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The *CJHP* is an academic journal that focuses on how pharmacists in hospitals and other collaborative health care settings optimize safe and effective drug use for patients in Canada and throughout the world.

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International Hospital Pharmacy: Learning from Each Other

Rebekah J Moles

Over the past 2 years, the *Canadian Journal of Hospital Pharmacy* (*CJHP*) has published the series "International Perspectives on Pharmacy Practice", describing health care systems and pharmacy practice in diverse countries from all of the World Health Organization (WHO) regions (www.who.int/about/regions/en/). The series has included updates from Australia, South Africa, Belgium, Saudi Arabia, the United States, Nepal, Jordan, Japan, Italy, Brazil, and Kenya (see Box 1); the final articles of the series, concerning practice in Hong Kong and Thailand, respectively, will be published in 2018. Part of *CJHP*'s vision is to share information on "patient-centred pharmacy practice in hospitals and other collaborative health care settings . . . throughout the world", and the series was designed to help meet this vision.

Box 1: Articles in the *CJHP* Series "International Perspectives on Pharmacy Practice"

Moles R, Stehlik P. Pharmacy practice in Australia. *Can J Hosp Pharm*. 2015;68(5):418-26.
Gray A, Riddin J, Jugathpal J. Health care and pharmacy practice in South Africa. *Can J Hosp Pharm*. 2016;69(1):36-41.
De Rijdt T, Desplenter F. Hospital pharmacy in Belgium: from moving boxes to providing optimal therapy. *Can J Hosp Pharm*. 2016;69(2):156-66.
Al-jedai A, Qaisi S, Al-meman A. Pharmacy practice and the health care system in Saudi Arabia. *Can J Hosp Pharm*. 2016;69(3):231-7.
Scott D. United States health care system: a pharmacy perspective. *Can J Hosp Pharm*. 2016;69(4):306-15.
Ranjit E. Pharmacy practice in Nepal. *Can J Hosp Pharm*. 2016;69(6):493-500.
Nazer LH, Tuffaha H. Health care and pharmacy practice in Jordan. *Can J Hosp Pharm*. 2017;70(2):150-5.
Nakagawa S, Kume N. Pharmacy practice in Japan. *Can J Hosp Pharm*. 2017;70(3):232-42.
Polidori P, Cifani C, Polidori P. Roles of hospital and territorial pharmacists within the Italian National Healthcare Service. *Can J Hosp Pharm*. 2017;70(4):309-15.
Melo CA, Galato D, Maniero HK, Pena Frade JCQ, Palhano TJ, da Silva WB, et al. Pharmacy in Brazil: progress and challenges on the road to expanding clinical practice. *Can J Hosp Pharm*. 2017;70(5):381-90.
Aywak D, Jaguga CDP, Nkonge NG, Kinuthia R, Ambale C, Awle IA. Pharmacy practice in Kenya. *Can J Hosp Pharm*. 2017;70(6):456-62.

Other ways for pharmacists to learn about practice around the globe are to travel to international conferences and to learn from their counterparts in other countries. A great place to start is through the International Pharmaceutical Federation (FIP). FIP is a global federation representing 4 million pharmacists and pharmaceutical scientists. This nongovernmental organization has had an official relationship with the WHO since 1948. Through its partnerships and extensive global pharmacy and pharmaceutical sciences network, as well as through practice and emerging scientific innovations, FIP supports the development of the pharmacy profession to meet the world's health care needs.[1]

The structure of FIP is complex, but essentially there are 2 main components: the Board of Pharmaceutical Sciences (BPS) and the Board of Pharmaceutical Practice (BPP). A third overarching body, known as FIP Education (FIP*Ed*), was formed recently to oversee pharmacy educational matters. The Young Pharmacists Group of FIP is open to younger pharmacists, and FIP also supports the International Pharmaceutical Students' Federation. The BPS contains 9 special interest groups, and the BPP has 8 sections, including the Hospital Pharmacy Section. When you join FIP as an individual member, your membership includes affiliation with one section of your choice; you may then join other sections for a nominal fee of 15 euros each, with no limit on the number of additional sections.

The Hospital Pharmacy Section is the second-largest section (after the Community Pharmacy Section) and is arguably the most active. The section's objectives (www.fip.org/hospital_pharmacy) are to further hospital pharmacy in all its aspects:

- to promote the exchange of views on professional subjects relating to the duties and responsibilities of hospital pharmacists
- to promote pharmaceutical care for patients in hospital-related facilities
- to foster continuous education programs for hospital pharmacists
- to promote realization of the goals of FIP as they apply to hospital pharmacists

- to pay particular attention to the needs of developing countries
- to promote integrating pharmacy services through communication and collaboration with other sections

The Section's vision for hospital pharmacy is set out in the *Revised FIP Basel Statements on the Future of Hospital Pharmacy*,[2] a set of consensus statements initially developed at the inaugural FIP Global Conference on the Future of Hospital Pharmacy in Basel, Switzerland, in 2008[3] and updated in Bangkok, Thailand, in 2014.[2] The work of updating these statements has been described and their relevance summarized in a previous *CJHP* editorial,[4] and research pertaining to the Basel Statements has also been published in this journal.[5,6] The work of the research committee of the Hospital Pharmacy Section, known as the World Hospital Pharmacy Research Consortium, has also been highlighted in *CJHP*.[7]

In addition to its active research group, the Hospital Pharmacy Section of FIP also undertakes many other activities to meet its goals, including organizing excellent educational programs and workshops at the FIP annual conferences, providing regular webinars, and connecting to members through regular newsletters and social media. The most recent FIP conference was held in Seoul, Republic of Korea; the 2018 edition will be in Glasgow, Scotland; and after that, attendees will be off to Abu Dhabi, United Arab Emirates.

The Executive Committee of the Hospital Pharmacy Section consists of the President, Past President, Treasurer, Secretary, Assistant Secretary, and a Vice President from each of the WHO regions. Any member of the section is eligible to be a member of the Executive Committee, with positions typically having 4-year terms. Another way to get involved in the Hospital Pharmacy Section is through one of the committees: the Basel Statements Promotion Committee, the Communications Committee, the Finance Committee, the Membership Committee, and the Research Committee.

Another active program supported by FIP is called Pharmabridge. This voluntary initiative is intended to strengthen pharmacy services in low-income and emerging countries. It was "established to link individuals and institutions together to actively exchange resources and training in pharmacy practice, pharmaceutical science, pharmaceutical industry and professional pharmacy education"(http://fip.org/www/index.php?page=pharmabridge). Through Pharmabridge, pharmacists from developing countries can visit developed countries and participate in a coordinated program that establishes institutional and personal connections across borders. This is another way to learn from our international colleagues, and participating in Pharmabridge might be something that you and your institution could consider in the future.

If, like me, you have an interest in learning about pharmacy outside your own setting, reading widely, travelling internationally, and getting involved will really help to open your eyes to new ideas. However, what I find when I read about hospital pharmacy in different parts of the world, or when I hear inspiring speakers at the FIP Congresses, is that there are always more similarities than differences around this vast world of ours. Furthermore, we all have the same goal: to improve patient care. Yet it is where there are differences that we are challenged to learn or try new things, or to help others to achieve desired outcomes by sharing our own experiences. If you would like to find out more about FIP and become more internationally focused, please visit the FIP website (www.fip.org) or contact me or other members of the FIP Hospital Pharmacy Section.

References

1. *International Pharmaceutical Federation annual report 2016: putting people first*. The Hague (Netherlands): International Pharmaceutical Federation; 2016 [cited 2017 Dec 22]. Available from: http://fip.org/files/fip/FIP_Annual_Report_2016.pdf
2. 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.
3. The Basel Statements on the future of hospital pharmacy. *Am J Health Syst Pharm.* 2009;66(5 Suppl 3):S61-6.
4. Moles RJ, Vermeulen L, Penm J, Ivey M. The Basel Statements: updated and relevant to all [editorial]. *Can J Hosp Pharm*. 2016;69(2):101-2.
5. Poh J, Vaillancourt R, Lamarre D, Oyella J. Use of the 2008 Basel consensus statements to assess, realign, and monitor pharmacy practice at a tertiary care hospital in northern Uganda: illustrative case study. *Can J Hosp Pharm.* 2013;66(5):318-27.
6. Penm J, Chaar B, Moles RJ. Use of the International Pharmaceutical Federation's Basel Statements to assess and advance hospital pharmacy practice: a scoping review. *Can J Hosp Pharm*. 2016;69(2):131-7.
7. Moles R, Chaar B, Penm J. The World Hospital Pharmacy Research Consortium—monitoring global practice in relation to the Basel Statements [editorial]. *Can J Hosp Pharm*. 2014;67(5):331-2.

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Competing interests: None declared.

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La pharmacie hospitalière internationale : apprendre les uns des autres

par Rebekah J. Moles

Au cours des deux dernières années, le *Journal canadien de la pharmacie hospitalière* (JCPH) a publié la série « Perspectives internationales sur la pratique pharmaceutique » où sont présentés les systèmes de santé et la pratique de la pharmacie de divers pays des six régions de l'Organisation mondiale de la Santé (OMS) (http://www.who.int/about/regions/fr/). La série comprend des comptes rendus de l'Australie, de l'Afrique du Sud, de la Belgique, de l'Arabie saoudite, des États-Unis, du Népal, de la Jordanie, du Japon, de l'Italie, du Brésil et du Kenya (consultez l'encadré 1 dans la version anglaise de cet éditorial, à la page 3 du numéro); les derniers articles de la série, qui porteront sur la pratique à Hong Kong et en Thaïlande, seront publiés en 2018. Une partie de la vision du JCPH est de partager de l'information sur la « pratique de la pharmacie centrée sur le patient dans les hôpitaux et les autres milieux de soins de santé misant sur la collaboration […] ailleurs dans le monde » : la série a ainsi été conçue pour aider à réaliser cette vision.

Les pharmaciens peuvent aussi apprendre sur la pratique à l'étranger en se rendant à des conférences internationales ou en apprenant de leurs homologues d'autres pays. La Fédération internationale pharmaceutique (FIP) s'avère un excellent point de départ. Cette organisation représente 4 millions de pharmaciens et de scientifiques du médicament. Cette organisation non gouvernementale entretient des relations officielles avec l'OMS depuis 1948. Grâce à ses partenariats et à son large réseau international en pharmacie et en sciences pharmaceutiques ainsi qu'aux innovations dans le domaine de la pratique et aux progrès scientifiques, la FIP appuie le développement de la profession de pharmacie afin de répondre aux besoins mondiaux en santé[1].

La structure de la FIP est complexe mais se compose essentiellement de deux organes principaux : le Conseil des sciences pharmaceutiques (Board of Pharmaceutical Sciences [BPS]) et le Conseil de la pratique pharmaceutique (Board of Pharmaceutical Practice [BPP]). Un troisième organe prééminent, FIP Éducation (FIP*Ed*), a été mis sur pied récemment pour veiller aux questions relatives à la formation en pharmacie. De plus, le Young Pharmacists Group de la FIP s'adresse aux diplômés plus récents et la FIP soutient aussi l'International Pharmaceutical Students' Federation. Le BPS compte neuf groupes d'intérêts spéciaux et le BPP est composé de huit sections, dont celle de la pharmacie hospitalière. Lorsqu'une personne devient membre de la FIP, elle est affiliée à la section de son choix. Il lui est ensuite possible de s'inscrire à d'autres sections, sans restriction quant au nombre, pour la modique somme de 15 euros par section.

La section de la pharmacie hospitalière est la deuxième en importance (après celle de la pharmacie communautaire) et c'est sans doute la plus dynamique. L'objectif de la section (www.fip.org/hospital_pharmacy) est de faire évoluer chacune des dimensions de la pharmacie hospitalière, soit :

- favoriser les échanges d'idées sur des sujets professionnels qui touchent aux devoirs et responsabilités des pharmaciens d'hôpitaux;
- promouvoir les soins pharmaceutiques pour les patients dans les établissements de santé;
- favoriser les programmes de formation continue pour les pharmaciens d'hôpitaux;
- encourager l'atteinte des objectifs de la FIP lorsqu'ils s'appliquent aux pharmaciens d'hôpitaux;
- porter une attention particulière aux besoins des pays en développement;
- encourager l'intégration des services de pharmacie par la communication et la collaboration avec les autres sections.

La vision de la section pour la pharmacie hospitalière est exposée dans les déclarations de Bâle révisées sur l'avenir de la pharmacie hospitalière[2] : il s'agit d'un ensemble de déclarations consensuelles conçues initialement en 2008 à la première Conférence mondiale sur l'avenir de la pharmacie hospitalière à Bâle en Suisse[3], puis mises à jour en 2014 à Bangkok en Thaïlande[2]. Le travail fait pour mettre ces déclarations à jour a été décrit et leur pertinence a été résumée dans un précédent éditorial du JCPH[4] et des recherches liées aux déclarations de Bâle ont aussi été publiées dans ce journal[5,6]. Le rôle du comité de

recherche de la section de la pharmacie hospitalière, qui s'appelle le World Hospital Pharmacy Research Consortium, a aussi été présenté dans le JCPH[7].

En plus du travail de son groupe de recherche dynamique, la section de la pharmacie hospitalière de la FIP mène aussi beaucoup d'autres activités pour atteindre ses objectifs : elle organise notamment d'excellents programmes et ateliers de formation lors des conférences annuelles de la FIP, elle offre régulièrement des webinaires et elle communique avec les membres par l'intermédiaire d'infolettres et des médias sociaux. La dernière conférence de la FIP a eu lieu à Séoul en Corée du Sud, l'édition de 2018 se tiendra à Glasgow en Écosse, puis les congressistes iront à Abu Dhabi aux Émirats arabes unis.

Le comité de direction de la section de la pharmacie hospitalière est composé d'un président, d'un président sortant, d'un trésorier, d'un secrétaire, d'un secrétaire adjoint et, pour chacune des régions de l'OMS, d'un vice-président. Tout membre de la section a la possibilité de siéger au comité de direction où les mandats sont normalement de quatre ans. Une autre façon de s'impliquer dans la section de la pharmacie hospitalière est de se joindre à l'un de ses comités : le comité de promotion des déclarations de Bâle, le comité des communications, le comité des finances, le comité d'adhésion et le comité de la recherche.

Un autre programme populaire à participation volontaire soutenu par la FIP s'appelle Pharmabridge. Il a pour objectif de renforcer les services de pharmacie dans les pays à faible revenu et les pays émergents. Il a été mis en place pour mettre en relation des personnes avec des établissements afin qu'ils échangent activement des ressources et de la formation dans les domaines de la pratique de la pharmacie, des sciences pharmaceutiques, de l'industrie pharmaceutique et de l'enseignement professionnel de la pharmacie (http://fip.org/www/index.php?page=pharmabridge). Grâce à Pharmabridge, les pharmaciens des pays en développement peuvent se rendre dans les pays développés et participer à un programme coordonné qui crée des liens organisationnels et personnels au-delà des frontières. Il s'agit d'une autre façon d'apprendre de nos collègues à l'étranger. D'ailleurs, peut-être que vous et votre établissement songerez aussi à participer à Pharmabridge dans l'avenir.

