTIs in a Canadian pediatric ED.

METHODS

Study Design and Participants

A retrospective case series was performed at the Alberta Children's Hospital, where patients up to 17 years of age are seen. There is currently no guideline for management of UTIs at this hospital. The study was based on a sample of convenience. Patient visits to the ED from September 1, 2020, through February 28, 2021, were included if UTI was listed as a potential diagnosis, urinalysis and urine culture had been performed, and any growth was reported from the culture. Patients were excluded if they had been referred to the Ambulatory Parenteral Therapy Clinic for IV antibiotics or if they had been admitted.

The following data were collected (by J.K.) from electronic charts: demographic characteristics, results of urinalysis and culture, antibiotic prescribed, time to reporting of susceptibilities, any documented follow-up, and return visits to the ED within 14 days. It was assumed that pathogens other than *Staphylococcus aureus* or coagulase-negative staphylococci that were susceptible to cephalexin were also susceptible to cefixime. Approximately 10% of the charts (n = 20) were reviewed by a second investigator (T.T.) to confirm accuracy in the interpretation of follow-up documentation and intervention coding.

This study was approved by the Health Research Ethics Board at the University of Alberta. Parental consent was waived, and the STROBE guidelines[4] were followed.

Definitions

A positive urinalysis result was defined as any of the following: positive for leukocyte esterase (at any level) or nitrites, leukocyte count above 5 white blood cells per high-power field, or bacteria present on microscopy. A positive result on urine culture was defined as 10^7 colony-forming units per litre (CFU/L) or above for a midstream urine sample or an in–out catheter specimen, or any growth from a suprapubic aspirate specimen. Lower colony counts were considered to represent negative culture results. Cultures with mixed growth were excluded unless the urinalysis results were abnormal and the colony count for all organisms met the definition of a positive urine culture result. Upper UTI (pyelonephritis) was defined by temperature of 38°C or above in the ED and/or documentation of fever at home. Afebrile cases were assumed to be lower UTI (cystitis).

Objectives

The primary objective of the study was to determine the least-broad-spectrum antibiotic that would have covered an arbitrarily chosen minimum 80% of cases with positive urine culture results for patients with upper and lower UTIs. Coverage of 100% of isolates would be ideal but would likely require empiric parenteral antibiotics. The reason for considering upper and lower UTIs separately was that for some antibiotics (specifically cephalexin and nitrofurantoin), even if the minimal inhibitory concentration (MIC) is low, it is not clear that concentration in the renal parenchyma will be adequate to cure upper UTI; there appear to be no published studies on use of these antibiotics for upper UTI.

The secondary objective was to determine how often the duration of therapy fit with CPS guidelines, which recommend 7 to 10 days for upper UTI and 2 to 4 days for older children (not further defined) with lower UTI.[3] A Cochrane review[5] and guidelines from the UK National Institute for Health and Care Excellence[6] support the shorter duration for lower UTI in children as young as 3 months of age.

Data analysis was limited to descriptive statistics.

RESULTS

Charts were reviewed for 232 patients seen during the study period, of whom 44 (19%) were excluded because they had been admitted (n = 20) or referred (n = 24) to the Ambulatory Parenteral Therapy Clinic. The remaining 188 patients (86.7% female; median age 5.0 [interquartile range 1.6–9.4] years) met the inclusion criteria (Table 1). Forty-one (21.8%) of the 188 patients had a history of UTI. Urinalysis results were positive in 183 (97.3%) of the cases. Eighty-three (44.1%) of the patients had fever at home or in the ED.

Empiric antibiotics were started in the ED for 184 (97.8%) of the 188 patients, specifically cefixime (n = 156, 84.8%),

with 5 of these patients also receiving 1 dose of ceftriaxone in the ED; amoxicillin–clavulanate (n = 8, 4.3%); nitrofurantoin (n = 7, 3.8%); trimethoprim–sulfamethoxazole (TMP–SMX; n = 6, 3.3%); amoxicillin (n = 4, 2.2%); ciprofloxacin (n = 2, 1.1%); and cephalexin (n = 1, 0.5%). Urine culture results met the study definition of "positive" for 170 patients (92.4% of the 184 with initiation of antibiotics), of whom 95 (55.9%) had lower UTIs. Organisms and susceptibilities (which were reported a mean of 2.01 [standard deviation 0.56] days after the ED visit) are shown in Table 2. The 95 urinary isolates from lower UTIs were susceptible to cephalexin (n = 81, 85.3%, cefixime (n = 78, 82.1%), nitrofurantoin (n = 76, 80.0%), TMP–SMX (n = 64, 67.4%), and amoxicillin (n = 55, 57.9%). The 75 urinary isolates from upper UTIs were susceptible to cefixime (n = 71, 94.7%), TMP–SMX (n = 57, 76.0%), and amoxicillin (n = 48, 64.0%). Of the 156 isolates treated with cefixime, 153 (98.1%) were susceptible to one or both of cephalexin and nitrofurantoin.

TABLE 1. Characteristics of 188 Children Discharged from an Emergency Department with a Diagnosis of Urinary Tract Infection

Characteristic	No. (%) of Patients[a] (n = 188)
Sex, female	163 (86.7)
Age	
Median (IQR)	5.0 (1.6–9.4) years
2 months to 3 years	78 (41.5)
4–12 years	83 (44.1)
13–18 years	27 (14.4)
Febrile[b]	83 (44.1)
Comorbidities/history	
History of UTI	41 (21.8)
Structural kidney/bladder abnormalities[c]	11 (5.9)
Immunosuppression	0
Other[d]	14 (7.4)
Antibiotic use within 7 days before the ED visit	9 (4.8)
Trimethoprim–sulfamethoxazole	2
Trimethoprim	1
Nitrofurantoin	4
Cephalexin	1
Cefixime	1
Urine collection method	
Midstream	126 (67.0)
In-out catheter	62 (33.0)
Positive urinalysis result[e]	183 (97.3)
Positive result on urine culture[f]	170 (90.4)

CFU = colony-forming unit, ED = emergency department, IQR = interquartile range, UTI = urinary tract infection.
[a]Except where indicated otherwise.
[b]Defined as temperature ≥ 38.0°C and/or clinician documentation of fever or parent reported fever at home before ED visit.
[c]Vesicoureteral reflux, bladder diverticulum, duplex ureter, hydronephrosis, pyeloplasty/stent, neurogenic bladder.
[d]Viral meningitis, asthma, herpes simplex virus, COVID-19, epilepsy, meningomyelocele, renal stone, depression, constipation.
[e]A urinalysis result was considered positive if at least 1 of the following was true: leukocyte esterase or nitrite was detected, urine white blood cell count was > 5 cells per high-power field, or bacteria was present on microscopy.
[f]Positive result on urine culture was defined as ≥ 10^7 CFU/L for clean-catch midstream urine, ≥ 10^7 CFU/L for an in–out catheter specimen, and any growth from a suprapubic aspirate specimen.

The mean prescribed duration of antibiotics was 8.3 days for the 95 patients with a lower UTI and 9.1 days for the 75 patients with an upper UTI, for a mean difference of 0.80 days (95% confidence interval [CI] 0.05–1.54 days). For patients with a lower UTI, the duration of therapy was specified in the chart for 74 of the 95 cases: 5 days (n = 3), 7 days (n = 47), 10 days (n = 20), or 14 days (n = 4), with no patients having the recommended duration of 2–4 days. For patients with an upper UTI, the duration of therapy was specified in the chart for 62 of the 75 cases: 7 days (n = 24), 10 days (n = 33), and 14 days (n = 5).

Follow-up was documented for all but 2 patients. Antibiotic interventions at follow-up included changing antibiotics because of resistance of the empiric choice (n = 7), narrowing empiric treatment to an alternative antibiotic (n = 3), and initiating an antibiotic (for 2 of the 4 patients not initially treated). Antibiotics were not discontinued for any of the 14 children with negative culture results. There were a total of 13 visits to the ED within 14 days, of which 9 were related to the initial UTI: worsening of UTI symptoms (n = 4, none of whom had an isolate resistant to the prescribed antibiotic); difficulties in administering oral cefixime (n = 2); and adverse effects of antibiotics, specifically 1 case each of diarrhea (patient receiving cefixime), rash (patient receiving TMP–SMX), and fussiness with poor feeding (patient receiving cefixime). None of these patients required admission to hospital.

Agreement between the 2 investigators who reviewed the charts was 100%.

DISCUSSION

More than 80% of urinary isolates were susceptible to cefixime, nitrofurantoin, cephalexin, and amoxicillin–clavulanate. Cefixime was by far the most frequently prescribed antibiotic for UTIs in this study. Although almost all patients could have been changed to a narrower-spectrum antibiotic once susceptibilities were available, this happened in only 3 cases. Changing therapy after ED discharge is a logistical challenge and is costly to parents, which highlights the importance of ensuring optimal initial empiric prescribing. Only 14 (7.6%) of the 184 patients who were started on antibiotics did not have a UTI, compared with 46% in another recent Canadian study,[8] which suggests that clinicians in our organization rarely prescribed antibiotics if the urinalysis results were negative.

Nitrofurantoin is not recommended for upper UTI because renal penetration is poor, but this drug should be considered for lower UTI given that almost all isolates were susceptible. However, nitrofurantoin requires 4 times daily administration except for adolescents, who can take the macrocrystal/monohydrate capsule twice daily.

Cephalexin is another empiric antibiotic that is appropriate for lower UTIs, given it covered almost all isolates. Rates of susceptibility to cephalexin have increased in recent years after the Clinical and Laboratory Standards Institute's introduction of urinary cefazolin-surrogate testing in 2014 (after the CPS guideline[3] was written), which corrected errors in reporting of cephalexin resistance that had resulted from cephalothin-surrogate testing.[7] However, the MIC breakpoint for cephalexin reported in our laboratory is based on the treatment of lower UTI. In the absence of reporting of breakpoints for upper UTI, cephalexin should be reserved for lower UTI. Traditional 4 times daily dosing is a barrier to compliance, but the product monograph states that twice-daily dosing can be used for children with lower UTI.[9]

TABLE 2. Susceptibility of Isolates from Urine Cultures of Children Seen in a Pediatric Emergency Department[a]

Isolate and Variable	Amoxicillin–ampicillin	Amoxicillin–clavulanate	Cephalexin	Gentamicin	Nitrofurantoin	Trimethoprim–sulfamethoxazole	Ceftriaxone	Cefixime	Cefazolin[b]	Ciprofloxacin	Tobramycin	Carbapenems[b,c]
Escherichia coli (*n* = 135)[c,d]												
No. of patients/cultures	135	135	135	135	135	135	9[e]	3[e]	10[e]	3[e]	5[e]	1[e]
Susceptible	63%	7%	97%	97%	99%	78%	100%	67%	0%	100%	20%	100%
Resistant	37%	8%	3%	3%	1%	22%	0%	33%	100%	0%	0%	0%
Intermediate resistance	0%	5%	0%	0%	0%	0%	0%	0%	0%	0%	80%	0%
Proteus mirabilis (*n* = 8)												
No. of patients/cultures	8	–	8	8	8	8	1	–	1	–	–	–
Susceptible	100%	–	100%	100%	12%	100%	100%	–	0%	–	–	–
Resistant	0%	–	0%	0%	88%	0%	0%	–	100%	–	–	–
Intermediate resistance	0%	–	0%	0%	0%	0%	0%	–	–	–	–	–
Klebsiella pneumoniae (*n* = 7)[d]												
No. of patients/cultures	6	6	6	6	6	5	–	–	–	3	–	–
Susceptible	0%	100%	100%	100%	17%	100%	–	–	–	100%	–	–
Resistant	100%	0%	0%	0%	0%	0%	–	–	–	0%	–	–
Intermediate resistance	0%	0%	0%	0%	83%	0%	–	–	–	0%	–	–
Citrobacter sp. (*n* = 3)												
No. of patients/cultures	3	3	3	3	3	3	–	–	2	–	–	–
Susceptible	0%	33%	33%	100%	67%	100%	–	–	0%	–	–	–
Resistant	100%	67%	67%	0%	33%	0%	–	–	100%	–	–	–
Intermediate resistance	0%	0%	0%	0%	0%	0%	–	–	0%	–	–	–
Enterococcus faecalis (*n* = 6)[d]												
No. of patients/cultures	6	–	–	–	6	–	–	–	–	–	–	–
Susceptible	100%	–	–	–	100%	–	–	–	–	–	–	–
Resistant	0%	–	–	–	0%	–	–	–	–	–	–	–
Intermediate resistance	0%	–	–	–	0%	–	–	–	–	–	–	–

CFU = colony-forming unit, MIC = minimum inhibitory concentration, UTI = urinary tract infection.

[a]Two patients had 2 organisms each. In addition, the table includes results for 3 patients who did not meet the study definition of a positive urine culture result. Other organisms: *Klebsiella oxytoca* (*n* = 2), *Staphylococcus aureus* (*n* = 1), coagulase-negative *Staphylococcus* (*n* = 5), *Streptococcus agalactiae* (*n* = 4), *Aerococcus urinae* (*n* = 1), *Enterococcus faecium* (ampicillin sensitive) (*n* = 1), *Staphylococcus saprophyticus* (*n* = 2).

[b]Six of the 10 *E. coli* cultures with cefazolin resistance had concurrent cephalexin susceptibility. Cefazolin is used as a surrogate for cephalexin and when used specifically for lower UTI has a higher MIC breakpoint (≤ 16 µg/mL) than when it is used for any infection other than lower UTI (for which MIC breakpoint is ≤ 2 µg/mL).[7] Therefore, in cases where the bacteria is reported as resistant to cefazolin but susceptible to cephalexin, cephalexin can be used for lower UTIs, but there is uncertainty as to whether cefazolin or cephalexin should be used for upper UTIs.

[c]One isolate had extended-spectrum β-lactamase (ESBL) resistance.

[d]Two cultures had 2 organisms with more than 10^7 CFU/L: *E. coli* and *E. faecalis* in combination; *E. coli* and *K. pneumoniae* in combination.

[e]Only reported according to local microbiology lab algorithm based on resistance or clinician request.

Other centres have reported the use of cephalexin rather than cefixime for empiric therapy of both upper and lower UTIs. In a study conducted in Seattle, Washington, use of cephalexin for uncomplicated UTIs treated in the ED and for inpatients increased from 19% to 80% once a guideline was introduced.[10] In a similar Kaiser Permanente study limited to outpatients, use of cephalexin increased from 29% to 53% with introduction of a guideline.[11] A study conducted in Toronto, Ontario, showed that 57% of patients seen in the ED were discharged on cephalexin.[8] None of these studies reported outcome data, but an abstract from a Philadelphia, Pennsylvania, study reported treatment failure in only 13% (95% CI 10%–15%) of 761 children treated with cephalexin versus 19% (95% CI 16%–21%) of 1010 treated with TMP–SMX and 36% (95% CI 31%–41%) of 363 treated with amoxicillin.[12] None of these 4 studies excluded children with upper UTI, and the Toronto study noted that the majority of patients had upper UTIs.[8]

Almost all isolates were susceptible to amoxicillin–clavulanate. However, this option has a broader spectrum of activity and costs more than cefixime or cephalexin, and many clinicians consider it more likely to cause diarrhea.

Adult guidelines caution that β-lactams have lower efficacy and are associated with more adverse events than other classes of antibiotics when used to treat UTI,[13] but this does not seem to be a concern in children: almost all of the patients in our study were treated with a β-lactam, with only 4 (2.4%) of 170 re-presenting with persistent symptoms.

For every child, the prescribed duration was longer than the 2- to 4-day course recommended for lower UTI,[3] but for most the prescribed duration fell within the recommended 7- to 10-day course for upper UTI. However, evidence is emerging that 7 days is sufficient for upper UTI.[14] As for lower UTI, traditional dogma is that the duration of β-lactam therapy should be longer than for other antibiotics,[7] but the previously mentioned Kaiser Permanente study successfully used a 3-day course of cephalexin.[11] In a recent trial, children with upper or lower UTI with clinical improvement on day 5 were randomly assigned to stop therapy or continue another 5 days of treatment.[15] Cure rate was inferior among the children with fever who stopped therapy after 5 days, but was still 96% (versus 99%), indicating that even in children with upper UTIs, 5 days of therapy may be sufficient if there is clinical improvement at the end of treatment.

This study had all the inherent limitations of a retrospective chart review. The definitions of UTI are not consistent across the pediatric literature. Our methodology did not allow us to determine factors that might have led to longer courses of antibiotic therapy, nor could we analyze the results of follow-up appointments outside the ED. Data on duration of antibiotic therapy were missing for some patients. In addition, the prescribed duration of antibiotics may have differed from the actual duration. Practice changes occurred in ED settings during the COVID-19 pandemic, which may have affected the results. Our results will not be applicable in all jurisdictions, given that antimicrobial susceptibilities vary. Cephalexin breakpoints have not been established for rare pathogens such as *Citrobacter*.

CONCLUSION

Less-broad-spectrum antibiotics and shorter duration of antibiotic therapy could be used for UTIs in this pediatric ED, and these conclusions could probably be applied in many other Canadian EDs. Consideration should be given to recommending cephalexin and nitrofurantoin as appropriate empiric antibiotics for children with suspected lower UTI except in cases with previous resistant urinary isolates. The main priority for future studies should be to determine the efficacy of cephalexin for upper UTIs. Clinicians should be encouraged to order therapy of shorter duration, in particular in cases of lower UTI.

References

1. Kazi BA, Buffone GJ, Revell PA, Chandramohan L, Dowlin MD, Crus AT. Performance characteristics of urinalyses for the diagnosis of pediatric urinary tract infection. *Am J Fam Med.* 2013;31(9):1405-7
2. Roberts KB. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. *Pediatrics.* 2011;128(3):595-610.
3. *Urinary tract infection in infants and children: Diagnosis and management* [position statement]. Canadian Paediatric Society; 2014 [reaffirmed 2020; cited 2020 Jul 20]. Available from: https://www.cps.ca/en/documents/position/urinary-tract-infections-in-children
4. *STROBE statement—checklist of items that should be included in reports of observational studies*. EQUATOR Network; 2015 [cited 2023 Mar 9]. Available from: https://www.equator-network.org/wp-content/uploads/2015/10/STROBE_checklist_v4_combined.pdf
5. Hodson EM, Craig JC, Martin S, Moyer VA. Short versus standard duration oral antibiotic therapy for acute urinary tract infection in children. *Cochrane Database Syst Rev*. 2003;(1):CD003966.
6. *UTI (lower): antimicrobial prescribing*. National Institute for Health and Care Excellence (UK); 2022 May [cited 2023 Mar 9]. Available from: https://www.nice.org.uk/guidance/ng109/resources/visual-summary-pdf-6544021069
7. Nguyen HM, Graber CJ. A critical review of cephalexin and cefadroxil for the treatment of acute uncomplicated lower urinary tract infection in the era of "bad bugs, few drugs". *Int J Antimicrob Agents*. 2020; 56(4):106085
8. Alghounaim M, Ostrow O, Timberlake K, Richardson SE, Koyle M, Science M. Antibiotic prescription practice for pediatric urinary tract infection in a tertiary center. *Pediatr Emerg Care*. 2021;37(3):150-4.
9. Keflex [product monograph]. Pendopharm, Division of Pharmascience; 2018 [cited 2023 Mar 9]. Available from: https://pdf.hres.ca/dpd_pm/00045523.PDF
10. Poole NM, Kronman MP, Rutman L, Weissman SJ, Migita RT, Caglar D, et al. Improving antibiotic prescribing for children with urinary tract infection in emergency and urgent care settings. *Pediatr Emerg Care.* 2020;36(6):e332-e339.
11. Daley MF, Arnold Rehring SM, Glenn KA, Reifler LM, Steiner JF. Improving antibiotic prescribing for pediatric urinary tract infections in outpatient settings. *Pediatrics.* 2020;145(4):e20192503.
12. Beus JM, Cowden CL, Metjian TA, Dona D, Ngo JS, Spyridakis E, et al. Cephalexin for outpatient urinary tract infections in children [abstract]. *Open Forum Infect Dis*. 2015;2(Suppl 1):1572.

13. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis.* 2011; 52(5):e103-e120.
14. Fox MT, Amoah J, Hsu AJ, Herzke CA, Gerber JS, Tamma PD. Comparative effectiveness of antibiotic treatment duration in children with pyelonephritis. *JAMA Netw Open*. 2020;3(5):e203951.
15. Zaoutis T, Shaikh N, Fisher BT, Coffin SE, Bhatnagar S, Downes KJ, et al. Short course therapy for urinary tract infections in children: the SCOUT randomized clinical trial. *JAMA Pediatr*. 2023;177(8):782-9.

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Competing interests: For activities unrelated to the study reported here, Cora Constantinescu has received honoraria from the Federation of Canadian Women in Medicine, GSK, Merck, and Pfizer. Joan Robinson serves as Chair of the Data Safety and Monitoring Board for a University of Alberta group A *Streptococcus* vaccine and as Divisional Director for Pediatric Infectious Disease at the University of Alberta. No other competing interests were declared.

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Funding: This study was funded through the Major Innovation Fund Project entitled "Antimicrobial Resistance – A One Health Approach Project".

Acknowledgements: In-kind support and human resources for this study were provided by AHS Pharmacy Services; analytic support was provided by the AHS Physician Learning Program.

Effect of Pharmacist-Initiated Interventions on Duration of Antibiotic Therapy for Acute Exacerbation of Chronic Obstructive Pulmonary Disease and Community-Acquired Pneumonia

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Can J Hosp Pharm. 2023;76(4):296-301 https://doi.org/10.4212/cjhp.3421

ABSTRACT

Background: Current guidelines for the treatment of acute exacerbation of chronic obstructive pulmonary disease (AECOPD) and community-acquired pneumonia (CAP) recommend 5 days of antimicrobial therapy. Despite these recommendations, the duration of therapy exceeds 5 days for up to 70% of patients, with most superfluous prescribing occurring upon discharge from hospital. Shortening the duration of antibiotic therapy could decrease adverse events, resistance, and costs.

Objective: To determine whether a pharmacist-initiated modification to the duration of antibiotic therapy prescribed for the treatment of AECOPD or CAP reduced the duration of antibiotic prescriptions.

Methods: In this prospective, single-centre study of adult inpatients receiving antibiotics for the treatment of AECOPD or CAP between October 2020 and March 2021, pharmacists assigned a 5-day duration to antimicrobials prescribed for these indications. For patients discharged before completion of therapy, the antibiotic start date and intended duration were included on the discharge prescription. Study patients were matched 1:1 with historical controls to compare the total duration of antibiotic therapy with and without the intervention.

Results: A total of 100 patients (66 with CAP and 34 with AECOPD) met the inclusion criteria and had their antibiotic treatment duration modified to 5 days. Mean total duration of antibiotic therapy was 5.31 days in the intervention group and 7.11 days in the control group ($p < 0.001$). Outpatient antibiotic prescribing was 0.86 days in the intervention group and 3.2 days in the control group ($p < 0.001$). In both groups, the rates of readmission at 30 and 90 days were 19% and 31%, respectively.

Conclusions: Pharmacist-initiated modification of antimicrobial therapy resulted in shortening of the duration of therapy by almost 2 days. Including information about treatment duration on the discharge prescription reduced outpatient prescribing without affecting readmission rates.

Keywords: community-acquired pneumonia, acute exacerbation of chronic obstructive pulmonary disease, antibiotic duration, antimicrobial stewardship, pharmacist

RÉSUMÉ

Contexte : Les lignes directrices actuelles relatives au traitement de l'exacerbation aiguë de la maladie pulmonaire obstructive chronique (MPOC) et de la pneumonie extra-hospitalière (PEH) recommandent 5 jours de traitement antimicrobien. Malgré ces recommandations, la durée du traitement dépasse 5 jours pour jusqu'à 70 % des patients, et la plupart des prescriptions superflues se produisent au moment du congé de l'hôpital. Le raccourcissement de la durée de l'antibiothérapie pourrait réduire les événements indésirables, la résistance et les coûts.

Objectif : Déterminer si une modification de la durée de l'antibiothérapie prescrite pour le traitement de l'exacerbation aiguë de la MPOC ou de la PEH, initiée par le pharmacien, réduit la durée des prescriptions d'antibiotiques.

Méthodes : Dans cette étude prospective monocentrique portant sur des patients adultes hospitalisés ayant reçu des antibiotiques pour le traitement de l'exacerbation aiguë de la MPOC ou de la PEH entre octobre 2020 et mars 2021, les pharmaciens ont attribué une durée de 5 jours aux antimicrobiens prescrits pour ces indications. Pour les patients quittant l'hôpital avant la fin du traitement, la date de début de l'antibiothérapie et la durée prévue figuraient sur l'ordonnance de décharge. Les patients de l'étude ont été jumelés 1:1 avec des témoins historiques pour comparer la durée totale de l'antibiothérapie avec et sans l'intervention.

Résultats : Au total, 100 patients (66 avec une PEH et 34 avec une exacerbation aiguë de la MPOC) répondaient aux critères d'inclusion et ont vu leur durée de traitement antibiotique modifiée à 5 jours. La durée totale moyenne de l'antibiothérapie était de 5,31 jours dans le groupe d'intervention et de 7,11 jours dans le groupe témoin ($p < 0,001$). La prescription d'antibiotiques en ambulatoire était de 0,86 jour dans le groupe d'intervention et de 3,2 jours dans le groupe témoin ($p < 0,001$). Dans les deux groupes, les taux de réadmission à 30 et 90 jours étaient de 19 % et 31 %, respectivement.

Conclusions : La modification du traitement antimicrobien initiée par le pharmacien a entraîné un raccourcissement de la durée du traitement de près de 2 jours. L'inclusion d'informations sur la durée du traitement sur l'ordonnance de départ a réduit la prescription ambulatoire sans avoir d'incidence sur les taux de réadmission.

Mots-clés : pneumonie extra-hospitalière, exacerbation aiguë de la maladie pulmonaire obstructive chronique, durée de l'antibiothérapie, gestion des antimicrobiens, pharmacien

INTRODUCTION

Antimicrobial resistance is one of the greatest threats to health care. Given that antimicrobial use accelerates the development of resistance, overuse and misuse of these drugs must be decreased to preserve their effectiveness.[1] Lower respiratory tract infection is the most common indication for the use of antimicrobials in Canadian hospitals.[1] Thus, avoiding unnecessarily long durations of antimicrobial therapy for the treatment of respiratory tract infections may have a significant impact on antimicrobial use and resistance.

Courses of antibiotic therapy with duration exceeding that recommended in therapeutic guidelines are most often prescribed for respiratory tract infections.[2] Antibiotic therapy is recommended for selected patients experiencing acute exacerbation of chronic obstructive pulmonary disease (AECOPD); however, approximately 90% of antibiotic prescriptions for the treatment of AECOPD exceed the current recommended treatment duration of 5 days.[3]

Historically, community-acquired pneumonia (CAP) was treated with 7- to 14-day courses of antibiotics.[4] In recent clinical trials, shorter courses of antibiotic therapy were non-inferior to longer courses for the treatment of CAP with respect to clinical success, mortality, and readmission rates.[5,6] The therapeutic guidelines of the American Thoracic Society and the Infectious Diseases Society of America recommend a 5-day duration of antibiotic therapy for the treatment of CAP, provided the patient has reached clinical stability.[7] A systematic review and meta-analysis supported this recommendation, showing that short courses (6 days or less) of antibiotic therapy did not increase mortality and resulted in fewer adverse events relative to long courses of treatment (7 days or more).[8] These adverse events included, but were not limited to, diarrhea, headache, nausea, and rash.[8] Despite guideline recommendations and literature supporting short-course therapy, a retrospective study of hospitalized patients with pneumonia demonstrated that two-thirds of patients received antibiotic therapy of excess duration, beyond 5 days.[2] Most of this excess prescribing of antibiotics (93%) occurred at discharge. Each excess day of treatment was associated with a 5% increase in the odds of an antibiotic-associated adverse event occurring after discharge.[8]

The principles of antimicrobial stewardship include using antibiotics only when necessary, selecting the optimal agent at the correct dose, and treating patients for the appropriate duration. The intervention that could most easily reduce antibiotic use and that is considered to be the safest and most attainable is to treat infections for only as long as necessary to achieve optimal cure rates.[9] Decreased exposure to antibiotics achieved through shorter-course regimens can decrease the selective pressure of resistant strains, leading to lower rates of infection and less colonization with drug-resistant organisms.

Short-course strategies have equivalent clinical outcomes compared with longer courses and are associated with lower rates of infection recurrence, superinfection, antibiotic resistance, and incidence of adverse effects from antibiotic use.[6] Within our institution, all antimicrobial prescriptions for hospital inpatients are electronically assigned a duration of 7 days; however, this practice is no longer supported for antibiotics prescribed for the treatment of AECOPD or CAP and may result in detrimental consequences. The objective of this study was to determine whether a pharmacist-initiated modification to the duration of antibiotic therapy prescribed for the treatment of AECOPD or CAP reduced total antibiotic prescribing (defined as days of therapy).

METHODS

Study Design

This prospective, single-centre study was designed to include all hospital inpatients at Windsor Regional Hospital – Ouellette Campus (WRH-OC) who received antibiotics for the treatment of AECOPD or CAP between October 15, 2020, and March 31, 2021. Approval for this study was granted by the Windsor Regional Hospital Research Ethics Board. The WRH-OC is a 350-bed community teaching hospital, serving a population of about 400 000 people in Windsor and Essex County. The hospital is responsible for all acute care services and provides the following types of care: complex trauma care, renal dialysis, cardiac care, stroke treatment and neurosurgery, intensive care, and acute mental health care. At the time of this study, the hospital used a paper chart system with paper-based medication orders. Study patients were matched 1:1 with historical controls who had been admitted 1 year before (October 2019 to March 2020). The controls were selected from a historical database and were matched on age, biological sex, and antibiotic indication. The target sample size was 100 patients in the intervention group matched with 100 historical control patients. Data were collected by means of a paper chart review.

Patient Eligibility

Patients were included if they were 18 years of age or older, had been admitted to hospital with a diagnosis of AECOPD or CAP, and had received an antibiotic prescription for treatment of AECOPD or CAP (specifically ceftriaxone, azithromycin, moxifloxacin, cefuroxime, amoxicillin/clavulanic acid, or doxycycline). To be considered for pharmacist-initiated modification of antibiotic duration, patients had to meet clinical stability criteria, defined as temperature 37.8°C or lower for 48 hours and no more than one of the following: systolic blood pressure less than 90 mm Hg, heart rate greater than 100/min, respiratory rate greater

than 24/min, oxygen saturation less than 90% (on room air), or partial pressure of oxygen less than 60 mm Hg.

Patients were excluded if they had any of the following: HIV, neutropenia (defined as absolute neutrophil count less than 1×10^9/L), treatment in a critical care area, chronic immunosuppression (defined as receipt of immunosuppression for solid organ transplant, receipt of 10 mg/day or more of prednisone or equivalent for longer than 30 days, or receipt of other immunosuppressive agents), need for a chest tube or diagnosis of empyema, infection due to an pathogen that required a longer duration of therapy (*Pseudomonas aeruginosa, Staphylococcus aureus, Legionella* sp.), residence in a nursing home or acute care hospital within the previous 14 days, a condition complicated by an extrapulmonary infection (e.g., meningitis, endocarditis), or infection secondary to COVID-19.

Study Groups

Before this study was initiated, prescribers were informed of the guideline-recommended changes to the duration of antibiotic therapy prescribed for the treatment of AECOPD or CAP. Prescribers were notified both verbally at their respective departmental meetings and by means of an electronic memo outlining the institution's policy permitting pharmacists to assign a 5-day duration of therapy for patients receiving antibiotics for the treatment of AECOPD or CAP, provided the patients met the study's inclusion criteria. The study was initiated on the day the new policy was implemented.