Si, tout comme moi, vous voulez en apprendre davantage sur la pharmacie en dehors de votre milieu, alors lire abondamment, voyager à l'étranger et s'engager vous permettra vraiment de découvrir de nouvelles idées. Cela dit, j'ai remarqué une chose en lisant sur la pharmacie hospitalière exercée dans différents endroits du monde et en écoutant des conférenciers inspirants dans les congrès de la FIP : il y a toujours plus de similitudes que de différences dans notre vaste monde. En outre, nous avons tous le même but : améliorer les soins aux patients. Mais ce sont nos différences qui nous amènent à nous dépasser et à apprendre ou à essayer de nouvelles choses, ce sont elles qui nous poussent à aider les autres à atteindre leurs objectifs en leur faisant part de nos propres expériences. Si vous souhaitez en apprendre davantage à propos de la FIP et être plus orienté vers l'international, veuillez consulter le site Web de la FIP (www.fip.org) ou communiquer avec moi ou un autre membre de la section de la pharmacie hospitalière de la FIP.

[Traduction par l'éditeur]

References

1. *International Pharmaceutical Federation annual report 2016: putting people first*. La Haye (Pays-Bas) : International Pharmaceutical Federation; 2016. Publié au : http://fip.org/files/fip/FIP_Annual_Report_2016.pdf. Consulté le 22 décembre 2017.
2. 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.
3. The Basel Statements on the future of hospital pharmacy. *Am J Health Syst Pharm.* 2009;66(5 Suppl 3):S61-6.
4. Moles RJ, Vermeulen L, Penm J, Ivey M. Les déclarations de Bâle : mises à jour et pertinentes pour tous [éditorial]. *Can J Hosp Pharm.* 2016;69(2):101-2.
5. Poh J, Vaillancourt R, Lamarre D, Oyella J. Use of the 2008 Basel consensus statements to assess, realign, and monitor pharmacy practice at a tertiary care hospital in northern Uganda: illustrative case study. *Can J Hosp Pharm.* 2013; 66(5):318-27.
6. Penm J, Chaar B, Moles RJ. Use of the International Pharmaceutical Federation's Basel Statements to assess and advance hospital pharmacy practice: a scoping review. *Can J Hosp Pharm*. 2016;69(2):131-7.
7. Moles R, Chaar B, Penm J. Le World Hospital Pharmacy Research Consortium — Suivi de la pratique dans le monde relativement aux déclarations de Bâle [éditorial]. *Can J Hosp Pharm*. 2014;67(5):331-2.

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ORIGINAL RESEARCH

Interaction between Psychotropic Medications and Alcohol: Perceptions among Patients Attending an Adult Mental Health Day Hospital Program

Cynthia Cheng, Fatima Mithoowani, Thomas Ungar, and Monica Lee

ABSTRACT

Background: Interaction between alcohol and certain medications can lead to adverse consequences. Individuals with mental health disorders are particularly vulnerable because of their psychotropic medications, which are typically taken over extended periods and which are known to have pharmacokinetic and pharmacodynamic interactions with alcohol. It is unknown what education these patients receive from their health care providers and how such interactions are managed.

Objectives: To determine whether individuals with mental health disorders are aware of alcohol–drug interactions and if so, how they use such information.

Methods: A questionnaire was developed to explore the perceptions of mental health patients concerning alcohol–drug interactions. The questionnaire included questions in 3 domains: knowledge of potential alcohol–drug interactions, consumption of alcohol while taking psychotropic medications, and source of advice regarding the interactions. Attendees of an adult mental health day hospital program were invited to participate.

Results: A total of 131 participants answered the questionnaire between July 2014 and February 2015; 31 of the questionnaires were incomplete and were excluded from analysis. Of the 100 participants included in the analyses, 75 reported having received counselling from a health care provider about alcohol–drug interactions, and 49 of these reported following the advice provided. The most common advice reported by participants was to avoid alcohol consumption while taking medications. Serious adverse effects, such as worsening of a psychiatric condition, admission to hospital, and increased drowsiness, were reported by 23 participants. Sixty-nine participants considered physicians to be the best source of information about these interactions.

Conclusions: Most participants reported that they had received information about strategies to avoid negative consequences from alcohol–drug interactions. Nevertheless, consumption of alcohol occurred, and almost one-quarter of participants reported a serious adverse effect related to consuming alcohol. These self-reported data indicate that patients do not

RÉSUMÉ

Contexte : L'interaction entre l'alcool et certains médicaments peut mener à des conséquences cliniques. Les personnes atteintes de troubles mentaux y sont particulièrement vulnérables à cause des médicaments psychotropes qu'ils prennent d'habitude sur une période prolongée et pour lesquels les interactions pharmacocinétiques et pharmacodynamiques avec l'alcool sont notoires. On ne sait pas quels conseils ces patients reçoivent de leurs fournisseurs de soins de santé et comment de telles interactions sont gérées.

Objectifs : Déterminer si les personnes atteintes de troubles mentaux sont conscientes des interactions entre l'alcool et les médicaments et, si oui, dévoiler comment elles agissent à la lumière de cette information.

Méthodes : On a mis au point un questionnaire pour enquêter sur les perceptions qu'ont les patients atteints de troubles mentaux des interactions alcool-médicaments. Les questions y étaient regroupées en trois catégories : conscience des interactions potentielles alcool-médicaments, consommation d'alcool en prenant des psychotropes et source des conseils sur les interactions. Les participants à un programme hospitalier de jour pour adultes atteints de troubles mentaux ont été invités à participer à l'étude.

Résultats : Au total, 131 participants ont rempli le questionnaire entre juillet 2014 et février 2015; 31 des questionnaires étaient incomplets et ont été exclus de l'analyse. Parmi les 100 participants inclus dans les analyses, 75 ont indiqué avoir reçu des conseils d'un fournisseur de soins de santé sur les interactions alcool-médicaments et 49 d'entre eux ont affirmé avoir suivi les conseils offerts. Le conseil le plus fréquent selon les répondants était d'éviter la consommation d'alcool lorsqu'on prend des médicaments. De graves réactions indésirables, telles que la détérioration d'un trouble psychiatrique, l'admission à l'hôpital et une somnolence accrue, ont été soulignées par 23 participants. Soixante-neuf participants considéraient les médecins comme les meilleures sources d'information à propos de ces interactions.

Conclusions : La plupart des participants ont indiqué avoir reçu de l'information sur les stratégies permettant d'éviter les conséquences des interactions alcool-médicaments. Certains ont tout de même consommé

necessarily follow the advice of their health care providers. Future studies should explore reasons for the gap between advice and action and how to minimize it.

Keywords: psychotropic drugs, alcohol, drug–alcohol interactions, perception, questionnaire, mental health

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de l'alcool et près du quart des participants ont signalé une réaction indésirable grave liée à la consommation d'alcool. Ces données autodéclarées révèlent que les patients ne suivent pas nécessairement les conseils de leurs fournisseurs de soins de santé. Des études ultérieures devraient se pencher sur les raisons expliquant l'écart entre les conseils et les actions et sur les solutions pour réduire cet écart.

Mots clés : médicaments psychotropes, alcool, interactions médicament-alcool, perception, questionnaire, santé mentale

INTRODUCTION

According to a Canadian study published in 2012, 80% of males and 74% of females aged 15 years or older reported consuming alcohol within the past year (data for 2010).[1] Alcohol interacts with many over-the-counter and prescription drugs, including psychotropic medications such as antidepressants, anxiolytics, and antipsychotics, which are commonly prescribed for the treatment of mental health disorders. The mechanism by which alcohol interacts with medications can be pharmacokinetic or pharmacodynamic in nature. Acute alcohol ingestion may inhibit the enzymes responsible for drug metabolism, increasing the risk of adverse effects from a medication by prolonging and enhancing its availability. Conversely, chronic alcohol ingestion may induce certain enzymes, resulting in enhanced drug elimination and diminished therapeutic effects. Medications can also alter the metabolism of alcohol, increase alcohol-related adverse effects, and lower the threshold for intoxication. When combined with psychotropic medications, alcohol may potentiate the drugs' inhibitory effects on the central nervous system, which can impair an individual's ability to function.[2] It has been estimated that alcohol–medication interactions may be a factor in at least 25% of all emergency room visits.[3]

Several studies have evaluated patterns of use of alcohol and interacting medications in various populations.[4-7] In a population-based study in the United States, Breslow and others[8] found that 41.5% of adult current drinkers used alcohol-interactive medications, the most commonly used medication classes being cardiovascular agents and central nervous system agents. Although literature about the interactions between psychotropic medications and alcohol in Canada is sparse, one Canadian study reported the prevalence of heavy alcohol consumption among benzodiazepine users in the previous week as 7.2%; current benzodiazepine users were less likely than non-current users to have recently consumed any alcohol.[9] Psychotropic medications are often prescribed for long-term treatment of chronic mental health conditions; as such, it is important for patients to understand the serious negative consequences and risks that may result from alcohol–drug interactions. Health care professionals, such as physicians, nurses, and pharmacists, may give patients information related to their medications. However, it is unknown whether patients are aware of potential interactions with alcohol or whether they follow any advice that is provided.

The goal of this study was to explore the knowledge of and perceptions about alcohol–drug interactions among individuals attending the Adult Mental Health Day Hospital Program at North York General Hospital, in Toronto, Ontario. This was a baseline study, with participants being asked to complete the study survey before any interaction with the program's clinicians.

METHODS

Questionnaire

A literature search was conducted to determine whether a similar validated survey existed to help answer the research questions. No prior studies on this topic were found, so the authors developed a self-administered questionnaire to investigate patients' knowledge about and specific advice received regarding alcohol intake while using prescription medications. The questionnaire was developed through consensus among 3 of the authors (C.C., F.M., M.L.). Questions were formulated on the basis of what the authors thought would best answer the research questions. The questionnaire was then distributed to 5 non–health care professionals, who evaluated readability of the content, layout, and style. Feedback was incorporated to improve readability of the questions. However, the questionnaire was not pretested with individuals similar to those in the intended study sample, and it has not been validated.

The questionnaire consisted of a section concerning demographic characteristics and an additional 9 questions addressing the following 3 domains: knowledge of drug–alcohol interactions, consumption of alcohol while taking psychotropic medications, and source of advice regarding alcohol–drug interactions. The complete questionnaire is available in Appendix 1

(https://www.cjhp-online.ca/index.php/cjhp/issue/view/125/showToc). A convenience sample of 100 acceptable surveys was chosen.

Participant Selection

Individuals newly enrolled in the Adult Mental Health Day Hospital Program (referred to hereafter as "the Day Hospital Program") at North York General Hospital were invited to complete the questionnaire. One component of the program involves pharmacy teachings, which include discussions of alcohol use. Therefore, patients who had previously been enrolled in the program, as well as current program enrollees, were excluded, to avoid study participation by patients with knowledge gained through program experience.

The Day Hospital Program is a 3-week outpatient program that was developed as an alternative to traditional inpatient treatment for those not requiring inpatient care and as a transitional "step-down" program for patients with subacute conditions. The program provides assessment and treatment services and promotes recovery. Those eligible for the program are adults 18 years of age or older who, in the clinical judgement of the referring physician (family practice physician or psychiatrist), are in acute emotional distress and require immediate and intensive intervention, yet have sufficient support to continue living in the community.[10] Patients who have recently been discharged from a hospital are also eligible. There is no specific timeframe used to define a "recent discharge"; eligible inpatients usually receive a referral during the hospital stay and are placed on a waitlist.

Within the Day Hospital Program, patients have the opportunity to work with an interdisciplinary team to learn about symptom management, treatment modalities, and coping skills, and to receive care for stabilization and treatment of their mental health condition. At the time of this study, the interdisciplinary team consisted of an occupational therapist, a social worker, psychiatrists (including T.U.), a psychologist, nurses, and pharmacists (C.C., F.M.). Among other activities, patients participate in twice-weekly group medication education sessions conducted by pharmacists, which include a brief discussion of alcohol use while taking psychotropic medications. The Day Hospital population was selected for this study because its participants represent a cohort transitioning toward outpatient management of their mental health conditions. They have more contact with health care providers than do outpatients not enrolled in this type of program, and can provide insight into perceptions and knowledge of drug–alcohol interactions.

Data Collection

The introduction letter and questionnaire were included in the orientation package that patients received from the unit secretary on their first day of the Day Hospital Program, before contact with any health care professional (including the program's pharmacists). Each patient was given an hour to complete the orientation package and was given the choice of completing the anonymous questionnaire for this study. Questionnaires were collected by the unit secretary and placed in a tamper-resistant box. Incomplete questionnaires (those with 3 or more questions left unanswered) were excluded from the analysis. All responses were entered into a spreadsheet (Excel 2010, Microsoft Corporation, Redmond, Washington) by one investigator (C.C.). A second investigator (F.M.) verified the data entry for accuracy. Descriptive statistics were used to summarize the data. Written consent was not requested, because completion of the anonymous survey was deemed to imply consent to participate in the study. The research protocol was reviewed and approved by the North York General Hospital Research Ethics Board in June 2014.

RESULTS

Over the 8-month study period (July 2014 to February 2015), all 506 patients who were newly admitted to the Day Hospital Program were invited to participate in the study. Of 131 surveys submitted, 31 were incomplete and were therefore excluded from analysis; therefore, 100 surveys were included in the analysis.

Demographic and Clinical Characteristics

The study sample consisted of 46 male participants, 52 female participants, and 2 participants who did not disclose their sex. Fifty-eight of the 100 respondents were 39 years of age or younger. Eighty-eight had taken at least one psychotropic medication, with antidepressants and benzodiazepines being the

Table 1. Characteristics of Participants

Characteristic	No. of Participants (*n* = 100)
Age (years)	
18–29	33
30–39	25
40–49	15
50–59	16
60–69	8
Did not disclose	3
Sex	
Men	46
Women	52
Did not disclose	2
Medications taken*	
Benzodiazepines	42
Antidepressants	46
Antipsychotics	24
Mood stabilizers	22
Stimulants	3
None	12

*Some participants reported taking more than one type of medication.

most common (Table 1). Nine participants indicated that they had previously required an intervention for alcohol misuse, and 14 stated that alcohol has been a factor in past hospital admissions. Figure 1 depicts the current alcohol consumption reported by the participants. Of the 100 respondents, most (87) reported consuming alcohol once a week or less frequently.