Hospital inpatients for whom antibiotics were prescribed for the treatment of AECOPD or CAP were identified by the infectious diseases pharmacist (L.N.) from a computer-generated list of all inpatients receiving antibiotic therapy. For patients who met the inclusion criteria, the pharmacist modified the duration of therapy to 5 days through a written order in the patient's paper chart. Once the order was entered into the pharmacy's computer system, the notation "duration of therapy modified to 5 days for AECOPD/CAP" was printed beneath the antibiotic drug name on the respective medication administration record, along with the start date and intended stop date of the medication.

Although all pharmacists were aware of the new policy authorizing pharmacists to modify the duration of antibiotic therapy prescribed for the treatment of AECOPD or CAP, most of the modifications were performed by the infectious diseases pharmacist, given the nature of workflow at WRH-OC. Twenty-four hours before the discontinuation of antibiotic therapy, a notification was placed in the patient chart alerting the prescriber of the impending discontinuation. This gave the prescriber an opportunity to extend antibiotic therapy beyond 5 days, if necessary. If the patient was discharged before the completion of antibiotic therapy, the electronic discharge prescription was amended to show the start date and intended duration of antibiotic therapy.

The control group consisted of hospital inpatients for whom antibiotics were prescribed for the treatment of AECOPD or CAP between October 2019 and March 2020. These patients were identified using diagnostic codes.

Endpoints

The primary endpoint was duration (in days) of antibiotic prescribing for treatment of AECOPD or CAP, including days of antibiotics received in hospital and after discharge, with pharmacist-initiated modification to the duration of therapy prescribed. In situations where the patient was discharged before the completion of antibiotic therapy, the antibiotic start date and intended stop date were printed on the computer-generated discharge prescription. Ultimately, the prescriber selected the duration of antibiotic therapy on the discharge prescription. The secondary endpoints were the rates of readmission within 30 days and 90 days of discharge.

Data Analysis

The primary outcome, duration of antibiotic prescribing, was analyzed with descriptive statistics, using a *t* test. A nonparametric test was used to confirm the results of the *t* tests. Categorical variables were compared with χ^2 tests. A multivariate linear regression analysis was performed for the primary outcome to account for the following confounders: age, biological sex, indication, and whether a patient was discharged with antibiotics. All effects were considered significant at $p < 0.05$.

RESULTS

Between October 15, 2020, and March 31, 2021, a total of 254 patients were assessed for eligibility; of these, 100 patients met the inclusion criteria (Figure 1). These patients were matched 1:1 with 100 historical control patients from the previous year. Baseline characteristics were balanced between the 2 groups (Table 1). No further data were collected for patients excluded from the study.

Primary Endpoints

The mean total intended duration of antibiotic therapy was 7.11 days in the control group and 5.31 days in the intervention group ($p < 0.001$) (Figure 2). The duration of inpatient antibiotic prescribing was 3.91 days and 4.45 days in the control and intervention groups, respectively ($p = 0.026$). The duration of outpatient antibiotic prescribing was 3.20 days in the control group and 0.86 days in the intervention group ($p < 0.001$). Multivariate analysis confirmed the results for the total duration of antibiotic therapy.

A total of 79 patients in the control group had antibiotics prescribed at discharge, compared with 32 patients in the intervention group ($p < 0.001$). Of patients discharged

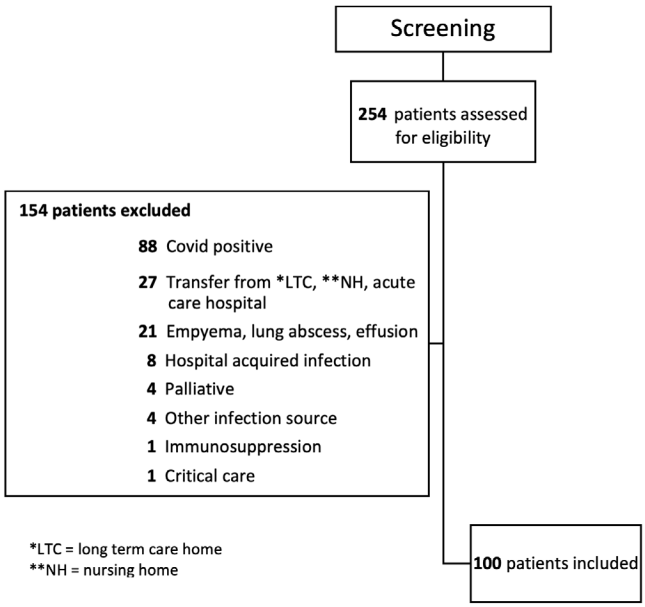

FIGURE 1. Study flow diagram.

with antibiotics, the discharge prescription extended the total duration of antibiotic therapy beyond 5 days for 86% (68/79) of patients in the control group and 31% (10/32) of patients in the intervention group.

Secondary Endpoints

The readmission rate at 30 days after discharge was 19% in both the control and intervention groups. Of readmissions by 30 days, 11 patients in the control group and 6 patients in the intervention group were readmitted because of a respiratory tract infection. The readmission rate at 90 days was 31% in both the control and intervention groups.

DISCUSSION

Among hospital inpatients receiving antibiotic therapy for the treatment of AECOPD or CAP, a pharmacist-initiated modification to duration of therapy significantly reduced total antibiotic prescribing. More specifically, the total duration of antibiotic therapy was reduced by 1.8 days in patients for whom the pharmacist modified the duration of therapy.

According to the workflow at WRH-OC, the infectious diseases pharmacist is responsible for assessing antibiotic therapy for all patients in non–critical care areas. Throughout the period of this study, the infectious diseases pharmacist was responsible for modifying the duration of antibiotic prescriptions for inpatients and outpatients. However, in the future, the goal is for all pharmacists to be capable of adjusting the duration of antibiotic therapy from 7 days to 5 days for patients for whom this change is appropriate.

The prescribed duration of inpatient antibiotic therapy was slightly greater in the intervention group relative to the controls, which may be attributed to longer lengths

TABLE 1. Baseline Characteristics of Study Participants

Characteristic	Study Group; No. (%) of Participants: Control (n = 100)	Intervention (n = 100)
Age (years) (mean ± SD)	72.6 ± 14.1	71.9 ± 14.8
Biological sex		
Male	51 (51)	51 (51)
Female	49 (49)	49 (49)
Diagnosis		
Acute exacerbation of COPD	34 (34)	33 (33)
Community-acquired pneumonia	66 (66)	67 (67)

COPD = chronic obstructive pulmonary disease, SD = standard deviation.

of stay for these patients; however, length of stay was not an endpoint in the current study. Multiple factors may have contributed to longer lengths of hospital stay in the intervention group. For example, the timing of this study coincided with the second wave of COVID-19 in Ontario, and many patients had to have a negative result on COVID-19 swab testing within 24 hours of repatriation to another health care facility. The need for this timely COVID-19 swab resulted in some patients remaining in hospital while awaiting test results, despite being medically stable for discharge. Additionally, during the COVID-19 pandemic, the widespread phenomenon of medical avoidance resulted in many patients either avoiding or delaying medical care.[10] During the study timeframe, fear of contracting COVID-19 in hospital may have resulted in only those patients with severe illness presenting to hospital; therefore, the increased length of stay may reflect increased severity of illness.

The most significant impact on antibiotic treatment duration occurred with discharge prescribing. Vaughn and

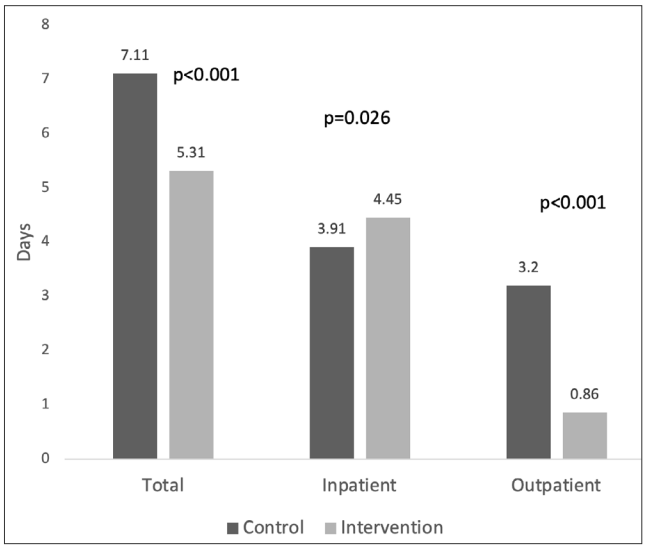

FIGURE 2. Mean duration of antibiotic use.

others[9] demonstrated that the majority of excess prescribing occurs on discharge, as the clock seems to be restarted at that point, with patients receiving prescriptions for full courses of therapy on discharge. To optimize "discharge stewardship", we included both the antibiotic start date and the intended duration of therapy on the electronic discharge prescription. Improved documentation at discharge resulted in reduced antibiotic prescribing, with only one-third of patients receiving a discharge prescription for antibiotics, a reduction of 2.34 days of outpatient prescribing relative to the control group. After adjustment for confounders, it was determined that patients discharged without a prescription were more likely to have a shorter total course of antibiotic therapy. The difference between the control and intervention groups, however, was still consistent with our initial results, indicating that the intervention group received fewer days of antibiotic therapy than the control group. In addition, consistent with previous studies, readmission rates were not affected by shorter courses of antibiotic therapy. Patient readmission rates were collected for patients readmitted to either campus of Windsor Regional Hospital or any acute care hospital in Ontario within 30 and 90 days of study enrolment. However, some readmissions might not have been captured, especially if a patient was readmitted to a hospital outside Windsor.

Prescriber education before initiation of this study likely contributed to stakeholder buy-in and successful reduction in the total duration of therapy. Significantly fewer patients in the intervention group were discharged on antibiotics. In contrast to what occurred for the control group, the minimal excess prescribing at discharge rarely extended the total duration of therapy beyond 5 days in the intervention group. Prescribers quickly adjusted to the change in duration of therapy, and, as time passed, the infectious diseeases pharmacist made fewer modifications to duration of therapy; more specifically, prescribers were almost 3 times more likely to prescribe a total antibiotic duration of 5 days without pharmacist modification in the intervention group, relative to the control group. Antimicrobial stewardship activities did not differ between the control and intervention periods, other than the implementation of this policy and the prescriber education related to this intervention. It is difficult to determine whether the reduction in antibiotic utilization was affected more by prescriber education or by policy implementation; however, it is likely that both factors contributed.

Our study had several limitations. First, not all patients with AECOPD or CAP were included in this study; rather, only patients admitted from Monday through Friday were included, because these were the days when the infectious diseases pharmacist was available to review patients' charts. Therefore, the duration of therapy might not have been modified for patients admitted on the weekend and discharged by Monday morning. Second, we did not track outpatient adherence with antibiotic therapy. Instead, we used the discharge prescription to track outpatient antibiotic prescribing. Our study measured antibiotic prescribing patterns of physicians and the impact that pharmacists can have on these prescribing patterns. Third, we did not control for the severity of illness in either group. This may have led to an imbalance between the groups, which might in turn have affected the total duration of antibiotics in a specific group or the length of the hospital stay. Despite not controlling for the severity of illness, a previous trial demonstrated that even patients with more severe infection did as well with short-course therapy.[5] Fourth, pharmacists did not confirm the diagnosis of AECOPD or CAP by either physical or radiographic findings in either the intervention or the control group. Rather, the diagnosis was based on documentation by the prescriber for patients in the study group and by diagnostic codes for patients in the control group.

Additionally, lower-than-normal patient volumes within the hospital due to the COVID-19 pandemic and the diagnostic uncertainty for patients presenting with symptoms of respiratory tract infection made it difficult to identify patients eligible for this study. Furthermore, as mentioned previously, COVID-19 may have contributed to longer lengths of hospital stay and greater severity of illness among patients in the intervention group.

CONCLUSION

In this study, pharmacist-initiated modifications adhering to guideline recommendations for AECOPD and CAP reduced the duration of inpatient and outpatient antibiotic prescriptions.

References

1. Frenette C, Sperlea D, German GJ, Afra K, Boswell J, Chang S, et al. The 2017 global point prevalence survey of antimicrobial consumption and resistance in Canadian hospitals. *Antimicrob Resist Infect Control*. 2020;9(1):104.
2. Pouwels KB, Hopkins S, Llewelyn MJ, Walker AS, McNulty CA, Robotham JV. Duration of antibiotic treatment for common infections in English primary care: cross sectional analysis and comparison with guidelines. *BMJ*. 2019;364:I440.
3. *Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: 2020 report*. Global Initiative for Chronic Obstructive Lung Disease; 2020 [cited 2020 Oct 15]. Available from: https://goldcopd.org/wp-content/uploads/2019/12/GOLD-2020-FINAL-ver1.2-03Dec19_WMV.pdf
4. Niederman MS, Mandell LA, Anzueto A, Bass JB, Broughton WA, Campbell GD, et al. Guidelines for the management of adults with community-acquired pneumonia. Diagnosis, assessment of severity, antimicrobial therapy, and prevention. *Am J Respir Crit Care Med*. 2001; 163(7):1730-54.
5. Uranga A, España P, Bilbao A, Quintana JM, Arriaga I, Intxausti M, et al. Duration of antibiotic treatment in community-acquired pneumonia. A multicenter randomized clinical trial. *JAMA Intern Med*. 2016; 176(9):1257-65.
6. Spellberg B. The new antibiotic mantra – "shorter is better" [editorial]. *JAMA Intern Med*. 2016;176(9):1254-5.
7. Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K,

et al. Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med*. 2019;200(7):e45-e67.
8. Tansarli GS, Mylonakis E. Systematic review and meta-analysis of the efficacy of short-course antibiotic treatments for community-acquired pneumonia in adults. *Antimicrob Agents Chemother*. 2018; 62(9):e00635-18.
9. Vaughn VM, Flanders SA, Snyder A, Conlon A, Rogers MAM, Malani AN, et al. Excess antibiotic treatment duration and adverse events in patients hospitalized with pneumonia: a multihospital cohort study. *Ann Intern Med*. 2019;171(3):153-63.
10. Czeisler MÉ, Marynak K, Clarke KE, Salah Z, Shakya I, Thierry JM, et al. Delay or avoidance of medical care because of COVID-19–related concerns — United States, June 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(36):1250-7.

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Competing interests: None declared.

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Funding: None received.

Acknowledgements: The authors would like to thank Dr Abdulkadir Hussein for statistical support.

ON THE FRONT COVER

Kananaskis Country, Alberta

This photograph was taken by Emily Cowley during a fall hiking trip with friends in Kananaskis Country in Alberta. In the small pond, you can see the reflection of Little Arethusa offering incredible views of the Arethusa Cirque filled with larches. Emily captured this image using her Samsung Galaxy S22.

Emily Cowley is a clinical pharmacist in the Cardiovascular Intensive Care Unit at the Mazankowski Alberta Heart Institute in Edmonton, Alberta. In her spare time, Emily enjoys hiking in the Rocky Mountains, travelling, and listening to Taylor Swift.

Pathways to Developing Clinical Pharmacist Practitioners: Is There a Better Way Forward? (Path-CPP)

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Can J Hosp Pharm. 2023;76(4):302-8 https://doi.org/10.4212/cjhp.3384

ABSTRACT

Background: Clinical Pharmacist Practitioners (CPPs) are independent care providers who practise to their full scope and have a positive impact on the quality of patient care. Ideally, all pharmacists in Canada would perform at this level. However, there is significant diversity in pharmacy practice across the country and among practice settings. It would be valuable to better understand how pharmacists attain CPP-level practice and what strategies might enable more pharmacists to practise at this level.

Objectives: To understand the perceptions of current CPPs and stakeholders in the health care system regarding the status of the CPP role in Canada and to propose pathways that would facilitate the attainment and recognition of CPP-level practice.

Methods: A qualitative study was conducted using semistructured interviews of peer-nominated CPPs and health care system stakeholders. Interviews were recorded, transcribed, and then analyzed using thematic analysis.

Results: Interviews involving 13 CPPs and 6 health care system stakeholders, conducted between March and July 2020, yielded 3 theme categories related to CPP roles, each containing subthemes, and 3 distinct themes relating to pathways forward. The 3 pathway themes were the following: that a legislative solution for expanded pharmacist scope is needed, that a new degree program is not required for pharmacy in Canada, and that a unified national credential signifying high-level practice might allow for better recognition of CPPs.

Conclusions: The full potential of pharmacists practising with advanced scope of practice in Canada has yet to be realized. Although significant external challenges exist, pharmacists must reframe the narrative by clearly articulating and defining their role within the Canadian health care system to increase CPP-level practice.

Keywords: clinical pharmacist practitioner (CPP), pathway, Canada, qualitative research, thematic analysis

RÉSUMÉ

Contexte : Les praticiens cliniciens sont des prestataires de soins indépendants qui exercent toutes leurs compétences et ont une incidence positive sur la qualité des soins aux patients. Idéalement, tous les pharmaciens au Canada devraient exercer à ce niveau. Cependant, la pratique de la pharmacie diffère grandement au pays et selon le milieu d'exercice. Il serait utile de mieux comprendre comment les pharmaciens atteignent le niveau de pratique de praticiens clinicien et quelles stratégies pourraient permettre à davantage d'entre eux d'exercer à ce niveau.

Objectifs : Comprendre les perceptions des praticiens cliniciens actuels et des parties prenantes du système de soins de santé concernant le statut du rôle des praticiens cliniciens au Canada et proposer des voies visant à faciliter la réalisation de la pratique au niveau de praticien clinicien et la reconnaissance de celle-ci.

Méthodes : Une étude qualitative a été menée à l'aide d'entretiens semi-structurés avec des praticiens cliniciens désignés par leurs pairs et des parties prenantes du système de soins de santé. Les entretiens ont été enregistrés, retranscrits, puis analysés à l'aide d'une analyse thématique.

Résultats : Des entretiens impliquant 13 praticiens cliniciens et 6 parties prenantes du système de soins de santé, menés entre mars et juillet 2020, ont permis de distinguer trois catégories thématiques liées aux rôles des praticiens cliniciens, chacune contenant des sous-thèmes, ainsi que trois thèmes distincts concernant les voies à suivre. Ces trois derniers thèmes étaient les suivants : la nécessité d'une solution législative pour l'élargissement du champ des compétences des pharmaciens; le fait qu'un nouveau programme diplômant ne soit pas requis pour la pharmacie au Canada; et l'idée qu'une accréditation nationale unifiée signifiant une pratique de haut niveau pourrait permettre de mieux reconnaître les praticiens cliniciens.

Conclusions : Le plein potentiel des pharmaciens exerçant avec une portée de pratique avancée au Canada reste encore à réaliser. Malgré l'existence de défis externes importants, les pharmaciens doivent reformuler le récit en articulant et en définissant clairement leur rôle au sein du système de soins de santé canadien afin d'accroître la pratique au niveau de praticien clinicien.

Mots-clés : praticien clinicien, voie, Canada, recherche qualitative, analyse thématique

INTRODUCTION

The profession of pharmacy in Canadian health care has evolved from traditional dispensing roles toward a focus on direct patient care requiring highly trained practitioners.[1-3] This transition has arisen because of a shifting health care landscape and demographic changes that have increased the health care needs of the population.[1,2] To meet these needs, regulatory bodies in multiple provinces have expanded pharmacists' scope of practice.[2] The pharmacy educational model has also changed to meet the demand for greater numbers of highly trained pharmacists. Faculties across Canada have transitioned from a Bachelor of Science in Pharmacy degree to entry-to-practice Doctor of Pharmacy programs. Numerous post–entry degree educational opportunities also exist. These changes have enabled pharmacists to take a greater role in the health care system, and pharmacists increasingly have the required skills to practise as independent direct patient care providers. Although a definition of this independent pharmacist practitioner role would be beneficial, one does not clearly exist in the Canadian literature.

For the purposes of the study reported here, we refer to this role as the Clinical Pharmacist Practitioner (CPP). A CPP is a pharmacotherapy expert who practises independently at their full scope, conducts thorough patient assessments, responds to consultations, monitors and adjusts drug therapy, provides education to patients and colleagues, and may prescribe independently or in collaboration with other health care professionals.[4,5]

Currently in Canada, there are many pharmacists in diverse settings whose practice meets this definition.[6] However, overall, they represent a small proportion of pharmacists, and most pharmacists continue to practise in traditional dispensing roles. Additionally, despite various training options, there is no single pathway to achieving the competencies of a CPP. Given substantial evidence of their impact, greater uptake of CPPs could provide significant benefits to patients and the health care system.[3,6]

There is a need to better understand how pharmacists develop into CPPs and the pathways that lead them there. In addition, to utilize CPPs to their maximum potential, a better understanding from health care system stakeholders of their perceptions of CPPs is essential. The objectives of this study were to describe the qualities, characteristics, and pathways that have contributed to pharmacists developing into CPPs and to determine what changes are needed to help more pharmacists achieve this expertise and fulfill these roles.

METHODS

A qualitative descriptive study was conducted using semi-structured key informant interviews. The consolidated criteria for reporting qualitative studies (COREQ) were consulted to ensure transparent reporting.[7]

Two groups of participants were included. The first group consisted of Canadian pharmacists who fit our definition of a CPP, who were nominated by members of the study team or by colleagues and invited to participate. To be eligible, these participants had to be registered Canadian pharmacists with at least 3 years of practice experience. The second group consisted of Canadian health care system stakeholders who provided external perspectives on the issues that CPP respondents articulated. These participants were recruited from relevant academic, regulatory, and practice domains. There were no exclusion criteria for this participant group. All participants were engaged through email communication.

Study recruitment consisted of purposive and snowball sampling.[8,9] The study team, which included pharmacy professionals meeting the definition of a CPP, nominated potential participants from their professional networks. In addition, 8 clinical pharmacy practice leaders from 6 Canadian provinces were engaged to nominate CPPs in their respective provinces. Finally, study participants were asked to suggest CPP colleagues for consideration.

The interview questions (Appendix 1 and Appendix 2, available from https://www.cjhp-online.ca/index.php/cjhp/issue/view/216) were informed by a literature review and were developed with input from study team members to elucidate the qualities and characteristics of CPPs and the steps that might be taken to normalize this level of practice.[9-13] A pilot interview was carried out with 1 CPP participant in March 2020, and questions were subsequently refined by 2 of the study investigators (R.P., M.L.).

Participant interviews lasted from 30 to 45 minutes and were carried out by telephone or virtually by video conferencing software between March and July 2020 by R.P. Participant recruitment and interviews were continued until the interview data produced little or no new information relevant to answering the research question ("informational redundancy"). Study ethics approval was obtained from the UBC-PHC Research Ethics Board.

Interview audio recordings were transcribed verbatim, and the text was organized using NVivo 12 Pro (version 12.6.0.959) by one investigator (R.P.). Thematic analysis of interview transcripts was conducted by 2 study investigators (R.P., a hospital pharmacy resident, and M.L., a hospital pharmacist with education and administrative roles), who performed independent coding in an iterative fashion as participants were recruited and interviewed.[14] Both of these investigators reflected on and articulated their internal biases before undertaking the analysis. They independently generated initial codes and collated these codes into potential themes. One of the investigators (R.P.) reviewed the transcripts in NVivo for coding, and the other (M.L.) reviewed the transcripts manually. These 2 investigators met multiple times throughout the process to discuss codes and themes generated, with ongoing refinement. During later meetings, they created thematic maps of the analysis to

ensure the themes fit in relation to the coded extracts. These codes and themes were further interrogated by discussion with the broader study team before finalization.

Member checking was then performed to ensure that the themes aligned with what participants meant during their interviews. Participants were contacted by email with a survey from Qualtrics XM survey software (version 11, 2020), which had a 1-month response deadline. A copy of the preliminary themes was provided with the survey.

RESULTS

Participant Characteristics

Forty-one CPPs and 13 health care system stakeholders were identified as potential participants. A total of 19 participants (13 CPPs and 6 health care system stakeholders) agreed to participate and provided informed consent. A summary of participant characteristics is presented in Table 1. Although participants were recruited from across the country, the majority were from British Columbia.

Thematic Analysis

From the CPP interviews, we identified 3 theme categories, each with its own associated themes related to perceptions of CPP roles. We also identified themes related to normalizing CPP roles, which we categorized as "pathways forward". The theme categories, associated themes, and representative quotes are presented in Tables 2 and 3 and are further described below.

TABLE 1. Participant Characteristics

Characteristic	No. of Participants
Clinical Pharmacist Practitioners	*n* = 13
Province	
British Columbia	9
Alberta	2
Manitoba	1
Quebec	1
Practice setting	
Hospital	8
Ambulatory	3
Community	2
Average practice experience (years)	20.2
Pharmacist stakeholders	*n* = 4
Province	
British Columbia	2
Ontario	2
Practice setting	
Academia	2
Regulatory	1
Clinical advocacy	1
Nonpharmacist stakeholders	*n* = 2
Profession	
Nurse practitioner[a]	2
Practice setting	
Hospital	1
Ambulatory	1

[a]Both of the nonpharmacist stakeholders were from British Columbia.

CPP Role

Hallmarks of a Clinical Pharmacist Practitioner

Current CPPs cited internal motivation, strong mentorship, and endorsement of diverse professional pathways as factors in their achievement of CPP practice. In particular, mentorship was cited as a critical factor that helped shape practice. One participant stated the importance of "Mentorship and having that relationship to discuss kind of what your career goals are and modeling your practice" (Participant 2). The importance of strong mentorship was echoed by nearly all CPPs.

Participants endorsed the desirability of having diverse professional pathways to becoming a CPP. When asked whether training needs to be streamlined into a single degree or pathway, one participant stated, "The training has already been established. …The necessary skills are already there I think for a lot of these advanced practitioners" (Participant 6). This quotation aligns strongly with responses received from the majority of the CPP group.

Dissatisfaction with the Status Quo for Pharmacy Practice

CPPs indicated their feeling that pharmacists are underutilized within the Canadian health care system and that the pharmacist's role is not well understood by nonpharmacists. Participants also reported some role uncertainty within the profession itself. This uncertainty was thought to stem from significant heterogeneity within the profession: "There is no singular vision as to what we are and what we do, which is a big reason why we struggle as individuals with our identity and as a profession with our identity" (Participant 11).

Nearly all participants felt it was unrealistic and unnecessary to expect CPP-level practice from all pharmacists. However, there was a sense that it would be valuable to have ways to engage pharmacists who aspire to this level of practice early in their career to help them achieve it. One participant stated, "I don't think everyone's motivated enough to want to do that [CPP]. I think more importantly we need to identify who would want to do it and ensure those people are getting to their career goals … to train them or find them mentorship so that they can reach that" (Participant 2).

Need for Pharmacists to Reframe Their Role and Better Advocate for Themselves within the Health Care System

CPPs felt that pharmacists across all practice settings need to move beyond fears of ambiguity and start to welcome clinician roles. One participant stated, "We have to ask ourselves as a profession, do we want to be a double check to

the system and therefore never push forward into sort of a provider role, even though we're potentially teaching the providers" (Participant 12).

Multiple participants indicated that the Canadian profession of pharmacy needs greater numbers of practising CPPs to promote the role and train future CPPs. One participant said, "The more we have individuals that practise at higher levels and that really integrate themselves as part of the team, the more that becomes the norm, then the more it will be recognized" (Participant 3).

A lack of unified leadership and advocacy within the Canadian pharmacy profession was consistently cited as a barrier to progress. One participant stated, "We are honestly our own worst enemy because we're doers and we're not promoters. We're not strong advocates of ourselves. … So, we need a stronger organization" (Participant 10).

Multiple participants cited pharmacy culture and professional identity as barriers to change, specifically noting role uncertainly both within and outside of the profession, the lack of acceptance of clinician roles, and the need for

TABLE 2. Themes Related to Clinical Pharmacist Practitioner (CPP) Role

Category	Associated Themes
Hallmarks of a clinical pharmacist practitioner	• Internal motivation • Strong mentorship • Support from colleagues and teams • Endorsement of diverse professional pathways to CPP • Current training programs are sufficient
Dissatisfaction with the status quo for pharmacy practice	• Regulators and health care decision-makers do not recognize the capabilities of CPPs • The pharmacist's role is not understood by patients and some health professionals • Not all pharmacists or people applying to pharmacy aspire to CPP-level practice • Pharmacists need to change their mentality/culture surrounding their role in patient care before they can convince others within the health care system of the need for an expanded role
Need for pharmacists to reframe their role and better advocate for themselves in the health care system	• The profession of pharmacy needs to embrace the role of patient care provider across all practice settings • A critical mass of CPPs providing high-quality patient care could change perceptions • Pharmacists and pharmacy leaders need to better promote, market, and advocate for CPP roles • To increase uptake, CPP needs to be a defined role, with a clear description of the skill set and what this practitioner brings to the table

TABLE 3. Thematic Analysis: Pathways Forward

Pathway to Normalizing CPP Roles	Illustrative Quotations
Legislative solution for expanded pharmacist scope is needed in all provinces (e.g., APA in Alberta)	• "I think we do need, I think every province in Canada could flip the switch on the legislative ability. They need to have a process of how they're going to give the authority to people, like you have to work through if they need an application process what have you, but we have one in Alberta, it's not like you'd have to start from scratch. Adopt the process and then people gotta get doing it" (Participant 1).
A new degree program (like programs for nurse practitioners) is *not* required for pharmacy in Canada	• "No, I think the model's already been established within the CSHP residency training model. General PGY1 residency program and then a specialized residency program with PGY2. That's a well-established model. And I don't think there's a need to recreate the wheel" (Participant 6).
A unified national credential that signifies high-level practice may allow for better recognition of CPPs	• "Nothing's formally in our credentialing, other than in the workplace that's been created by the health authorities, but nothing that's, you know BC based, even Canada based. That's really helpful in differentiating yourself from others, the States do have their board certification program which is somewhat helpful" (Participant 6). • "I think the only other thing I would say would be it would be nice if there was a national approach that could be done" (Participant 13). • "I think one of the challenges with this type of position is that there's no set standard for credentialing for somebody in this type of role so we don't have sort of a specialist type of recognition, whether it be from the regulatory college perspective or even within hospitals to sort of have a standardized expectation of what the role would look like across the country" (Participant 17). • "Even if we provide these credentials, if other people don't recognize what those roles are. Then that, it's just an extra few letters at the end of your name that may or may not mean anything different" (Participant 2).

APA = additional prescribing authorization, BC = British Columbia, CPP = Clinical Pharmacist Practitioner, CSHP = Canadian Society of Hospital Pharmacists, PGY1 and PGY2 = postgraduate year 1 and 2.

increased leadership and advocacy highlighted within the previous 2 theme categories.

Participants identified a need to move past the aforementioned role uncertainty and to define pharmacists' niche within the health care system: "And what becomes clear is that we as a group of pharmacists maybe haven't really defined what that is [our role]. And so, other practitioners don't ultimately know what you're going to do" (Participant 1). The CPP group frequently identified chronic disease management as being an important role for pharmacists.

Pathways Forward

Study participants highlighted a number of potential solutions to normalizing CPP roles (Table 3).

Legislative Solution for Expanded Pharmacist Scope Is Needed in All Provinces

A legislative solution that allows for prescribing, as well as ordering and monitoring laboratory tests, is imperative if pharmacists are to become independent practitioners within the Canadian health care system. To achieve this goal nationally, there are several barriers to overcome, including significant heterogeneity within the profession and the lack of a unified vision, as noted by participants.

Participants practising in provinces where a legislative solution has already been implemented (e.g., Alberta, Manitoba) noted that prescribing authority helps them to provide patient care and increases efficiency in practice. It also gives those who possess the skills a pathway to put their skill set to optimal use.

A New Degree Program Is NOT Required for Pharmacy in Canada

Most participants felt that the pharmacy profession does not need to redesign the Canadian pharmacy education system. It was felt that the entry-level PharmD degree, along with available residency programs, provides sufficient training for CPP-level practice. It was noted that more post–entry-to-practice training seats are needed, especially for advanced residency programs, given that the majority of postbaccalaureate PharmD degrees are no longer available in Canada.

A Unified National Credential that Signifies High-Level Practice May Allow for Better Recognition of CPPs

Although not all participants agreed, many of them felt that a unified national credential signifying high-level practice could be valuable. However, it was clear that such a credential would need to be rolled out thoughtfully by engaging key stakeholders and ensuring that the credential is meaningful. Participants did not feel the pharmacy profession lacks the skills or training for CPP roles. Instead, it was proposed that a credentialing system could demarcate a level of practice that is already in existence (i.e., CPPs) and allow that to be recognized by others within the Canadian health care system. By identifying this role, validating it with a credential, and then speaking the same language about it nationally, the pharmacy profession could progress.

Perspectives of Health Care System Stakeholders

Pharmacists

There were too few participants in the pharmacist health care system stakeholder group to formally identify themes specific to this group. However, their perspectives aligned closely with the feedback provided by the CPPs relating to role uncertainty, pharmacy culture, heterogeneity of pharmacy practice, and a lack of strong leadership and advocacy. One participant stated, "There's a whole series of perceptions from the other health care providers about what the role of the pharmacist is, so a barrier is sometimes simply role uncertainty" (Participant 19). Another participant echoed this sentiment, saying "I think the first problem is pharmacists themselves. I don't think we have internalized clinician ways of being as our actual identity" (Participant 18). Regarding leadership and advocacy, another participant stated, "Just having a unified voice and mission for what it is we want our profession to do in our health care system is something that I think is gravely lacking in our country" (Participant 19).

Pharmacist health care system stakeholders agreed that an advanced credential could be useful, but noted that pharmacists would need to be purposeful about how it is rolled out. A participant cautioned, "We just need to be careful of things like credential creep and degree creep and adding new titles and new training … we already have huge numbers of pharmacists across the world saying they're over trained to dispense meds" (Participant 18). Pharmacist health care system stakeholders agreed that chronic disease management could be an important role for CPPs.

Nonpharmacists

The study's 2 external stakeholders (nurse practitioners) expressed uncertainty about pharmacists' physical assessment skills and confusion about their training and degree designations. These stakeholders specifically mentioned the term "PharmD", which to them had previously denoted a pharmacist with advanced training but is now the entry-to-practice degree.

Member Checking

Nine (47%) of the 19 study participants provided responses to the member-checking survey. Options regarding agreement with individual themes were yes, no, or "other", with the possibility of providing free-text comments. Agreement with the various themes identified in the study ranged from 78% to 89%, indicating that most respondents agreed with the themes identified.

DISCUSSION

This study was designed to gain a better understanding of what is required to enable more pharmacists to practise at

the highest level of scope and independence in Canada. We described individuals who practise at this level as "Clinical Pharmacist Practitioners" or CPPs. We explored the perspectives of current CPPs and captured insights from a limited number of health care system stakeholders.

Key findings were that current CPPs felt it was unrealistic to expect CPP-level practice from all pharmacists. There was also clear agreement that novel training programs are not needed to develop more CPPs. When participants were asked about barriers to pharmacists attaining CPP-level practice, there was a strong sense that external barriers, such as inconsistent legislation to support pharmacist prescribing across provinces, need to be addressed. However, many barriers internal to the profession also exist. These include pharmacy culture, role uncertainty, and lack of strong advocacy, which align closely with issues that have been previously noted in the literature.[15,16]

Although barriers do exist, many pharmacists still manage to practise at the CPP level. The addition of clinical pharmacy services to patient care has been shown to result in better patient outcomes, including improved quality of medication use and reduced rates of hospital readmissions.[3,17] Tsuyuki and colleagues have shown in multiple studies that pharmacists have a large impact in health care outcomes and costs when managing conditions such as hypertension, heart failure, dyslipidemia, diabetes, and urinary tract infections.[18] In the United States, the implementation of CPPs into primary care settings has shown that they are able to provide services comparable in efficacy to those of primary care providers for chronic disease management.[4] This literature provides further validity to themes among participants in the current study indicating that many pharmacists already have the necessary skills for CPP-level practice.

In the consideration of possible pathways forward, one solution proposed by the CPPs participating in this study was the development of a unified national credential, which would signify high-level practice. Such a credential would be less focused on certification in a particular specialty and more on the level of practice demonstrated by the individual. This seems like a logical approach, especially if we accept the CPPs' assertion that the goal would not be to achieve this level of practice for all pharmacists. Similarly, given that current CPPs did not endorse a single preferred training pathway and because no current single-degree designation confers "pharmacist practitioner" status, there needs to be an alternate way to highlight these individuals. A certification could provide much needed clarity both within the profession and to external stakeholders who struggle to understand pharmacists' capabilities.

Several pharmacy organizations outside of Canada have attempted to address challenges associated with heterogeneity in pharmacy practice. The United Kingdom and Australia have developed frameworks for advanced pharmacy practice, which include key competency clusters on which pharmacists are ranked.[19-21] Another approach, used in the United States, involves credentialing systems, such as certification through the Board of Pharmaceutical Specialties (BPS).[22] Some study participants pointed to this as a rigorous model in delineating advanced practice. Although Canada does not have a comparable pharmacy specialty credentialing system or separate designation, a survey of Canadian hospital pharmacists in 2015 showed support for the implementation of an analogous system.[23,24] If Canada were to pursue a similar credentialing system, those developed elsewhere could serve as a guide.

Although respondents did not express the need for a new degree program, the uptake of nurse practitioners in Canada offers learning that could be utilized in CPP expansion. For example, CPPs practising under expanded scopes of practice could potentially perform roles analogous to those performed by nurse practitioners to reduce health care costs and increase health care access.[25]

This study had multiple limitations. Most participants were from British Columbia and were practising in the hospital setting; as such, the study findings may not reflect the views of pharmacists practising elsewhere and in different practice settings. The peer nomination process may have introduced selection bias, through potential inclusion of participants supportive of the CPP role. Subjective thematic analysis of qualitative data could have introduced the internal biases of investigators. The authors reflected upon these internal biases to minimize their impact on data analysis; in addition, participant triangulation was incorporated through alignment of CPP themes and health care system stakeholder perspectives, and investigator triangulation with thematic analysis conducted by multiple team members was used to increase the validity of findings. Lastly, we were able to engage only a small number of nonpharmacist stakeholders. Going forward, physicians and patients will need to be engaged to determine the role of CPPs in the Canadian health care system and to determine whether there is a societal need for this role.

Despite these limitations, this study adds unique perspectives of primarily Canadian hospital-based CPPs and selected health care system stakeholders on barriers and facilitators of advanced pharmacy practice, as well as pathways forward in normalizing CPP roles. Future studies could further elucidate what optimal credentialing could look like for Canadian pharmacists in CPP roles.

CONCLUSION

The full potential of pharmacists practising with advanced scope of practice in Canada has yet to be realized. The heterogeneous image that the pharmacy profession projects, pharmacy culture, and role uncertainty within the profession and in how pharmacists are perceived remain

as substantial issues within pharmacy practice in Canada. Pathways for increasing CPP-level practice are attainable; however, pharmacists first need to clearly define their role within the Canadian health care system, and a legislative solution is required for expanded pharmacist scope in all provinces.

References

1. Guérin A, Bussières JF. Anticipated changes in pharmacy practice by 2025: a survey of hospital pharmacy residents. *Can J Hosp Pharm*. 2016; 69(5):388-93.
2. Bhatia S, Simpson SH, Bungard T. Provincial comparison of pharmacist prescribing in Canada using Alberta's model as the reference point. *Can J Hosp Pharm*. 2017;70(5):349-57.
3. Kaboli PJ, Hoth AB, McClimon BJ, Schnipper JL. Clinical pharmacists and inpatient medical care: a systematic review. *Arch Intern Med*. 2006;166(9):955-64.
4. Kislan MM, Bernstein AT, Fearrington LR, Ives TJ. Advanced Practice Pharmacists: a retrospective evaluation of the efficacy and cost of ClinicaL Pharmacist PractitionErs managing ambulatory Medicare patients in North Carolina (APPLE-NC). *BMC Health Serv Res.* 2016;16:607.
5. Scott MA, Heck JE, Wilson CG. The integral role of the clinical pharmacist practitioner in primary care. *N C Med J*. 2017;78(3):181-5.
6. Shalansky S. The Advanced Pharmacist Practitioner: a new series in the *Canadian Journal of Hospital Pharmacy*. *Can J Hosp Pharm*. 2019; 72(1):42-8.
7. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *Int J Qual Health Care*. 2007;19(6):349-57.
8. Anderson C. Presenting and evaluating qualitative research. *Am J Pharm Educ*. 2010;74(8):141.
9. Donald M, King-Shier K, Tsuyuki RT, Al Hamarneh YN, Jones CA, Manns B, et al. Patient, family physician and community pharmacist perspectives on expanded pharmacy scope of practice: a qualitative study. *CMAJ Open*. 2017;5(1):E205-E212.
10. Guirguis LM, Makowsky MJ, Hughes CA, Sadowski CA, Schindel TJ, Yuksel N. How have pharmacists in different practice settings integrated prescribing privileges into practice in Alberta? A qualitative exploration. *J Clin Pharm Ther*. 2014;39(4):390-8.
11. Hughes CA, Makowsky M, Sadowski CA, Schindel TJ, Yuksel N, Guirguis LM. What prescribing means to pharmacists: a qualitative exploration of practising pharmacists in Alberta. *Int J Pharm Pract*. 2014;22(4):283-91.
12. Wheeler A, Crump K, Lee M, Li L, Patel A, Yang R, et al. Collaborative prescribing: a qualitative exploration of a role for pharmacists in mental health. *Res Soc Admin Pharm*. 2012;8(3):179-92.
13. Wright DJ, Adams RJ, Blacklock J, Corlett SA, Harmston R, McWilliams M, et al. Longitudinal qualitative evaluation of pharmacist integration into the urgent care setting. *Integr Pharm Res Pract*. 2018;7:93-104.
14. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol*. 2006;3(2):77-101.
15. Rosenthal M, Austin Z, Tsuyuki RT. Are pharmacists the ultimate barrier to pharmacy practice change? *Can Pharm J*. 2010;143(1):37-42.
16. Frankel GEC, Austin Z. Responsibility and confidence: identifying barriers to advanced pharmacy practice. *Can Pharm J*. 2013;146(3):155-61.
17. Makowsky MJ, Koshman SL, Midodzi WK, Tsuyuki RT. Capturing outcomes of clinical activities performed by a rounding pharmacist practicing in a team environment: the COLLABORATE study. *Med Care*. 2009;47(6):642-50.
18. Tsuyuki RT. FAQs (frequent asinine questions) on pharmacists' scope of practice. *Can Pharm J*. 2018;151(4):212-3.
19. Galbraith K, Coombes I, Matthews A, Rowett D, Bader LR, Bates I. Advanced pharmacy practice: aligning national action with global targets. *J Pharm Pract Res*. 2017;47(2):131-5.
20. Jackson S, Martin G, Bergin J, Clark B, Stupans I, Yeates G, et al. An advanced pharmacy practice framework for Australia. *Pharmacy (Basel)*. 2015;3(2):13-26.
21. Udoh A, Bruno A, Bates I, Galbraith K. Transnational comparability of advanced pharmacy practice developmental frameworks: a country-level crossover mapping study. *Int J Pharm Pract*. 2018;26(6):550-9.
22. Bruno A, editor. A*dvanced practice and specialisation in pharmacy: global report*. International Pharmaceutical Federation; 2015 [cited 2019 Nov 6]. 78 pp. Available from: https://www.fip.org/files/fip/PharmacyEducation/Adv_and_Spec_Survey/FIPEd_Advanced_2015_web_v2.pdf
23. Penm J, MacKinnon NJ, Jorgenson D, Ying J, Smith J. Need for formal specialization in pharmacy in Canada: a survey of hospital pharmacists. *Can J Hosp Pharm*. 2016;69(5):356-66.
24. *Needs assessment of specialization in pharmacy in Canada*. Canadian Pharmacists Association; 2015 Jul [cited 2019 Oct 26]. Available from: https://www.pharmacists.ca/cpha-ca/assets/File/pharmacy-in-canada/blueprint/Needs%20Assessment%20of%20Specialization%20in%20Pharmacy%20in%20Canada%20-%20Final%20Report.pdf
25. Gould ON, Johnstone D, Wasylkiw L. Nurse practitioners in Canada: beginnings, benefits, and barriers. *J Am Acad Nurse Pract*. 2007; 19(4):165-71.

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Competing interests: For activities unrelated to the study described here, Kerry Wilbur has received a CSHP research grant and consulting fees from the University of Waterloo. No other competing interests were declared.

Disclaimer: Stephen Shalansky is the Editor of the *Canadian Journal of Hospital Pharmacy*. He did not participate in the editorial decision-making for this article.

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Funding: None received.

Treatments and Outcomes of Critically Ill Patients with *Candida* spp. Colonization of the Lower Respiratory Tract in Regina, Saskatchewan

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Can J Hosp Pharm. 2023;76(4):309-13 https://doi.org/10.4212/cjhp.3408

ABSTRACT

Background: Among critically ill patients receiving mechanical ventilation, *Candida* spp. are commonly detected in the lower respiratory tract (LRT). This is generally considered to represent colonization.

Objective: To evaluate the use of antifungal treatments and the clinical outcomes of patients with *Candida* colonization of the LRT.

Methods: This retrospective analysis involved consecutive patients admitted to the intensive care unit between April 2016 and May 2021with positive results on *Candida* spp. testing of LRT samples. Data related to antifungal treatment and clinical outcomes were analyzed descriptively, and multivariable logistic regression was performed.

Results: Of 200 patients initially identified, 160 (80%) died in hospital. Antifungal therapy was given to 103 (51.5%) of the patients, with treatment being more likely among those with shock and those who received parenteral nutrition. Mortality was high among patients with positive *Candida* results on LRT culture, regardless of treatment. Multivariable logistic regression, with adjustment for age, sex, comorbidities, and sequential organ failure assessment (SOFA) score, showed that antifungal treatment was associated with lower odds of death (odds ratio 0.39, 95% confidence interval 0.17–0.87) compared with no treatment ($p = 0.021$).

Conclusions: This study showed higher mortality rates than have been reported previously. Further investigation into the role of antifungal therapy among critically ill patients with *Candida* spp. colonization is required.

Keywords: *Candida*, critical care, antifungal

RÉSUMÉ

Contexte : Chez les patients gravement malades recevant une ventilation mécanique, les *Candida* spp. sont fréquemment détectées dans les voies respiratoires inférieures (VRI) – une situation généralement considérée comme une colonisation.

Objectif : Évaluer l'utilisation d'un traitement antifongique et les résultats cliniques chez les patients présentant une colonisation par *Candida* dans les VRI.

Méthodes : Cette analyse rétrospective portait sur des patients consécutifs de l'unité de soins intensifs ayant obtenu un résultat positif au test de *Candida* sur les isolats des VRI entre avril 2016 et mai 2021. Les données relatives au traitement antifongique et aux résultats cliniques ont été analysées de manière descriptive, et une régression logistique multivariable a été effectuée.

Résultats : Parmi les 200 patients initialement recensés, 160 (80 %) sont décédés à l'hôpital. Une thérapie antifongique a été administrée à 103 (51,5 %) des patients, et le traitement était plus probable chez ceux en état de choc et ceux ayant reçu une nutrition parentérale. Les patients ayant été déclarés positifs pour la *Candida* dans la culture des VRI présentaient un taux de mortalité élevé, indépendamment du traitement. Une régression logistique multivariable, avec ajustement pour l'âge, le sexe, les comorbidités et le score SOFA (*sequential organ failure assessment*), a montré que le traitement antifongique était associé à une probabilité de décès réduite (rapport de cotes 0,39; intervalle de confiance à 95 % 0,17-0,87), par rapport à l'absence de traitement ($p = 0,021$).

Conclusions : Cette étude a révélé des taux de mortalité plus élevés que ce qui avait été rapporté précédemment. Une enquête plus approfondie sur le rôle de la thérapie antifongique chez les patients gravement malades présentant une colonisation par *Candida* spp. est nécessaire.

Mots-clés : *Candida*, soins intensifs, traitement antifongique

INTRODUCTION

Critically ill patients in the intensive care unit (ICU) who are receiving mechanical ventilation are at increased risk of nosocomial infections, such as ventilator-associated pneumonia, which in turn increases their risk of morbidity and mortality.[1] Although *Candida* spp. are commonly detected in the lower respiratory tract (LRT), they are generally considered colonizers rather than a pathogenic cause of infection; therefore, empiric antifungal treatment is not recommended.[2-4] It is estimated that *Candida* spp. colonization of the respiratory tract may be present in more than half of critically ill patients undergoing mechanical ventilation.[5] In a Canadian study of ICU patients with suspected ventilator-associated pneumonia, those with *Candida* spp. in LRT samples had higher in-hospital mortality than those

without yeast (34.2% versus 21%) and almost double the hospital length of stay (59.9 versus 38.6 days).[6] A European study evaluating ICU patients with *Candida* spp. pulmonary colonization reported in-hospital mortality of 40%: 52% for those who received antifungal therapy and 35% for those who did not.[7]

The objectives of our study were to examine the use of antifungals in ICU patients with LRT samples testing positive for *Candida* spp. and to investigate their clinical outcomes.

METHODS

We performed a retrospective analysis for a cohort of all adult patients (at least 18 years of age) admitted consecutively, between April 2016 and May 2021, to a medical or surgical ICU in Regina, Saskatchewan, with *Candida* spp. identified in LRT samples (i.e., sputum, endotracheal tube aspirate, bronchoalveolar lavage, or mini–bronchoalveolar lavage, as labelled in the laboratory database). We collected demographic data, risk factors for invasive infection,[8] and antifungal treatment choice. Continuous variables are presented as means or medians, dependent on normality, as assessed by skewness and kurtosis. We compared patients with and without treatment for *Candida* spp. using the *t* test or Wilcoxon rank-sum test, dependent on normality. Categorical variables are presented as counts (with percentages), with comparisons using the χ^2 test.

We conducted a propensity score matching analysis for in-hospital mortality using matched cohorts, with 1:1 nearest-neighbour matching for age, sex, Charlson comorbidity index, sequential organ failure assessment (SOFA) score, and the *Candida* score (defined as multifocal *Candida* spp. colonization, use of parenteral nutrition, surgery on ICU admission, and severe sepsis)[9,10] using a caliper of 0.2, the standard deviation of the logit of the propensity score.

All statistical analyses were performed using Stata 15.1/MP (StataCorp), with a 2-sided p value less than 0.05 considered statistically significant.

RESULTS

A total of 200 patients admitted to the ICU between April 2016 and May 2021 met the study's inclusion criteria. The median age was 64 (interquartile range [IQR] 55–74) years, and 100 (50%) of the patients were female (Table 1). The mean SOFA score on admission to the ICU was 10 (standard deviation 3), and the median duration of intubation was 21.5 (IQR 5–37) days. Median length of stay in the ICU was 12 (IQR 4–14) days, and median hospital stay was 24 (IQR 8–29) days. Nearly 94% of patients (n = 187) received antibiotic therapy before a positive result on fungal LRT culture, whereas only 51.5% (n = 103) received antifungal treatment. Patients were more likely to be given antifungal therapy if they had experienced shock or received parenteral nutrition.

In total, 160 (80%) of the patients died in hospital (Table 1). Univariable logistic regression comparing antifungal-treated patients with untreated patients yielded an odds ratio (OR) for death of 0.44 (95% confidence interval [CI] 0.21–0.90) (Table 2). In the multivariable logistic

TABLE 1 (Part 1 of 2). Patient Demographic Characteristics and Outcomes

Characteristic	Patient Group; No. (%) of Patients[a]	
	Treated with Antifungal (n = 103)	Untreated (n = 97)
Age (years) (median and IQR)	63 (53–72)	65 (56–74)
Sex, female	50 (48.5)	50 (51.5)
Diagnosis on admission to ICU		
Respiratory failure	32 (31.1)	31 (33.0)
Sepsis	26 (25.2)	18 (18.6)
Postsurgery	8 (7.8)	4 (4.1)
Neurology	7 (6.8)	3 (3.1)
Post-arrest	3 (2.9)	6 (6.2)
Cancer complications	1 (1.0)	6 (6.2)
Other	26 (25.2)	28 (28.9)
Charlson comorbidity index (median and IQR)	1 (1–2)	1 (1–3)
COVID-19 infection	14 (13.6)	16 (16.5)
SOFA score (mean ± SD)	10 ± 4	10 ± 3
Candida score (mean ± SD)	2.2 ± 1.4	1.2 ± 1.2
CPIS on day of first fungal culture (mean ± SD)	4 ± 2	4 ± 2

TABLE 1 (Part 2 of 2). Patient Demographic Characteristics and Outcomes

Characteristic	Patient Group; No. (%) of Patients[a]	
	Treated with Antifungal (*n* = 103)	Untreated (*n* = 97)
Resource intensity weight (mean ± SD)	11 ± 7.4	6.2 ± 5.8
Risk factors for invasive candidiasis		
Systemic antibiotic	98 (95.1)	89 (91.8)
Septic shock	74 (71.8)	46 (47.4)
Parenteral nutrition	20 (19.4)	2 (2.1)
Surgery	14 (13.6)	7 (7.2)
Immunosuppression	10 (9.7)	7 (7.2)
Central venous catheter	3 (2.9)	1 (1.0)
Yeast identified		
Yeast not specified[b]	60 (58.2)	70 (72.1)
Candida albicans	27 (26.2)	23 (23.7)
Candida glabrata	6 (5.8)	1 (1.0)
Candida tropicalis	8 (7.8)	2 (2.1)
Candida krusei	1 (1.0)	1 (1.0)
Other *Candida* spp.	6 (5.8)	1 (1.0)
Aspergillus spp.	1 (1.0)	1 (1.0)
Primary location of respiratory yeast as identified in laboratory labelling		
Sputum	26 (25.2)	24 (24.7)
Endotracheal tube aspirate	47 (45.6)	50 (51.5)
Bronchoalveolar lavage	23 (22.3)	10 (10.3)
Mini–bronchoalveolar lavage	7 (6.8)	13 (13.4)
Yeast identified at second site	43 (41.7)	11 (11.3)
Urine	29	10
Blood	2	1
Ascites	2	0
Skin or soft-tissue swab	6	0
Line[c]	2	0
Other[d]	2	0
Lung imaging on day before or after the day of sampling with positive result on LRT culture[e]		
No infiltrate	29 (28.2)	32 (33.0)
Diffuse or patchy infiltrate	68 (66.0)	58 (60.0)
Distinct infiltrates	6 (5.8)	7 (7.2)
Antifungal, terminal therapy		
Fluconazole	61 (59.2)	NA
Caspofungin/micafungin	40 (38.8)	NA
Amphotericin B	1 (1.0)	NA
Voriconazole	1 (1.0)	NA
In-hospital death	76 (73.8)	84 (86.6)
Hospital length of stay (days) (median and IQR)	22 (12–40)	10 (4–14)
ICU length of stay (days) (median and IQR)	12 (6–20)	5 (3–10)

CPIS = clinical pulmonary infection score, ICU = intensive care unit, IQR = interquartile range, LRT = lower respiratory tract, NA = not applicable, SD = standard deviation, SOFA = sequential organ failure assessment.

[a]Except where indicated otherwise.

[b]In 2018, the institution's Medical Microbiology department stopped differentiating yeast identified on respiratory culture unless the treating physician makes a specific request.

[c]Femoral central line (*n* = 1) and hemodialysis line (*n* = 1) after the line was removed.

[d]Hernia mesh following removal (*n* = 1) and hepatic drain (*n* = 1).

[e]Computed tomography was used if available; otherwise, chest radiography was used.

TABLE 2. Effect of Antifungal Therapy on In-Hospital Mortality among ICU Patients with Yeast Identified In Lower Respiratory Tract Samples

Analysis	Odds Ratio (95% CI)	*p* Value
Univariable analysis	0.44 (0.21–0.90)	0.026
Multivariable logistic regression[a]	0.39 (0.17–0.87)	0.021
Propensity score–matched logistic regression (n = 61 each group)	0.41 (0.17–1.01)	0.053
Sensitivity analyses		
Effect of fluconazole	0.31 (0.13–0.77)	0.011
Effect of caspofungin/micafungin	0.59 (0.21–1.70)	0.33
Multivariable logistic regression[a] after excluding all patients with secondary sites except urine and wound swab source (n = 191)	0.39 (0.17–0.87)	0.024

CI = confidence interval, ICU = intensive care unit, SOFA = sequential organ failure assessment.
[a]With adjustment for age, sex, comorbidities, and SOFA score.

regression, after adjustment for age, sex, Charlson comorbidity index, and SOFA score, antifungal treatment was associated with OR for death of 0.39 (95% CI 0.17–0.87). In sensitivity analyses, fluconazole was associated with reduced odds of death (OR 0.31, 95% CI 0.13–0.77), whereas the results with caspofungin/micafungin were nonsignificant (OR 0.59, 95% CI 0.21–1.70). In a further sensitivity analysis with exclusion of patients who had secondary sites (excluding urine and wound swabs) that were positive for *Candida* spp. at any time in their ICU admission, the results were similar to our primary analysis. Antifungal treatment was associated with lower odds for death after multivariable logistic regression (OR 0.39, 95% CI 0.17–0.87). However, this difference was not evident after propensity score matching (OR 0.41, 95% CI 0.17–1.01).

DISCUSSION

Current guidelines recommend against exposing patients to antifungal therapy when *Candida* spp. are identified on LRT culture, as therapy may not confer benefit in this situation.[3] However, there is a lack of high-quality studies evaluating antifungal therapy in such cases. There is also evidence suggesting that *Candida* spp. isolated through high-quality sampling, such as bronchoalveolar lavage, may represent contamination and thus antifungal therapy is not required.[11] In our study, we found that a high proportion of patients with *Candida* spp. isolated from the LRT were treated with antifungal therapy, despite these recommendations. Treated patients were more likely to have presented with sepsis, to have had surgery, to have received parenteral nutrition, and/or to have a higher *Candida* score. It is possible that the clinicians at our centre perceived a higher risk for these patients and chose to initiate antifungal therapy, despite the recommendations noted above. However, only a small proportion of these patients (n = 15) had a *Candida* score above 3, which indicates that most patients did not have a higher risk of invasive infection.[10]

Notably, we found a potential association between antifungal treatment and reduced mortality; however, we cannot rule out the possibility that residual confounding, time-varying exposures, and selection bias influenced the results. Our findings are discordant with previous work suggesting that exposure to antifungal treatment does not offer additional benefit to patients.[7,12] Interestingly, there were differences between patients who received azole and those who received echinocandin antifungal treatment. However, our work was exploratory in nature and suggests the need for high-quality studies to evaluate the role of antifungal therapy in relation to *Candida* spp. colonization.

With a lack of high-quality studies to guide decision-making, clinicians are left to decide on antifungal treatment for *Candida* spp. colonization on a case-by-case basis. No drug is benign, and any exposure to therapy may lead to an adverse event. Although clinicians may definitively initiate antifungal therapy in the setting of candidemia or a histopathologic diagnosis of multifocal *Candida* spp. infection, there are also several common situations in which a clinician may choose to treat (e.g., if the patient is immunocompromised, if the patient has a high *Candida* score or colonization of multiple sites, or if a line cannot be readily removed). There are also some very limited data pointing toward a potential additive cross-kingdom interaction between *Candida* spp. and bacterial respiratory infection, whereby treatment may confer benefit.[13]

Our study had some important limitations. Because of the retrospective nature of the study and its small sample size, we were unable to completely control for residual confounding, time-varying covariates, and/or selection bias, despite multivariable modelling and propensity score matching. Of note, this cohort of patients had a higher-than-expected mortality rate (80%), which is greater than our centre's overall reported ICU mortality rate (about 20%) and mortality rates previously described in the literature on *Candida* spp. colonization.[6,14] Given that ICU patients accrue *Candida* spp. colonization over time or after exposure

to broad-spectrum antibiotics, this cohort's high mortality rate may reflect underlying population selection bias and/or severity of illness.[15-17] Time-varying exposures and immortal time bias may also play a role, as patients who have survived longer may be more likely to be exposed to antifungal therapy. An additional limitation is that several types of respiratory samples are labelled as "sputum" in our institution's laboratory's database, regardless of how the sample was collected. Despite this labelling, 97% of samples were collected while patients were intubated. A sensitivity analysis that removed the 3% of patients who were not intubated did not yield a significant change in the statistical findings. Additionally, many of the fungal respiratory isolates were labelled as "yeast (not specified)" because of changes in the laboratory's procedures. Previous work showed decreases in exposure to antifungal therapy by half when fungal respiratory cultures were labelled in this way[18]; however, when this change was made at our centre halfway through our data collection period, there was a decrease of only 6%. Our dataset tracked diagnosis of bacterial infections but did not track the pathogens isolated; thus, we were unable to assess specific bacterial contributions to our results. Our centre is unable to test for β-D-glucan levels without sending samples to a third-party laboratory, which delays assessment. Consequently, this test is not ordered routinely at our institution. Finally, no patients in our study had histopathologic sampling to confirm the presence of true fungal infection.

CONCLUSION

The findings of this study suggest the need for further high-quality investigation into the utility of antifungal therapy for critically ill patients with *Candida* spp. isolates in the LRT.

References

1. Muscedere JG, Martin CM, Heyland DK. The impact of ventilator-associated pneumonia on the Canadian health care system. *J Crit Care*. 2008;23(1):5-10.
2. Bow EJ, Evans G, Fuller J, Laverdière M, Rotstein C, Rennie R, et al. Canadian clinical practice guidelines for invasive candidiasis in adults. *Can J Infect Dis Med Microbiol*. 2010;21(4):e122-e150.
3. Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, et al. Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2016;62(4):e1-e50.
4. Martin-Loeches I, Antonelli M, Cuenca-Estrella M, Dimopoulos G, Einav S, De Waele JJ, et al. ESICM/ESCMID task force on practical management of invasive candidiasis in critically ill patients. *Intensive Care Med*. 2019;45(6):789-805.
5. Pendleton KM, Huffnagle GB, Dickson RP. The significance of *Candida* in the human respiratory tract: our evolving understanding. *Pathog Dis*. 2017;75(3):ftx029.
6. Delisle MS, Williamson DR, Perreault MM, Albert M, Jiang X, Heyland DK. The clinical significance of *Candida* colonization of respiratory tract secretions in critically ill patients. *J Crit Care*. 2008;23(1):11-7.
7. Lindau S, Nadermann M, Ackermann H, Bingold TM, Stephan C, Kempf VA, et al. Antifungal therapy in patients with pulmonary *Candida* spp. colonization may have no beneficial effects. *J Intensive Care*. 2015;3(1):31.
8. Thomas-Rüddel DO, Schlattmann P, Pletz M, Kurzai O, Bloos F. Risk factors for invasive *Candida* infection in critically ill patients, a systematic review and meta-analysis. *Chest*. 2022;161(2):345-55.
9. León C, Ruiz-Santana S, Saavedra P, Almirante B, Nolla-Salas J, Alvarez-Lermaet F, et al. A bedside scoring system ("*Candida* score") for early antifungal treatment in nonneutropenic critically ill patients with *Candida* colonization. *Crit Care Med*. 2006;34(3):730-7.
10. León C, Ruiz-Santana S, Saavedra P, Galván B, Blanco A, Castro C, et al. Usefulness of the "*Candida* score" for discriminating between *Candida* colonization and invasive candidiasis in non-neutropenic critically ill patients: a prospective multicenter study. *Crit Care Med*. 2009;37(5):1624-33.
11. Wood GC, Mueller EW, Croce MA, Boucher BA, Fabian TC. *Candida* sp. isolated from bronchoalveolar lavage: clinical significance in critically ill trauma patients. *Intensive Care Med*. 2006;32(4):599-603.
12. Ioannou P, Vouidaski A, Spernovasilis N, Alexopoulou C, Papazachariou A, Paraschou E, et al. *Candida* spp. isolation from critically ill patients' respiratory tract. Does antifungal treatment affect survival? *Germs*. 2021;11(4):536-43.
13. Meena DS, Kumar D. *Candida* pneumonia: an innocent bystander or a silent killer? *Med Princ Pract*. 2022;31(1):98-102.
14. Sy E, Gupta C, Shahab Z, Fortin N, Kassir S, Mailman J, et al. Long-term safety of directly discharging patients home from the ICU compared to ward transfer. *J Intensive Care Med*. 2022;37(10):1344-52.
15. Huang D, Qi M, Hu Y, Yu M, Liang Z. The impact of *Candida* spp. airway colonization on clinical outcomes in patients with ventilator-associated pneumonia: a systematic review and meta-analysis. *Am J Infect Control*. 2020;48(6):695-701.
16. Samonis G, Anastassiadou H, Dassiou M, Tselentis Y, Bodey GP. Effects of broad-spectrum antibiotics on colonization of gastrointestinal tracts of mice by *Candida albicans*. *Antimicrob Agents Chemother*. 1994;38(3):602-3.
17. Schulte DM, Sethi A, Gangnon R, Duster M, Maki DG, Safdar N. Risk factors for *Candida* colonization and co-colonization with multi-drug resistant organisms at admission. *Antimicrob Resist Infect Control*. 2015;4:46.
18. Barenfanger J, Arakere P, Dela Cruz R, Imran A, Drake C, Lawhorn J, et al. Improved outcomes associated with limiting identification of *Candida* spp. in respiratory secretions. *J Clin Microbiol*. 2003;41(12):5645-9.