Knowledge of Drug–Alcohol Interaction

Seventy-five of the respondents acknowledged that they had received advice about taking psychotropic medications and drinking alcohol (Figure 2). Fifty-six (75%) of these 75 respondents reported that the information they had received was sufficient, and 8 (11%) indicated that the information was not sufficient. Only 49 (65%) of the 75 stated that they had followed the advice received. The most common advice received was to avoid alcohol consumption while on medications (49 of 75 [65%]), followed by limiting the number of alcoholic drinks (19 of 75 [25%]) (Figure 3).

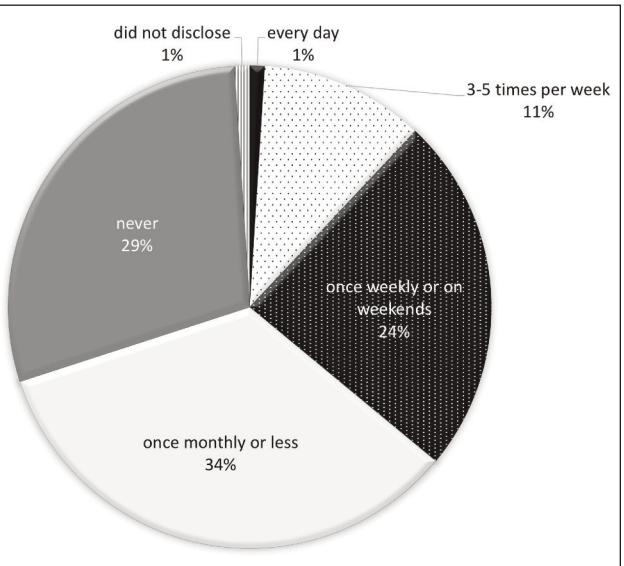

Figure 1. Reported frequency of current alcohol consumption among the 100 survey respondents.

Consumption of Alcohol while Taking Psychotropic Medications

Twenty-three respondents reported experiencing a serious adverse effect related to an interaction between their psychotropic medication and alcohol, specifically hospital admission (n = 5), worsening of their psychiatric condition (n = 7), and increase in drowsiness (n = 11) (Figure 4). Of these 23 respondents, 21 had received counselling regarding psychotropic medication use and alcohol consumption, although the questionnaire did not explore whether the counselling was received before or after the self-reported adverse effects. When asked whether they had considered the possibility of an alcohol–drug interaction before consuming alcohol, 33 of the 100 participants reported having thought about the interaction, and 14 reported a decision to deal with the consequences afterward. Three 3 respondents selected both of these options; by consensus, the authors assumed the worst scenario and counted these respondents only in the second category ("deal with the consequences").

Source of Advice Regarding Alcohol–Drug Interactions

Participants were asked to indicate all sources from which they had obtained information about alcohol–drug interactions (Figure 5, top). Family doctors, psychiatrists, and pharmacists were the most frequently identified sources of the interaction information, followed by the internet. Friends, family, and addiction counsellors were less commonly identified sources. With respect to which health care professionals were considered best to discuss alcohol use and psychotropic medications, psychiatrists ranked first and family doctors second, followed by addiction counsellors and pharmacists (Figure 5, bottom).

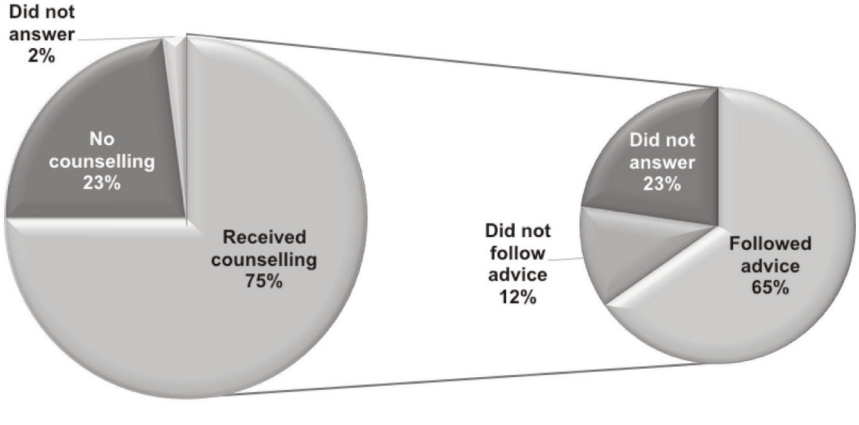

Figure 2. Proportion of participants reporting that they received counselling about drug–alcohol interactions (n = 100) and whether they followed the advice (n = 75).

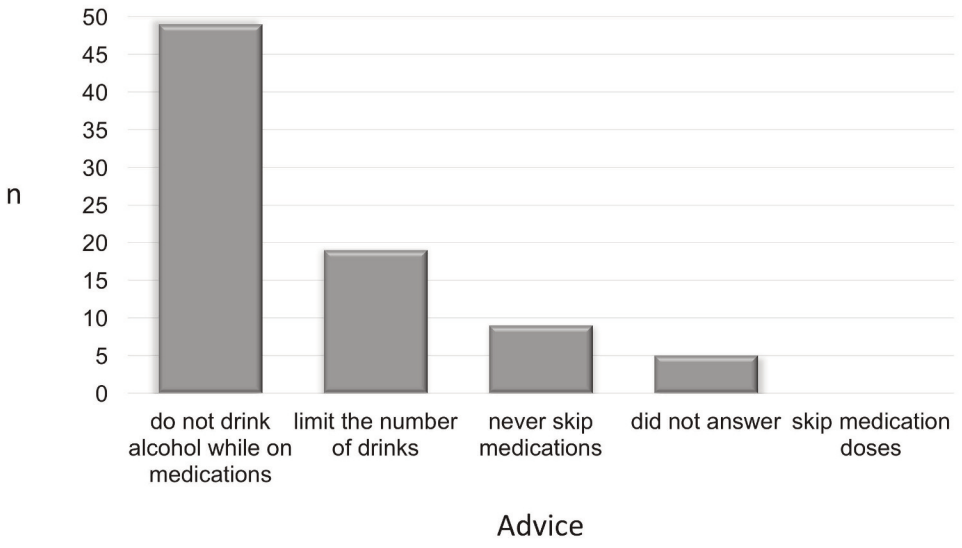

Figure 3. Advice that participants received about drug–alcohol interactions, based on selection from a specified list in the questionnaire (*n* = 75; sum of data is greater than 75 because some respondents reporting receiving more than one type of advice).

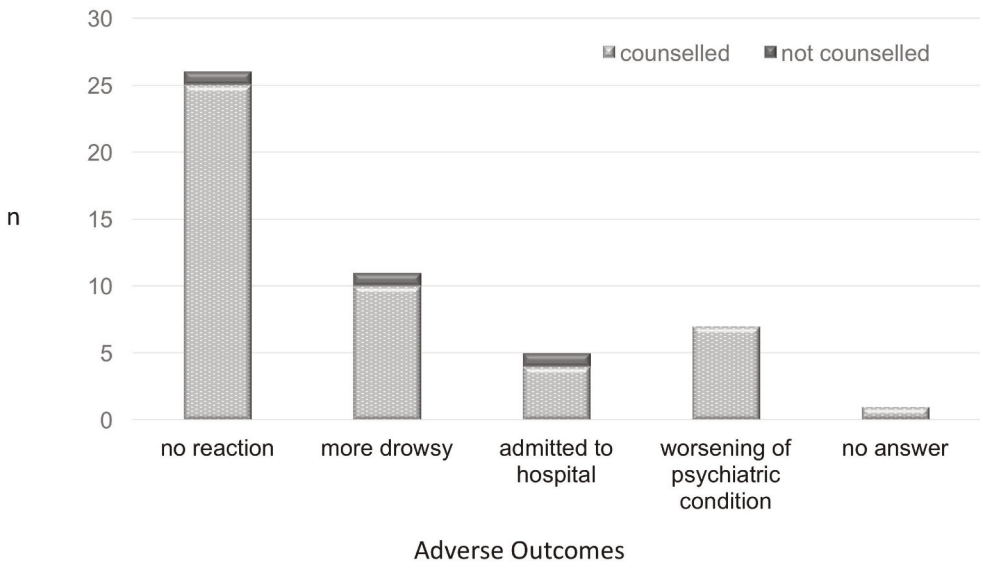

Figure 4. Reactions associated with drug–alcohol interactions at any time in the past.

DISCUSSION

About a quarter of patients newly admitted to the Day Hospital Program participated in this survey. The participants were primarily young adults under the age of 40, with about equal representation of men and women. Although the questionnaire was not designed to collect information about participants' psychiatric diagnoses, the majority reported having taken benzodiazepines or antidepressants (or both). About three-quarters of the study sample admitted to consuming alcohol at least occasionally, which is similar to the pattern of social drinking reported by Health Canada for 2012, whereby 78.4% of respondents stated having had at least one drink in the past year.[11]

A large proportion of participants (75%) recalled being counselled about drug–alcohol interactions. This finding contrasts with a previous study, which reported that only 15.7% of US adults had ever discussed alcohol use with a health professional.[12] This difference might be attributable to the populations studied:

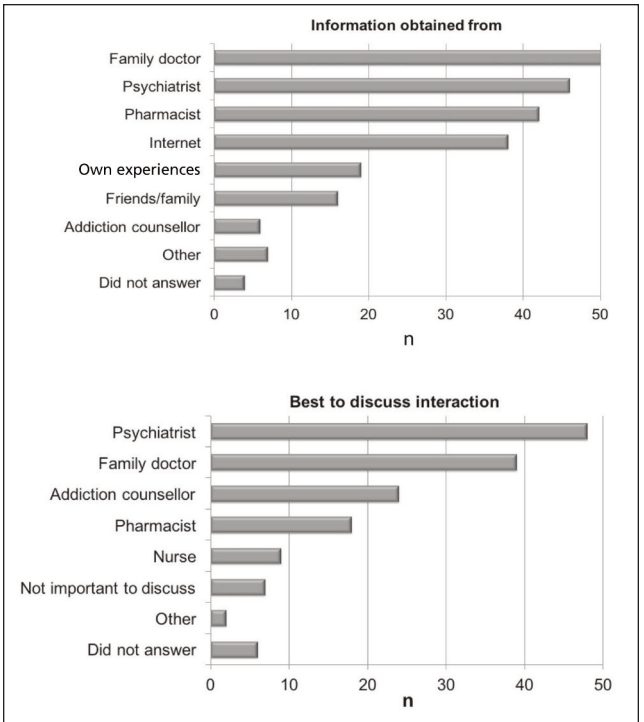

Figure 5. Top: Sources of counselling about drug–alcohol interaction reported by participants (n = 100). Bottom: Sources that participants thought were the best for provision of counselling (n = 100). For both parts of this figure, respondents could select more than one answer from a list provided.

perhaps more emphasis is placed on drug–alcohol interactions during counselling about mental health medications than is the case for other medications for chronic conditions.

At present, there is no consensus on how clinicians should counsel patients on potential interactions between alcohol and psychotropic medications. Most patients in this study reported being advised not to drink alcohol while taking psychotropic medications or to limit the amount of alcohol consumed, consistent with recommendations in product monographs and standard drug references. Although the majority of respondents considered this information to be sufficient, some participants admitted not following this advice. More importantly, about a quarter of all respondents reported perceived harm as a result of a drug–alcohol interaction, including serious consequences such as hospital admission and worsening of their psychiatric conditions. The current study did not explore reasons why participants did not follow advice from health care professionals, but we hypothesize the following: challenges associated with avoiding alcohol completely when taking an interacting medication for a chronic condition, lack of a strong therapeutic alliance between the provider and patient,[13] inadequate health literacy, insufficient time for proper counselling, and emotional barriers involving self-medication. Future studies should explore these hypotheses to gain further insight on how adverse outcomes from drug–alcohol interactions can be minimized.

With respect to the health care professionals that the patients thought would be best to discuss alcohol use and psychotropic medications, psychiatrists and family physicians received top rankings, followed by addiction counsellors and pharmacists. It was unclear why pharmacists were not considered best suited to provide drug interaction information in this population. Further studies should explore mental health patients' perceptions of various health care professionals in providing drug interaction advice.

This study had several limitations. It relied on self-reporting by participants, and previous studies have shown that individuals often under-report the amount of alcohol consumed when they are asked to self-report.[14] Only about 25% of the patients newly admitted to the Day Hospital Program chose to participate in this study, which could have resulted in selection bias. A literature search revealed no previous questionnaires examining the use of alcohol by patients who were taking medications, so a new questionnaire was created to gather self-reported data and comments for this study; however, this questionnaire has not been validated. Although the readability of the questionnaire was evaluated by non–health care professionals, it was not pretested with individuals similar to the intended study sample. Some patients may have found the questionnaire difficult to navigate, and 31 questionnaires were excluded from the analysis because 3 or more questions had been left unanswered. For future studies, methods should be employed to ensure completion of the survey, such as use of electronic questionnaires or interviewers. This survey did not explore the temporal relationship between a patient's behaviour and the timing of counselling, nor was there any direct evidence of the type of counselling provided by clinicians. Finally, all participants were from the outpatient psychiatric day hospital program at a single site, which limits the generalizability of results to other patient groups.

CONCLUSION

Most of the participants in this study, drawn from patients attending the Adult Mental Health Day Hospital Program at North York General Hospital, reported having received information about alcohol–drug interactions from a health care provider. Nevertheless, some participants consumed alcohol and medications concurrently, and perceived that alcohol–drug interactions had caused them harm. The study results suggest that there may be a gap between professionals' recommendations and patients' behaviour. Future studies should explore which strategies can best minimize adverse consequences resulting from alcohol–drug interactions.