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Competing interests: None declared.

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Funding: This study was funded by a University of Saskatchewan, College of Medicine Dean's Summer Research Student Project grant.

BRIEF RESEARCH REPORT

Hiding in Plain Sight: Quantifying Salbutamol and Ipratropium Inhaler Wastage in Hospitals

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Can J Hosp Pharm. 2023;76(4):314-6 https://doi.org/10.4212/cjhp.3405

ABSTRACT

Background: Previous studies have found significant inhaler wastage in the inpatient setting, which contributes to unnecessary health care expenditures. Wastage may involve inhalers available in automated dispensing cabinets (ADCs).

Objectives: To evaluate whether salbutamol and ipratropium inhalers were unnecessarily withdrawn from ADCs for hospital inpatients.

Methods: This cross-sectional study included patients from 16 health care facilities in British Columbia. ADC reports were run for the period August 2021 to January 2022 to identify salbutamol and ipratropium inhalers removed from ADCs.

Results: Over the study period, 8.3% (2180/26 324) of salbutamol and ipratropium inhalers were withdrawn from ADCs unnecessarily for the same patient encounter within a 2-day timeframe, and another 1118 (4.2%) represented instances when multiple inhalers were withdrawn for the same patient at the same time. Overall, 12.5% (3298/26 324) of all salbutamol and ipratropium inhalers were withdrawn unnecessarily. The total cost of these inhalers was about $31 600 over the 6-month period.

Conclusions: This evaluation revealed considerable wastage of inhalers, leading to wasted expenditures. Other health authorities should conduct similar analyses to determine whether similar problems exist in their settings.

Keywords: drug waste, health care expenditure, salbutamol, ipratropium, metered dose inhalers

RÉSUMÉ

Contexte : De précédentes études ont mis au jour un gaspillage important d'inhalateurs en milieu hospitalier, ce qui contribue à des dépenses de soins de santé inutiles. Ce gaspillage peut comprendre des inhalateurs disponibles dans des cabinet de distribution automatisé (CDA).

Objectif : Évaluer si les inhalateurs de salbutamol et d'ipratropium ont été inutilement retirés des CDA pour les patients hospitalisés.

Méthodes : Cette étude transversale comprenait des patients provenant de 16 établissements de soins de santé en Colombie-Britannique. Des rapports portant sur les CDA ont été générés pour la période d'août 2021 à janvier 2022 afin de recenser les inhalateurs de salbutamol et d'ipratropium qui ont été retirés des CDA.

Résultats : Pendant la période de l'étude, 8,3 % (2180/26 324) des inhalateurs de salbutamol et d'ipratropium ont été inutilement retirés des CDA pour la même rencontre avec le patient dans une fenêtre de 2 jours, et dans le cas de 1118 (4,2 %) inhalateurs, plusieurs inhalateurs ont été retirées en même temps pour un même patient. Dans l'ensemble, 12,5 % (3298/26 324) de tous les inhalateurs de salbutamol et d'ipratropium ont été inutilement retirés. Le coût total de ces inhalateurs s'élevait à environ 31 600 $ sur une période de 6 mois.

Conclusions : Cette évaluation a révélé un gaspillage considérable d'inhalateurs, ce qui entraîne des dépenses inutiles. D'autres autorités sanitaires devraient mener des analyses similaires pour savoir si des problèmes similaires se produisent dans leurs établissements.

Mots-clés : gaspillage de médicaments, dépenses de soins de santé, salbutamol, ipratropium, inhalateurs doseurs

INTRODUCTION

Metered dose inhalers (MDIs) are used frequently for hospital inpatients, which in turn may lead to significant waste and potential negative environmental impacts because of the nature of the devices used (i.e., made of plastic) and the number of doses within each device. A study in the United Kingdom determined that 80% of MDIs collected from a single local district hospital still had doses remaining, and the authors estimated this would have been equivalent to 2.63 tonnes of carbon dioxide emissions.[1] Furthermore, current disposal procedures for unused or expired prescriptions in British Columbia involve incineration. Burning plastic actuators can release additional greenhouse gases, as well as carcinogens.[2]

Two previous evaluations showed significant loss/wastage of partly used inhalers within our large urban health region.[3,4] Reasons cited for these findings included loss of the devices on patient transfer and their ready availability as ward stock. On the basis of these evaluations, it was suspected that wastage might be associated with inhalers available in automated dispensing cabinets (ADCs). ADCs frequently contain the short-acting inhalers salbutamol and ipratropium to allow quick and easy access for nurses in patient care areas. Given that the devices are not dispensed from the pharmacy as labelled, patient-specific

inhalers, there is a risk that they will remain unlabelled after removal from the cabinet. Nurses are then unable to determine to whom unlabelled inhalers belong, so they must be discarded (to maintain infection-control practices) and new inhalers obtained.

The objective of this study was to evaluate whether more salbutamol and ipratropium inhalers were withdrawn from ADCs than was deemed necessary.

METHODS

This cross-sectional study included patients for whom at least 1 salbutamol or ipratropium inhaler was provided from an ADC, across 16 inpatient health care facilities in British Columbia comprising quaternary and tertiary sites (n = 4), urban community sites (n = 9), and rural locations (n = 3) and serving a mixed adult and pediatric population. Within our facilities, the majority of inhalers for these 2 medications are obtained from ADCs rather than being supplied as patient-specific items from the pharmacy. Transaction detail reports were run for the period August 1, 2021, to January 31, 2022, for all salbutamol and ipratropium inhalers removed from ADCs in all areas of every hospital, including the emergency department.

For purposes of the analysis, we made several assumptions. First, we assumed that patients would not need more than 1 inhaler of any type on the same day or the subsequent day. We chose this timeframe on the assumption that patients would not use all 200 doses in an inhaler within 2 days, even if they were being treated for acute asthma exacerbation (2 puffs qid + PRN) or were being mechanically ventilated (10 puffs q4h + PRN). We therefore counted the number of instances when an additional inhaler was withdrawn for the same patient encounter within a 2-day timeframe; these were deemed to represent unnecessary withdrawals from the ADC. Second, we identified instances when multiple inhalers were withdrawn for the same patient at the same time and counted the number of extra inhalers removed; these were also deemed unnecessary. From these data, we calculated the total number and percentage of unnecessary inhalers. Third, we calculated the number of unnecessary inhalers per patient encounter by dividing the total number of unnecessary inhalers by the number of patient encounters in which the patient received salbutamol or ipratropium in the study period. Finally, we calculated the cost associated with unnecessary withdrawals of salbutamol and ipratropium inhalers.

RESULTS

During the study period, a total of 26 324 inhalers were withdrawn from ADCs at the 16 study sites. We found that 2180 (8.3%) of these inhalers were withdrawn unnecessarily for the same patient encounter within a 2-day timeframe, and another 1118 (4.2%) represented instances when multiple inhalers were withdrawn for the same patient at the same time. As such, a total of 3298 (12.5%) inhalers overall, or 1 in every 8 inhalers, were withdrawn unnecessarily (Table 1). We calculated that 1 of every 4.3 patient encounters involved an unnecessary inhaler, and the cost of these inhalers was about $31 600 over the 6-month period.

DISCUSSION

To our knowledge, this study is the first to use ADC transaction reports to quantify the number of extra inhalers withdrawn unnecessarily (i.e., for the same patient encounter within a short period or involving multiple inhalers for a given patient at the same time). This method can be applied in a reasonably efficient manner and is easily replicated. In addition, the results help to pinpoint ADC availability as a significant contributor to inhaler wastage within the hospital system.

One potential cause that we identified is the lack of automation for generating patient-specific labels for multidose inhalers at the time of withdrawal from an ADC. Busy nursing staff may not always take the extra step of manually requesting a patient label each time, which results in unlabelled inhalers that must be discarded, according to infection control protocols. As a result of this study, we have worked with ADC system administration to reprogram some of the ADCs to automatically print patient-specific labels for inhalers, and post-implementation evaluation of this intervention is currently underway. Furthermore, a survey targeting nursing staff is being developed to identify where medications are stored on the unit and to characterize the patient transfer process, in hopes of identifying additional simple strategies to reduce this type of waste.

TABLE 1. Unnecessary Inhalers Withdrawn from Automated Dispensing Cabinets (ADCs)

Drug	Total No. of Inhalers Withdrawn from ADC	No. (%) Additional Inhalers Withdrawn in 2-Day Period	No. (%) of Excess Inhalers Withdrawn at One Time	Total No. (%) of Inhalers Deemed Withdrawn Unnecessarily
Salbutamol	16 672	1356 (8.1)	755 (4.5)	2111 (12.7)
Ipratropium	9 652	824 (8.5)	363 (3.8)	1187 (12.3)
Total	26 324	2180 (8.3)	1118 (4.2)	3298 (12.5)

This study had multiple limitations. We did not assess the withdrawal of additional inhalers outside the 2-day timeframe; however, inhalers withdrawn over much longer periods could be deemed unnecessary if the initial inhaler still had doses remaining. We did not review orders placed for individual patients to determine whether one inhaler had been withdrawn for a regularly scheduled dose and a second inhaler against a PRN order. Therefore, this study likely underestimates the total inhaler waste from ADCs that is occurring in our facilities. Finally, we assumed that any extra inhalers withdrawn were used or wasted and not returned to stock.

CONCLUSION

This analysis demonstrates a quick and easy way to quantify inhaler waste at the point of the ADC. Unnecessary inhaler waste places a significant financial burden on already limited health care budgets and has a negative environmental impact. We encourage other health care institutions and health authorities to conduct similar analyses to determine whether similar problems exist elsewhere.

References

1. Dipper A, Anning L, Zorzi A, Thrush L, Schulz T, Higbee D, et al. Reducing plastic waste, carbon footprint and cost: inhaler recycling at Musgrove Park Hospital [abstract]. *Eur Respir J.* 2018 [cited 2022 Nov 28];52 Suppl 62:PA3158. Available from: https://erj.ersjournals.com/content/52/suppl_62/PA3158
2. Appiah-Anane S, Waldon K. Reducing plastic waste from inhalers in general practice. *J Med Optim*. 2021 [cited 2023 Aug 21];7(1). Available from: https://www.pmhealthcare.co.uk/uploads/imagelib/pdfs/Journal_articles_by_issue/JoMO%20Mar%202021/Reducing%20Plastic%20waste%20from%20Inhalers%20in%20General%20practice.pdf
3. Aeng ESY, Dhaliwal MM, Tejani AM. A cautionary tale of multiple-dose drug products: fluticasone and salmeterol combination inhaler waste. *J Eval Clin Pract*. 2020;26(6):1699-702.
4. Aeng ESY, McDougal KC, Allegretto-Smith EM, Tejani AM. Hidden costs of multiple-dose products: quantifying ipratropium inhaler wastage in the hospital setting. *Can J Hosp Pharm*. 2021;74(2):117-21.

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Competing interests: For activities unrelated to this study, Aaron Tejani has received consulting fees for expert advice related to a legal case; speaker's fees for presentations to divisions of family practice in British Columbia, the BC Ministry of Health, and hospital rounds; and payment for advisory board participation for the ACTION ADE study (Vancouver General Hospital). No other competing interests were declared.

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Funding: None received.

Acknowledgements: The authors thank Deborah Heidary for generating medication-use reports and Cindy Lau for generating reports from the Omnicell automated dispensing cabinets.

Optimal Therapeutic Drug Monitoring Strategy for IV Aminoglycosides and IV Vancomycin in People with Cystic Fibrosis: A Systematic Review

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Can J Hosp Pharm. 2023;76(4):317-23 https://doi.org/10.4212/cjhp.3429

ABSTRACT

Background: Given altered pharmacokinetics in people with cystic fibrosis (pwCF), there is debate regarding optimal strategies for therapeutic drug monitoring (TDM) for aminoglycosides and vancomycin administered intravenously.

Objectives: To determine the TDM strategy for IV aminoglycosides and IV vancomycin associated with optimal clinical outcomes in pwCF.

Data Sources: Several databases (MEDLINE, Embase, CINAHL, Web of Science, Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov) were searched from inception to November 15, 2020, with searches rerun on February 13, 2023.

Study Selection and Data Extraction: Full articles evaluating TDM strategies and clinical outcomes in pwCF receiving IV aminoglycosides or IV vancomycin were included.

Data Synthesis: Three studies met the inclusion criteria for IV aminoglycosides, and 1 study met the inclusion criteria for IV vancomycin. Data are presented with descriptive analyses.

Conclusions: The available evidence is insufficient to determine an optimal TDM strategy for IV aminoglycoside or IV vancomycin therapy in pwCF.

Keywords: cystic fibrosis, therapeutic drug monitoring, aminoglycosides, vancomycin, systematic review

RÉSUMÉ

Contexte : Étant donné que la pharmacocinétique des personnes atteintes de fibrose kystique est altérée, un débat existe concernant les stratégies optimales de suivi thérapeutique des médicaments (STM) pour les aminoglycosides et la vancomycine administrés par voie intraveineuse.

Objectif : Déterminer la stratégie de suivi thérapeutique des médicaments pour les aminoglycosides et la vancomycine par voie intraveineuse associée aux résultats cliniques optimaux chez les personnes atteintes de fibrose kystique.

Sources des données : Plusieurs bases de données (MEDLINE, Embase, CINAHL, Web of Science, Cochrane Central Register of Controlled Trials et ClinicalTrials.gov) ont été consultées depuis leur création jusqu'au 15 novembre 2020, avec des recherches répétées le 13 février 2023.

Sélection des études et extraction des données : Les articles en texte intégral évaluant les stratégies de suivi thérapeutique des médicaments et les résultats cliniques chez les personnes atteintes de fibrose kystique recevant des aminoglycosides ou de la vancomycine par voie intraveineuse ont été inclus.

Synthèse des données : Trois études répondaient aux critères d'inclusion pour les aminoglycosides par voie intraveineuse, et une étude répondait aux critères d'inclusion pour la vancomycine par voie intraveineuse. Les données s'accompagnent d'analyses descriptives.

Conclusions : Les éléments probants disponibles sont insuffisants pour déterminer une stratégie optimale de suivi thérapeutique des médicaments pour la thérapie par aminoglycosides par voie intraveineuse ou la vancomycine par voie intraveineuse chez les personnes atteintes de fibrose kystique.

Mots-clés : fibrose kystique, suivi thérapeutique des médicaments, aminoglycosides, vancomycine, revue systématique, suivi thérapeutique pharmacologique

INTRODUCTION

People with cystic fibrosis (pwCF) are prone to bacterial respiratory infections, which result in chronic inflammation and pulmonary exacerbations.[1] These problems lead to progressive decline in lung function and ultimately respiratory failure, which is the most common cause of death in pwCF.[2] As such, optimal antibiotic dosing is imperative. Antibiotic dosing in pwCF may be complicated by higher clearance and volume of distribution,[1,3] which in turn may necessitate higher doses relative to populations without cystic fibrosis (CF).[4] Dosing of certain antibiotics is optimized with therapeutic drug monitoring (TDM). Two of the most commonly used antibiotics in pwCF are aminoglycosides and vancomycin, administered intravenously.[5]

Aminoglycosides are concentration-dependent bactericidal agents.[6] In non-CF populations, a target ratio of maximum serum concentration (C_{max}) to minimum

inhibitory concentration (MIC) (C_{max}/MIC) of 8–10 has been associated with better clinical outcomes.[6,7] The ratio of area under the curve (AUC) to MIC (AUC/MIC) has also been associated with better outcomes.[8,9] Three reviews have summarized aminoglycoside pharmacokinetics and pharmacodynamics (PK/PD) and TDM for pwCF,[10-12] but the determination of optimal monitoring strategies was identified as a topic in need of further study.[10,12]

Vancomycin is a time-dependent bactericidal agent.[13] Recent updates to guidelines for serious methicillin-resistant *Staphylococcus aureus* infections have recommended AUC/MIC-based monitoring in place of previously recommended trough-based monitoring.[14] A systematic review challenged this recommendation because of inconsistent data showing benefit.[15] Two reviews have examined IV vancomycin PK and TDM in pwCF, but neither addressed clinical outcomes.[11,16]

To our knowledge, no review of this topic to date has applied a systematic methodology. The objective of this systematic review was to determine whether there is a TDM strategy for pwCF receiving IV aminoglycosides or IV vancomycin that optimizes clinical outcomes.

METHODS

Search Strategy

The MEDLINE, Embase, CINAHL, Web of Science Core Collection, and ClinicalTrials.gov databases were systematically searched up to November 15, 2020; the search was later rerun to include literature up to February 13, 2023. The reference lists of relevant studies were reviewed for additional studies not identified in the database searches. The systematic review protocol was registered with PROSPERO (CRD42020212941).

Selection of Studies

Studies comparing TDM strategies and clinical outcomes in pwCF who received an IV aminoglycoside or IV vancomycin were included. To be eligible for inclusion, the TDM strategies had to be described in enough detail to be reproducible. Nonhuman and in vitro studies, studies without full published reports, and those not available in English were excluded. Pairs of authors independently screened all studies identified in both the initial (J.J., N.G.) and subsequent (J.J., R.D.) searches. Discrepancies were resolved by consulting 2 additional authors (V.S., R.D.).

Outcomes

The primary outcomes of interest were change in lung function (e.g., percent or absolute change in forced expiratory volume in 1 second [FEV_1]), percent baseline lung function at end of treatment, symptom resolution, radiographic changes, and toxicity. The secondary outcomes of interest were death, duration of hospitalization, time to achieve therapeutic drug levels, treatment failure, daily antibiotic exposure, antibiotic dosing regimen, and timing of antibiotic level(s) measurement relative to the dose.

Data Extraction and Management

Relevant data, including first author, year of publication, study design, participant characteristics, and clinical outcomes, were extracted and tabulated.

Quality Assessment

All of the included studies were assessed independently for risk of bias by 2 reviewers (J.J., N.G.), who used the National Heart, Lung, and Blood Institute (US) quality assessment tool for observational cohort and cross-sectional studies.[17] An overall rating of "good", "fair", or "poor" was assigned to each report after discussion and consensus. Discrepancies were resolved by consulting the third and fourth authors (V.S., R.D.).

Data Analysis

Descriptive analyses were used to assess the extracted data.

RESULTS

Therapeutic Drug Monitoring Strategy

Aminoglycosides

Of the 4030 records identified in the initial search, 1 study[18] met the inclusion criteria (Figure 1); 2 additional studies were identified in the subsequent search.[19,20] The characteristics of included studies are summarized in Table 1.

Burkhardt and others[18] compared extended-interval and conventional dosing of tobramycin, retrospectively correlating the AUC achieved during a 24-hour interval (AUC_{24})/MIC and C_{max}/MIC with lung function at day 14 of treatment. Both AUC_{24}/MIC and C_{max}/MIC had a log–linear relationship with percent predicted FEV_1 ($ppFEV_1$) (extended-interval dosing: $r^2 = 0.62$ and 0.31, respectively; conventional dosing: $r^2 = 0.63$ and 0.17, respectively).[18] For equal values of AUC_{24}/MIC, extended-interval dosing was associated with a higher $ppFEV_1$ at day 14 relative to conventional dosing.[18] The relationship between lung function improvement and C_{max}/MIC was not dependent on dosing interval.[18]

Landmesser and others[19] conducted a retrospective chart review comparing the predictive value of AUC_{24} and C_{max} for change in absolute FEV_1. Of patients who achieved an AUC_{24} of at least 80 mg*h/L, 75.8% had a return to baseline FEV_1, compared with 61.5% of those with an AUC_{24} less than 80 mg*h/L ($p = 0.147$).[19] Similarly, 80.3% of patients who achieved the target C_{max} of at least 8 times the highest-documented MIC for *Pseudomonas aeruginosa* had a return to baseline FEV_1, compared with 65.6% who did not achieve the aforementioned target C_{max}/MIC ($p = 0.065$).[19] Acute kidney injury (AKI) was more frequent among those who received multiple daily doses than among those with

extended-interval dosing ($p = 0.047$), but was not associated with increasing AUC_{24} or C_{max}.[19]

The ambidirectional cohort study by Hemmann and others[20] compared trough-only and patient-specific PK monitoring for tobramycin and amikacin using 2- and 8-hour post-dose levels. There was no significant difference between groups for change in $ppFEV_1$, antibiotic duration, length of stay, or nephrotoxicity.[20] In the patient-specific PK group, 75% of participants required dose adjustments after initial measurement of serum concentration, whereas none of those in the trough-only group required dose adjustments ($p < 0.001$); the majority of adjustments involved a decrease in dose interval to avoid a prolonged drug-free interval.[20]

Vancomycin

No studies identified in the initial search met the inclusion criteria (Figure 1), but 1 study was identified when the search was rerun. Mitchell and others[21] retrospectively compared trough- and AUC-based monitoring. Among adults, 86.5% in the AUC-based monitoring group and 56.5% in the trough-based monitoring group had a return to baseline $ppFEV_1$ ($p = 0.002$); notably, 50% of those with return to baseline in the AUC-based monitoring group and 20% in the trough-based monitoring group were receiving a CF transmembrane conductance regulator (CFTR) modulator.[21] Among pediatric patients, 67% in the AUC-based monitoring group and 80% in the trough-based monitoring group had return to baseline $ppFEV_1$ ($p = 0.458$), and among these patients, 58% in the AUC-based monitoring group and 75% in the trough-based monitoring groups were receiving a CFTR modulator.[21] Time to next exacerbation and AKI incidence were not significantly different between groups.[21] AKIs of higher severity occurred only in adults in the trough-based monitoring group; however, concomitant nephrotoxic medications were more prevalent in this group.[21] Median total daily dose for AUC- versus trough-based monitoring was 40 mg/kg and 52 mg/kg, respectively, among adults and 60 mg/kg and 58 mg/kg, respectively, among pediatric patients.[21] Overall, lower troughs were observed in the AUC group.[21]

Quality Assessment

Three of the included studies were deemed to be of "good" quality,[19-21] and 1 study was deemed to be of "fair" quality.[18]

DISCUSSION

The objective of this systematic review was to determine if there is a TDM strategy for IV aminoglycosides and IV vancomycin associated with optimal clinical outcomes in pwCF.

Aminoglycosides

Results from the 2 studies comparing C_{max} with AUC_{24} were conflicting.[18,19] Burkhardt and others[18] suggested that C_{max}/MIC may be a better measure for clinical outcomes, given that the relationship with $ppFEV_1$ was not affected

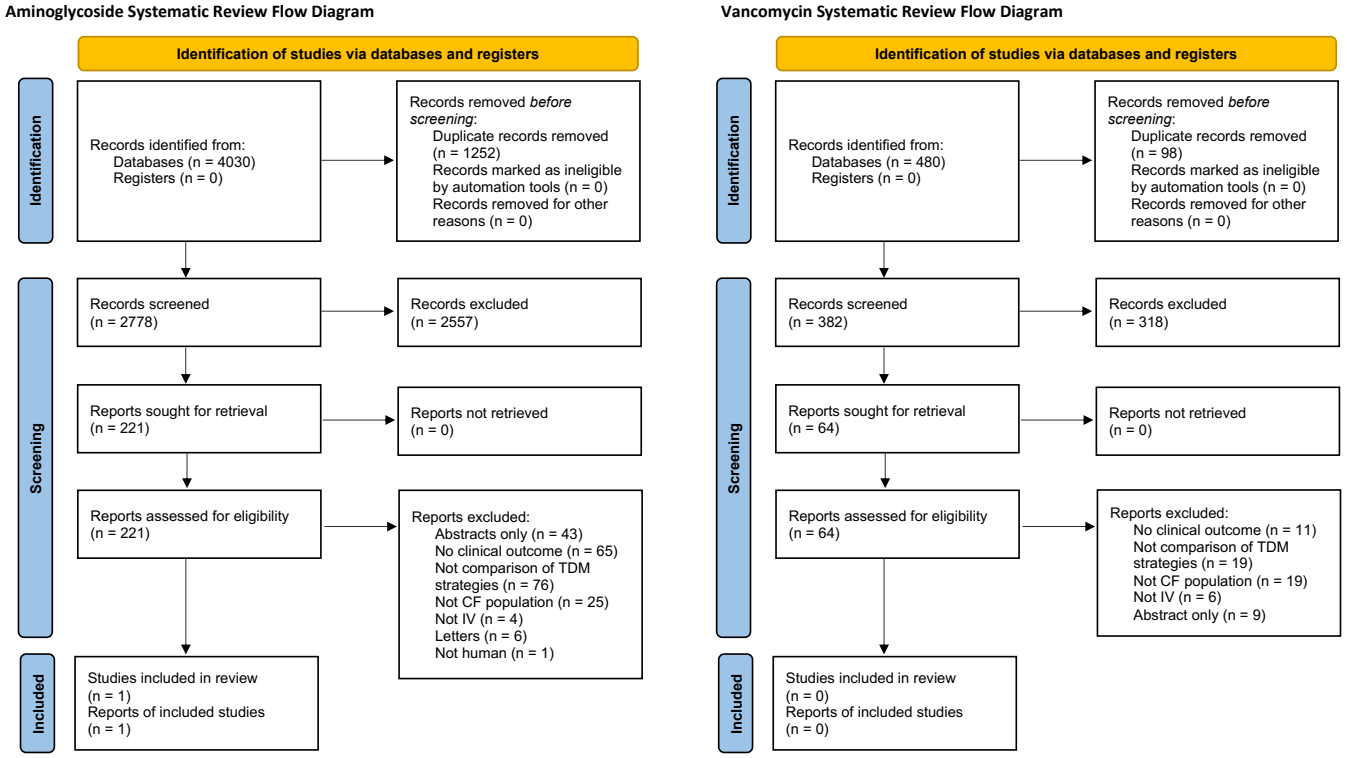

FIGURE 1. PRISMA flow diagram of study selection based on initial search, performed on November 15, 2020. CF = cystic fibrosis, TDM = therapeutic drug monitoring.

by dosing interval. This suggestion is congruent with the concentration-dependent antimicrobial activity of aminoglycosides[6] but was contradicted by the observed log–linear correlation between ppFEV$_1$ and C_{max}/MIC being lower than the correlation between ppFEV$_1$ and AUC$_{24}$/MIC.[18] Notably, some patients had improvement in FEV$_1$ despite low C_{max}/MIC and AUC$_{24}$/MIC, and these were excluded from the log–linear model.[18] Similarly, Landmesser and others[19] observed that more than 60% of patients had return to baseline FEV$_1$ despite not achieving C_{max} or AUC$_{24}$ targets; there was no statistical difference from patients who achieved these targets, but the study was likely not powered to detect such a difference. The AKI risk also was not correlated with AUC$_{24}$/MIC or C_{max}/MIC, but the risk increased with multiple daily doses relative to extended-interval dosing.[19] Exploratory analyses of a retrospective review evaluating the impact of aminoglycoside PK exposure on clinical outcomes in pwCF indicated that AUC and C_{max} were not associated with FEV$_1$ recovery, and no optimal threshold for either parameter was identified for this outcome.[22]

TABLE 1 (Part 1 of 2). Summary of Characteristics and Results of Included Studies for TDM Strategies in People with Cystic Fibrosis

Reference and Study Design	Population	Regimen	TDM Strategies Compared	Results
Aminoglycosides				
Burkhardt et al. (2006)[18] Single centre, open-label RCT	n = 33 adults, age range 19–37 years *Exclusions:* pre-existing renal insufficiency or hearing impairment; aminoglycoside or β-lactam hypersensitivity; pregnancy	Tobramycin 10 mg/kg divided q8h (n = 16) vs q24h (n = 17) × 14 days Target C_{tr} and C_{pk}: • q8h: < 2 mg/L, 5–20 mg/L • q24h: < 1 mg/L, 20–40 mg/L	C_{max}/MIC vs AUC$_{24}$/MIC	• Log–linear correlation between C_{max}/MIC and AUC$_{24}$/MIC with ppFEV$_1$ at 14 days (C_{max}/MIC: r^2 = 0.17 [q8h], 0.31 [q24h]; AUC$_{24}$/MIC: r^2 = 0.63 [q8h], 0.62 [q24h]) • For equal AUC$_{24}$/MIC value, better improvement in ppFEV$_1$ with q24h than with q8h dosing • C_{max}/MIC outcome not dependent on q24h vs q8h dosing • Toxicity not reported
Landmesser et al. (2021)[19] Retrospective chart review (Aug. 1, 2015, to Aug. 31, 2019)	n = 66 patients (151 encounters), age range 0.8–61 years • n = 19 pediatric patients (≥ 1 month old; 44 encounters) • n = 47 adult patients (107 encounters) *Exclusions: Pseudomonas aeruginosa* not identified in sputum culture; pre-existing CKD; 2 post-dose drug levels not obtained during admission, after ≥ 20% dose change, or after change in dose interval due to fluctuating renal function	Tobramycin • Dose adjusted to achieve calculated C_{tr} < 0.5 mg/L and C_{pk} ≥ 12 mg/L • 85% received q24h dosing	C_{max} (target ≥ 8× highest-documented MIC for *P. aeruginosa*) vs AUC$_{24}$ (target 80–120 mg*h/L)	• Of patient encounters in which AUC$_{24}$ was ≥ 80 mg*h/L or target C_{max} was achieved, absolute FEV$_1$, returned to baseline in 75.8% (p = 0.147) and 80.3% (p = 0.065), respectively • Difference in mean C_{max} and AUC$_{24}$ for patient encounters in which FEV$_1$ did and did not return to baseline was NSS • No association between increasing AUC$_{24}$ or C_{max} and development of AKI • Increased incidence of AKI with multiple daily doses vs extended-interval dosing (50% vs 29% of encounters, respectively; p = 0.047)
Hemmann et al. (2022)[20] Ambidirectional cohort study (June 1, 2018, to Feb. 8, 2021)	n = 53 pediatric patients (< 18 years), mean age 10.6 years *Exclusions:* did not receive monitoring per assigned cohort; second admission within 30 days of the previous admission	Tobramycin 10 mg/kg q24h or amikacin 30 mg/kg IV q24h • In intervention group, dose adjusted to achieve target C_{max}, C_{min}, and DFI	Control (cohort 1): trough-only monitoring (n = 21: June 1, 2018, to Feb. 28, 2019) Intervention (cohort 2): patient-specific PK calculations (n = 32: June 1, 2019, to Feb. 8, 2021) • levels measured 2 and 8 h post-dose • trough level used if no indication to repeat PK calculations[a]	• No difference in change in ppFEV$_1$ from admission to discharge between cohorts 1 and 2 (11.4% vs 13.9%; p = 0.55) • Difference in duration of antibiotics and length of stay NSS between cohorts 1 and 2 • Dose adjustment after initial level(s)[b]: 75% in cohort 2 vs 0% in cohort 1 (p < 0.001) • Nephrotoxicity (SCr 1.5× baseline): 6.3% in cohort 2[c] vs 0% in cohort 1 (NSS)

TABLE 1 (Part 2 of 2). Summary of Characteristics and Results of Included Studies for TDM Strategies in People with Cystic Fibrosis

Reference and Study Design	Population	Regimen	TDM Strategies Compared	Results
Vancomycin				
Mitchell et al. (2022)[21] Retrospective chart review (Oct. 1, 2015, to Jan. 31, 2021)	$n = 60$[d] (155 encounters), age range 0.25–55 years • $n = 26$ pediatric patients (42 encounters) • $n = 36$ adult patients (113 encounters) *Exclusions:* < 5 days of IV vancomycin during or after transplant	Initial dose per institutional policy, then adjusted to achieve TDM target	Trough-only monitoring (Oct. 1, 2015, to Oct. 1, 2018), target 10–20 mg/L AUC monitoring (Oct. 2, 2018, to Jan. 31, 2021), target 400–600 mg*h/L (calculated using 2-point estimate)	• Return to baseline $ppFEV_1$ for trough vs AUC monitoring in adults[e]: 56.5% vs 86.5% ($p = 0.002$) • Return to baseline $ppFEV_1$ for trough vs AUC monitoring in pediatric patients[f]: 80% vs 67% ($p = 0.458$) • Difference in median time to next exacerbation NSS between groups in adult or pediatric study populations • Median TDD for trough monitoring: adult 52 (IQR 42–70) mg/kg, pediatric 58 (IQR 55–70) mg/kg • Median TDD for AUC monitoring: adult 40 (IQR 34–54) mg/kg, pediatric 60 (IQR 54–72) mg/kg • Incidence of AKI NSS between trough and AUC monitoring, both overall (17% vs 12%, respectively; $p = 0.451$) and in adult and pediatric subgroups • Grade 2 and 3 AKI[g] in 1 adult each in trough-monitoring group; all other AKIs were grade 1[g]

AKI = acute kidney injury, AUC = area under the curve, AUC_{24} = area under the curve in 24 h, AUC_{24}/MIC = ratio of area under the curve in 24 h to minimum inhibitory concentration, CFTR = cystic fibrosis transmembrane conductance regulator, CKD = chronic kidney disease, C_{max}/MIC = ratio of maximum concentration to minimum inhibitory concentration, C_{max} = maximum concentration, C_{min} = minimum concentration, C_{pk} = peak concentration, C_{tr} = trough concentration, DFI = drug-free interval, FEV_1 = forced expiratory volume in 1 second, IQR = interquartile range, MIC = minimum inhibitory concentration, NSS = not statistically significant, PK = pharmacokinetic, $ppFEV_1$ = percent predicted forced expiratory volume in 1 second, RCT = randomized controlled trial, SCr = serum creatinine, TDD = total daily dose, TDM = therapeutic drug monitoring.

[a]Patient-specific PK calculations were completed at least once every 6 months for admitted patients, sooner if patient had any of the following criteria: ≥ 30% change in SCr, ≥ 20% change in weight, significant change in fluid status, or admission to pediatric intensive care unit.[20]

[b]Change in dose after initial measurement of aminoglycoside serum concentration(s) was the primary outcome of this study.[20]

[c]The 2 patients who experienced SCr 1.5× baseline were receiving concurrent nephrotoxic medications and had a history of SCr elevations while receiving aminoglycosides.

[d]The total numbers of adult and pediatric patients sum to 62 but represent only 60 unique individuals, as 2 patients had admissions included in both the pediatric and adult cohorts.[21]

[e]Of adult patients in the trough- and AUC-monitoring groups with return to baseline FEV_1, 20% and 50%, respectively, were receiving concomitant CFTR modulator therapy.[21]

[f]Of pediatric patients in the trough- and AUC-monitoring groups with return to baseline FEV_1, 75% and 58%, respectively, were receiving concomitant CFTR modulator therapy.[21]

[g]Per Kidney Disease Improving Global Outcomes (KDIGO) criteria.[21]

Concerns have been raised about observed increases in *P. aeruginosa* MIC with extended-interval dosing, potentially because of the prolonged drug-free interval[18]; the majority of dose adjustments in the study by Hemmann and others[20] were in order to shorten the drug-free interval, but this did not result in better clinical outcomes. Moreover, antimicrobial sensitivity testing does not reliably predict clinical outcomes in pwCF.[23]

The aforementioned findings raise the question: Is aminoglycoside TDM strategy or dosing regimen more important for clinical outcomes? The available literature suggests that extended-interval dosing maximizes C_{max}/MIC and the post-antibiotic effect, while decreasing risk for AKI.[10,12]

Vancomycin

Although the study results suggest greater return to baseline $ppFEV_1$ among adults with AUC-based monitoring than those with trough-based monitoring, the disproportionate number of patients who were receiving CFTR modulators is a potential confounder.[21] The relatively smaller disparity

in CFTR modulator use and higher baseline ppFEV$_1$ among pediatric patients may account for the lack of observed difference between the study groups.[21]

Mitchell and others[21] did not report whether the difference between groups in vancomycin total daily dose was statistically significant. However, the decrease in total daily dose for adults in the AUC-based monitoring group and lower troughs observed in the AUC-based monitoring group overall may translate to clinical benefit, given the evidence suggesting that AKI risk with vancomycin increases with higher troughs and AUC.[14]

Limitations

The primary limitation of this systematic review was the small number of studies that met the inclusion criteria. This likely reflects a lack of studies evaluating these outcomes in pwCF, as we utilized a robust search strategy in multiple databases and reviewed the grey literature to minimize the risk of publication bias. The potential for selection bias was addressed by having 2 reviewers independently screen for and identify eligible studies. No studies were excluded as a result of the TDM strategy being non-reproducible. All included studies had a small sample size, which limited generalizability as well as statistical power to detect outcome differences. Moreover, 3 of the 4 studies involved retrospective analysis of data, which carries an intrinsic risk for confounding variables. There were insufficient data from the included studies to evaluate optimal TDM targets in pwCF.

CONCLUSION

Available evidence is insufficient to determine an optimal TDM strategy for IV aminoglycosides or IV vancomycin in pwCF. Prospective randomized controlled trials (RCTs) are required to better evaluate the correlation of aminoglycoside AUC_{24}/MIC and C_{max}/MIC with clinical outcomes in pwCF, as well as to elucidate the impact of conventional versus extended-interval dosing. Similarly, RCTs are required to compare the clinical outcomes of different vancomycin TDM strategies in pwCF. Future studies involving pwCF should also explore whether optimal TDM strategy varies by age group and should focus on determining optimal TDM targets. In the era of highly effective CFTR modulators, achieving the necessary sample size to evaluate these outcomes may prove difficult; therefore, it is imperative that the CF community collaborate in attempts to fill these important gaps in the literature.

References

1. Rowe SM, Miller S, Sorscher EJ. Cystic fibrosis. *N Engl J Med*. 2005; 352(19):1992-2001.
2. *Patient registry 2020 annual data report*. Cystic Fibrosis Foundation; 2021 [cited 2023 Aug 24]. Available from: https://www.cff.org/sites/default/files/2021-10/2019-Patient-Registry-Annual-Data-Report.pdf
3. Castagnola E, Cangemi G, Mesini A, Castellani C, Martelli A, Cattaneo D, et al. Pharmacokinetics and pharmacodynamics of antibiotics in cystic fibrosis: a narrative review. *Int J Antimicrob Agents*. 2021;58(3):106381.
4. Horrevorts AM, Driessen OM, Michel MF, Kerrebijn KF. Pharmacokinetics of antimicrobial drugs in cystic fibrosis. Aminoglycoside antibiotics. *Chest*. 1988;94(2 Suppl):120S-125S.
5. Döring G, Flume P, Heijerman H, Elborn JS; Consensus Study Group. Treatment of lung infection in patients with cystic fibrosis: current and future strategies. *J Cyst Fibros*. 2012;11(6):461-79.
6. Moore RD, Lietman PS, Smith CR. Clinical response to aminoglycoside therapy: importance of the ratio of peak concentration to minimal inhibitory concentration. *J Infect Dis*. 1987;155(1):93-9.
7. Burgess DS. Use of pharmacokinetics and pharmacodynamics to optimize antimicrobial treatment of *Pseudomonas aeruginosa* infections. *Arch Clin Infect Dis*. 2005;40(Suppl 2):S99-S104.
8. Mouton JW, Jacobs N, Tiddens H, Horrevorts AM. Pharmacodynamics of tobramycin in patients with cystic fibrosis. *Diagn Microbiol Infect Dis*. 2005;52(2):123-7.
9. Bland CM, Pai MP, Lodise TP. Reappraisal of contemporary pharmacokinetic and pharmacodynamic principles for informing aminoglycoside dosing. *Pharmacotherapy*. 2018;38(12):1229-38.
10. Young DC, Zobell JT, Stockmann C, Waters CD, Ampofo K, Sherwin CMT, et al. Optimization of anti-pseudomonal antibiotics for cystic fibrosis pulmonary exacerbations: V. Aminoglycosides. *Pediatr Pulmonol*. 2013;48(11):1047-61.
11. Magréault S, Roy C, Launay M, Sermet-Gaudelus I, Jullien V. Pharmacokinetic and pharmacodynamic optimization of antibiotic therapy in cystic fibrosis patients: current evidences, gaps in knowledge and future directions. *Clin Pharmacokinet*. 2021;60(4):409-45.
12. Ochs MA, Dillman NO, Caverly LJ, Chaffee VD. Aminoglycoside dosing and monitoring for *Pseudomonas aeruginosa* during acute pulmonary exacerbations in cystic fibrosis. *Pediatr Pulmonol*. 2021;56(12):3634-43.
13. Craig WA. Basic pharmacodynamics of antibacterials with clinical applications to the use of β-lactams, glycopeptides, and linezolid. *Infect Dis Clin North Am*. 2003;17(3):479-501.
14. Rybak MJ, Le J, Lodise TP, Levine DP, Bradley JS, Liu C, et al. Therapeutic monitoring of vancomycin for serious methicillin-resistant *Staphylococcus aureus* infections: a revised consensus guideline and review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. *Am J Health Syst Pharm*. 2020;77(11):835-64.
15. Dalton BR, Rajakumar I, Langevin A, Ondro C, Sabuda D, Griener TP, et al. Vancomycin area under the curve to minimum inhibitory concentration ratio predicting clinical outcome: a systematic review and meta-analysis with pooled sensitivity and specificity. *Clin Microbiol Infect*. 2020;26(4):436-46.
16. Epps QJ, Epps KL, Young DC, Zobell JT. State of the art in cystic fibrosis pharmacology—optimization of antimicrobials in the treatment of cystic fibrosis pulmonary exacerbations: I. Anti-methicillin-resistant *Staphylococcus aureus* (MRSA) antibiotics. *Pediatr Pulmonol*. 2020;55(1):33-57.
17. Quality assessment tool for observational cohort and cross-sectional studies. In: *Study quality assessment tools* [website]. National Institutes of Health, National Heart, Lung, and Blood Institute; [cited Mar 21 2021]. Available from: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools
18. Burkhardt O, Lehmann C, Madabushi R, Kumar V, Derendorf H, Welte T. Once-daily tobramycin in cystic fibrosis: better for clinical outcome than thrice-daily tobramycin but more resistance development? *J Antimicrob Chemother*. 2006;58(4):822-9.
19. Landmesser KB, Autry EB, Gardner BM, Bosko KA, Schadler A, Kuhn RJ. Comparison of the predictive value of area under the curve versus maximum serum concentration of intravenous tobramycin in cystic fibrosis patients treated for an acute pulmonary exacerbation. *Pediatr Pulmonol*. 2021;56(10):3209-16.
20. Hemmann B, Woods E, Makhlouf T, Gillette C, Perry C, Subramanian M, et al. Impact of patient-specific aminoglycoside monitoring

for treatment of pediatric cystic fibrosis pulmonary exacerbations. *J Pediatr Pharmacol Ther*. 2022;27(7):655-62.
21. Mitchell B, Kormelink L, Kuhn R, Schadler A, Autry E. Retrospective review of vancomycin monitoring via trough only versus two-point estimated area under the curve in pediatric and adult patients with cystic fibrosis. *Pediatr Pulmonol.* 2022;58(1):239-45.
22. Hoff BM, Scheetz MH, Jain M, Cullina JF, Rhodes NJ. Exploring the relationship between FEV_1 loss and recovery and aminoglycoside pharmacokinetics in adult patients with cystic fibrosis: implications for clinical dosing strategies. *Pharmacotherapy.* 2020;40(6):584-91.
23. Somayaji R, Parkins MD, Shah A, Martiniano SL, Tunney MM, Kahle JS, et al.; Antimicrobial Resistance in Cystic Fibrosis International Working Group. Antimicrobial susceptibility testing (AST) and associated clinical outcomes in individuals with cystic fibrosis: a systematic review. *J Cyst Fibros*. 2019;18(2):236-43.

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Competing interests: None declared.

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Funding: None received.

Misunderstandings about Tonicity and Osmolality Can Lead to Patient Harm

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Can J Hosp Pharm. 2023;76(4):324-6 https://doi.org/10.4212/cjhp.3417

INTRODUCTION

Hyponatremia, the most common electrolyte disorder in hospitalized patients, is associated with both morbidity and mortality.[1-6] The use of hypotonic IV fluids has been identified as an important potential cause of hospital-acquired hyponatremia, especially among children.[1-6] During patient care rounds, one of the authors (J.R.M.) serendipitously discovered a bag of hypotonic IV fluid that was inappropriately labelled (at the manufacturing level). This observation prompted a more in-depth review of IV fluid labelling practices across randomly selected Canadian and US manufacturers to better understand the scope of this issue.

WHY ARE HOSPITALIZED PATIENTS AT RISK FOR HYPONATREMIA?

Risk factors for non-osmotic release of antidiuretic hormone (ADH) include pain, nausea, stress, and certain medications. Hospitalized patients regularly experience these symptoms and often have changes to their medication regime, which may impair their ability to excrete free water because of fluctuations in ADH release. In the setting of increased ADH, the free water available in hypotonic IV solutions can rapidly lead to clinically significant hyponatremia.[1-6]

WHAT IS TONICITY AND OSMOLALITY?

It is important for clinicians to understand the difference between tonicity and osmolality. Tonicity is a property of a solution with reference to a particular membrane, whereas osmolality is a property of a solution that is independent of any membrane.[3,5] Solutes such as dextrose (which can freely enter the cell under normal conditions) contribute to the osmolality of a solution, but they do not alter tonicity.[3,5] Although the difference between tonicity and osmolality may seem inconsequential, consider how a lack of awareness of this difference might lead to potential harm when an IV solution is prescribed.

In a patient with normal serum sodium, administration of a hyperosmolar IV solution without sodium (e.g., 10% dextrose in water, D10W) could lead to hyponatremia because the solution being administered is very hypotonic. In contrast, D10NS—an IV solution with the same concentration of dextrose but, concurrently, 0.9% sodium chloride (NaCl)—would not be expected to cause hyponatremia, because the NaCl contributes to tonicity (i.e., the solution is hyperosmotic yet isotonic).

Put another way, administration of 1000 mL of D5W is analogous to administering 1000 mL of electrolyte-free water, given that dextrose, once administered under normal physiologic conditions, will be quickly metabolized, leaving only free water. Similarly, administration of 1000 mL of 0.45% NaCl can be considered equivalent to administering 500 mL of isotonic (0.9%) NaCl plus 500 mL of free water. Finally, no free water is administered when 1000 mL of isotonic (0.9%) NaCl is given.

WHY IS THIS A PARTICULAR CONCERN IN YOUNGER PATIENTS?

Because of physiological differences, children are at higher risk than adults for hyponatremia-related complications.[3] Cases of iatrogenic hyponatremia in children (and adults) have been outlined in recent publications by the Institute for Safe Medication Practices Canada.[7,8] Partly in response to these reports, our local children's hospital established a policy listing several hypotonic solutions, which are mostly restricted to critical care areas.[9] The American Academy of Pediatrics[5] and the Canadian Paediatric Society[1] recommend the use of isotonic IV solutions as the standard for fluid maintenance in children, with the recognition that hypotonic IV solutions can be used in specific circumstances but only with careful monitoring.

CONFUSING THE ISSUE: LABELLING OF IV SOLUTIONS IN NORTH AMERICA

Given that the differences between osmolality and tonicity are well established, we reviewed the labelling and product monographs of selected dextrose-containing IV solutions

produced by a random selection of Canadian and US manufacturers. We conducted a Google search using the term "leading IV manufacturers Canada" and chose the first 3 manufacturers generated by the search. We reviewed labelling and monograph information from the Canadian and US subsidiaries of all 3 companies; in 1 case, the Canadian and US labelling was the same, so only the US labelling is reported here (Table 1). We found several examples of isotonic and hypotonic IV solutions that were designated as "hypertonic" both in the product monograph and on individual bags of IV fluid. Of the 5 manufacturers screened (Table 1), only 1 manufacturer's monograph indicated that dextrose-containing fluids could become hypotonic in vivo because of rapid metabolism.

A total of 28 IV solutions were reviewed, 27 of which had incorrect information in their respective monographs,

TABLE 1. Labelling of Individual IV Fluid Bags and Product Monographs from Randomly Selected North American Manufacturers[a]

Company and IV Solution	Osmolality (Compared with Plasma)	Tonicity	Bag Labelled as Hypertonic	Designated as Hypertonic in Monograph
Canada				
B. Braun Medical Inc, Mississauga, Ontario				
Dextrose 10%	Hyperosmolar	Hypotonic	Yes	Yes
Dextrose 5% in 0.45% NaCl		Hypotonic	Yes	Yes
Dextrose 5% in 0.9% NaCl		Isotonic	Yes	Yes
Baxter Corporation, Mississauga, Ontario				
Dextrose 10%	Hyperosmolar	Hypotonic	Yes	No
Dextrose 10% in 0.9% NaCl		Isotonic	Yes	No
Dextrose 5% in 0.45% NaCl		Hypotonic	Yes	No
Dextrose 5% in 0.9% NaCl		Isotonic	Yes	No
Dextrose 5% in lactated Ringer's solution		Isotonic	Yes	Yes
United States				
B. Braun Medical Inc, Bethlehem, Pennsylvania				
Dextrose 10%	Hyperosmolar	Hypotonic	Yes	Yes
Dextrose 10% in 0.2% NaCl		Hypotonic	Yes	Yes
Dextrose 10% in 0.45% NaCl		Hypotonic	Yes	Yes
Dextrose 5% in 0.2% NaCl		Hypotonic	No	No
Dextrose 5% in 0.33% NaCl		Hypotonic	Yes	Yes
Dextrose 5% in 0.45% NaCl		Hypotonic	Yes	Yes
Dextrose 5% in 0.9% NaCl		Isotonic	Yes	Yes
Dextrose 5% in lactated Ringer's solution		Isotonic	Yes	Yes
Baxter Healthcare Corp, Deerfield, Illinois				
Dextrose 10%	Hyperosmolar	Hypotonic	Yes	Yes[b]
Dextrose 5% in 0.2% NaCl		Hypotonic	No	Yes[c]
Dextrose 5% in 0.33% NaCl		Hypotonic	No	Yes[c]
Dextrose 5% in 0.45% NaCl		Hypotonic	Yes	Yes[c]
Dextrose 5% in 0.9% NaCl		Isotonic	Yes	Yes[c]
Dextrose 5% in lactated Ringer's solution		Isotonic	Yes	No
ICU Medical Inc, San Clemente, California				
Dextrose 10%	Hyperosmolar	Hypotonic	No	Yes
Dextrose 5% in 0.225% NaCl		Hypotonic	No	Yes
Dextrose 5% in 0.3% NaCl		Hypotonic	No	Yes
Dextrose 5% in 0.45% NaCl		Hypotonic	No	Yes
Dextrose 5% in 0.9% NaCl		Isotonic	No	Yes
Dextrose 5% in lactated Ringer's solution		Isotonic	No	Yes

[a]This review included dextrose (> 5%) solutions and dextrose/saline-containing (≥ 5% dextrose) solutions listed in each manufacturer's online catalogue. Solutions containing ≥ 20 mmol KCl/L were excluded.
[b]Labelling and monograph contain the following statement: "10% Dextrose Injection is a hypertonic solution. In the body, however, glucose containing fluids can become extremely physiologically hypotonic due to rapid glucose metabolization."
[c]Labelling and monograph contain the following statement: "Dextrose and sodium chloride injection is a hypertonic solution. In the body, however, glucose containing fluids can become extremely physiologically hypotonic due to rapid glucose metabolization."

labelling, or both. Of the 18 hypotonic fluids that we reviewed, 11 (61%) were incorrectly labelled as "hypertonic" on the IV bag.

MISLABELLING: AN ACADEMIC CONCERN OR TRUE HARM?

In our review, most of the solutions labelled as hypertonic are in fact hyperosmolar but not hypertonic. While it may be worthwhile to know the osmolarity of IV solutions (for example, hyperosmolar solutions may be associated with an increased risk of venous irritation[10]), the tonicity needs to be correctly described on both the label and product monograph to help ensure appropriate fluid selection in the clinical environment.

Hospital policies may help to provide guidance around the principles of IV fluid therapy. As previously noted, our local children's hospital has established a policy regarding IV fluid administration. This policy lists several hypotonic solutions (for example, D5W, D10W, D5W + 0.2% NaCl, and dextrose 3.3% + 0.3% NaCl) which should not be routinely stocked outside of critical care areas,[9] in part to avoid inadvertent administration when not clinically indicated. Moreover, the policy requires some hypotonic solutions (some of which are labelled as hypertonic by the manufacturer) to be labelled with a sticker reading "high-risk hypotonic solution". Clearly, labelling a bag of IV solution with separate, yet conflicting, information is less than ideal. Correcting the labelling of these products at the time of manufacture would be a better approach to avoid potential errors.

We acknowledge that clinicians do not make decisions about IV fluid administration on the basis of product labelling, but rather according to education and teaching that would be gained through medical training. Therefore, the realized clinical impact of this labelling error has likely been negligible. However, the potential for severe harm, especially in pediatric patients, cannot be overstated. The inadvertent administration of hypotonic fluid that is labelled as hypertonic could be catastrophic and could result in morbidity and mortality.[6] Therefore, we should not wait for a negative outcome but rather should recommend that companies change their product labelling so that negative outcomes can be avoided altogether.

CONCLUSION

We intend to submit our observations regarding inappropriate IV solution labelling to Canadian and US regulatory bodies in the hope that our analysis spurs changes toward more accurate labelling in the future.

References

1. Friedman JN. Risk of acute hyponatremia in hospitalized children and youth receiving maintenance intravenous fluids. Canadian Paediatric Society; 2018 [cited 2022 Oct 25]. Available from: https://www.cps.ca/en/documents/position/acute-hyponatremia-in-hospitalized-children-and-youth
2. Friedman JN, Beck CE, DeGroot J, Geary DF, Sklansky DJ, Freedman SB. Comparison of isotonic and hypotonic intravenous maintenance fluids. a randomized clinical trial. *JAMA Pediatr*. 2015;169(5):445-51.
3. Playfor SD. Hypotonic intravenous solutions in children. *Expert Opin Drug Saf*. 2004;3(1):67-73.
4. *Patient safety alert 22: Reducing the risk of hyponatraemia when administering intravenous infusions to children*. National Safety Patient Agency (UK); 2007 Mar 28 [cited 2022 Oct 25]. Available from: https://media.gosh.nhs.uk/documents/NPSA_Reducing_the_risk_ofs_fluids_to_children.pdf
5. Feld LG, Neuspiel DR, Foster BA, Leu MG, Garber MD, Austin K, et al.; Subcommittee on Fluid and Electrolyte Therapy. Clinical practice guideline: maintenance intravenous fluids in children. *Pediatrics*. 2018;142(6):e20183083
6. Henry DA. In the clinic: Hyponatremia. *Ann Intern Med*. 2015; 163(3):ITC1-19.
7. Knowledge and monitoring deficits contribute to hospital-acquired hyponatremia. *ISMP Can Saf Bull*. 2015;15(11):1-5.
8. Hospital-acquired acute hyponatremia: two reports of pediatric deaths. *ISMP Can Saf Bull*. 2009;9(7):1-4.
9. Clinical practice guideline no. 80.30: IV fluids – infants, children and adolescents (prescribing, administration, safe storage/labeling). IWK Health Centre; 2014.
10. Uslusoy E, Mete S. Predisposing factors to phlebitis in patients with peripheral intravenous catheters: a descriptive study. *J Am Acad Nurse Pract*. 2008;20(4):172-80.

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Competing interests: For activities unrelated to the work reported here, Karthik Tennankore received an investigator-initiated grant from Otsuka; consulting fees from Baxter, Bayer, Otsuka, Astra Zeneca, GSK, and Vifor; and speaker's fees from Bayer, Otsuka, Vifor, and Bayer; Dr Tennankore has also participated on an advisory board for Quanta. No other competing interests were declared.

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Funding: None received.

The New Brunswick Pharmacy Assessment Clinic: A Novel, Pharmacist-Led, Virtual Collaborative Practice Hub for the Assessment and Prescribing of Nirmatrelvir/Ritonavir for Patients with COVID-19

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Can J Hosp Pharm. 2023;76(4):327-30 https://doi.org/10.4212/cjhp.3365

INTRODUCTION

Collaborative practice agreements (CPAs) are formal regulatory agreements, differing in scope, area, and format from one jurisdiction or institution to another, between pharmacists and physicians.[1] CPAs outline roles and responsibilities that may be delegated to a pharmacist in addition to what is identified as the baseline scope of practice, such as therapeutic drug monitoring and concurrent medication modification.[2] These agreements have resulted in improved pharmacist job satisfaction, overall patient satisfaction, and positive economic impacts.[3-10] Despite these benefits, the CPA model continues to be underutilized in Canada. For example, in the province of New Brunswick, only 22 (2.3%) of 943 licensed pharmacists held an active CPA in mid-2022. This situation represents a missed opportunity in a strained health care system.[11,12]

The authorization of nirmatrelvir/ritonavir by Health Canada on January 17, 2022, led to the establishment of a regional CPA for assessment and prescribing of this medication for New Brunswickers with COVID-19. Nirmatrelvir/ritonavir is an orally administered antiviral for the treatment of mild to moderate COVID-19 infections, in those at high risk for progression to severe disease.[13] A limited initial supply of the drug required careful triage to ensure that those who would benefit most from this treatment were given access.[14,15] At the outset, provincial and territorial governments were tasked with developing individualized nirmatrelvir/ritonavir distribution plans.[16] In most jurisdictions, assessment and prescribing of nirmatrelvir/ritonavir was initially performed by primary care providers.[17,18] New Brunswick opted to establish a CPA that allowed a selected group of hospital pharmacists to perform patient triage and to be the initial sole prescribers for nirmatrelvir/ritonavir therapy.

In consultation with the Horizon and Vitalité Health Networks (New Brunswick's 2 regional health authorities [RHAs]), and with assistance from the New Brunswick College of Pharmacists, a pharmacist-led CPA permitting nirmatrelvir/ritonavir prescribing was developed. This novel approach to nirmatrelvir/ritonavir assessment and prescribing was undertaken by the Office of the Chief Medical Officer of Health because of an already-increasing burden on primary care providers, with pharmacists being considered well suited to take on this new and important role.[19-22] Development of this CPA model took into consideration the requirement for bilingual service and the need for equitable, widespread access across rural and urban communities.[18] To meet care needs, a virtual pharmacist-run nirmatrelvir/ritonavir assessment clinic, named the Pharmacy Assessment Clinic (PAC), was created in less than a week. The PAC operated 7 days per week from January 24 to April 11, 2022. After the PAC closing date, assessment and prescribing duties were extended to all primary care providers within New Brunswick, in addition to the PAC pharmacists.

To the authors' knowledge, at the time of clinic development, the PAC was a first-of-its-kind pharmacist-led model of care for the assessment and prescribing of nirmatrelvir/ritonavir, with pharmacists as the sole prescribers in the province. In subsequent months, similar models would be employed in other provinces, such as Nova Scotia, where its use continues.

DESCRIPTION OF THE PROGRAM

Clinic Structure

Between the time of clinic development and the date of clinic dissolution, 16 hospital pharmacists staffed within both RHAs were reassigned from regular patient care duties

or were temporarily hired to work in the PAC. Pharmacists undertook self-guided training and applied for a CPA for the assessment and prescribing of nirmatrelvir/ritonavir with the New Brunswick College of Pharmacists. As part of this agreement, 13 physicians were available as prescribing collaborators to provide guidance on a rotating on-call basis. Brief virtual team huddles, held on weekday mornings, involved the PAC pharmacists, administrative assistants, and RHA pharmacy managers. These meetings facilitated real-time review of evidence, discussion of complicated drug therapy problems, operational changes, and staff concerns. Regular discussions between clinic staff and pharmacy managers enabled streamlining of processes and continuing education for pharmacists. Additionally, a clinical guideline with assessment tools, recommendations, and resources was developed and added to the RHAs' antimicrobial stewardship application.

Clinic Format

A virtual clinic model was established for the PAC with support from provincial information technology services (Figure 1). This model allowed pharmacists to work remotely and to provide care from any location in the province. Each PAC pharmacist was provided with a mobile telephone and a laptop computer with software and virtual private network access, which were necessary to provide the services in a paperless environment. The PAC members had access to a shared Microsoft Outlook inbox, which was set up to accept email-to-email and fax-to-email transmissions. A toll-free clinic phone number was also created for referral and drug information purposes, with voicemail messages sent to the shared Outlook inbox as voice files.

Patient referrals were submitted by designated public health nurses, extra-mural nurses, First Nations health centres, and long-term care facilities once a positive result on polymerase chain reaction testing was confirmed and the patient agreed to be assessed further for the opportunity to receive a prescription for nirmatrelvir/ritonavir. Nurse screeners used a standardized assessment form to gather information on patient demographic characteristics, date of symptom onset, date of COVID-19 diagnosis, and vaccination status. Assessment forms were subsequently faxed or emailed to the shared PAC inbox.