References

1. Thomas G. *Alcohol Price Policy Series, Report 1 of 3: Levels and patterns of alcohol use in Canada.* Ottawa (ON): Canadian Centre on Substance Abuse; 2012 [cited 2016 Aug 28]. Available from: www.ccsa.ca/Resource%20Library/CCSA-Patterns-Alcohol-Use-Policy-Canada-2012-en.pdf

2. Weathermon R, Crabb DW. Alcohol and medication interactions. *Alcohol Res Health.* 1999;23(1):40-54.
3. Holder HD. *Effects of alcohol, alone and in combination with medications.* Walnut Creek (CA): Prevention Research Center; 1992.
4. Adam WL. Potential for adverse drug-alcohol interactions among retirement community residents. *J Am Geriatr Soc.* 1995;43(9):1021-5.
5. Forster LE, Pollow R, Stoller EP. Alcohol use and potential risk for alcohol-related adverse drug reactions among community-based elderly. *J Community Health*. 1993;18(4):225-39.
6. Jalbert JJ, Quilliam BJ, Lapane KL. A profile of concurrent alcohol and alcohol-interactive prescription drug use in the US population. *J Gen Intern Med*. 2008;23(9):1318-23.
7. Pringle KE, Ahern FM, Heller DA, Gold CH, Brown TV. Potential for alcohol and prescription drug interactions in older people. *J Am Geriatr Soc.* 2005;53(11):1930-6.
8. Breslow RA, Dong C, White A. Prevalence of alcohol-interactive prescription medication use among current drinkers: United States, 1999-2010. *Alochol Clin Exp Res*. 2015;39(2):371-9.
9. Veldhuizen S, Wade TJ, Cairney J. Alcohol consumption among Canadians taking benzodiazepines and related drugs. *Pharmacoepidemiol Drug Saf.* 2009;18(3):203-10.
10. Partial hospitalization program. Toronto (ON): North York General Hospital; 2016 [cited 2016 Jul 27]. Available from: www.nygh.on.ca/Default.aspx?cid=1205&lang=1
11. Canadian alcohol and drug use monitoring survey. Ottawa (ON): Health Canada; 2014 [cited 2016 Jul 28]. Available from: www.hc-sc.gc.ca/hc-ps/drugs-drogues/stat/_2012/summary-sommaire-eng.php
12. McKnight-Eily LR, Liu Y, Brewer RD, Kanny D, Lu H, Denny CH, et al. Vital signs: communication between health professionals and their patients about alcohol use — 44 states and the District of Columbia, 2011. *MMWR.* 2014;63(1):16-22.
13. Levesque A, Li HZ, Pahal JS. Factors related to patients' adherence to medication and lifestyle change recommendations: data from Canada. *Int J Psychol Stud.* 2012;4(2):42-55.
14. Monk RL, Heim D, Qureshi A, Price A. "I have no clue what I drunk last night" using smartphone technology to compare in-vivo and retrospective self-reports of alcohol consumption. *PLoS One*. 2015;10(5):e0126209.

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ON THE FRONT COVER

Mont Sainte-Anne Beaupré, Quebec

This winter landscape shot was taken in early March atop Mont Sainte-Anne, the highest ski peak in eastern Canada. CSHP member François Cauchon, the President and CEO of BCE Pharma, used an iPhone 7 to take the photo.

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

ORIGINAL RESEARCH

Meropenem Assessment before and after Implementation of a Small-Dose, Short-Interval Standard Dosing Regimen

Ivy Chow, Vincent Mabasa, and Connor Chan

ABSTRACT

Background: Small-dose, short-interval dosing for meropenem has been shown to yield pharmacokinetic and pharmacodynamic properties similar to those associated with traditional dosing of this drug. However, few studies have examined clinical outcomes in the general population.

Objectives: To characterize differences in effects between a small-dose, short-interval dosing regimen for meropenem (500 mg every 6 h) and the traditional regimen (1000 mg every 8 h) on clinical outcomes and costs to the health care system.

Methods: This retrospective cohort study included 194 patients who received the traditional meropenem dosage (July 2006 to August 2008) and 188 patients who received the small-dose, short-interval regimen (December 2008 and October 2009) at a large tertiary care hospital and a community hospital. The primary outcome (clinical success), the secondary outcomes (30-day in-hospital mortality, time to defervescence, duration of therapy, and length of stay), and drug costs were compared between cohorts.

Results: The 2 cohorts did not differ significantly in terms of baseline characteristics. There was no statistically significant difference between the small-dose, short-interval regimen and the traditional dosing regimen in terms of the primary outcome: clinical success was achieved in 83.5% (162/194) and 80.8% (152/188) of the patients, respectively. Likewise, there was no statistically significant difference in any of the secondary outcomes. The average drug cost per patient per visit was $222.23 with small-dose, short-interval dosing and $355.90 with traditional dosing, a significant difference of more than $130 per patient per visit.

Conclusion: The small-dose, short-interval meropenem dosing regimen resulted in clinical outcomes similar to those achieved with the traditional dosing regimen at significantly lower cost.

Keywords: meropenem, pharmacodynamics, stewardship, dosing, outcomes

RÉSUMÉ

Contexte : Selon des études, un schéma posologique de méropénème avec administration d'une faible dose à intervalle réduit produit des résultats pharmacocinétiques et pharmacodynamiques semblables à ceux obtenus avec une posologie traditionnelle. Mais peu d'études ont examiné les résultats cliniques dans la population générale.

Objectif : Offrir un portrait des différences entre les effets d'un schéma posologique de méropénème avec administration d'une faible dose à intervalle réduit (500 mg toutes les 6 heures) et d'une posologie traditionnelle (1000 mg toutes les 8 heures) pour ce qui est des résultats cliniques et des coûts pour le système de santé.

Méthodes : La présente étude de cohorte rétrospective incluait 194 patients ayant reçu le méropénème selon le schéma posologique traditionnel (entre juillet 2006 et août 2008) et 188 patients l'ayant reçu avec administration d'une faible dose à intervalle réduit (entre décembre 2008 et octobre 2009) dans un grand hôpital de soins tertiaires et un hôpital communautaire. Le principal paramètre d'évaluation (succès clinique), les paramètres d'évaluation secondaires (taux de mortalité à l'hôpital dans les 30 jours, période de défervescence, durée du traitement et durée du séjour) et les coûts des médicaments ont été comparés entre les cohortes.

Résultats : Les deux cohortes n'étaient pas significativement différentes en ce qui touche aux caractéristiques de base. Il n'y avait aucune différence statistiquement significative entre le schéma posologique avec administration d'une faible dose à intervalle réduit et la posologie traditionnelle en ce qui concerne le principal paramètre d'évaluation : le succès clinique a été obtenu respectivement chez 83,5 % (162/194) et chez 80,8 % (152/188) des patients. De même, aucune différence statistiquement significative n'a été relevée pour les paramètres d'évaluation secondaires. Par contre, le coût moyen des médicaments par patient par visite était de 222,23 $ pour le schéma posologique avec administration d'une faible dose à intervalle réduit et de 355,90 $ pour la posologie traditionnelle, une différence significative de plus de 130 $ par patient par visite ($p < 0{,}001$).

Conclusion : Le schéma posologique de méropénème avec administration d'une faible dose à intervalle réduit produisait des résultats cliniques semblables à ceux de le posologie traditionnelle, et ce, pour un prix significativement plus faible.

Mots clés : méropénème, pharmacodynamie, gestion responsable, posologie, résultats

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INTRODUCTION

Meropenem is a broad-spectrum parenteral carbapenem antibiotic that is active against most gram-positive and gram-negative bacteria.[1] Given its broad spectrum of activity, it is often reserved for more complicated bacterial infections. Like other ß-lactam antibiotics, meropenem exerts time-dependent bactericidal activity that is maximized by optimizing the time when free drug concentration exceeds the minimum inhibitory concentration (MIC) for a given pathogen ($\%fT_{>MIC}$).[1,2] The commonly cited range of $\%fT_{>MIC}$ for meropenem is 20%–40%, although it appears to be based on minimal scientific investigation.[2] The traditional meropenem dosage is 1000 mg every 8 h. Alternative regimens that have been tried involve prolonged infusion times or a small-dose, short-interval approach, with the goal of achieving similar pharmacodynamic targets while minimizing drug cost.[2] One of the more common alternatives, 500 mg every 6 h, has shown equivalency in terms of $\%fT_{>MIC}$ in 4 separate Monte Carlo simulation studies[3-6] and also in a recent systematic review.[2]

Three previous retrospective studies have compared the clinical efficacy and cost savings of the small-dose, short-interval meropenem dosing regimen (500 mg every 6 h) with those of the traditional regimen.[7-9] Patel and others[7] reviewed the charts of 192 patients who received the small-dose, short-interval regimen and 100 patients who received the traditional regimen and found similar mortality rates (11.5% and 8%, respectively), clinical success rates (92.1% and 90.1%, respectively), and median durations of meropenem therapy (4 and 5 days, respectively). However, there was a statistically significant reduction in the median time to resolution of infection with the small-dose, short-interval regimen (1.5 and 3 days, respectively; $p < 0.0001$).[7] Kotapati and others[8] conducted a chart review for 45 patients who received small-dose, short-interval dosing and 40 patients who received traditional dosing, finding no difference in meropenem-related length of stay (7 and 7.5 days, respectively), clinical success rates (78% and 82%, respectively), microbiological eradication rates (63% and 79%, respectively), or median time to resolution of infection (4 and 4.5 days, respectively). Finally, in a retrospective analysis, Arnold and others[9] found no statistically significant differences in time to defervescence (2 and 3 days, respectively), need for additional antibiotics (17% and 14%, respectively), treatment duration (8 days for both groups), or in-hospital mortality (7% for both groups). Drug cost savings with the small-dose, short-interval regimen were substantial across all studies, ranging from US$151 to US$406 saved per patient per visit.[7-9]

Given the available evidence on alternative dosing of meropenem, the Fraser Health Authority Infectious Diseases Subcommittee introduced new guidelines for this drug in October 2008, recommending that clinicians adopt the standardized small-dose, short-interval regimen (500 mg IV every 6 h) for most infections in patients with adequate renal function (estimated glomerular filtration rate [eGFR] ≥ 50 mL/min).[6,7,10] Dosage adjustments for patients with reduced renal function (eGFR < 50 mL/min) were also included.[10] However, it was recognized that these recommendations were based on small, single-centre studies targeting specific infections and excluding patients with impaired renal function (eGFR < 25 mL/min). Also, the previous cost savings literature was based on the US health care system. The current study was undertaken to build upon the existing evidence by characterizing clinical efficacy in a larger population of patients with a broader spectrum of infections and a broader range of renal function. We also wanted to generate results that would be generalizable to the Canadian health care setting.

The primary objective of this study was to characterize differences in clinical outcomes between the small-dose, short-interval meropenem dosing regimen of 500 mg every 6 h and the traditional dosing regimen of 1000 mg every 8 h. Additionally, we examined the potential cost savings that could be achieved by using this small-dose, short-interval approach.

METHODS

Study Design

This study was a chart review at a tertiary care hospital and a community hospital. The study was approved by the Fraser Health Research Ethics Board. Informed consent was not required because of the retrospective nature of the study.

Inclusion Criteria

All patients who received a minimum of 72 h of traditionally dosed meropenem (1000 mg IV every 8 h) were eligible for inclusion in the historical cohort. All patients who received a minimum of 72 h of the small-dose, short-interval meropenem regimen (500 mg IV every 6 h) were eligible for inclusion in the alternative cohort. The inclusion periods were based on release of the Infectious Diseases Subcommittee guidelines in October 2008, avoiding the 2 months immediately before and after release (to allow for clinician adaptation) and extending long enough to achieve the desired sample size. Adjustment in dosing frequency according to renal function was acceptable if it followed the adjustment recommendations in the guidelines, as outlined in Table 1. These dosage adjustments differed from those of the manufacturer but allowed for adjustment for patients with estimated eGFR below 25 mL/min. Eligible patients were identified from the prescription database report of the Fraser Health Authority's medication-use evaluation team. From this pool of eligible patients, the required sample population was randomly selected for the analysis through random sequence generation.

Exclusion Criteria

Patients were excluded if they were younger than 18 years of age, had a body mass index greater than 40 kg/m^2, were receiving

Table 1. Meropenem Dosage Adjustment According to Estimated Glomerular Filtration Rate (eGFR)

	Meropenem Dosing Regimen by eGFR			
Regimen	**eGFR ≥ 50 mL/min**	**eGFR 25–49 mL/min**	**eGFR 10–24 mL/min**	**eGFR < 10 mL/min**
Traditional*	1000 mg IV q8h	1000 mg IV q12h	1000 mg IV q12h	1000 mg IV q24h
Small-dose, short-interval	500 mg IV q6h	500 mg IV q8h	500 mg IV q12h	500 mg IV q24h

*Traditional dosing regimen adapted from Aronoff and others.[10]

dialysis, or were pregnant. Patients with infections necessitating higher-than-usual meropenem concentrations (primarily cystic fibrosis and meningitis) were also excluded. Those whose antibiotic dose was not adjusted according to renal function within 48 h were excluded, as were patients with a meropenem dosing regimen other than the traditional regimen or the small-dose, short-interval regimen, as described in Table 1. Patients with solitary infections (i.e., having a single source, such as isolated pneumonia or urinary tract infection) caused by a meropenem-resistant organism confirmed by culture and susceptibility testing were excluded.

Data Collection

Baseline clinical and demographic characteristics, microbiological data, and meropenem dosing information were collected from the charts selected for review. Clinical data, including temperature, leukocyte count, neutrophil count, and any relevant notation within the progress notes pertaining to the patient's infection, were also recorded for comparison between cohorts. The data were collected by one investigator (C.C.) using both electronic and paper-based medical records.

The primary efficacy end point, clinical success rate, was defined as the percentage of patients with elevation of peripheral temperature (> 37.5°C), leukocyte count (> 11×10^9/L), and/or neutrophil count (> 8×10^9/L) at initiation of meropenem who experienced normalization of or reduction from baseline in temperature (normally ≤ 37.5°C), leukocyte count (normally ≤ 11×10^9/L), and neutrophil count (normally ≤ 8×10^9/L) along with signs of clinical resolution or improvement as noted in the patient chart. Clinical success could be either complete (i.e., total improvement within the duration of meropenem therapy) or partial (i.e., a trend in improvement, defined as consecutive values for temperature, leukocyte count, or neutrophil count decreasing toward normal, with de-escalation or discontinuation of antibiotics before full resolution). The secondary efficacy outcomes were in-hospital mortality, meropenem-related length of stay, duration of meropenem therapy, and time to defervescence. In-hospital mortality was defined as patient death during the admission in which meropenem was administered. Mortality was further stratified as infection-related and non–infection-related on the basis of clinician notes; if the cause of death was not specified, it was conservatively assumed that the death was related to an infectious process. Meropenem-related length of stay was defined as the length of time from initiation of meropenem therapy to discharge. Time to defervescence, captured only for those with elevated temperature at the start of meropenem therapy, was measured as the time from meropenem initiation to the point of normal body temperature, defined as consecutive temperatures below or equal to 37.5°C. Any discrepancies or ambiguities were discussed among the 3 investigators until a general consensus was reached.

Subgroup analysis was performed for more acutely ill populations, specifically patients admitted to the intensive care unit (ICU) and patients with *Pseudomonas aeruginosa* infections.

A historical cost analysis was conducted to determine whether there were any actual savings between 2006 and 2009. In addition, because there was a transition to use of generic meropenem in 2012 within the health authority, a prorated cost analysis was also conducted using meropenem pricing as of April 2015. For both the historical and current-pricing comparisons, the costs were determined by multiplying the total number of doses received by patients in the study by the cost per dose.

Statistical Analysis

Given the decreased time to infection resolution with the small-dose, short-interval meropenem dosing regimen observed by Patel and others[7] in what was, at the time of study inception, the largest clinical investigation published to date, we used a superiority study design. Using the clinical cure rate in that trial, with a small predicted difference in effect size and $\alpha = 0.05$, we determined that 186 patients were needed in each cohort for 80% statistical power. Based on an estimated 33% exclusion rate, 250 patients were randomly selected per cohort. All categorical data (baseline demographic characteristics and outcomes) were analyzed using χ^2 analysis or the Fisher exact test; continuous outcomes were compared with either the Student *t* test or Wilcoxon sum–rank test as appropriate. Differences between the 2 cohorts were adjusted by regression analysis as appropriate. Statistical significance included any 2-sided *p* value less than or equal to 0.05. All statistical analyses were carried out using Microsoft Excel 2010 (Microsoft Corp, Redmond, Washington). Data collection, statistical analysis, and manuscript creation were conducted without any financial support or corporate input.

RESULTS

To obtain the required sample size for the historical cohort, we included patients who received a minimum of 72 h of traditionally dosed meropenem from July 16, 2006, to August

16, 2008. To obtain the required sample size for the alternative cohort, we included patients who received a minimum of 72 h of the small-dose, short-interval meropenem regimen from December 16, 2008, to October 16, 2009.

After application of the exclusion criteria, the cohort with traditional dosing of meropenem had 194 patients and the cohort with small-dose, short-interval dosing had 188 patients (Figure 1). Both the reasons for exclusion and the numbers of patients excluded were similar between groups. No statistically significant differences were found between cohorts in terms of baseline characteristics or frequency of comorbidities (Table 2). Likewise, microbiological isolates and concomitant antibiotic usage were similar between groups (Table 3). The only statistically significant difference was related to the source of infection, there being more urinary tract infections in the small-dose, short-interval cohort (37.8% versus 27.3%; $p = 0.04$).

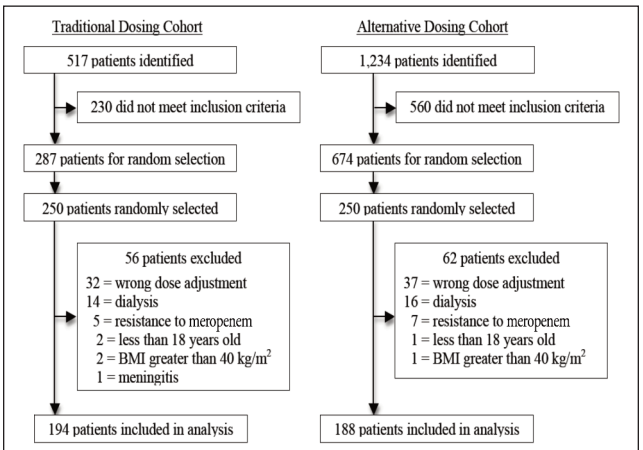

Figure 1. Study flow chart. BMI = body mass index.

Table 2. Baseline Characteristics of Patients Who Received Traditional or Small-Dose, Short-Interval Dosing of Meropenem

Characteristic	Dosing Regimen*; Mean ± SD or No. (%) of Patients†	
	Traditional Dosing (*n* = 194)	Small-Dose, Short-Interval Dosing (*n* = 188)
Age (years)	64.9 ± 14.5	66.1 ± 17.3
Weight (kg)	73.4 ± 25.3	72.8 ± 18.7
Height (m)	1.66 ± 0.1	1.67 ± 0.1
BMI (kg/m^2)	24.4 ± 5.1	25.1 ± 5.2
Sex, male	99 (51.0)	96 (51.1)
Length of stay (days)	11.6 ± 31.1	10.9 ± 25.1
eGFR (mL/min)	67.6 ± 30.0	68.4 ± 33.0
≥ 50 mL/min	147 (75.8)	128 (68.1)
25-49 mL/min	31 (16.0)	44 (23.4)
10-24 mL/min	13 (6.7)	16 (8.5)
<10 mL/min	3 (1.5)	0 (0.0)
ICU admission	19 (9.8)	23 (12.2)
Comorbidity		
Hypertension	78 (40.2)	92 (48.9)
Diabetes mellitus	55 (28.4)	59 (31.4)
Coronary artery disease	42 (21.6)	42 (22.3)
Congestive heart failure	24 (12.4)	32 (17.0)
Cerebrovascular disease	20 (10.3)	22 (11.7)
Cancer	71 (36.6)	57 (30.3)
Lung disease	38 (19.6)	38 (20.2)
Liver disease	20 (10.3)	19 (10.1)
Kidney disease	31 (16.0)	34 (18.1)
Neutropenia (ANC < 1000 cells/μL)	16 (8.2)	9 (4.8)
Immunodeficiency	3 (1.5)	5 (2.7)
Auto-inflammatory disease	10 (5.2)	8 (4.3)
Concomitant antibiotics	96 (49.5)	87 (46.3)
Metronidazole	29 (14.9)	23 (12.2)
Vancomycin	33 (17.0)	34 (18.1)
Fluoroquinolone	26 (13.4)	32 (17.0)
Other	23 (11.9)	27 (14.4)

ANC = absolute neutrophil count, BMI = body mass index,
eGFR = estimated glomerular filtration rate, ICU = intensive care unit
*Traditional = 1000 mg IV q8h; small-dose, short-interval = 500 mg IV q6h.
†For all characteristics, $p > 0.05$.

Table 3. Source of Infection and Bacteria Identified for Patients Who Received Traditional or Small-Dose, Short-Interval Dosing of Meropenem

Characteristic of Infection	Dosing Regimen*; No. (%) of Patients	
	Traditional Dosing (*n* = 194)	Small-Dose, Short-Interval Dosing (*n* = 188)
Microbial source		
Blood	76 (39.2)	70 (37.2)
Abdomen	50 (25.8)	42 (22.3)
Urinary tract†	53 (27.3)	71 (37.8)
Skin and soft tissue	19 (9.8)	11 (5.9)
Lung	76 (39.2)	71 (37.8)
Stool	5 (2.6)	3 (1.6)
Bone and connective tissue	2 (1.0)	0 (0.0)
Multiple	70 (36.1)	64 (34.0)
Microbial isolates		
Escherichia coli	35 (18.0)	43 (22.9)
Enterococcus spp.	13 (6.7)	17 (9.0)
Multidrug-susceptible *Staphylococcus aureus*	12 (6.2)	7 (3.7)
Pseudomonas aeruginosa	10 (5.2)	15 (8.0)
SPICE organisms (*Serratia* spp., *Providencia* spp., *Morganella* spp., *Citrobacter* spp., *Enterobacter* spp., *Proteus vulgaris*)	9 (4.6)	7 (3.7)
Klebsiella spp.	4 (2.1)	3 (1.6)
Proteus mirabilis	4 (2.1)	2 (1.1)
Corynebacterium spp.	4 (2.1)	2 (1.1)
Viridans group *Streptococcus*	3 (1.5)	0 (0.0)
Group B *Streptococcus*	2 (1.0)	4 (2.1)
Multidrug-resistant *Staphylococcus aureus*	2 (1.0)	4 (2.1)
Acinetobacter spp.	1 (0.5)	4 (2.1)
Streptococcus pneumoniae	1 (0.5)	1 (0.5)
Anaerobes	2 (1.0)	5 (2.7)
Polymicrobial	22 (11.3)	22 (11.7)

*Traditional = 1000 mg IV q8h; small-dose, short-interval = 500 mg IV q6h.
†Urinary tract was the source of infection for a significantly greater proportion of patients in the small-dose, short-interval group ($p = 0.04$). For all other variables in this table, there was no statistically significant difference.

In terms of the primary outcome, there was no statistically significant difference in clinical success rate (whether partial or complete) between the traditional dosing regimen and the small-dose, short-interval dosing regimen (83.5% versus 80.8%; $p = 0.51$). In addition, no differences were identified between the traditional dosing regimen and the small-dose, short-interval dosing regimen in terms of proportion of patients with complete clinical success (Table 4). A subgroup comparison involving patients admitted to the intensive care unit (ICU) showed no difference in the primary outcome of clinical success between the traditional and the small-dose, short-interval regimen. Similarly, there was no between-group difference in success rate for patients with *P. aeruginosa* infection (Table 5). Finally, no significant differences were identified in any of the secondary clinical outcomes, specifically mortality, duration of therapy, meropenem-related length of stay, and time to defervescence (Table 6).

The cost analysis revealed a statistically significant difference in drug cost per patient per visit in favour of the small-dose, short-interval regimen. Historically, the mean cost per patient per visit was $1016.97 for the traditional regimen and $627.21 for the small-dose, short-interval regimen. Using costs prorated to April 2015, the mean cost per patient per visit was $355.90 for the traditional regimen and $222.23 for the small-dose, short-interval regimen ($p < 0.001$). The overall savings with the small-dose, short-interval regimen were $79 417.44 and $27 279.48 with historical and current pricing, respectively.

DISCUSSION

At a time when increasing demand on the health care system puts increased strain on health care budgets, practice innovations must be instituted to minimize costs. Use of a small-dose, short-interval dosing regimen for meropenem represents an effort to incorporate pharmacodynamic properties into decision-making, with the objective of decreasing drug costs. Data showing similar

Table 4. Clinical Success for Patients Who Received Traditional or Small-Dose, Short-Interval Dosing of Meropenem

Category of Success	Dosing Regimen*; No. (%) of Patients		RR (95% CI)
	Traditional Dosing (*n* = 194)	Small-Dose, Short-Interval Dosing (*n* = 188)	
Clinical success (partial or complete)†	162 (83.5)	152 (80.8)	0.97 (0.88–1.07)
Complete success only‡	102 (52.6)	94 (50.0)	0.95 (0.77–1.17)

CI = confidence interval, RR = relative risk.
*Traditional = 1000 mg IV q8h; small-dose, short-interval = 500 mg IV q6h.
†Data for patients with either complete or partial clinical success. The *complete clinical success rate* was defined on the basis of normalization of peripheral temperature (to ≤ 37.5°C), leukocyte count (to ≤ 11 × 10^9/L), and/or neutrophil count (to ≤ 8 × 10^9/L), along with signs of clinical resolution as noted in the patient chart. Clinical success was deemed not to have been achieved if the patient died during the admission or if therapy was stopped because of a serious adverse event. The *partial clinical success rate* was defined on the basis of reduction in temperature, leukocyte count, and neutrophil count from initially elevated values (but without full resolution), along with signs of clinical improvement from baseline as noted in patient chart. For further detail, please see Methods, under "Data Collection".
‡Excludes patients with partial success.

Table 5. Subgroup Analyses of Clinical Success for Patients Who Received Traditional or Small-Dose, Short-Interval Dosing of Meropenem

Subgroup	Dosing Regimen*; No. (%) of Patients		RR (95% CI)
	Traditional Dosing	Small-Dose, Short-Interval Dosing	
Patients in the ICU	15/19 (79)	15/23 (65)	0.83 (0.59–1.29)
Patients with *Pseudomonas aeruginosa* infection	9/10 (90)	11/15 (73)	0.82 (0.67–1.33)

CI = confidence interval, ICU = intensive care unit, RR = relative risk.
*Traditional = 1000 mg IV q8h; small-dose, short-interval = 500 mg IV q6h.

Table 6. Secondary Outcomes among Patients Who Received Traditional or Small-Dose, Short-Interval Dosing of Meropenem

Outcome	Dosing Regimen*; No. (%) of Patients or Mean Value		*p* Value
	Traditional Dosing (*n* = 194)	Small-Dose, Short-Interval Dosing (*n* = 188)	
30 day all-cause mortality	18 (9.2)	27 (14.4)	0.15
30 day infection-related mortality	9 (4.6)	12 (6.4)	0.51
Duration of meropenem therapy (days)	6.9	6.9	0.93
Meropenem-related length of stay (days)	24.5	27.8	0.27
Time to defervescence (days)	2.2	2.1	0.62

*Traditional = 1000 mg IV q8h; small-dose, short-interval = 500 mg IV q6h.

$\%fT_{>MIC}$ between traditional and small-dose, short-interval meropenem dosing regimens suggest that clinical effects should be similar even with the administration of 33% less medication over a 24-h period with the latter approach. Accordingly, the handful of studies[7-9] examining clinical outcomes of alternative dosing strategies have suggested, at a minimum, equivalence in outcomes such as clinical cure rate and mortality, with possible superiority in terms of time to resolution of the infection.[7] We used a superiority trial design based on the observed decrease in time to infection resolution to determine whether there was a similar advantage in terms of clinical success rate with the small-dose, short-interval dosing regimen relative to traditional dosing. Our objective was to build upon existing evidence while broadening applicability. One aspect of our approach was to remove limitations of renal function as an exclusion criterion; by incorporating patients with any eGFR, provided they were not receiving dialysis, we were able to capture a more critically ill population, who might be more likely to receive meropenem therapy. Whereas previous studies excluded patients who were afebrile throughout their antibiotic therapy and patients with neutropenia, we included patients without fever, as well as those with febrile neutropenia, using a collection of clinical signs and

symptoms and laboratory values to determine whether clinical success was achieved.[7-9] The intention was to encompass as broad a patient population as possible for maximal applicability to practice.

This study had clinical success rates in keeping with the previous investigation by Kotapati and others,[8] but lower than those found in a larger study by Patel and others.[7] Inclusion in the current study of patients with more severe renal dysfunction and a greater proportion of patients with malignancy may have been factors contributing to the lower success rate reported here. We also chose a conservative threshold for elevated peripheral temperature (> 37.5°C) on the basis of previous febrile neutropenia studies,[11,12] not accounting for circadian differences and differences in location of temperature readings. However, we did not identify superiority of the small-dose, short-interval dosing regimen in terms of the primary outcome. Findings of no significant difference in length of stay and in-hospital mortality were also consistent with previous studies; however, in contrast with observations by Patel and others,[7] we found no decrease in time to defervescence. Of note, there was a trend toward a higher mortality rate with the small-dose, short-interval regimen (14.4% versus 9.2%, $p = 0.15$): however, when mortality was stratified by its relation to infection, the rates were similar between the 2 regimens (Table 6). Indeed, in the small-dose, short-interval group, a greater proportion of the mortality rate was related to malignancy than to meropenem failure. Given that mortality was a secondary end point, additional studies with sufficient statistical power are needed to confirm the results.