Role of the Pharmacist

The PAC pharmacists triaged referrals by urgency, according to the time since symptom onset, with patients on day 5 of symptoms being prioritized in light of evidence-based initiation time sensitivity.[23] Upon receipt of referrals, the PAC pharmacists completed virtual assessments through direct consultation of electronic health records. Assessment components included, but were not limited to, pharmacokinetic and pharmacodynamic drug interactions, date of symptom onset, laboratory values (notably renal and hepatic function),

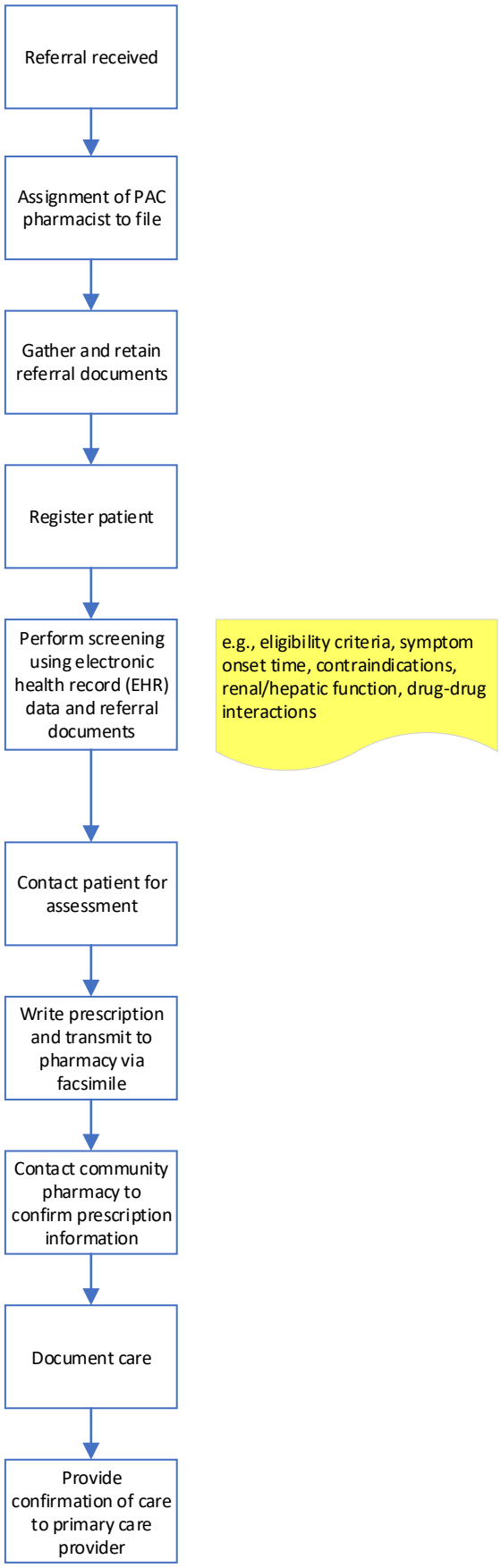

FIGURE 1. Workflow process map for the Pharmacy Assessment Clinic.

and patient preference. Explicit consent for care was obtained by telephone, with the PAC pharmacists providing patient-centred and evidence-informed education about the risks and benefits of therapy. Substitute decision-makers provided consent when the patient was unable to do so.

The PAC pharmacists had 3 options upon completion of each patient assessment: to prescribe a full dose of nirmatrelvir/ritonavir, to prescribe a half dose of the medication (if estimated glomerular filtration rate was 30–60 mL/min), or to not authorize a prescription. A standardized template was used for all prescriptions. This template contained a section for additional medication changes made to address concomitant drug–drug interactions. The PAC pharmacist then faxed the prescription to one of several designated community pharmacies across the province, for further assessment and dispensing. The community pharmacists were able to reach the PAC by phone if they had any questions about the prescription. In addition, PAC pharmacists confirmed all issued prescriptions with patients' primary care providers. All follow-up care was performed in collaboration with dispensing community pharmacies or the patient's primary care provider.

EVALUATION OF THE PROGRAM

Preliminary data for the period January 24 to April 11, 2022, showed a total of 1112 referrals for nirmatrelvir/ritonavir received by the PAC. Of these, more than two-thirds (n = 413, 37.1%) resulted in prescriptions being sent to community pharmacies; for the remaining 699 referrals (62.9%), no prescription was sent. An initial roster of 17 community pharmacies in New Brunswick, selected by the provincial Department of Health, dispensed nirmatrelvir/ritonavir to patients. The number of community pharmacies gradually increased as the inventory of medication allowed, with all community pharmacies granted ordering and dispensing privileges by April 11, 2022.

Subjective and objective data analysis of the virtual pharmacist-led hub clinic and its impact on the health care of New Brunswickers is ongoing, with research and ethics board approvals obtained. Several modes of data collection and analysis may be used in these evaluations, including surveys of stakeholders, interviews with clinic management figures, and intervention-specific analyses of the care provided.

IMPLICATIONS AND SIGNIFICANCE FOR PRACTICE

The involvement of clinical pharmacists in the care of patients with diagnoses of infectious diseases is not a novel concept, nor is pharmacist assessment and prescribing in this realm. What is unique, however, is the accessibility of this clinical model, which provided virtual pharmacologic assessment and clinical interventions to patients in New Brunswick, regardless of location, mobility, or necessity for isolation due to illness. Given the complicated drug interaction profile of nirmatrelvir/ritonavir, in addition to the need to ensure equitable distribution of limited resources, hospital pharmacists provided a crucial service to residents of New Brunswick.

This innovative clinical model of assessment and prescribing could be carried forward into other areas of clinical pharmacy practice. Notably, it could work particularly well when access to medication and care is limited, when clinical assessment is complex, or when specialized medication-related expertise is required. This model offers an innovative method to utilize both CPAs and the extensive knowledge of pharmacists. Several subareas within the health care domain that could be considered for this centralized, referral-based clinical model include HIV pre-exposure prophylaxis, antimicrobial stewardship, symptomatic management during oncology treatments, and management of chronic disease states such as hypertension and diabetes mellitus.

CONCLUSION

Pharmacists have been, and continue to be, regarded as the medication experts within the broader health care team. The authors believe this concept was proven and exceeded through the New Brunswick PAC. Through technology, collaboration, clinical expertise, and the ability to provide care in both official languages, the PAC provided timely and judicious care to patients in the entire province at a time when such care was needed most.

References

1. *Advancing team-based care through collaborative practice agreements: a resource and implementation guide for adding pharmacists to the care team.* US Department of Health and Human Services, Centers for Disease Control and Prevention; 2017 [cited 2022 Jun 29]. Available from: https://www.cdc.gov/dhdsp/pubs/docs/cpa-team-based-care.pdf
2. Kelly DV, Bishop L, Young S, Hawboldt J, Phillips L, Montgomery Keough T. Pharmacist and physician views on collaborative practice. *Can Pharm J (Ott).* 2013;146(4):218-26.
3. Pearson GJ. Remote pharmacist practice model of collaboration in primary care: potential for benefit or an opportunity lost? *Circ Cardiovasc Qual Outcomes.* 2018;11(6):e004801.
4. Brock KA, Doucette WR. Collaborative working relationships between pharmacists and physicians: an exploratory study. *J Am Pharm Assoc (2003).* 2004;44(3):358-65.
5. Zillich AJ, McDonough RP, Carter BL, Doucette WR. Influential characteristics of physician/pharmacist collaborative relationships. *Ann Pharmacother.* 2004;38(5):764-70.
6. Yuksel N, Eberhart G, Bungard TJ. Prescribing by pharmacists in Alberta. *Am J Health Syst Pharm.* 2008;65(22):2126-32.
7. Bungard TJ, Schindel TJ, Brocklebank C. A description of a multistaged professional development course for practising pharmacists in anticoagulation management. *Can Pharm J (Ott).* 2012;145(1):14-16.e1.
8. Lott BE, Anderson EJ, Zapata LV, Cooley J, Forbes S, Taylor AM, et al. Expanding pharmacists' roles: pharmacists' perspectives on barriers and facilitators to collaborative practice. *J Am Pharm Assoc (2003).* 2021;61(2):213-220.e1.

9. Bryk A, Koontz S, Mayor J, Betcher J, Tombleson R, Bookout R, et al. Characterization of collaborative practice agreements held by hematopoietic stem cell transplant pharmacists. *J Oncol Pharm Pract.* 2019;25(3):558-66.
10. *Collaborative practice agreements and pharmacists' patient care services: a resource for pharmacists.* US Department of Health and Human Services, Centers for Disease Control and Prevention; 2013 [cited 2022 June 29]. Available from: https://www.cdc.gov/dhdsp/pubs/docs/translational_tools_pharmacists.pdf
11. *National statistics.* National Association of Pharmacy Regulatory Authorities; 2022 Jan 1 [cited 2022 Jun 29]. Available from: https://www.napra.ca/national-statistics
12. *Find a pharmacy professional* [official register]. New Brunswick College of Pharmacists; 2022 Jul [cited 2022 Jul 25]. Available from: https://nbcp-opnb.alinityapp.com/client/publicdirectory
13. *Considerations for the use of nirmatrelvir/ritonavir (brand name Paxlovid) to treat COVID-19.* Government of Canada; 2022 Jun 22 [cited 2022 Jun 29]. Available from: https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/guidance-documents/considerations-nirmatrelvir-ritonavir-paxlovid.html
14. *Archived: Considerations for the use of nirmatrelvir/ritonavir to treat COVID-19 in the context of limited supply [2022-02-24].* Government of Canada; 2022 Feb 24 [cited 2022 Jun 29]. Available from: https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/guidance-documents/considerations-nirmatrelvir-ritonavir-paxlovid/archived.html
15. *CADTH drug implementation advice: nirmatrelvir and ritonavir (Paxlovid).* CADTH; 2022 Jan 17 [cited 2022 Jun 29]. Available from: https://www.cadth.ca/sites/default/files/pdf/HD0007%20Paxlovid_Final.pdf
16. *Oral COVID-19 treatment (Paxlovid™).* Gouvernement du Québec; 2022 May 4 [cited 2022 Jun 29]. Available from: https://www.quebec.ca/en/health/health-issues/a-z/2019-coronavirus/symptoms-transmission-treatment/oral-treatment-against-covid-19-paxlovidmc
17. Bossé O. Très peu utilisé, le Paxlovid maintenant prescrit par les pharmaciens. *Le soleil.* 2022 Mar 31 [cited 2022 Jun 29]. Available from: https://www.lesoleil.com/2022/04/01/tres-peu-utilise-le-paxlovid-maintenant-prescrit-par-les-pharmaciens-b5204e175cd66be1c1571e6caa240ddd
18. *New Brunswick population report February 2022.* Government of New Brunswick; 2022 Feb [cited 2022 Jun 29]. Available from: https://www.nbjobs.ca/sites/default/files/2022-02-07-LMI-Population-Report-EN_0.pdf
19. de Moissac D, Bowen S. Impact of language barriers on quality of care and patient safety for official language minority francophones in Canada. *J Patient Exp.* 2019;6(1):24-32.
20. Cooper J, Crandall L. Planning for a pandemic and preparing for the future. *Can Pharm J (Ott).* 2006;139(4):59-60.
21. Jalili M, Niroomand M, Hadavand F, Zeinali K, Fotouhi A. Burnout among healthcare professionals during COVID-19 pandemic: a cross-sectional study. *Int Arch Occup Environ Health.* 2021;94(6):1345-52.
22. Gebru AA, Birhanu T, Wendimu E, Ayalew AF, Mulat S, Abasimel HZ, et al. Global burden of COVID-19: situational analysis and review. *Hum Antibodies.* 2021;29(2):139-48.
23. Famularo DE, Koloski J, Marathe J, Au A, Hamilton S, Mordino J, et al. Pharmacist-driven assessment and prescribing of COVID-19 therapeutics: a large, tertiary academic medical center's experience. *Am J Health Syst Pharm.* 2022;79(21):1880-93.

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Competing interests: For activities unrelated to the study reported here, Heather Naylor has received speaker's fees from Otsuka (conference presentation). No other competing interests were declared.

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Funding: None received.

Acknowledgements: The authors acknowledge Dr Anastasia Shiamptanis and Cathy Purvis of the New Brunswick College of Pharmacists, as well as Dr Natalie Banville (Senior Vice President, Client Programs and Medical Affairs, Vitalité Health Network) and Dr Susan Brien (Senior Vice President, Medical, Academic and Research Affairs, Horizon Health Network), for their assistance and support in the development of the Pharmacy Assessment Clinic and the preparation of this manuscript.

Pharmaceutical Care and Services in French Minority Settings across Canada

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Can J Hosp Pharm. 2023;76(4):331-3 https://doi.org/10.4212/cjhp.3407

INTRODUCTION

Research has shown that francophone minority populations across Canada are in poorer health (perceived and actual) than the anglophone majority.[1] According to the 2021 census of the Canadian population, French Canadians are by far Canada's largest minority, with 21.4% of Canadians reporting French as their mother tongue.[2] A report published in 2021 by the Consortium national de formation en santé (CNFS) showed that pharmacists were the least accessible health care providers in Canada when it comes to offering services in French.[3] The University of Ottawa and its Office of Francophone Affairs developed and is implementing a new undergraduate (entry-to-practice) Doctor of Pharmacy (PharmD) program to be offered in French starting in September 2023.

The objectives of this article are to describe the needs of the Canadian population for health care services offered in French by pharmacists outside of Quebec and to briefly introduce the new PharmD program that will be offered in Ottawa, Ontario.

DESCRIPTION

As of 2022, there were 10 pharmacy programs in Canadian universities. Such programs are offered in English at 2 other Ontario institutions (University of Toronto, with about 240 students in 2022, and University of Waterloo, with about 120 students).[4,5] There are no other pharmacy training programs offered in French in the province of Ontario. Current student enrolment for the English programs amounts to a total of 360 for this province, which had an estimated population of more than 14 million in 2022.[6]

Two pharmacy training programs are offered in French in Canada, both in the province of Quebec (Université Laval, with about 190 students, and Université de Montréal, with about 200 students).[7,8] Given the total of 390 pharmacy students, enrolment in Quebec, which had an estimated population of more than 8.5 million in 2022,[6] has been greater than enrolment in Ontario (before initiation of the new PharmD program).

Understanding health care challenges in French minority settings outside of Quebec was an important step in the development of the new PharmD program. A minority official language setting is defined as a situation where there is a potential significant demand for services in the French minority official language, the place of residence is a province or territory outside of Quebec, and the mother tongue or home language (spoken most often or on a secondary basis) includes French as a single response on the census questionnaire or in combination with another language.[2] Educating future pharmacists has been an aspiration for the University of Ottawa since the early 1990s, and this was the university's fourth attempt to create such a program. This time, the university learned from its previous experiences, several internal analyses, and a variety of external assessments with a view to demonstrating the need to train more bilingual pharmacists outside of Quebec.

Some of the findings of these background analyses are summarized below.

Health of Francophones in Minority Settings

Research has shown that francophone minority populations across Canada are in poorer health (perceived and actual) than the anglophone majority.[1] In addition, francophones in minority communities are generally older, less educated, and in a less favourable economic situation. A recent study showed that francophones who were treated by a French-speaking physician in Canada had 24% lower odds of death than those who received care from a non-French-speaking physician.[9] For allophones, the results were even more striking, with 54% lower odds of death.[9] Although language is not considered to be a determinant of health, it plays a key role with regard to access to health services, quality of care, and patient safety.

Accessibility to Pharmacy Services in French

Over the past 25 years, considerable effort has gone into implementing health care training programs for francophones throughout Canada, but pharmacy has not benefited

from this momentum. This situation could explain the fact that outside the province of Quebec, the proportion of pharmacists able to speak French is significantly underrepresented relative to other health care professionals. As noted above, the CNFS recently reported that pharmacists are the least accessible health care providers in Canada in terms of services offered in French outside Quebec.[3] In Ontario, there is a maldistribution of French-speaking pharmacists, which may limit the ability of francophone patients to receive pharmacy services in their preferred language.[10] In that study, the distribution of pharmacists was assessed in relation to the larger concentration of the francophone population, geography (north versus south), and community type (rural versus urban), and was found to vary according to each of these characteristics.[10]

Pharmacists' Expanded Scope of Practice across Ontario and Canada

In several provinces and territories, the pharmacist's role has evolved in recent years to include a broader range of primary care services not limited to vaccination. For example, in recent months, Ontario and Yukon have expanded pharmacists' scope of practice to include prescribing medications for common minor ailments.[11,12] In these jurisdictions, the patient can now look to the pharmacist to receive treatments that, in the past, would have been provided by a physician or other health care professional. Pharmacists have become an integral component of the continuum of care, which leads to the need for more training resources.

Increased Demand for Pharmacists Able to Offer Services in French

In addition to many changes in the pharmacist's scope of practice, the demand for pharmacists is expected to increase in the coming years because of population growth, aging of the population, the increasing complexity of health care, the development of new drugs, and an increase in the number of medications prescribed.

These factors, as well as existing data consulted in the course of planning for the new program and certain data collected specifically to assess pharmacy services available in French, all support the current and future need for French-speaking pharmacists in Canadian francophone minority communities.

Overall, estimates based on the 2021 census of Canada demonstrate the need for an additional 750 French-speaking pharmacists in Canada outside of Quebec by 2026.[2] The training of pharmacists in French in Ontario will help to address the challenge of offering pharmaceutical services and care in French, mitigating anticipated pharmacist shortages and making the profession more accessible to the francophone minority population.

IMPLICATIONS: A NEW DOCTOR OF PHARMACY PROGRAM

Following work to better understand needs and interest, a team of experts (including pedagogical specialists, pharmacists, faculty members, and external representatives) was set up to develop the program in its entirety. Training will be adapted to local needs and will focus on various innovative educational elements. For example, this new undergraduate pharmacy program will be the first in Canada based on entrustable professional activities (EPAs). The EPAs were further broken down by competency, aligned with both the 2017 educational outcomes of the Association of Faculties of Pharmacy of Canada (AFPC) [13] and the 2014 professional competencies for Canadian pharmacists at entry to practice of the National Association of Pharmacy Regulatory Authorities (NAPRA).[14] Teaching methods will be based on active and experiential learning, planned formative and certificative assessment, and integrated interprofessionalism. The curriculum design will follow a spiral pedagogical method. The 2 main goals of a spiral curriculum are building continuity from one year to the next in all areas of study (vertical integration) and building interrelationships among these disciplines (horizontal integration). Integration helps create a schema that allows for effective teaching of complex and higher-order thinking skills, which in turn facilitates the development of proficiency in problem-solving abilities that are not usually addressed by a traditional curriculum.[15]

Starting in September 2023, the new undergraduate PharmD program offered at the University of Ottawa will train 60 students per cohort per year who will be able to practise as pharmacists in various inpatient and outpatient care settings. This program, offered in French, is aimed primarily at francophones from Ontario, as well as francophones from elsewhere in Canada, with the objective of meeting the need for bilingual pharmacists in minority settings.

In addition to meeting the standards of practice set by 2017 AFPC educational outcomes and 2014 NAPRA entry-to-practice competencies,[13,14] a PharmD graduate from the University of Ottawa will have the following skills and abilities:

- communicating effectively with members of the francophone minority community to provide personalized care that meets local needs
- using current scientific evidence to responsibly optimize comprehensive drug therapy for patients and disseminate information in both official languages
- being confident and autonomous to practise in both official languages
- maintaining current skills to proactively contribute to local health services and collaborate optimally with others
- sharing knowledge in the community and with other health care providers to educate the population and contribute to health promotion.

CONCLUSION

Studies have shown that the health of the francophone population in minority settings across Canada is poor, with limited access to services affecting the quality of care. Of all health care providers, pharmacists are the least accessible to offer pharmaceutical care and services in French outside of Quebec. The training of bilingual pharmacists is key to addressing these challenges and better serving the population. The new pharmacy program at the University of Ottawa will be the only undergraduate PharmD program in Canada based on EPAs and will have the main objective of meeting the need for increased accessibility of pharmaceutical care and services by bilingual pharmacists in minority settings across Ontario and Canada as a whole.

References

1. Bouchard L, Gilbert A, Landry R, Deveau K. Social capital, health, and francophone minorities. *Can J Public Health.* 2006;97 Suppl 2:S16-S20.
2. *Census of population* [2021]. Statistics Canada; [cited 2022 Dec 30]. Available from: https://www12.statcan.gc.ca/census-recensement/index-eng.cfm
3. Diaz Pinsent Mercier Research Inc. *Accès aux services en santé dans la langue officielle de leur choix par les minorités francophones hors Québec. Analyse de données secondaires.* Consortium national de formation en santé; 2021 May 3 [cited 2022 Dec 30]. Available from: https://cnfs.net/wp-content/uploads/2021/06/DPM-Acc%C3%A8s_services_en_sant%C3%A9_langue_officielle_minorit%C3%A9s_francophones_hors_Qu%C3%A9bec_Rapport_3mai2021.pdf
4. Programs: Doctor of Pharmacy (PharmD): Frequently asked questions [webpage]. University of Toronto, Leslie Dan Faculty of Pharmacy; [cited 2022 Dec 30]. Available from: https://www.pharmacy.utoronto.ca/programs/doctor-pharmacy-pharmd/frequently-asked-questions#:~:text=Approximately%20240%20students%20are%20admitted%20to%20the%20PharmD%20program%20each%20year
5. Pharmacy: Future students: Doctor of Pharmacy (PharmD) [webpage]. University of Waterloo, School of Pharmacy; [cited 2022 Dec 30]. Available from: https://uwaterloo.ca/pharmacy/future-students/doctor-pharmacy-pharmd
6. Ontario population 2022 [webpage]. [cited 2022 Dec 30]. Available from: https://canadapopulation.org/ontario-population/
7. Faculté de pharmacie : Doctorat de 1er cycle en pharmacie [webpage]. Université de Montréal, Faculté de pharmacie; [cited 2022 Dec 30]. Available from: https://admission.umontreal.ca/programmes/doctorat-de-1er-cycle-en-pharmacie/#:~:text=Le%20Pharm.,annuelle%20est%20de%20200%20%C3%A9tudiants
8. Faculté de pharmacie : Programmes : Doctorat de premier cycle en pharmacie [webpage]. Université Laval; [cited 2022 Dec 30]. Available from: https://www.pha.ulaval.ca/etudes/programmes/doctorat-de-premier-cycle-en-pharmacie
9. Seale E, Reaume M, Batista R, Eddeen AB, Roberts R, Rhodes E, et al. Patient–physician language concordance and quality and safety outcomes among frail home care recipients admitted to hospital in Ontario, Canada. *CMAJ.* 2022;194(26):E899E908.
10. Timony PE, Waite N, Houle S, Violette R, Gauthier AP. The pharmacist is in: the availability and distribution of French-speaking pharmacists in Ontario. *Minor Linguist Soc.* 2022;18:175-96.
11. Government of Yukon expands services for pharmacists to include prescribing [news release]. Government of Yukon; 2022 Dec 28 [cited 2022 Dec 30]. Available from: https://yukon.ca/en/news/government-yukon-expands-services-pharmacists-include-prescribing
12. Expanded scope of practice: minor ailments. Ontario College of Pharmacists; 2022 [cited 2022 Dec 30]. Available from: https://www.ocpinfo.com/practice-education/expanded-scope-of-practice/minor-ailment/
13. *AFPC educational outcomes for first professionnal degree programs in pharmacy in Canada 2017*. Association of Faculties of Pharmacy of Canada; 2017 Jun [cited 2022 Dec 30]. Available from: http://www.afpc.info/system/files/public/AFPC-Educational%20Outcomes%202017_final%20Jun2017.pdf
14. *Professional competencies for Canadian pharmacists at entry to practice*. National Association of Pharmacy Regulatory Authorities; 2014 Mar [cited 2022 Dec 30]. Available from: https://napra.ca/wp-content/uploads/2022/09/NAPRA-Comp-for-Cdn-PHARMACISTS-at-Entry-to-Practice-March-2014-b.pdf
15. Dowding TJ. The application of a spiral curriculum model to technical training curricula. *Educ Technol.* 1993;33(7):18-28.

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Funding: None received.

Acknowledgements: For their support in the creation of the program described here, the authors thank the University of Ottawa PharmD Working Group (Pierre Moreau, educational consultant and past dean of pharmacy, Kuwait University; Pierre Giguère, pharmacist; Daniel Figeys, director of the new School of Pharmaceutical Sciences, University of Ottawa; Patrick Leclair, family physician practising in a minority setting and director of the Health and Wellness Clinic, University of Ottawa; and John Leddy, professor in the Faculty of Medicine, University of Ottawa) and the Office of Francophone Affairs, Faculty of Medicine, University of Ottawa.

Periprocedural Management with Therapeutic Tinzaparin for a Hemodialysis Patient with a Mechanical Heart Valve

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Can J Hosp Pharm. 2023;76(4):334-6 https://doi.org/10.4212/cjhp.3402

INTRODUCTION

Warfarin remains the mainstay for preventing thrombosis in patients with mechanical heart valves.[1] Inevitably, these patients require screening or interventional procedures at some point, during which the warfarin therapy must be held and a shorter-acting agent (e.g., low-molecular-weight heparin [LMWH] or unfractionated heparin) used to limit the duration of subtherapeutic anticoagulation.[2] Unfractionated heparin has typically been used for patients undergoing hemodialysis (HD). However, unlike the situation for LMWH, which can be administered in an ambulatory setting, administration and monitoring of IV unfractionated heparin require hospitalization. The LMWHs are primarily cleared by the kidney; therefore, the main concern about their use in this setting is the risk of accumulation in patients with creatinine clearance (CrCl) below 30 mL/min.[3] Tinzaparin is the largest LMWH and the least dependent on renal clearance.[3] Data suggest that accumulation does not occur with therapeutic doses of tinzaparin in patients with CrCl above 20 mL/min; hence, utilization of this drug is not recommended when CrCl is below 20 mL/min.[3]

Here, we describe an HD-dependent patient who was taking warfarin after mechanical heart valve replacement and who received therapeutic tinzaparin for periprocedural bridging related to hernia surgery, because there was a need to avoid hospitalization.

CASE REPORT

A 36-year-old man who was undergoing HD and was taking warfarin because of an On-X mechanical aortic valve replacement (Artivion) (with preferred international normalized ratio [INR] target of 2.0–2.5, as specified by the cardiology team) noted a swelling approximately the size of his palm in the right inguinal area.* The swelling caused enough pain to prematurely stop the HD sessions, and laparotomy was required to repair the right inguinal hernia.

*The patient provided verbal consent for publication of this case report.

At the age of 9 years, the patient had been given a diagnosis of congenital polycystic kidney disease, and he had been undergoing nocturnal intermittent HD 3 times weekly (duration 6 hours, blood flow rate 400 mL/min, dialysate flow rate 500 mL/min for all sessions). He had major depressive disorder, type 2 diabetes mellitus, and secondary hyperparathyroidism with parathyroid resection at the age of 33. Dermatological conditions were psoriasis and leukocytoclastic vasculitis. Gastrointestinal conditions were adenomyomatosis of the gallbladder and cholelithiasis. Cardiovascular conditions were dyslipidemia, hypertension, borderline aortic root/ascending aorta dilatation, pacemaker insertion for complete heart block, and *Staphylococcus aureus* infectious endocarditis of the bicuspid aortic valve. The aortic valve was initially replaced with a tissue valve at age 33; however, the patient experienced aneurysmal outpouching below the aortic valve with a fistula to the right atrium, necessitating re-operation 2 months later with implantation of the mechanical valve.

Outpatient medications were calcium carbonate 1000 mg 3 times daily, calcitriol 0.25 µg daily, darbepoetin alfa 150 µg administered intravenously every 14 days, insulin aspart administered subcutaneously twice daily, insulin glargine administered subcutaneously once daily, a general-purpose multivitamin daily, pantoprazole magnesium 40 mg daily, repaglinide 1 mg 3 times daily, warfarin daily as directed by the anticoagulation clinic, and acetylsalicylic acid (ASA) 81 mg daily.

The anticoagulation clinic, which managed the patient's warfarin therapy, was consulted for periprocedural anticoagulation management, in light of a strong preference to avoid hospitalization. The patient's recent laboratory results included body mass index 29.9 (height 182 cm, weight 99 kg), serum creatinine 606 µmol/L, estimated glomerular filtration rate 9 mL/min/1.73 m^2, and calculated CrCl 18 mL/min. Although data support a target INR of 1.5–2.0 for low-risk patients with a mechanical On-X aortic valve who are receiving ASA therapy, a collective decision was

made to target this patient's INR at 2.0–3.0, and preferably between 2.0 and 2.5, given the bleeding risk associated with HD.[3] The weekly warfarin requirement at 3 months before surgery was 35 mg (5 mg daily), with weekly INR results between 1.7 and 2.8. Three weeks before the procedure, the maintenance dose of warfarin was increased to 6 mg one day of the week, with 5 mg on all other days of the week.

The patient's periprocedural anticoagulation with tinzaparin is outlined in Figure 1. As per periprocedural guidelines,[2] ASA was continued throughout periprocedural management. No bleeding or clotting complications were noted during the procedure, and intraoperative blood loss was about 50 mL. Six days later, the INR was 1.8, whereupon the anticoagulation clinic implemented a higher daily warfarin maintenance dose of 6 mg on 2 days of the week, with 5 mg on all other days of the week. Fourteen days after the procedure, the patient's INR was 1.7, whereupon the anticoagulation clinic implemented a further weekly dose increase, to 6 mg on 3 days of the week, with 5 mg on all other days of the week. One week later, his INR was therapeutic, at 2.1. Notably, the postprocedure warfarin dose escalation was conservative, given data supporting a target INR of 1.5–2.0 (with ASA) for patients with an On-X aortic valve.[3]

DISCUSSION

Pharmacokinetic and pharmacodynamic studies of tinzaparin have outlined excellent bioavailability and predictable pharmacodynamic properties, and under ideal circumstances (CrCl > 20 mL/min) monitoring for accumulation of the drug is not needed.[4] The elimination half-life is 3–4 hours, with metabolism involving both the renal and reticuloendothelial systems.[4]

Evidence for the use of LMWH in HD patients requiring periprocedural management of warfarin is limited. A single randomized controlled trial (RCT) investigated anti-Xa levels 20–24 hours after administration of 3 therapeutic doses of either tinzaparin or dalteparin just before HD.[5] Notably, procedures were scheduled to occur the day after HD and were cancelled if repeat anti-Xa levels exceeded 0.2 IU/mL. Mean (standard deviation [SD]) predialysis trough anti-Xa levels suggested accumulation of both tinzaparin (n = 17 patients; 0.37 [SD 0.23] IU/mL) and dalteparin (n = 12 patients; 0.62 [SD 0.41] IU/mL). Other limited evidence for tinzaparin in HD patients is from settings outside of periprocedural management.[6-8] For example, the IRIS substudy, involving 87 patients with renal impairment who received therapeutic doses of tinzaparin (over a mean of 8.7 days), showed no statistically significant difference in accumulation between groups with moderate (CrCl 30–60 mL/min) and severe (CrCl ≤ 30 mL/min) renal impairment.[6] In these 2 groups, mean peak anti-Xa levels were 0.86 (SD 0.34) and 0.87 (SD 0.31), respectively. The Trivet study involved 148 patients, including 7 patients with CrCl below 20 mL/min and 25 HD-dependent patients who received daily therapeutic doses of tinzaparin for 7 days, with samples drawn for monitoring of anti-Xa levels before the third to fifth dose (first measurement) and before the fifth to seventh dose (second measurement).[7] The highest reported mean anti-Xa levels were 0.41 IU/mL and 0.35 IU/mL after the first and second measurements, respectively. Another study recommended against empiric dose adjustment of tinzaparin in those with moderate (which would have entailed a 25% dose reduction) or severe (which would have entailed a 50% dose reduction) renal insufficiency, as defined above, given that subtherapeutic peak anti-Xa levels could introduce the risk of treatment failure.[8]

In light of this evidence and to mitigate LMWH accumulation, we altered our typical periprocedural management strategy.[2] We chose tinzaparin as the anticoagulant because of its favourable pharmacokinetic properties and the need to avoid hospitalization. Weight-based dosing for this patient would have necessitated a total dose of 17 325 IU; using prefilled syringes and taking into account previous clinical experience, we

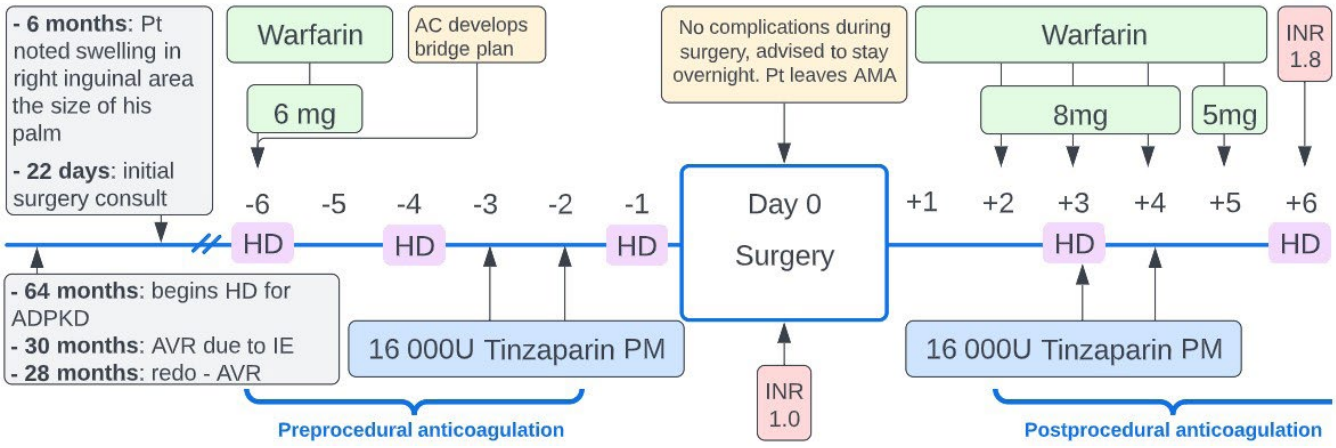

FIGURE 1. Case overview. AC = anticoagulation clinic, ADPKD = autosomal dominant polycystic kidney disease, AMA = against medical advice, AVR = aortic valve replacement, HD = hemodialysis, IE = infectious endocarditis, INR = international normalized ratio, PM = evening.

made the first of 3 empiric alterations by rounding the total dose down to 16 000 IU, instead of up to 18 000 IU. Second, in contrast to the RCT summarized above,[5] we administered 2 instead of 3 doses of tinzaparin before the procedure. Third, the final injection was administered at least 36 hours before the procedure. Given that the authors of the RCT[5] reported accumulation of LMWH, we aimed to limit drug accumulation by empirically reducing our patient's dose, providing fewer injections, and allowing more time between the last injection and the procedure. To monitor these modifications, a sample for measurement of anti-Xa level was to be drawn just before the procedure; however, because of a clinical error, this measurement was not performed.