The purpose of examining the ICU subgroup was to quantify the effect of administering less drug overall in a more acutely ill population. Likewise, we analyzed the subgroup of patients with *P. aeruginosa* infections to determine whether there was any difference in clinical effect according to the regimen used. Both subgroup analyses showed no difference in clinical success rate between dosing regimens, although the numbers of patients within these subgroups were small relative to the entire study population (i.e., 42 ICU patients and 25 patients infected with *P. aeruginosa* out of 382 patients in the study as a whole), and the subgroup analyses were not powered to detect a difference. Additional studies of sufficient statistical power are needed to assess the critically ill population and those infected with more virulent organisms.

With the secondary cost analysis, we hoped to quantify potential cost savings in terms of Canadian dollars, given that previous pharmacoeconomic analyses were done in the United States. Similar to previous studies, we found significant cost savings with use of the small-dose, short-interval regimen. Given that mean treatment duration was similar for the 2 cohorts (6.9 days for both), the cost savings can be attributed to the use of 33% less meropenem per day with the small-dose, short-interval regimen. In recognition of the substantial cost difference between brand and generic medication, we conservatively prorated costs to April 2015 in the current-pricing comparison. Cost savings were notable in terms of both prorated and historical pricing, although the magnitude of savings was substantially less when the conservative estimate was used ($27 279.48 versus $79 417.44).

This investigation had some limitations. First, the retrospective nature of the study likely introduced unavoidable confounders that may have affected the results. However, by maximizing the sample size and randomly selecting the patient population, we were able to obtain 2 cohorts with similar baseline characteristics (most notably in terms of comorbidities and renal function). The only patient characteristic that differed significantly, the presence of a urinary infection, did not affect the statistical results when examined by regression analysis.

In addition, the superiority design of the study inhibited our ability to conclude clinical equivalence between the 2 dosing regimens. An ideal study would use a non-inferiority design, but such a trial would require tens of thousands of patients, given the high clinical success rate and the minimal difference in outcomes between dosing regimens. Given the sporadic use of meropenem before emergence of extended-spectrum ß-lactamase organisms, it would have been difficult to obtain sufficient patients eligible for inclusion in the study. The inclusion time period for the traditional dosing cohort reflected this lack of patients, in that we had to use 2 years of data for this cohort but only 1 year of data for the small-dose, short-interval cohort (2006–2008 versus 2008–2009). Further broadening of the inclusion period would have introduced temporal confounders such as changes in practice standards that would have affected the clinical outcomes. Despite this limitation, we feel that these results, in combination with a growing body of evidence suggesting similar clinical success rates in other settings, will allow decision-makers to more confidently assume clinical equivalence between these dosing regimens.

This study did not include a safety comparison between the dosing regimens. However, we examined 2 dosing regimens of the same medication (which were shown to exhibit similar pharmacokinetic and pharmacodynamics parameters), so we felt that such an investigation would likely not have added value to these results.

As is the case for other studies in the infectious disease literature, there was inter-clinician variability in the primary outcome of clinical success (e.g., radiographic improvement, decrease in symptoms). To minimize this variability, we took a conservative approach: in the absence of data from physician progress notes and in the absence of objective outcomes such as defervescence or leukocyte count, we assumed clinical failure.

Finally, the cost analysis was restricted to drug cost alone and did not incorporate material costs (e.g., tubing, IV bags), dispensary preparation time, or nursing administration factors. It might be argued that use of broad-spectrum antibiotics such as meropenem may be curtailed by initiatives such as antimicrobial stewardship

and that drug cost alone is not sufficient to determine overall savings. Future in-depth pharmacoeconomic studies may be required to further delineate the actual cost savings that can be realized with a small-dose, short-interval meropenem dosing regimen based on current practices.

CONCLUSION

To our knowledge, this study is the largest to date comparing the clinical effects of a small-dose, short-interval meropenem dosing regimen with the traditional dosing regimen, and the only one to include patients with all stages of renal dysfunction. The investigation did not reveal any statistically significant differences in clinical efficacy outcomes: therefore, we conclude that meropenem 500 mg every 6 h is not superior to meropenem 1000 mg every 8 h. However, use of the small-dose, short-interval dosing regimen was associated with significant drug cost savings (more than Can$130 per patient per visit). This pharmacoeconomic advantage and the lack of evidence to suggest worse patient outcomes indicate that the small-dose, short-interval regimen could be adopted system-wide. Further studies are needed to confirm these results, especially in-depth pharmacoeconomic studies to delineate overall cost savings.

References

1. Merrem [product monograph]. In: Repchinsky C, editor-in-chief. *e-CPS*. Ottawa (ON): Canadian Pharmacists Association; 2012 [cited 2013 Jun 22]. Available from: https://www-e-therapeutics-ca. Subscription required to access content.
2. Perrott J, Mabasa VH, Ensom MHH. Comparing outcomes of meropenem administration strategies based on pharmacokinetic and pharmacodynamic principles: a qualitative systematic review. *Ann Pharmacother.* 2010;44(3):557-64.
3. Lomaestro BM, Drusano GL. Pharmacodynamic evaluation of extending the administration time of meropenem using a Monte Carlo simulation. *Antimicrob Agents Chemother.* 2005;49(1):461-3.
4. Wang H, Zhang B, Ni Y, Kuti JL, Chen B, Chen M, et al. Pharmacodynamic target attainment of seven antimicrobials against gram-negative bacteria collected from China in 2003 and 2004. *Int J Antimicrob Agents.* 2007;30(5):452-7.
5. Zelenitsky S, Zvonar R, Ariano R. Monte Carlo simulations (MCSs) of meropenem in patients with varying degrees of renal function [abstract]. *Can J Hosp Pharm*. 2009;62(1):68.
6. Kuti JL, Maglio D, Nightingale CH, Nicolau DP. Economic benefit of a meropenem dosage strategy based on pharmacodynamic concepts. *Am J Heatlh Syst Pharm.* 2003;60(6):565-8.
7. Patel GW, Duquaine SM, McKinnon PS. Clinical outcomes and cost minimization with an alternative dosing regimen for meropenem in a community hospital. *Pharmacotherapy.* 2007;27(12):1637-43.
8. Kotapati S, Nicolau DP, Nightingale CH, Kuti JL. Clinical and economic benefits of a meropenem dosage strategy based on pharmacodynamic concepts. *Am J Health Syst Pharm*. 2004;61(12):1264-70.
9. Arnold HM, McKinnon PS, Augustin KM, Hladnik LM, Casabar E, Reichley RM, et al. Assessment of an alternative meropenem dosing strategy compared with imipenem-cilastatin or traditional meropenem dosing after cefepime failure or intolerance in adults with neutropenic fever. *Pharmacotherapy.* 2009;29(8):914-23.
10. Aronoff GR, Berns JS, Brier ME, Golpher TA, Morrison G, Singer I, et al., editors. *Drug prescribing in renal failure: dosing guidelines for adults.* 4th ed. Philadelphia (PA): American College of Physicians; 1999.
11. Fehér C, Rovira M, Soriano A, Esteve J, Martínez JA, Marco F, et al. Effect of meropenem administraton in extended infusion on the clinical outcome of febrile neutropenia: a retrospective observational study. *J Antimicrob Chemother*. 2014;69(9):2556-62.
12. Tamura K, Matsuoka H, Tsukada J, Masuda M, Ikeda S, Matsuishi E, et al. Cefepime or carbapenem treatment for febrile neutropenia as a single agent is as effective as a combination of 4th generation cephalosporin + aminoglycosides: comparative study. *Am J Hematol*. 2002;71(4):248-55.

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ORIGINAL RESEARCH

Effectiveness of Injectable Ibuprofen Salts and Indomethacin to Treat Patent Ductus Arteriosus in Preterm Infants: Observational Cohort Study

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ABSTRACT

Background: There is no injectable ibuprofen product marketed to treat patent ductus arteriosus (PDA) in newborns in Canada. The authors' institution has used ibuprofen arginine in the past. In the absence of published evidence supporting use of this salt form of ibuprofen for neonatal PDA, a retrospective analysis was undertaken.

Objective: To compare the effectiveness and adverse effects of ibuprofen arginine, ibuprofen tromethamine, and indomethacin in the treatment of PDA.

Methods: This retrospective observational cohort study, for patients admitted between 2009 and 2015, included preterm infants with symptomatic PDA who received at least one dose of injectable indomethacin, ibuprofen tromethamine, or ibuprofen arginine. Three effectiveness end points were analyzed: closure after one course of treatment, repeat medical treatment, and surgical ligation. The secondary end points included acute kidney injury, necrotizing enterocolitis, chronic lung disease, and time to full enteral feeding.

Results: A total of 179 infants were included. There were no differences among groups in terms of closure after one course of treatment (37/54 [69%] with indomethacin, 42/70 [60%] with ibuprofen tromethamine, and 28/55 [51%] with ibuprofen arginine; $p = 0.21$) or surgical ligation (10/54 [19%] with indomethacin, 13/70 [19%] with ibuprofen tromethamine, and 12/55 [22%] with ibuprofen arginine; $p = 0.88$). However, there was a difference regarding use of a repeat course of treatment, ibuprofen arginine having the highest rate (8/54 [15%] with indomethacin, 18/70 [26%] with ibuprofen tromethamine, and 20/55 [36%] with ibuprofen arginine; $p = 0.04$). After adjustment for gestational age, the association between ibuprofen arginine and increased use of a repeat course of treatment remained significant. The groups did not differ with respect to adverse effects.

Conclusion: These results highlight the potential for differences in effectiveness among various salt forms of injectable ibuprofen and indomethacin. Because of the small sample size and retrospective methodology, confirmation of the present results through a larger prospective study is needed.

RÉSUMÉ

Contexte : Il n'y a pas sur le marché de produit injectable à base d'ibuprofène pour traiter la persistance du canal artériel (PCA) chez le nouveau-né au Canada. L'ibuprofène arginine a été utilisé auparavant dans l'établissement de santé des auteurs. En l'absence de données publiées appuyant l'utilisation de ce médicament sous forme de ce sel pour traiter la PCA chez le nouveau-né, une analyse rétrospective a été réalisée.

Objectif : Comparer l'efficacité et les effets indésirables de l'ibuprofène arginine, de l'ibuprofène trométhamine et de l'indométhacine dans le traitement de la PCA.

Méthodes : Cette étude de cohorte observationnelle rétrospective, au sujet de patients hospitalisés entre 2009 et 2015, incluait des nourrissons prématurés atteints d'une PCA symptomatique ayant reçu par injection au moins une dose d'indométhacine, d'ibuprofène trométhamine ou d'ibuprofène arginine. Trois paramètres d'évaluation de l'efficacité ont été analysés : la fermeture après un seul traitement, la répétition du traitement médical et la ligature chirurgicale. Les paramètres d'évaluation secondaires étaient les cas d'insuffisance rénale aiguë, d'entérocolite nécrosante et de maladie pulmonaire chronique ainsi que le temps pour atteindre l'alimentation entérale complète.

Résultats : Au total, 179 nourrissons ont été admis à l'étude. Aucune différence n'a été relevée entre les groupes en ce qui touche à la fermeture après un seul traitement (37/54 [69 %] pour l'indométhacine, 42/70 [60 %] pour l'ibuprofène trométhamine et 28/55 [51 %] pour l'ibuprofène arginine; $p = 0{,}21$) ou à la ligature chirurgicale (10/54 [19 %] pour l'indométhacine, 13/70 [19 %] pour l'ibuprofène trométhamine et 12/55 [22 %] pour l'ibuprofène arginine; $p = 0{,}88$). Cependant, une différence a été observée pour ce qui est de la répétition du traitement et l'ibuprofène arginine a obtenu le taux le plus élevé (8/54 [15 %] pour l'indométhacine, 18/70 [26 %] pour l'ibuprofène trométhamine et 20/55 [36 %] pour l'ibuprofène arginine; $p = 0{,}04$). Après ajustement pour l'âge gestationnel, l'association entre l'utilisation de l'ibuprofène arginine et une augmentation du recours à un second traitement demeurait significative. Il n'y avait pas de différence entre les groupes en ce qui touche aux effets indésirables.

Keywords: ductus arteriosus, patent; infant, newborn; indomethacin; ibuprofen; ibuprofen arginine

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Conclusion : Ces résultats soulignent la possible différence d'efficacité parmi les divers sels d'ibuprofène injectable et l'indométhacine. Cependant, en raison de la petite taille de l'échantillon et de l'emploi d'une méthodologie rétrospective, une étude prospective plus importante doit être menée pour confirmer les résultats de la présente étude.

Mots clés : persistance du canal artériel, nouveau-né, nourrisson, indométhacine, ibuprofène, ibuprofène arginine

INTRODUCTION

About 55% of infants born with body weight less than 1000 g have a symptomatic patent ductus arteriosus (PDA) requiring medical treatment.[1,2] A persistent PDA can lead to undesirable pulmonary, renal, and gastrointestinal (GI) effects, thus warranting medical or surgical treatment.[3-9] A 2010 meta-analysis reported that ibuprofen was as effective as indomethacin in closing a PDA and reduced the risk of necrotizing enterocolitis (odds ratio [OR] 0.68) and renal insufficiency (OR 0.28 for urine output declining to < 1 mL/kg per hour) relative to indomethacin.[10]

Until early 2010, indomethacin was the sole treatment option for PDA at the Foothills Medical Centre, a 39-bed level 3 neonatal intensive care unit (NICU) in Calgary, Alberta. At that time, a shortage of indomethacin led to use of injectable ibuprofen, which is available in various salt forms. Starting in 2010, ibuprofen tromethamine was obtained through Health Canada's Special Access Programme and was used for PDA treatment in the unit. From 2011 to 2013, both indomethacin and ibuprofen tromethamine were available and used for this purpose. In 2013, ibuprofen arginine came onto the Canadian market; given its apparently more reliable availability and lower cost, it was adopted as first-line treatment for symptomatic PDA. Of note, the salt form used in most initial ibuprofen efficacy trials has been ibuprofen lysine, which is available in the United States and Europe.[11-16] Although many studies do not indicate the salt form of injectable ibuprofen used, ibuprofen tromethamine[17,18] and ibuprofen arginine[19] have also been studied.