Our patient had a good outcome, as did most patients in the RCT.[5] Of the 17 patients who received tinzaparin, only 1 experienced a major bleed (after a traumatic arteriovenous fistula puncture). Also in the RCT, prophylactic doses of tinzaparin were administered postoperatively until the INR value was above 2.0, with 63% of patients having undetectable predialysis anti-Xa levels and the remaining having a mean anti-Xa of 0.14 (SD 0.02) IU/mL, which suggested the absence of clinically relevant accumulation.[5] In our case, the surgeon recommended restarting therapeutic anticoagulation 72 hours after the procedure. Given the delayed impact of warfarin on INR, we restarted warfarin 48 hours after the procedure and administered therapeutic doses of tinzaparin for 72 hours after the procedure. To expedite re-establishment of therapeutic INR, our practice is to restart warfarin with 3 bolus doses (1.5 times the maintenance dose), as opposed to resuming maintenance dosing directly.[9] Two days after the second dose of tinzaparin in this case, anti-Xa levels were ordered during HD, but again the samples were not drawn. After 2 doses, the tinzaparin was discontinued because of concerns about potential accumulation with prolonged use, the lack of measurement of anti-Xa level, the increased risk of bleeding from the incision site, and the inherently increased risk of bleeding in HD patients.

Our analysis of this case is limited by the fact that despite being ordered, anti-Xa levels were not measured; this lack of data precludes any quantitative conclusions related to the accumulation of tinzaparin. We note, however, that the surgeon reported a typical amount of blood loss during the procedure, and the patient had no poor outcomes, arguably the most important observation in this case.

CONCLUSION

We have described a modified periprocedural management strategy for a patient undergoing HD, in which we endeavoured to mitigate tinzaparin accumulation by using a lower-dose prefilled syringe, ensuring a limited number of tinzaparin injections (2 before and 2 after the procedure), and lengthening the interval between the last tinzaparin injection and the procedure to at least 36 hours. Despite the lack of measurement of anti-Xa levels, we were reassured by the absence of adverse outcomes, with a typical amount of blood loss during the procedure itself. To our knowledge, no other case reports of this nature are available, and we propose that our case offers a thoughtful example of ambulatory-based periprocedural management for HD. Further investigation is needed before LMWH (specifically tinzaparin) can be recommended in this patient population.

References

1. Whitlock RP, Sun JC, Fremes SE, Rubens FD, Teoh KH. Antithrombotic and thrombolytic therapy for valvular disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest.* 2012;141(2 Suppl):e576S-e600S.
2. Douketis JD, Spyropoulos AC, Murad MH, Arcelus JI, Dager WE, Dunn AS, et al. Perioperative management of antithrombotic therapy: an American College of Chest Physicians clinical practice guideline. *Chest.* 2022; 162(5):e207-e243.
3. Puskas J, Gerdisch M, Nichols D, Quinn R, Anderson C, Rhenman B, et al. Reduced anticoagulation after mechanical aortic valve replacement: interim results from the prospective randomized on-X valve anticoagulation clinical trial randomized Food and Drug Administration investigational device exemption trial. *J Thorac Cardiovas Surg.* 2014;147(4):1202-11.
4. Helfer H, Siguret V, Mahé I. Tinzaparin sodium pharmacokinetics in patients with chronic kidney disease: practical implications. *Am J Cardiovasc Drugs.* 2020;20(3):223-8.
5. Rodger MA, Ramsay T, MacKinnon M, Westphal M, Wells PS, McCormick B, et al. Tinzaparin versus dalteparin for periprocedure prophylaxis of thromboembolic events in hemodialysis patients: a randomized trial. *Am J Kidney Dis.* 2012;60(3):427-34.
6. Siguret V, Gouin-Thibault I, Pautas E, Leizorovicz A. No accumulation of the peak anti-factor Xa activity of tinzaparin in elderly patients with moderate-to-severe renal impairment: the IRIS substudy. *J Thromb Haemost.* 2011;9(10):1966-72.
7. Lim W, Crowther M, Wang L, Douketis JD, Schnurr T, Moreau C, et al. Serial trough anti-Xa levels to assess low molecular weight heparin accumulation in patients with chronic kidney disease: analysis of Crcl <30 ml/min from the Trivet study. *Blood*. 2016;128(22):90.
8. Olie RH, Meertens NEL, Henskens YMC, ten Cate H. Empirically reduced dosages of tinzaparin in patients with moderate-to-severe renal insufficiency lead to inadequate anti-Xa levels. *Nephron*. 2017;137(2):113-23.
9. Bungard TJ, Mutch J, Ritchie B. A randomized trial of restarting warfarin at maintenance versus loading doses following an elective procedure. *J Thromb Thrombolysis,* 2017;44(4):507-15.

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Competing interests: Tammy Bungard has received an unrestricted quality improvement grant from Pfizer and has served (on a voluntary basis) as cochair of the Patient & Family Committee of Thrombosis Canada; she has also received Fragmin, Lovenox and Innohep cards, which allow drugs to be supplied to patients unable to afford their medications. No other competing interests were declared.

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Funding: None received.

Acetaminophen Dose Considerations in Frail and Malnourished Elderly Patients: A Case Report of Hepatotoxicity with Therapeutic Doses

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Can J Hosp Pharm. 2023;76(4):337-9 https://doi.org/10.4212/cjhp.3415

INTRODUCTION

Acetaminophen is a medication commonly used for older adults.[1] It is used not only to treat fever but also as a first-line analgesic for mild to moderate pain. Although it is generally well tolerated, the main concern with acetaminophen use is drug-induced liver injury. Indeed, acetaminophen is the most frequent cause of drug-induced hepatotoxicity. Hepatotoxicity occurs when supratherapeutic doses of acetaminophen are ingested voluntarily or inadvertently. The results of liver function tests (LFTs) can also be mildly elevated when therapeutic doses are used, but such elevations are usually transient and asymptomatic, and they resolve without lasting effect in healthy individuals.[2] Frail elderly people are at increased risk of acetaminophen-induced hepatotoxicity because they have diminished acetaminophen clearance, diminished glucuronidation, and diminished glutathione reserves and synthesis.[3] All of these factors create challenges for optimal dosing to prevent acetaminophen hepatotoxicity in frail elderly patients. Here, we present a case of acute liver injury associated with therapeutic acetaminophen use in a frail elderly patient.

CASE REPORT

A 69-year-old woman was admitted to the hospital for fracture of the eighth and ninth thoracic vertebrae after a fall.* Her home medications consisted of aripiprazole, citalopram, pantoprazole, vitamin D, vitamin B_{12}, and magnesium. She had a history of falls, intellectual disability, untreated diabetes, severe chronic malnourishment, hypothyroidism, anemia, chronic hyponatremia, bipolar disorder, hiatal hernia, and polyneuropathy. At 30.1 kg and 130 cm, she presented severe cachexia and sarcopenia. The patient reported drinking 2 or 3 beers daily, although her consumption was likely higher than stated, according to her social worker.

*The patient provided written informed consent for publication of her clinical details.

On admission, acetaminophen 650 mg PO 4 times daily was prescribed for pain, and a diazepam protocol was initiated for alcohol withdrawal syndrome. The patient presented with hypoglycemia upon admission (glucose 3.3 mmol/L), and her glycated hemoglobin (HbA1c) was 0.039 or 3.9%. No LFTs were done at the time of admission. However, her aspartate aminotransferase level had been within normal limits 2 months before the hospitalization (38 U/L; normal range 13–39 U/L).

The patient had a second episode of hypoglycemia on day 5 of admission, and LFTs were performed on day 6; the results showed liver injury (Table 1) with acute kidney injury. The differential diagnosis included acetaminophen toxicity, and upon testing at 90 minutes after her last dose, the acetaminophen level was found to be 388 µmol/L (58.7 mg/L; therapeutic serum concentration 66–132 µmol/L).

Abdominal and pelvic ultrasonography showed moderate diffuse liver steatosis without signs of cirrhosis, focal lesions, or biliary tract obstruction. Screening for viral hepatitis yielded negative results. On the same day, the patient became very drowsy with altered state of mind, despite having received no diazepam. She had no abdominal pain, nausea, or asterixis.

Following a gastroenterology consultation, acute liver injury caused by chronic acetaminophen intoxication was diagnosed, as no other causes could be identified. Acetaminophen was discontinued, and *N*-acetylcysteine (NAC) was given. Her LFT results started to improve (Table 1). However, on day 7, she started desaturating, and aspiration pneumonia was diagnosed. Her condition worsened rapidly, and she died of respiratory failure on day 8 of the admission.

DISCUSSION

Acetaminophen hepatotoxicity at therapeutic doses of 4 g/day has been reported in patients with risk factors such as advanced age, lower weight, and chronic alcohol use,[4,5] but not in frail older patients with severe malnutrition. The dose

TABLE 1. Results of Liver Function Tests 2 Months before and during Incident of Acetaminophen-Induced Hepatotoxicity

Timing	AST (U/L)	ALT (U/L)	Total Bilirubin (μmol/L)	INR
Normal range	13–39	8–31	7–23	0.9–1.2
2 months before	38	Not done	Not done	Not done
Day 6				
At 0645	3383	2231	Not done	Not done
At noon		Last dose of acetaminophen given: 650 mg PO		
At 1330	2472	2158	71	1.4
At 1815		21-h perfusion of NAC started		
Day 7	808	1359	75	1.4

ALT = alanine aminotransferase, AST = aspartate aminotransferase, INR = international normalized ratio, NAC = *N*-acetylcysteine.

of acetaminophen given to this patient had been adjusted for her age (2.6 g/day or 21.6 mg/kg per dose). Nonetheless, hepatotoxicity occurred after 6 days of treatment, with the patient's acetaminophen concentration reaching more than 2.5 times the upper limit of normal. The patient had multiple risk factors for hepatotoxicity, including her age, low weight, severe malnutrition (low glutathione production and reserves), and alcohol use (which would have induced the cytochrome P450 2E1 isozyme).

Some guidelines now recommend a maximum dose lower than 4 g/day for long-term use (i.e., more than 7–14 days), but they do not necessarily recommend any adjustment for short-term use, even for elderly patients.[6-8] However, local guidelines recommend a dosage of 15 mg/kg per dose 4 times daily in patients weighing less than 50 kg, regardless of the duration of use.[8] Given that this patient was at high risk for acetaminophen hepatotoxicity, it is unclear whether a weight-based dose adjustment or a dose of 2 g/day might have been sufficient to prevent the liver injury. The causality of the adverse drug reaction was estimated as "probable" on the Naranjo scale.[9]

There are limits to what we can infer from this case. We excluded the main causes of liver injury but could not formally exclude all possible causes of hepatitis. No LFTs were done upon admission, and it is therefore possible that a liver injury was already present, before any acetaminophen intake. Measurement of acetaminophen level was not repeated. A second level would have allowed us to calculate the half-life of elimination, which would in turn have permitted an evaluation of acetaminophen metabolism. Also, it was unknown whether the patient was already taking acetaminophen at home. Nonetheless, even if acetaminophen was not the main cause of her liver injury, it was a contributing factor, given the improvement in her LFT results after acetaminophen was stopped and NAC was given.

CONCLUSION

This case report suggests that for frail elderly patients at high risk of hepatotoxicity, a weight-based dosing strategy for acetaminophen (e.g., 15 mg/kg per dose qid), with monitoring by LFTs, should be applied or an alternative analgesic should be considered. If the decision is made to initiate acetaminophen, LFTs should be performed before initiating the drug and within the first week of treatment.

References

1. Conaghan PG, Arden N, Avouac B, Migliore A, Rizzoli R. Safety of paracetamol in osteoarthritis: what does the literature say? *Drugs Aging*. 2019;36(Suppl 1):7-14.
2. Acetaminophen. In: *LiverTox: clinical and research information on drug-induced liver injury*. National Institute of Diabetes and Digestive and Kidney Diseases; 2012 [updated 2016 Jan 28, cited 2022 Nov 3]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK548162/
3. O'Neil CK, Hanlon JT, Marcum ZA. Adverse effects of analgesics commonly used by older adults with osteoarthritis: focus on non-opioid and opioid analgesics. *Am J Geriatr Pharmacother*. 2012;10(6):331-42.
4. Ging P, Mikulich O, O'Reilly KM. Unexpected paracetamol (acetaminophen) hepatotoxicity at standard dosage in two older patients: time to rethink 1 g four times daily? *Age Ageing*. 2016;45(4):566-7.
5. Claridge LC, Eksteen B, Smith A, Shah T, Holt AP. Acute liver failure after administration of paracetamol at the maximum recommended daily dose in adults. *BMJ*. 2010;341:c6764.
6. Acetaminophen (paracetamol): drug information. In: *UpToDate*. Wolters Kluwer; [cited 2022 Nov 3]. Available from: https://www.uptodate.com. Subscription required to access content.
7. Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J, et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the management of osteoarthritis of the hand, hip, and knee. *Arthritis Care Res (Hoboken)*. 2020;72(2):149-62. Erratum in: *Arthritis Care Res (Hoboken)*. 2021;73(5):764.
8. Roy-Petit J, Laplante JK, Bergeron J. Annexe 12 : Gestion de la douleur chronique non cancéreuse en UCDG. In: *Guide de gestion médicamenteuse en UCDG*. RUSHGQ [Regroupement des unités de courte durée gériatriques et des services hospitaliers de gériatrie du Québec]; 2017 [updated 2021; cited 2022 Nov 3]. Available from: https://rushgq.org/wp-content/uploads/2021/10/Annexe_12_Fiche-douleur-chronique_RUSHGQ_20oct2021_FINALE.pdf
9. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981;30(2):239-45.

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Funding: None received.

Clozapine for Management of Neuropsychiatric Symptoms in Dementia with Lewy Bodies: Case Report and Literature Review

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Can J Hosp Pharm. 2023;76(4):340-5 https://doi.org/10.4212/cjhp.3390

INTRODUCTION

Dementias are a group of neurocognitive disorders characterized by a significant decline in one or more domains of cognition that interferes with a person's ability to function. According to the Canadian Chronic Disease Surveillance System, more than 402 000 older adults are living with some type of dementia, including Alzheimer disease, in Canada (excluding Saskatchewan).[1] Approximately 76 000 new cases of dementia are diagnosed each year, with a projected total annual health care cost of $16.6 billion for Canadians with dementia by 2031.[1] Dementia with Lewy bodies (DLB) is a type of dementia for which probable diagnosis requires the presence of dementia and at least 2 core clinical features.[2] The core clinical features of DLB are fluctuating cognition, recurrent visual hallucinations, rapid eye movement sleep behaviour disorder, and 1 or more features of parkinsonism, such as bradykinesia, rest tremor, and rigidity.[2] These symptoms can be very disabling and significantly affect quality of life for both patients and their families.

"Lewy body dementia" is an umbrella term for major neurocognitive disorders caused by Lewy body pathology. Parkinson disease dementia (PDD) and DLB are the 2 main syndromes within Lewy body dementia. Together, they constitute the second most common type of degenerative dementia in persons older than 65 years.[3] The major clinical feature that differentiates PDD and DLB is the relative timing of the onset of parkinsonism and dementia. In PDD, motor symptoms precede dementia by at least 1 year, but in DLB, they occur within 1 year of each other.[4] A systematic review estimated that the proportion of individuals with DLB ranged from 0% to 23% among people with dementia.[5]

The evidence base for the pharmacological management of DLB is limited and is founded on evidence related to Parkinson disease psychosis. Despite the paucity of randomized controlled trial data in DLB, acetylcholinesterase inhibitors, atypical antipsychotics such as quetiapine and clozapine, memantine, and nonpharmacological approaches are used for patients with DLB.[4] One major challenge in finding the optimal treatment is the interplay of neurotransmitters such as dopamine, acetylcholine, and serotonin and their opposing effects on neuropsychiatric symptoms such as hallucinations and motor symptoms in DLB. Clozapine is a tricyclic dibenzodiazepine antipsychotic with efficacy in treating hallucinations and psychosis in Parkinson disease without dementia[6] and is less likely than other medications to worsen motor symptoms because of its distinctive dopamine receptor binding.[7] However, the number of case studies describing the use of clozapine in DLB patients is limited.[8] Here, we describe a DLB patient whose severe hallucinations and other neuropsychiatric symptoms were managed by clozapine without adverse effects.

CASE REPORT

In mid-June 2021, a 76-year-old retired male member of the Canadian Armed Forces was admitted to our specialized dementia care unit from an acute care hospital for assessment and treatment of behavioural and psychological symptoms of dementia including hallucinations, aggression, and paranoia.* At the time, he had a diagnosis of unspecified dementia (suspected Lewy body dementia), post-traumatic stress disorder (PTSD), rapid eye movement sleep behaviour disorder, insomnia, type 2 diabetes mellitus, and hypertension.

In 2010, the patient had begun experiencing PTSD symptoms related to his prior military experiences. His symptoms of rapid eye movement sleep behaviour disorder progressed over time, and he was followed by a sleep clinic and a geriatric psychiatry clinic. He was started on quetiapine for his vivid visual hallucinations and olanzapine for

*The authors were unable to obtain patient consent. As per the study institution's research ethics guidelines, all potentially identifiable information not relevant to the case has been omitted.

better control of his neuropsychiatric symptoms, such as poor social communication and agitation.

In early June 2021, he was admitted to a community hospital for violent behaviours with cognitive decline, and a diagnosis of likely Lewy body dementia was made. Before admission, the patient had been hallucinating and claimed that some men were threatening him and his wife. A physician's assessment noted tremors on the patient's left side, with pill rolling and rigidity. Rivastigmine 1.5 mg twice daily was prescribed, along with olanzapine 2.5 mg daily and risperidone 0.25 mg twice daily as needed. His home medications of citalopram 20 mg daily, quetiapine 12.5 mg daily, and clonazepam 0.5 mg at bedtime were continued. Computed tomography showed hippocampus and occipital atrophy, with no acute changes and no hemorrhage. Because of wandering and episodes of falling, the medical team had to restrain him, which was emotionally challenging for his family. Therefore, after about 2 weeks, the family decided to transfer the patient to another hospital.

Upon admission to our institution's specialized dementia care unit, in mid-June, a physical assessment showed parkinsonian symptoms of cogwheel rigidity, unilateral hand tremor at rest, unsteady gait necessitating use of a walker for ambulation, and decreased blink rate. Despite the unsteady gait, the patient had no underlying signs of dizziness or syncope. His vital signs were normal, and initial white blood cell (WBC) count and absolute neutrophil count (ANC) were within normal limits (10.8×10^9/L and 7.3×10^9/L, respectively). His scheduled medications at the time of admission to our unit included olanzapine 2.5 mg daily, risperidone 0.25 mg twice daily, quetiapine 12.5 mg daily, rivastigmine 1.5 mg twice daily,and citalopram 20 mg daily.

Magnetic resonance imaging showed moderate diffuse brain atrophy with ventricular prominence and microangiopathic changes, but no ischemia or hemorrhage. A Montreal Cognitive Assessment test was done, in which the patient scored 9 out of 30, with cognitive deficits mainly in the domains of visual–spatial function, executive function, and memory.

The olanzapine and risperidone were discontinued, and quetiapine 12.5 mg 3 times daily as needed was prescribed. Given multiple "code white" episodes for violent and aggressive behaviours, the quetiapine dose was increased to 25 mg twice daily. Multiple breakthrough doses of parenteral lorazepam and loxapine were needed to control his behavioural and psychological symptoms of dementia in the following weeks. During the code white episodes, the patient was verbally and socially inappropriate toward staff members and showed physical aggression by lifting tables above his head and breaking objects. Given the safety risk to staff, the patient was not eligible to participate in recreational activities as part of his nonpharmacological treatment plan. With higher doses of quetiapine, no excessive sedation was observed, but the patient's gait was less steady after titration to the 100-mg daily dose.

With the updated daily dose of quetiapine 100 mg, a change to rivastigmine patch 13.3 mg, and initiation of trazodone 100 mg daily, the patient continued experiencing distressing visual hallucinations, delusions, incoherent speech, restlessness, fluctuations in mental function, periods of lethargy, and memory problems. His impaired cognition and psychotic symptoms had negatively affected his decision-making and activities of daily living, and his PTSD complicated the final diagnosis. Two weeks after admission to our institution, a diagnosis of probable DLB was made. The patient met the full diagnostic criteria for DLB, with the following 4 core clinical features: fluctuations in attention and alertness, prominent and well-formed visual hallucinations, parkinsonism, and rapid eye movement sleep behaviour disorder.

In July 2021, a neurological assessment of the patient's motor function showed cogwheel rigidity and paratonia throughout the upper and lower extremities, along with bilateral tremors in the upper limbs at rest. He exhibited an unsteady gait that necessitated the continued use of a walker. Quetiapine was discontinued, and clozapine was initiated at 6.25 mg daily, with very slow titration up to 50 mg daily. At this time, the patient was also receiving rivastigmine 13.3 mg transdermally daily and trazodone 50 mg 3 times per day. Citalopram was tapered down and discontinued in early August 2021. To monitor for agranulocytosis, the patient was registered with the Clozapine Support and Assistance Network, and weekly blood tests were arranged. His WBC count and ANC remained within normal limits. He tolerated clozapine very well and did not experience adverse effects of sedation, hypersalivation, or weight gain. Neither parkinsonian symptoms nor extrapyramidal symptoms (EPS) were observed. Approximately 2 weeks after initiation of clozapine, he was noticeably calmer and less agitated, and he was experiencing fewer hallucinations. Nonpharmacological strategies such as involvement in creative arts, painting and music therapy, yoga, physiotherapy, and occupational therapies were added to his treatment plan to decrease his agitation, as well as to improve his gait stability, function, and overall quality of life. These strategies also helped to improve his sleep, with minimal use of melatonin 5 mg at bedtime as needed for insomnia.

By November 2021, the patient's cognitive status had improved significantly on a stable dose of clozapine 50 mg daily. He still experienced some cogwheel rigidity, but it did not worsen during the titration of clozapine. The patient did have a fall that month and was found to have some mild orthostatic hypotension, which prompted a decrease in his candesartan dose. Subsequent assessments showed that he was no longer experiencing delusions and was having no periods of altered perception during the day, no periods of disorganized speech, and less frequent periods of restlessness with fluctuating mental function throughout the day. There

were no further occurrences of aggression or violent behaviour. His hallucinatory episodes improved, although he did have occasional hallucinations briefly in the evenings. These were not distressing to him, and he was easily redirected by nurses and other staff without the need to administer breakthrough medications. He was very cooperative with care, and his motor symptoms such as cogwheel rigidity and tremors remained essentially the same as before clozapine was initiated. His symptom control also led to improved quality of life, and he has been participating in social activities inside and outside the facility, such as going on bus trips and city tours. A timeline of changes in the patient's psychoactive medications is presented in Figure 1.

In February 2022, a neurological reassessment noted that the patient was functionally improved compared with his prior assessment (before initiation of clozapine treatment). He could stand easily from a seated position by pushing up from the chair. With his walker, he continued to take short steps with some foot dragging, but there was no gait festination, no turning en bloc, and no gait freezing. Physical examination showed asymmetric parkinsonism, with the right side being more rigid, tremulous, and bradykinetic than the left.

DISCUSSION

To date, Health Canada has not approved any medications for DLB, and all current treatments are therefore used off-label. For example, acetylcholinesterase inhibitors and memantine may improve cognitive and neuropsychiatric symptoms in DLB.[9] If antipsychotics are needed for severe or distressing psychotic symptoms, the typical antipsychotics are avoided in patients with DLB because these drugs have higher dopamine antagonism, with a higher risk for motor symptoms and EPS. Clinicians often select clozapine and quetiapine for patients with PDD and DLB because these drugs have lower affinity for D2 receptors, but the evidence for their efficacy in DLB is low.[8,10] The use of clozapine is limited because of the idiosyncratic and very low but serious risk of agranulocytosis (0.38% in more than 99 000 patients[11]), which requires frequent blood monitoring.[12] The efficacy of clozapine in treating psychotic symptoms in patients with Parkinson disease without worsening of motor symptoms has been demonstrated in randomized clinical trials.[13-15] Clozapine exhibits weak D2 antagonism, strong serotonin-2 receptor (5-HT2A) antagonism, and fast dissociation from the D2 receptor, leading to its favourable motor profile.[16] However, clinical trials have not been conducted with clozapine in patients with the sole diagnosis of DLB. There is also little evidence for the efficacy of nonpharmacological approaches, because research involving patients with DLB has been limited. Patient- or caregiver-focused education and training to manage psychiatric symptoms, the elimination of triggering environmental stimulants, exercise (both motor and cognitive), and cognitive behavioural therapy are commonly used, despite the limited evidence.[2,17] This case report aims to shed light on some of the pharmacological challenges in treating patients with DLB and adds

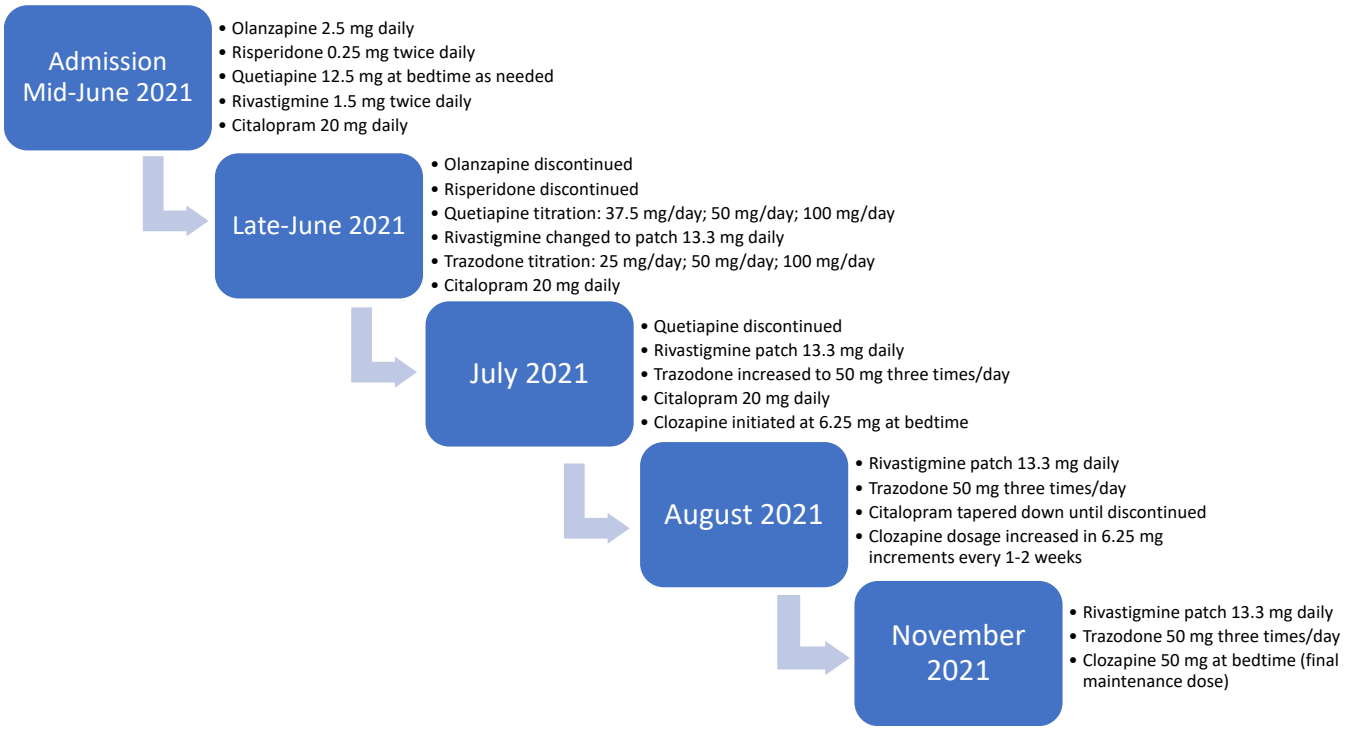

FIGURE 1. Timeline of changes in the patient's psychoactive medications.

to the evidence for the efficacy and safety of clozapine when the patient is monitored appropriately.

We conducted a literature search of randomized clinical trials, systematic reviews, meta-analyses, case reports, and retrospective chart reviews comparing clozapine with placebo, other pharmacological options, and nonpharmacological treatments for DLB. We searched several databases, specifically TRIP PRO, the Cochrane Database of Systematic Reviews, Embase, PubMed, MEDLINE, and PsycINFO, as well as the grey literature, from January 1993 to May 2022, with keywords for the population and interventions of interest: (clozapine OR Clozaril) AND (Lewy* OR dementia). Six case studies (5 in English and 1 in Dutch) documented the treatment of DLB patients with clozapine (Table 1).[18-23] We also found several systematic reviews based on these few case studies on the use of clozapine in DLB and therapeutic alternatives for DLB and PDD. Patient demographic characteristics, prior or concomitant use of acetylcholinesterase inhibitors or dopaminergic or antipsychotic drugs, and the outcomes of these 6 case studies (describing a total of 7 patients) are presented in Table 1. The primary goal of therapy in all of these case studies was to reduce the patient's symptoms, such as hallucination, delusions, and aggression, that were not mitigated with previous medication regimens. Neuroleptic sensitivity in 2 patients (described in a single case report) resulted in discontinuation of clozapine due to worsening hallucinations and confusion.[20] In the other 5 case studies, the goals of therapy were met, as the resolution of patients' hallmark symptoms was clinically significant and patients did not experience increased risk of falls or orthostatic hypotension due to clozapine. Among these 5 patients, 2 patients experienced EPS, which were treated with concomitant daily levodopa[21,22]; a third patient's EPS were minimal and did not interfere with his daily activities.[23] None of the 5 patients in these cases were reported to have experienced neuroleptic sensitivity syndrome or concerning changes in WBC count or ANC as a sign of agranulocytosis due to the use of clozapine. Agranulocytosis is a dangerous but reversible hematological condition that can be managed, if identified early, by regular blood monitoring. Patients may be rechallenged with clozapine once neutrophil counts return to normal.[24] Although there is no evidence derived from randomized clinical trials, these 6 case reports present important points about the efficacy of clozapine. We believe that clozapine can be safely used to improve the neuropsychiatric symptoms of DLB, if monitored appropriately.