Although the efficacy and safety of ibuprofen for treatment of PDA in neonates has been well described, published data on use of the arginine salt of this drug are limited to a single abstract.[19] A difference in pharmacological activity between salt forms is not expected, given that salts of the various ibuprofen products deliver similar amounts of ibuprofen (amount of ibuprofen in 10 mg of salt forms: lysine, 0.028 mmol; tromethamine, 0.030 mmol; arginine, 0.026 mmol). However, data on the use of ibuprofen tromethamine has indicated higher rates of necrotizing enterocolitis relative to placebo, and 3 cases of pulmonary hypertension have been reported.[17] These adverse effects are postulated to be related to the timing of administration of ibuprofen tromethamine (< 6 h from birth) or to an effect of the tromethamine buffer.[10] Arginine is a precursor of nitric oxide (NO), and ibuprofen arginine has been shown to release NO in animal models.[20] The role of NO in ductal patency has been demonstrated in animal models, and use of an NO synthase inhibitor in combination with indomethacin was associated with improved ductal closure rates in premature newborns relative to indomethacin alone.[21-24] These data provide a theoretical reason to doubt the effectiveness of ibuprofen arginine for PDA. In addition, a previous study that compared the effectiveness of ibuprofen arginine and indomethacin in preterm neonates demonstrated that ibuprofen arginine had a significantly lower closure rate after one course (37% versus 65%, $p = 0.006$) and a higher PDA ligation rate (15% versus 2%, $p = 0.03$).[19] For these reasons, an audit of the effectiveness of ibuprofen arginine for treatment of PDA was deemed prudent.

The objective of this study was to compare the effectiveness of ibuprofen arginine with that of indomethacin and ibuprofen tromethamine in terms of the following outcomes:

- closure of the PDA during initial course of medical therapy;
- failure of initial course of medical therapy, necessitating a repeat course of medical therapy;
- failure of medical treatment, necessitating surgical ligation of the PDA.

The secondary objectives were to compare the incidence of adverse effects of PDA treatment (GI bleeding, spontaneous intestinal perforation, acute kidney injury) and the incidence of necrotizing enterocolitis and chronic lung disease among the 3 groups.

METHODS

This retrospective, observational cohort study included all infants at the Foothills Medical Centre NICU with gestational

age less than 32 weeks and/or birth weight less than 1500 g who had symptomatic PDA requiring pharmacological intervention and received at least one dose of a study drug during the following 3 periods: March 2009 to February 2010 (the indomethacin cohort), March 2010 to February 2011 (the ibuprofen tromethamine cohort), and June 2013 to January 2015 (the ibuprofen arginine cohort). Infants with ductal dependent heart disease, major congenital anomalies, or a contraindication to ibuprofen or indomethacin (urine output < 1 mL/h in the preceding 12 h, serum creatinine > 120 μmol/L, platelet count $< 60 \times 10^9$/L, presence of necrotizing enterocolitis, or active bleeding) were excluded. Waiver of consent and the full protocol were approved by the University of Calgary Conjoint Health Research Ethics Board.

The computerized order entry system was used to identify infants who received ibuprofen or indomethacin during the 3 study periods. Medical records were reviewed for relevant data. Patients were followed until death or discharge from the NICU.

The decision to treat a PDA was based on clinical signs and symptoms, supplemented by echocardiography confirmation of a hemodynamically significant PDA. Indomethacin (Indocid P.D.A., Merck Frosst Canada) was given in 3 doses (if < 48 h of life, doses of 0.2, 0.1, and 0.1 mg/kg; if 2–7 days of life, doses of 0.2, 0.2, and 0.2 mg/kg; and if > 7 days of life, doses of 0.2, 0.25, and 0.25 mg/kg) at 12-h intervals. Ibuprofen tromethamine (Pedea, Orphan Europe SARL) was given in 3 doses (10, 5, and 5 mg/kg, respectively) at 24-h intervals. Data from these 2 groups of patients had been collected previously and formed the historical comparator groups for this study.[18] Ibuprofen arginine (Caldolor, Alveda Pharmaceuticals) was used at the same dosage as ibuprofen tromethamine.

All infants receiving these agents were monitored clinically and biochemically to look for ductal closure and possible medication-related side effects. In cases of persistent hemodynamically significant PDA (as documented by echocardiography), a repeat course of either agent was used unless contraindicated. Surgical ligation of PDA was considered for those with failure of 2 courses of pharmacological therapy and those with contraindications to the medications.

The primary outcome was effectiveness of treatment, as defined by the following criteria:

- closure of the PDA during the initial course of medical therapy (as confirmed by echocardiography or determined by clinical resolution of symptoms);
- failure of initial course of medical therapy, necessitating a repeat course;
- failure of treatment, necessitating surgical ligation of the PDA.

The following secondary end points were also assessed:

- GI bleeding;
- spontaneous intestinal perforation;
- necrotizing enterocolitis stage II or greater (based on modified Bells staging)[25];
- acute kidney injury (urine output < 0.5 mL/kg per hour for more than 8 h or increase in serum creatinine > 30 μmol/L within 72 h of medication administration or ≥ 50% from baseline)[26];
- diagnosis of chronic lung disease (oxygen requirement at 36 weeks corrected gestational age);
- age (days of life) when full enteral feeding was achieved.

Descriptive statistics (means and proportions) were used to describe the 3 study groups. Categorical variables were compared among the groups using the χ^2 test or the Fisher exact test, with a priori significance level of 0.05. Continuous variables were compared using analysis of variance. Patients with missing data were excluded from analysis for the applicable variable; hence, the sample size was reduced for some end points. To account for differences in baseline characteristics and other confounding factors, multivariable logistic regression was used to determine the influence of covariates on the study end points. Factors that differed among groups at a significance level of $p < 0.1$ in the bivariate analysis and those with a known association with PDA were considered for inclusion in the model.

RESULTS

The ibuprofen arginine cohort had lower mean birth weight ($p = 0.001$) and appeared to be more acutely ill than the other cohorts, with lower 5-minute APGAR scores ($p = 0.012$), higher SNAP-II scores (Score for Neonatal Acute Physiology) ($p < 0.001$), and a higher rate of antenatal steroid use ($p = 0.008$) (Table 1).

There were no significant differences among the groups in terms of complete or clinical PDA closure after one course of treatment ($p = 0.21$) and need for PDA ligation ($p = 0.88$) (Table 2). However, there was a difference in terms of need for a repeat course of medical treatment, the ibuprofen arginine group having a significantly higher rate than the other groups ($p = 0.04$). A post hoc analysis was performed on the proportion of patients who received both a repeat course of treatment and ligation surgery, but there was no significant difference among the groups ($p = 0.34$).

There did not appear to be any differences among the groups in terms of incidence of acute kidney injury; however, for this variable there was a high proportion of missing data for the ibuprofen arginine cohort (Table 2). Similarly, no differences were seen regarding incidence of necrotizing enterocolitis, chronic lung disease, time to achieve full enteral feeding, or death before NICU discharge. Because of low event rates, statistical analysis was not performed for the incidence of GI bleeding ($n = 2$ in indomethacin group, $n = 4$ in ibuprofen tromethamine group, $n = 0$ in ibuprofen arginine group) or intestinal perforation ($n = 0$ in indomethacin group, $n = 1$ in ibuprofen tromethamine group, $n = 4$ in ibuprofen arginine group).

Table 1. Characteristics of Patients and Their Mothers by Treatment Group

Characteristic	Treatment Group; No. (%) of Patients*			*p* Value†
	Indomethacin (*n* = 54)	Ibuprofen Tromethamine (*n* = 70)	Ibuprofen Arginine (*n* = 55)	
Gestational age (weeks) (mean ± SD)	26.9 ± 2.3	26.6 ± 2.1	26.2 ±1.8	0.24
Birth weight (g) (mean ± SD)	1004 ± 272	992 ± 347	811 ± 22‡	0.001
Sex, male	27 (50)	44 (63)	30 (55)	0.34
Multiple gestations	20 (37)	25 (36)	17 (31)	0.77
Prenatal steroids	46 (85)	55 (79)	54 (98) §¶	0.008
Chorioamnionitis	19 (35)	16 (23)	9 (16)	0.07
Cesarean section	30 (56)	38 (54)	39 (71)	0.13
APGAR score at 5 min (median and IQR)	7 (7–8)	7 (7–8)	6(5–7)**††	0.012
SNAP-II score (mean ± SD)	15.6 ± 13.0	14.1 ± 7.8	23.8 ± 17.1‡‡	< 0.001
IVH ≥ grade III	7 (13)	7 (10)	12 (22)	0.16

IQR = interquartile range, IVH = intraventricular hemorrhage, SD = standard deviation,
SNAP-II = Score for Neonatal Acute Physiology II.
*Except where indicated otherwise.
†The *p* values in this column refer to results of 3-way comparisons among all groups; significant results for pairwise comparisons are indicated with individual footnotes.
‡$p < 0.001$ for comparison of ibuprofen arginine with indomethacin in terms of birth weight.
§$p = 0.024$ for comparison of ibuprofen arginine with indomethacin in terms of prenatal steroids.
¶$p = 0.002$ for comparison of ibuprofen arginine with ibuprofen tromethamine in terms of prenatal steroids.
**$p = 0.004$ for comparison of ibuprofen arginine with indomethacin in terms of APGAR score.
††$p = 0.017$ for comparison of ibuprofen arginine with ibuprofen tromethamine in terms of APGAR score.
‡‡$p = 0.007$ for comparison of ibuprofen arginine with indomethacin in terms of SNAP-II score.

Logistic regression was performed on the 3 components of the primary end point. Factors that differed among groups at a significance level of $p < 0.1$ in the bivariate analysis (birth weight, antenatal steroids, APGAR score, SNAP-II score, age [days of life] at start of treatment) and the factor with a known association with PDA (chorioamnionitis)[27] were considered for inclusion in the model. Gestational age was substituted for birth weight because of collinearity of these 2 factors and because external factors have less influence on gestational age than on birth weight. APGAR score was not included because of collinearity with SNAP-II score. After adjustment, only gestational age showed a significant association with complete or clinical closure and with the need for surgical ligation. Use of ibuprofen arginine showed a significant association with repeat course of PDA treatment (Table 3).

DISCUSSION

In this retrospective analysis, the agent used for PDA treatment did not appear to affect the rate of clinical or complete closure after the initial course of treatment or the need for surgical ligation, which was reassuring. However, use of ibuprofen arginine appeared to be associated with greater use of repeat treatment courses. Given the similar quantity of ibuprofen delivered from its various salts, and meta-analytic data supporting similar efficacy between other ibuprofen salts and indomethacin,[10] this result was unexpected.

Potential explanations for this unexpected finding include the release of NO by ibuprofen arginine.[20] Although release of NO could theoretically reduce the effectiveness of ibuprofen arginine in PDA treatment, the amount of arginine provided through therapeutic doses of this agent is very low (0.024 mmol/kg daily; dose for prevention of necrotizing enterocolitis 1.5 mmol/kg daily).[28] It is possible that this is the explanation for the increased need for repeat courses of treatment, and that this study was too small to show differences in the other effectiveness end points. The closure rate was numerically lower with ibuprofen arginine (51%) than with indomethacin (69%) and ibuprofen tromethamine (60%), although the comparison did not reach statistical significance.

A more likely explanation is that these findings represent biases in practice. Given the study's retrospective and uncontrolled design, there was no standard decision-making model for initiation of medical treatment for PDA or for repetition of the course of treatment. The greater use of repeat courses of treatment with ibuprofen arginine could reflect increased clinician comfort with ibuprofen over indomethacin because of its more favourable safety profile.[10] The ibuprofen arginine cohort was the most recent cohort, and comfort with ibuprofen's safety profile may have been building over time. Greater use of repeat medical treatment with ibuprofen arginine could also represent growing skepticism toward ibuprofen's efficacy among neonatologists, which is supported by subjective observations at our centre. This skepticism may have influenced clinicians' decisions about whether or not an infant would benefit from a repeated course of treatment.

The results for closure and ligation rates reported here differ from those reported in the only other study examining use of ibuprofen arginine for PDA in preterm neonates.[19] That study

Table 2. Outcomes by Treatment Group

Characteristic	Treatment Group; No. (%) of Patients*			*p* Value†
	Indomethacin (*n* = 54)	Ibuprofen Tromethamine (*n* = 70)	Ibuprofen Arginine (*n* = 55)	
Age at start of treatment (days of life) (mean ± SD)	3.7 ± 2.5	5.5 ± 4.6‡	5.6 ± 5.2§	0.04
First course of treatment				
Completed	36 (67)	62 (89) ¶	45 (82)	0.01
Not completed	18 (33)	8 (11)	10 (18)	
Reason for non-completion				
Renal	9 (50)	2 (25)	3 (30)	
Gastrointestinal	1 (6)	2 (25)	0	
Bleeding	2 (11)	1 (13)	0	
Closure before completion	6 (33)	3 (37)	6 (60)	
Unknown	0	0	1 (10)	
Primary end point				
Complete or clinical closure after first course of treatnment	37 (69)	42 (60)	28 (51)	0.21
Received repeat course of treatment	8 (15)	18 (26)	20 (36)**	0.04
Underwent surgical ligation	10 (19)	13 (19)	12 (22)	0.88
Received both repeat course of treatment and surgical ligation	4 (7)	8 (11)	9 (16)	0.34
Secondary end points				
Acute kidney injury	11 (20)	10/69 (14)	2/10 (10)	0.49
Necrotizing enterocolitis ≥ stage II	5 (9)	5 (7)	8 (15)	0.38
Chronic lung disease	27/46 (59)	38/68 (56)	23/42 (55)	0.93
Age at full enteral feeding (days of life) (mean ± SD)	23.9 ± 11	24.3 ± 10	27.4 ± 16	0.28
Death before NICU discharge	2 (4)	3 (4)	4 (7)	0.65

NICU = neonatal intensive care unit, SD = standard deviation.
*Except where indicated otherwise. Where data were missing for some patients, both numerator and denominator are shown.
†The *p* values in this column refer to results of 3-way comparisons among all groups; significant results for pairwise comparisons are indicated with individual footnotes.
‡*p* = 0.013 for comparison of ibuprofen tromethamine with indomethacin in terms of age at start of treatment.
§*p* = 0.022 for comparison of ibuprofen arginine with indomethacin in terms of age at start of treatment.
¶*p* = 0.003 for comparison of ibuprofen tromethamine with indomethacin in terms of completion of first course of treatment.
***p* = 0.01 for comparison of ibuprofen arginine with indomethacin in terms of repeat course of treatment.

Table 3. Results of Regression Analysis (Relative to Indomethacin Control)

End Point	Comparison Group; Adjusted OR* (95% CI)	
	Ibuprofen Tromethamine	Ibuprofen Arginine
Closure after first course of treatment	0.75 (0.33–1.71)	0.60 (0.25–1.47)
Received repeat course of treatment	1.74 (0.60–5.02)	4.25 (1.34–13.4)
Underwent surgical ligation	0.73 (0.25–2.16)	1.00 (0.31–3.20)

CI = confidence interval, OR = odds ratio.
*Adjusted for gestational age, SNAP-II score, prenatal steroids, chorioamnionitis, and day of life at start of treatment.