The case that we have reported here highlights the efficacy and safety of clozapine in treating DLB core symptoms, such as cognitive fluctuation and hallucinations, without worsening motor symptoms or inducing side effects such as falls, neuroleptic sensitivity, or agranulocytosis. Because clozapine has α-adrenergic blockade and a higher risk of dizziness and orthostatic hypotension, especially in the geriatric population, we monitored the patient's orthostatic blood pressure routinely. Given the patient's history of constipation, he continued taking laxatives, and his bowel movements were monitored daily to allow mitigation of the additive anticholinergic side effects of clozapine. Upon admission to our specialized dementia care unit, the patient's risperidone and olanzapine were discontinued and replaced by quetiapine, given that his parkinsonian symptoms were likely due to the higher dopamine antagonism of risperidone and olanzapine relative to quetiapine.[9] Also,

TABLE 1. Case Studies Investigating the Use of Clozapine for Patients with Lewy Body Dementia

Study	Age (yr) and Sex	Cognitive Screening Test	Prior Medications	Clozapine Initial–Final Dose[a] (mg/day)	Concomitant Medications (mg/day)	Outcomes and Efficacy
Chacko et al. (1993)[18]	57, female	NR	Levodopa, selegiline, pergolide	25–75	None	Resolution of hallucinations, improved mood, and improved social communication
Geroldi et al. (1997)[19]	74, female	MMSE 19/30	Haloperidol	12.5–37.5	None	Satisfactory reduction of visual and tactile hallucinations
Burke et al. (1998)[20]	71, male 69, male	MMSE 27/30 MMSE 16/30	Selegiline, levodopa Pergolide, levodopa	6.25–12.5 6.25	None None	Clozapine discontinued because of increased confusion, hallucination, agitation, and behavioural symptoms
Majic et al. (2010)[21]	73, female	MMSE 20/30	Quetiapine, pipamperone, donepezil	200	Levodopa 375, donepezil 10	Resolution of hallucination and delusions, worsening of parkinsonism
Archie et al. (2013)[22]	77, male	NR	Quetiapine, rivastigmine	75	Levodopa 100	Resolution of hallucination and delusions
Bhamra et al. (2018)[23]	75, male	MMSE 23/30	Donepezil, rivastigmine	6.25–18.75	Rivastigmine patch 13.3	Resolution of hallucinations and agitation, improved mood

MMSE = Mini-Mental State Examination, NR = not reported.
[a]Where only one dose appears, the patient's dose did not change over the course of treatment.

olanzapine has anticholinergic side effects and a higher risk for metabolic syndrome that could affect the patient's diabetes. By approximately 12 months after clozapine initiation, the patient's positive outcomes persisted, and his mild, infrequent hallucinations and agitation had resolved. In compliance with Health Canada drug monitoring requirements,[25] blood monitoring was conducted weekly for the first 6 months and biweekly for another 6 months, during which time his WBC count and ANC were consistently within the normal limits (4–11 × 10^9 /L for both); this monitoring will continue in the future. Because of disease progression, his complete dependence on others for activities of daily living, and the difficulty of caring for him at home, there is currently no plan to discharge this patient. However, in cases where the patient can be discharged, the drug manufacturers offer a compassionate program for off-label use of clozapine, which assists patients with medication costs and a monitoring plan.[26] Given the serious risk of agranulocytosis associated with clozapine, patients, their health care providers, and their dispensing pharmacists must be enrolled in a registry specific to 1 of the 3 marketers of clozapine in Canada.[25] Alternatively, Veterans Affairs Canada has coverage for veterans, depending on their pension conditions.[27]

Pimavanserin is a selective serotonin 5-HT2A receptor inverse agonist that was recently approved by the US Food and Drug Administration (but is not marketed in Canada) for the treatment of hallucinations and delusions associated with Parkinson disease psychosis.[28] The effects and maximal benefit of this drug are not immediate and can take 2–6 weeks to achieve, which may not be ideal in acute care settings.[29] As of summer 2023, patients are being recruited to an open-label trial that will compare quetiapine and pimavanserin among patients with psychosis due to PDD or DLB.[30]

Ours was an observational case report with no control group for comparison. As with most case reports, unmeasured confounding, selection bias, and recall bias limit the generalizability of our findings. In 1 previous case report, the authors were able to conduct a variety of objective assessments such as the Mini-Mental State Examination before and after initiating clozapine to evaluate the outcomes,[23] but this type of testing was not applicable in our clinical setting. Therefore, our outcomes might reflect measurement and interviewer biases. Despite these caveats, this case report supports the use of clozapine for treating patients with DLB. There is a need for further research, through larger case series and placebo-controlled trials, to better assess the place of clozapine and other treatment options in guidelines for managing DLB.

CONCLUSION

In the patient case presented here, clozapine was an effective treatment option for persistent psychosis and aggression in DLB. Through its anticholinergic activity, this drug has a multitude of possible side effects that may significantly affect an older patient like the one described here, such as constipation and urinary retention.[25,26] Therefore, consideration must be given to identifying the side effects to which the person may be vulnerable, and appropriate monitoring plans should be put in place to monitor for and reduce the risks of these side effects. The use of low doses and slow titration remains appropriate and is the safest way to monitor for emerging side effects and to identify the lowest therapeutic dose.

References

1. Public Health Agency of Canada; Neurological Health Charities Canada. *Mapping connections: an understanding of neurological conditions in Canada*. Report HP35-45/2014E-PDF. Minister of Health (Canada); 2014 [cited 2023 Jan 18]. Available from: https://www.canada.ca/content/dam/phac-aspc/migration/phac-aspc/publicat/cd-mc/mc-ec/assets/pdf/mc-ec-eng.pdf
2. Mckeith IG, Boeve BF, Dickson DW, Halliday G, Taylor JP, Weintraub D, et al. Diagnosis and management of dementia with Lewy bodies: fourth consensus report of the DLB Consortium. *Neurology*. 2017;89(1):88-100.
3. Walker Z, Possin KL, Boeve BF, Aarsland D. Lewy body dementias. *Lancet*. 2015;386(10004):1683-97.
4. Kyle K, Bronstein JM. Treatment of psychosis in Parkinson's disease and dementia with Lewy bodies: a review. *Parkinsonism Relat Disord*. 2020;75:55-62.
5. Vann Jones SA, O'Brien JT. The prevalence and incidence of dementia with Lewy bodies: a systematic review of population and clinical studies. *Psychol Med*. 2014;44(4):673-83.
6. Seppi K, Chaudhuri KR, Coelho M, Fox SH, Katzenschlager R, Lloret SP, et al. Update on treatments for nonmotor symptoms of Parkinson's disease—an evidence-based medicine review. *Mov Disord*. 2019;34(2):180-98.
7. Kapur S, Seeman P. Does fast dissociation from the dopamine D(2) receptor explain the action of atypical antipsychotics?: A new hypothesis. *Am J Psychiatry*. 2001;158(3):360-9.
8. Taylor JP, McKeith IG, Burn DJ, Boeve BF, Weintraub D, Bamford C, et al. New evidence on the management of Lewy body dementia. *Lancet Neurol*. 2020;19(2):157-69.
9. Watts KE, Storr NJ, Barr PG, Rajkumar AP. Systematic review of pharmacological interventions for people with Lewy body dementia. *Aging Ment Health*. 2023;27(2):203-16.
10. Lee HB, Hanner JA, Yokley JL, Appleby B, Hurowitz L, Lyketsos CG. Clozapine for treatment-resistant agitation in dementia. *J Geriatr Psychiatry Neurol*. 2007;20(3):178-82.
11. Honigfeld G, Arellano F, Sethi J, Bianchini A, Schein J. Reducing clozapine-related morbidity and mortality: 5 years of experience with the Clozaril National Registry. *J Clin Psychiatry*. 1998;59 Suppl 3:3-7.
12. Goldman JG, Holden S. Treatment of psychosis and dementia in Parkinson's disease. *Curr Treat Options Neurol*. 2014;16(3):281.
13. Factor SA, Friedman JH, Lannon MC, Oakes D, Bourgeois K; Parkinson Study Group. Clozapine for the treatment of drug-induced psychosis in Parkinson's disease: results of the 12 week open label extension in the PSYCLOPS trial. *Mov Disord*. 2001;16(1):135-9.
14. Merims D, Balas M, Peretz C, Shabtai H, Giladi N. Rater-blinded, prospective comparison: quetiapine versus clozapine for Parkinson's disease psychosis. *Clin Neuropharmacol*. 2006;29(6):331-7.
15. Morgante L, Epifanio A, Spina E, et al. Quetiapine versus clozapine: a preliminary report of comparative effects on dopaminergic psychosis in patients with Parkinson's disease. *Neurol Sci*. 2002; 23 Suppl 2:S89-S90.
16. Meyer JM. Pharmacotherapy of psychosis and mania. In: Brunton LL, Hilal-Dandan R, Knollmann BC, editors. *Goodman & Gilman's: the pharmacological basis of therapeutics*. 13th ed. McGraw Hill; 2017.

17. Tripathi A, Gupta PK, Bansal T. Management of psychiatric disorders in patients with Parkinson's diseases. *Indian J Psychiatry*. 2022; 64(8):S330-S343.
18. Chacko RC, Hurley RA, Jankovic J. Clozapine use in diffuse Lewy body disease. *J Neuropsychiatry Clin Neurosci*. 1993;5(2):206-8.
19. Geroldi C, Frisoni GB, Bianchetti A, Trabucchi M. Drug treatment in Lewy body dementia. *Dement Geriatr Cogn Disord*. 1997;8(3):188-97.
20. Burke WJ, Pfeiffer RF, McComb RD. Neuroleptic sensitivity to clozapine in dementia with Lewy bodies. *J Neuropsychiatry Clin Neurosci*. 1998;10(2):227-9.
21. Majic T, Mell T, Heinz A, Rapp MA. Adjunct treatment with levodopa in a patient with dementia with Lewy bodies, delusions and severe neuroleptic hypersensitivity syndrome. *Int Psychogeriatr*. 2010; 22(4):678-9.
22. Archie A, Persoons P, Vandenbulcke M. [The use of clozapine and levodopa for the treatment of persistent visual hallucinations and parkinsonism in Lewy body dementia]. *Tijdschr Psychiatr*. 2013;55(4): 287-91. Article in Dutch.
23. Bhamra M, Rajkumar AP, Ffytche DH, Kalafatis C. Successful management of persistent distressing neuropsychiatric symptoms by clozapine in a patient suffering from dementia with Lewy bodies. *BMJ Case Rep.* 2018;2018:bcr2018224710.
24. Komaragiri A, Friedman JH. Multiple re-challenges for clozapine neutropenia in Parkinson's disease [letter]. *Parkinsonism Related Disord*. 2016;23:114-5.
25. Chandrakumar S, Warnock C, Powell V, Zhang M. 5 things you should know about clozapine. *Pharm Connect.* 2018 [cited 2022 Jun 3];25(2): 38-41. Available from: https://www.ocpinfo.com/library/pharmacy-connection/download/ocp_pharmacyconnection_spring2018.pdf
26. *CLOZARIL® handbook for healthcare professionals*. HLS Therapeutics Inc; 2020 [cited 2023 Jan 18]. Available from: https://clozaril.ca/wp-content/uploads/2019/09/Clozaril_HCP-Handbook_EN-1.pdf
27. Benefit information for Clozaril, accessed through drug formulary search form. In: *Prescription drug program (POC 10)*. Veterans Affairs Canada; 2019 Feb 11 [cited 2023 Aug 4]. Available from: https://www.veterans.gc.ca/eng/financial-support/medical-costs/treatment-benefits/poc10/search/results?tradename=clozaril
28. Cummings J, Isaacson S, Mills R, Williams H, Chi-Burris K, Corbett A, et al. Pimavanserin for patients with Parkinson's disease psychosis: a randomised, placebo-controlled phase 3 trial *Lancet*. 2014; 383(9916):533-40. Erratum in: *Lancet.* 2014;384(9937):28.
29. Tampi RR, Tampi DJ, Young JJ, Balachandran S, Hoq RA, Manikkara G. Evidence for using pimavanserin for the treatment of Parkinson's disease psychosis. *World J Psychiatry*. 2019;9(3):47-54.
30. Horn S. Comparing antipsychotic medications in LBD over time (CAMELOT). ClinicalTrials.gov identifier: NCT05590637. Updated 2022 Oct 21 [cited 2023 Jan 18]. Available from: https://clinicaltrials.gov/ct2/show/NCT05590637

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Competing interests: Chris Fan-Lun received a patient care grant from the Ontario Branch of the Canadian Society of Hospital Pharmacists (paid to the institution) and has received speaker's fees from the Regional Geriatric Program of Toronto. No other competing interests were declared.

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Funding: None received.

Acknowledgements: The authors thank the nurses and allied health staff at Dorothy Macham Home for sharing their insights and notes in their provision of patient-centred care.

Wise Words from the Good Doctor (Seuss)

Ashley Walus

https://doi.org/10.4212/cjhp.3526

> Congratulations!
> Today is your day.
> You're off to Great Places!
> You're off and away!
>
> You have brains in your head.
> You have feet in your shoes.
> You can steer yourself
> any direction you choose.
>
> —Dr Seuss (*Oh, the Places You'll Go.*
> Random House Children's Books; 1990)

These words from the good doctor are often seen at graduation—brimming with potential, they remind the reader that we have within us the tools we need to succeed. They convey the optimism that exists upon new beginnings: nothing can stop the brains in our heads and the feet in our shoes from helping us to do great things.

What's less popular in greeting cards and feel-good social media posts are the words that come later in Dr Seuss's poem:

> You will come to a place where the streets are
> not marked.
> Some windows are lighted. But mostly they're
> darked.
> A place you could sprain both your elbow and
> chin!
> Do you dare to stay out? Do you dare to go in?
> How much can you lose? How much can you win?

We have all seen our fair share of unmarked streets, darked windows, and sprained chins over the past three years in the profession of pharmacy. Whether it be the ongoing impacts of the COVID-19 pandemic on our health care system or the health human resource struggles we face nationwide, hospital pharmacy professionals have weathered more uncertainty in these last few years than many have ever experienced before. We lack a unified vision for pharmacy practice in Canada, which—as noted by Zack Dumont in a previous Executive Commentary (https://doi.org/10.4212/cjhp.3412)—has left us all without a guiding North Star upon which to focus our collective professional efforts.

Yet we have had successes. We have learned many valuable lessons from the pandemic, as shared in the latest *Hospital Pharmacy in Canada Survey Report* (https://www.cshp.ca/docs/pdfs/HPCS-2020-21-Report-ENG.pdf), and we have struck a CSHP task force to craft our vision for the profession we are all so passionate about. We have begun to build meaningful and fruitful relationships with the Indigenous Pharmacy Professionals of Canada and the Canadian Association of Pharmacy for the Environment, and we have also started the critical work of determining how CSHP can best support sustainability efforts within hospital pharmacy practice in response to our changing climate.

We are now at an inflection point. How much will we dare? What can we win or, conversely, lose? And in what direction will we choose to steer ourselves? CSHP is embarking on our next strategic planning cycle, and the resulting plan will be more outward-facing than our last one. We know our resources are not infinite, so we must be mindful of how our national organization can have the greatest impact on pharmacy practice issues. This may mean travelling down unmarked streets and rethinking how we support our members in their pursuit of excellence in patient care. It will mean working collectively to develop a plan that sets CSHP on a path to greater places than we have ever been, guided by the unified vision we are crafting now.

It may seem daunting to some, but with the brains in our heads, and the feet in our shoes, we will chart our next course together. Today is our day, so let's get going.

Ashley Walus, BScPharm, ACPR, MBA, is President Elect of the Canadian Society of Hospital Pharmacists.

De sages paroles du bon docteur (Seuss)

par Ashley Walus

https://doi.org/10.4212/cjhp.3540

> Félicitations!
> C'est aujourd'hui le grand jour.
> Tu mets les voiles, tu pars!
> Qui sait quand tu seras de retour!
>
> Ton cerveau est dans ta tête.
> Tes pieds sont dans tes chaussures.
> Libre à toi de te diriger
> vers n'importe quelles aventures.
>
> —Dr Seuss (*Oh, the Places You'll Go.*
> Random House Children's Books; 1990) *[trad. libre]*

Ces paroles du bon docteur sont souvent lues au moment de la remise des diplômes — débordant de potentiel, elles rappellent au lecteur que nous avons en nous les outils nécessaires pour réussir. Elles véhiculent l'optimisme qui règne au moment des nouveaux départs : rien ne peut empêcher notre esprit et notre corps de nous aider à accomplir de grandes choses.

Ce qui est moins populaire dans les cartes de vœux et les billets bienveillants sur les réseaux sociaux, ce sont les paroles qui viennent plus tard dans le poème du Dr Seuss :

> Tu arriveras à un endroit où les rues ne sont pas indiquées.
> Certaines fenêtres seront éclairées. Mais la plupart ne le seront pas.
> Un endroit où tu pourrais te tordre le coude et le menton!
> Oseras-tu rester dehors? Oseras-tu entrer?
> Combien as-tu à perdre? Qu'as-tu à y gagner?

Au cours de ces trois dernières années, en tant que pharmaciens, nous avons tous connu notre juste part de rues non marquées, de fenêtres sans lueur et d'entorses au menton. Qu'il s'agisse des conséquences continues de la pandémie de COVID-19 sur notre système de santé ou des difficultés dans les ressources humaines en santé auxquelles nous sommes confrontés à l'échelle nationale, les professionnels de la pharmacie hospitalière ont traversé plus d'incertitudes au cours des dernières années que beaucoup n'en ont jamais connues auparavant. Nous manquons d'une vision unifiée pour la pratique de la pharmacie au Canada. Comme l'a noté Zack Dumont dans un précédent mot de la direction (https://doi.org/10.4212/cjhp.3428), cette absence nous a tous laissés sans étoile polaire nous permettant d'orienter nos efforts professionnels collectifs.

Pourtant, nous avons connu des réussites. Nous avons tiré de nombreuses leçons précieuses de la pandémie, comme le mentionne le dernier Rapport du Sondage sur les pharmacies hospitalières canadiennes (https://www.cshp.ca/docs/pdfs/HPCS-2020-21-Report-FR.pdf), et nous avons constitué un groupe de travail de la SCPH ayant pour mission de façonner notre vision de la profession qui nous passionne tous. Nous avons commencé à établir des relations pertinentes et fructueuses avec les Professionnels et professionnelles autochtones de la pharmacie du Canada ainsi qu'avec la Canadian Association of Pharmacy for the Environment. Nous avons aussi commencé notre travail critique visant à déterminer comment la SCPH peut soutenir au mieux les efforts de durabilité au sein de la pratique de la pharmacie hospitalière en réponse à notre climat changeant.

Nous nous trouvons maintenant à un croisement. Jusqu'où irons-nous? Qu'avons-nous à gagner ou à perdre? Et dans quelle direction choisirons-nous de nous orienter? La SCPH entame son prochain cycle de planification stratégique et le plan qui en résultera sera plus orienté vers l'extérieur que le précédent. Nous savons que nos ressources ne sont pas infinies. Nous devons donc être conscients de la façon dont notre organisme national peut exercer le plus grand impact sur les questions portant sur la pratique de la pharmacie. Cela peut signifier parcourir des rues non marquées et repenser notre façon de soutenir nos membres dans leur poursuite de l'excellence en matière de soins aux patients. Cela signifiera travailler collectivement pour élaborer un plan qui place la SCPH sur une trajectoire menant à des horizons inexplorés plus vastes, tout en étant guidés par la vision unifiée que nous façonnons actuellement.

Cela peut sembler intimidant pour certains, mais avec le cerveau en tête et les pieds dans nos chaussures, nous définirons ensemble notre prochain cap. C'est aujourd'hui le grand jour… alors, levons l'ancre.

Ashley Walus, B. Sc. Pharm., ACPR, M.B.A., est présidente désignée de la Société canadienne des pharmaciens d'hôpitaux.

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APPENDIX 1: Interview questions.

1. First, we can start out by having you tell me about your story of overcoming a patient safety incident, including a brief summary of the event if you are comfortable, the emotional response you felt and how you handled those emotions.
    a. Interviewer may use active prompts to encourage responses to each portion of the question. For example:
        i. Would you be able to tell me more about how you overcame the emotions you felt?
        ii. Is there anything else you would like to mention?
2. If a disclosure to the patient or family was involved, what role did this play in your recovery? What made disclosure easier or more challenging?
3. How were your interactions with the patient or family throughout the story? Did they change over time? How did these interactions impact your emotions?
4. Did you disclose this event to colleagues? What role did this disclosure play in your recovery? What made disclosure easier or more challenging?
5. Did you feel that the incident was the result of a systemic process or due to error from a single person?
6. It is thought that a culture of perfectionism and individual blame plays a role towards shame, guilt and other negative emotions following a patient safety incident. Were these factors applicable to your experience? What other factors contributed to your emotional impact?
7. How has this experience changed you as a pharmacist? As a person?
8. Has the experience changed your behaviour? How so?
9. How could your institution better support you and other pharmacists following incidents?

Appendix to: Ney M, Landry C, Trinacty M, Joanisse M, Caron C. Emotional impact of medication-related patient safety incidents on Canadian hospital pharmacists: a mixed-methods study. *Can J Hosp Pharm*. 2023;76(4):267-74.

APPENDIX 1. Frequency of country of qualifying education in the sample of pharmacists.

Country	Frequency (%)[a] (*n* = 14 689)
Canada	7403 (50.4)
Egypt	1858 (12.65)
India	1448 (9.86)
USA	876 (5.96)
England	654 (4.45)
Philippines	295 (2.1)
Pakistan	276 (1.88)
Iran	269 (1.83)
Jordan	172 (1.17)
Iraq	115 (0.78)
Nigeria	106 (0.72)
Bangladesh	97 (0.66)
Australia	87 (0.59)
South Africa	75 (0.51)
South Korea	71 (0.48)
Syria	71 (0.48)
Yugoslavia	62 (0.42)
China	50 (0.34)
Jamaica	50 (0.34)
Poland	47 (0.32)
Russia	43 (0.29)
Romania	38 (0.26)
Ukraine	38 (0.26)
Lebanon	35 (0.24)
Taiwan	25 (0.17)
United Arab Emirates	23 (0.16)
Vietnam	19 (0.13)
Brazil	18 (0.12)
Israel	18 (0.12)
Scotland	17 (0.12)
Sudan	17 (0.12)
Italy	15 (0.1)
Ghana	14 (0.1)
Argentina	12 (0.08)
Japan	12 (0.08)
Saudi Arabia	12 (0.08)
Hungary	11 (0.07)
Trinidad and Tobago	11 (0.07)
Turkey	11 (0.07)
Ethiopia	10 (0.07)
Macedonia	10 (0.07)
Cuba	9 (0.06)
Germany	9 (0.06)
Palestine	8 (0.05)
Serbia	8 (0.05)
Albania	7 (0.05)
Kenya	7 (0.05)
Libya	7 (0.05)
Tanzania	7 (0.05)
Armenia	6 (0.04)
Bulgaria	6 (0.04)
Czech Republic	6 (0.04)
Ireland	6 (0.04)
Thailand	6 (0.04)
France	5 (0.03)
Korea	5 (0.03)
Malaysia	5 (0.03)
Nepal	5 (0.03)
New Zealand	5 (0.03)
Zimbabwe	5 (0.03)
Afghanistan	< 5
Algeria	< 5
Azerbaijan	< 5
Belarus	< 5
Belgium	< 5
Bosnia and Herzegovina	< 5
Chile	< 5
Colombia	< 5
Croatia	< 5
Ecuador	< 5
Eritrea	< 5
Greece	< 5
Guyana	< 5
Haiti	< 5
Indonesia	< 5
Kazakhstan	< 5
Kuwait	< 5
Kyrgyzstan	< 5
Lithuania	< 5
Malta	< 5
Mauritius	< 5
Mexico	< 5
Moldova	< 5
Northern Ireland	< 5
Norway	< 5
Oman	< 5
Peru	< 5
Portugal	< 5
Qatar	< 5
Singapore	< 5
Slovakia	< 5
Slovenia	< 5
Spain	< 5
Sweden	< 5
Tunisia	< 5
Uganda	< 5
Venezuela	< 5
Yemen	< 5
Zaire	< 5
Total	14 689

[a]The sum of percentages for countries with fewer than 5 graduates each was 0.52%

Appendix to: Patel D, Mickleborough T, Elbeddini A, Alsabbagh MW. Association between pharmacists' country of qualifying education and practising in a hospital setting: a cross-sectional Ontario study. *Can J Hosp Pharm.* 2023;76(4):282-9.

APPENDIX 2. Characteristics of pharmacists by location of qualifying education (Canadian vs IPG) when drug preparation premises were considered to be community pharmacies

Characteristic	Location of Qualifying Education			p Value[a]
	Canadian Graduates (*n* = 7403)	IPGs (*n* = 7286)	All (*n* = 14 689)	
No. (%) with at least 1 hospital practice site	2445 (33.0)	414 (5.7)	2859 (19.5)	< 0.001
No. (%) females	4679 (63.2)	3807 (52.3)	8486 (57.8)	< 0.001
Time since graduation (years) (mean ± SD)	17.4 ± 13.2	22.1 ± 11.0	19.7 ± 12.4	< 0.001
No. of declared sites of practice (mean ± SD)	1.6 ± 2.4	1.5 ± 1.5	1.6 ± 2.0	0.02

IPG = international pharmacy graduate, SD = standard deviation.
[a]Based on χ^2 or *t* test.

Appendix to: Patel D, Mickleborough T, Elbeddini A, Alsabbagh MW. Association between pharmacists' country of qualifying education and practising in a hospital setting: a cross-sectional Ontario study. *Can J Hosp Pharm.* 2023;76(4):282-9.

APPENDIX 1: Semistructured interview for clinical pharmacist practitioners.

Hello,
Thank you for taking the time out of your day to sit down with me and be involved in our study. If for any reason you decide you would no longer like to participate, you can let me know at any time. This interview should take 30–45 minutes of your time.

We are conducting semi structured interviews with Canadian clinical pharmacist practitioners with exemplary practices and Canadian health care system stakeholders, such as yourself, in order to ascertain perspectives on how pharmacists of the future may achieve clinical pharmacist practitioner roles and where these clinical pharmacist practitioners would fit into the current and future health care systems. Your feedback will supplement information in the existing literature from around the world on how clinical pharmacist practitioner roles may be established and incorporated into health care systems.

Our hope is to develop key themes gained from our semi structured interviews in order to provide a clear pathway for pharmacists of the future to practise within their full scope and take on clinical pharmacist practitioner roles within Canada.

We plan to record these semi structured interviews to allow for transcription and text-based analysis. We ask your permission to do so. The recording will only be used by our research group. If possible, please try to refrain from stating any personal identifying information, but if you do it will be de-identified upon transcription. A summary of the data analysis procedure and a summary of the results of the inquiry will be shared with you via Qualtrics survey tool to ensure that themes gathered align with what you intended during your interview, unless you have any objections to us doing so. Results of the study will ultimately be shared at a project defense at St. Paul's Hospital or Vancouver General Hospital in September 2020, we will seek to present poster results at local/national conferences, and we will aim to publish the findings in a peer-reviewed journal.

Demographic data (some data may be pre-populated from prior contact):

1) How long have you been practising as a pharmacist?	Numerical value
2) What is your current position?	Job title
3) How long have you been in your current role?	Numerical value
4) What setting do you practise in?	Hospital, community, ambulatory, academia, regulatory, or other
5) Does your practice involve direct patient care?	Y or N

Audio recording to begin after initial demographic data recorded

Questions:

1) What internal qualities and characteristics do you feel have contributed to your attainment of your current role and advanced practice?
2) What external factors do you think contributed?
3) How would you describe the pathway that you took to achieve your current practice role?
   - Formal training?
   - Informal training opportunities?
   - Other career advancement avenues?
4) What were some of the barriers/enablers that you encountered?
5) If you had to start all over again, are there any changes you would make to the path that you took? Or in other words, what advice would you give to a pharmacist starting out in their career who wants to end up in a similar position such as yours?
6) How could this level of practice/practice environment become the norm for all pharmacists? Do you think achieving that is a possibility? What changes would be required (e.g., training, regulatory, etc.)?
7) How do you think others perceive clinical pharmacist practitioners? How should we as a profession promote our role in the health care system?
8) What are your thoughts on credentialing or certifying pharmacists for advanced scope of practice as compared to training all pharmacists to achieve the same scope of practice?
9) Is a separate designation (such as the Nurse Practitioner designation that nursing has created) needed to achieve similar advancement within pharmacy?
10) My main purpose in the interview today is to use data gathered to begin to identify pathways for Canadian pharmacists to practise to their full scope and perhaps take on clinical pharmacist practitioner roles, is there anything else that you feel is important that we haven't discussed?

Appendix to: Parmar R, Legal M, Dahri K, Wilbur K, Shalansky S, Partovi N. Pathways to developing clinical pharmacist practitioners: is there a better way forward? (Path-CPP). *Can J Hosp Pharm*. 2023;76(4):302-8.

APPENDIX 2: Semistructured interview for health care system stakeholders.

Hello,
Thank you for taking the time out of your day to sit down with me and be involved in our study. If for any reason you decide you would no longer like to participate, you can let me know at any time. This interview should take 30-45 minutes of your time.

We are conducting semi structured interviews with Canadian clinical pharmacist practitioners with exemplary practices and Canadian health care system stakeholders, such as yourself, in order to ascertain perspectives on how pharmacists of the future may achieve clinical pharmacist practitioner roles and where these clinical pharmacist practitioners would fit into the current and future health care systems. Your feedback will supplement information in the existing literature from around the world on how clinical pharmacist practitioner roles may be established and incorporated into health care systems.

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Demographic data (some data may be pre-populated from prior contact):

1)	What is your current role?	Job title
2)	How long have you been in your current role?	Numerical value
3)	What setting do you practise in?	Hospital, community, ambulatory, academia, regulatory, or other
4)	Does your practice involve direct patient care?	Y or N

Audio recording to begin after initial demographic data recorded

Clinical Pharmacist Practitioner Description:

Clinical pharmacist practitioners are pharmacotherapy experts who practise independently, conduct thorough patient assessments, respond to consultations, monitor and adjust drug therapy, provide patient and colleague education, and may prescribe independently or in collaboration with other health professionals.

Questions:

1) Looking at an ideal description of a clinical pharmacist practitioner and their possible scope of practice, what do you see as their role and where would they fit into the Canadian health care system? How could they complement or work with other health care providers in the system?
2) What challenges, barriers or limitations do you see with having such an individual more involved in the health care system?
3) Based on what you know of pharmacists' training, what are qualities/skills of pharmacists that you feel would help them succeed in this type of role? What are qualities/skills you would be concerned that pharmacists could lack and may be required for this type of role?
4) Do you think a separate designation is required to have pharmacists with this scope of practice becoming more widespread?
5) Do you feel that having this type of pharmacist implemented in regular roles throughout the Canadian health care system would be useful? What additional value could this type of practitioner provide to patients/the health care system?
6) My main purpose in the interview today is to use data gathered to begin to develop a pathway for Canadian pharmacists to practise to their full scope and perhaps take on clinical pharmacist practitioner roles, is there anything else that you feel is important that we haven't discussed?

Appendix to: Parmar R, Legal M, Dahri K, Wilbur K, Shalansky S, Partovi N. Pathways to developing clinical pharmacist practitioners: is there a better way forward? (Path-CPP). *Can J Hosp Pharm*. 2023;76(4):302-8.