(*n* = 86 patients) reported that patients treated with ibuprofen arginine had significantly lower closure rates after one course of treatment (37% with ibuprofen arginine versus 65% with indomethacin, *p* = 0.006) and a higher PDA ligation rate (15% with ibuprofen arginine versus 2% with indomethacin, *p* = 0.03).[19] The differences observed here were much smaller (for closure, 51% with ibuprofen arginine versus 69% with indomethacin, *p* = 0.21; for ligation, 22% with ibuprofen arginine versus 19% with indomethacin, *p* = 0.88). These differences could reflect differences in selection of patients for medical treatment

and surgical referral, which would be supported by the significantly higher rates of ligation in our cohort. Further support for this theory is difficult to ascertain because the results of the previous study were published in abstract form only.[19]

Failure rates in both of the current ibuprofen cohorts were higher than what was reported in the meta-analysis (40% with ibuprofen tromethamine and 49% with ibuprofen arginine in the current study versus about 26% in the meta-analysis[10]). The lower rate reported previously could be related to patient selection, although there has also been some discussion in the literature about the need for higher ibuprofen doses, starting in 2005.[29] More recently, in 2012, Dani and others[30] reported improved rates of PDA closure with an ibuprofen dosing regimen of 20, 10, and 10 mg/kg given at 24-h intervals, with no increase in adverse effects. Use of this higher-dose regimen might improve closure rates seen at our centre, but would need to be evaluated before widespread adoption.

As reported in the meta-analysis,[10] the rates of acute kidney injury, chronic lung disease, necrotizing enterocolitis, and death in the present cohorts did not differ among treatment groups. However, the current study was likely too small to detect differences in these end points, and missing data because of inconsistent measurement of serum creatinine further reduced the sample size for acute kidney injury. There were no statistically significant differences in rate of necrotizing enterocolitis, although the rate was numerically higher in the ibuprofen arginine group (15% versus 9% with indomethacin and 7% with ibuprofen tromethamine, $p = 0.38$). There was also no difference among cohorts in the time needed to reach full enteral feeding, but again this was numerically (if not statistically) higher in the ibuprofen arginine group (27.4 days versus 23.9 with indomethacin and 24.3 days with ibuprofen tromethamine, $p = 0.28$). These observations may be due to the younger gestational age and lower birth weight of the ibuprofen arginine group at baseline. The incidence of GI bleeding and intestinal perforation were too low to analyze, and further examination of these outcomes in a larger study may be warranted.

During the periods of ibuprofen tromethamine and indomethacin use that were analyzed in this study, these were the only PDA treatment options available on the units. However, during the period when ibuprofen arginine was used, indomethacin was also available, and oral ibuprofen had become a more frequently used agent for PDA treatment. This difference in clinical context has the potential to confound our end points, as clinician bias may have played a role in selection of the initial agent, as well as the agent used for repeat courses of treatment. For example, 2 patients in the ibuprofen arginine group received indomethacin for their repeat course, and 1 patient in this group received oral ibuprofen.

To our knowledge, this study is the first to compare multiple salts of ibuprofen and indomethacin in terms of the end points of PDA treatment in neonates; however, it was limited by its retrospective observational design. The higher rate of repeat treatment courses with ibuprofen arginine could represent clinician bias in deciding when to use repeat courses, either because of comfort with ibuprofen's safety or skepticism about ibuprofen's effectiveness. The sample sizes were limited by the timelines for availability of the 3 agents, and the study was therefore too small to show differences in rates of the less common end points (i.e., adverse effects). Overall, confirmation of the present results through a larger prospective study would be ideal. The results would further inform Canadian neonatal clinicians' ability to use a more readily accessible injectable ibuprofen product, rather than one available only through Health Canada's Special Access Programme.

CONCLUSION

Ibuprofen arginine has been more accessible and less expensive than other PDA treatment options at the authors' centre, but the potential for differing effectiveness (based on the theoretical effects of NO and data presented only in abstract form) required that its use be audited before widespread adoption. Other salts of ibuprofen have been shown to have effects similar to those of indomethacin, with evidence of lower rates of necrotizing enterocolitis and renal dysfunction. Our data suggest similar closure rates after one course and similar surgical ligation rates, but an increased need for repeat courses of PDA treatment with ibuprofen arginine. This difference may represent clinician bias in initiating and repeating courses of medical treatment with ibuprofen that have developed over time. No significant differences were observed among the 3 treatments regarding adverse effects. The effectiveness of ibuprofen arginine should be examined in larger cohorts with appropriate randomization and controls.

References

1. Koch J, Hensley G, Roy L, Brown S, Ramaciotti C, Rosenfeld CR. Prevalence of spontaneous closure of the ductus arteriosus in neonates at a birth weight of 1000 grams or less. *Pediatrics.* 2006;117(4):1113-21.
2. Clyman RI. Ibuprofen and patent ductus arteriosus. *N Engl J Med.* 2000;343(10):728-30.
3. Scholl JE, Yanowitz TD. Pulmonary hemorrhage in very low birth weight infants: a case-control analysis. *J Pediatr*. 2015;166(4):1083-4.
4. Cotton RB, Stahlman MT, Kovar I, Catterton WZ. Medical management of small preterm infants with symptomatic patent ductus arteriosus. *J Pediatr.* 1978;92(3):467-73.
5. Mullaart RA, Hopman JC, Rotteveel JJ, Stoelinga GBA, De Haan AFJ, Daniëls O. Cerebral blood flow velocity and pulsation in neonatal respiratory distress syndrome and periventricular hemorrhage. *Pediatr Neurol*. 1997; 16(2):118-25.
6. Dollberg S, Lusky A, Reichman B. Patent ductus arteriosus, indomethacin and necrotizing enterocolitis in very low birth weight infants: a population-based study. *J Pediatric Gastroenterol Nutr.* 2005;40(2):184-8.
7. Schena F, Francescato G, Cappelleri A, Picciolli I, Mayer A, Mosca F, et al. Association between hemodynamically significant patent ductus arteriosus and bronchopulmonary dysplasia. *J Pediatr.* 2015;166(6):1488-92.

8. Noori S, McCoy M, Friedlich P, Bright B, Gottipati V, Seri I, et al. Failure of ductus arteriosus closure is associated with increased mortality in preterm infants. *Pediatrics*. 2009;123(1):e138-44.
9. Hamrick SEG, Hansmann G. Patent ductus arteriosus of the preterm infant. *Pediatrics*. 2010;125(5):1020-30.
10. Ohlsson A, Walia R, Shah SS. Ibuprofen for the treatment of patent ductus arteriosus in preterm and/or low birth weight infants. *Cochrane Database Syst Rev*. 2010;(4):CD003481.pub4.
11. Van Overmeire B, Smets K, Lecoutere D, Van de Broek H, Weyler J, De Groote K, et al. A comparison of ibuprofen and indomethacin for closure of patent ductus arteriosus. *N Engl J Med.* 2000;343(10):674-81.
12. Hammerman C, Shchors I, Jacobson S, Schimmel MS, Bromiker R, Kaplan M, et al . Ibuprofen versus continuous indomethacin in premature neonates with patent ductus arteriosus: is the difference in the mode of administration? *Pediatr Res.* 2008;64(3):291-7.
13. Lago P, Bettiol T, Salvadori S, Pitassi I, Vianello A, Chiandetti L, et al. Safety and efficacy of ibuprofen versus indomethacin in perterm infants treated for patent ductus arteriosus: a randomized controlled trial. *Eur J Pediatr.* 2002;161(4):202-7.
14. Mosca F, Bray M, Lattanzio M, Fumagalli M, Tosetto C. Comparative evaluation of the effects of indomethacin and ibuprofen on cerebral perfusion and oxygentation in preterm infants with patent ductus arteriosus. *J Pediatr.* 1997;131(4):549-54.
15. Su PH, Chen JY, Su CM, Huang TZ, Lee HS. Comparison of ibuprofen and indomethacin therapy for patent ductus arteriosus in preterm infants. *Pediatr Int*. 2003;45(6):665-70.
16. Van Overmeire B, Follens I, Hartmann S, Creten WL, Van Acker KJ. Treatment of patent ductus arteriosus with ibuprofen. *Arch Dis Child Fetal Neonatal Ed.* 1997;76(3):F179-84.
17. Gournay V, Roze JC, Kuster A, Daoud P, Cambonie G, Hascoet JM, et al. Prophylactic ibuprofen versus placebo in very premature infants: a randomised, double-blind, placebo-controlled trial. *Lancet.* 2004; 364(9449):1939-44.
18. Sivanandan S, Bali V, Soraisham AS, Harabor A, Kamaluddeen M. Effectiveness and safety of indomethacin versus ibuprofen for the treatment of patent ductus arteriosus in preterm infants. *Am J Perinatol*. 2013;30(9): 745-50.
19. Rogerson S, Thornley C, Schmoelzer G, Fox LM. Ibuprofen is less effective than indomethacin for closure of haemodynamically significant patent ductus arteriosus after 72 hours [abstract]. Combined 17th Congress of the Federation of Asian and Oceania Perinatal Societies and 16th Annual Congress of the Perinatal Society of Australia and New Zealand; 2012 Mar; Sydney, Australia. *J Paediatr Child Health.* 2012;48 Suppl S1:44-5.
20. De Palma C, Di Paola R, Perrotta C, Mazzon E, Cattaneo D, Trabucchi E, et al. Iburpofen-arginine generates nitric-oxide and has enhanced anti-inflammatory effects. *Pharmacol Res.* 2009;60(4):221-8.
21. Momma K, Toyono M. The role of nitric oxide in dilating the fetal ductus arteriosus in rats. *Pediatr Res.* 1999;46(3):311-5.
22. Richard C, Gao J, LaFleur B, Christman BW, Anderson J, Brown N, et al. Patency of the preterm fetal ductus arteriosus is regulated by endothelial nitric oxide synthase and is independent of vasa vasorum in the mouse. *Am J Physiol Regul Integr Comp Physiol*. 2004;287(3):R652-60.
23. Reese J, O'Mara PW, Poole SD, Brown N, Tolentino C, Eckman DM, et al. Regulation of the fetal mouse ductus arteriosus is dependent on interaction of nitric oxide and COX enzymes in the ductal wall. *Prostaglandins Other Lipid Mediat.* 2009;88(3-4):89-96.
24. Kellar RL, Tacy TA, Fields S, Ofenstein JP, Aranda JV, Clyman RI. Combined treatment with a nonselective nitric oxide synthase inhibitor (L-NMMA) and indomethacin increases ductus constriction in extremely premature newborns. *Pediatric Res*. 2005;58(6):1216-21.
25. Walsh MC, Kliegman RM. Necrotizing enterocolitis: treatment based on staging criteria. *Pediatr Clin North Am*. 1986;33(1):179-201.
26. Duzova A, Bakkaloglu A, Kalyoncu M, Poyrazoglu H, Delibas A, Ozkaya O, et al.; Turkish Society for Pediatric Nephrology Acute Kidney Injury Study Group. Etiology and outcome of acute kidney injury in children. *Pediatr Nephrol.* 2010;25(8):1453-61.
27. Park HW, Choi YS, Kim KS, Kim SN. Chorioamnionitis and patent ductus arteriosus: a systematic review and meta-analysis. *PLoS One*. 2015;10(9): e0138114.
28. Arginine hydrochloride [monograph]. In: *Lexicomp Online* [database]. Hudson (OH): Lexi-Comp; [cited 2016 Nov 12]. Available from: http://online.lexi.com/lco/action/home. Subscription required to access content.
29. Desfrere L, Zohar S, Morville P, Brunhes A, Chevret S, Pons G, et al. Dose-finding study of ibuprofen in patent ductus arteriosus using the continual reassessment method. *J Clin Pharm Ther*. 2005;30(2):121-32.
30. Dani C, Vangi V, Bertini G, Pratesi S, Lori I, Favelli F, et al. High-dose ibuprofen for patent ductus arteriosus in extremely preterm infants: a randomized controlled study. *Clin Pharmacol Ther*. 2012;91(4):590-6.

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Potential Negative Effects of Antimicrobial Allergy Labelling on Patient Care: A Systematic Review

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ABSTRACT

Background: Antimicrobial allergy labels, either self-reported or placed in a patient's medical record, are common, but in many cases they are not associated with a true immunoglobulin E–mediated allergic response.

Objective: To assess the impact of antimicrobial allergy labels on antimicrobial prescribing, resource utilization, and clinical outcomes.

Data Sources: The MEDLINE, Embase, CINAHL, and Scopus electronic databases were searched for the period 1990 to January 2016.

Study Selection: Controlled studies with the objective of assessing antimicrobial prescribing, resource utilization, and/or clinical outcomes associated with antimicrobial allergy labels were included.

Results: The search identified 560 unique citations, of which 7 articles met the inclusion criteria. One additional article identified by an expert in the field was also included. Four of the identified papers were limited to penicillin or other ß-lactam allergies. Six studies noted differences in antibiotic selection between patients with allergy labels and those without such labels. Broader-spectrum or second-line agents (e.g., vancomycin, clindamycin, and fluoroquinolones) were more commonly prescribed for patients with penicillin allergy labels. Antibiotic therapy costs were significantly higher for patients with allergy labels than for those without. The impact of allergy labels on clinical outcomes was mixed. One study indicated a longer length of hospital stay, 2 studies reported higher readmission rates, and 1 study reported a higher rate of antibiotic-resistant organisms for patients with allergy labels.

Conclusions: Most of the available literature is limited to penicillin or ß-lactam allergy. The growing body of knowledge supports the concept that ß-lactam allergy labels are not benign and that labelling in the absence of a true allergy has a negative effect on patient care. Allergy labelling appears to be associated with suboptimal antibiotic selection, greater treatment costs, prolonged length of stay, greater readmission rates, and higher prevalence of antibiotic-resistant organisms. There is an opportunity for antimicrobial stewardship programs to implement systematic allergy verification to optimize antimicrobial therapy and improve patient care.

Keywords: antimicrobial allergy labels, antibiotic allergy, antimicrobial stewardship, antibiotic stewardship

RÉSUMÉ

Contexte: Les mentions d'allergies aux antimicrobiens, soit autodéclarées soit consignées dans un dossier médical, sont fréquentes, mais dans bien des cas elles ne signalent pas une véritable réaction allergique à médiation par l'immunoglobuline E.

Objectif : Évaluer l'effet des mentions d'allergie aux antimicrobiens sur les habitudes de prescription d'antimicrobiens, l'utilisation des ressources et les résultats cliniques.

Sources des données : Les bases de données numériques MEDLINE, Embase, CINAHL et Scopus ont été interrogées pour la période allant de 1990 à janvier 2016.

Sélection des études : Les essais cliniques comparatifs dont l'objectif était d'évaluer les habitudes de prescription d'antimicrobiens, l'utilisation des ressources ou les résultats cliniques associés aux mentions d'allergie aux antimicrobiens ont été inclus.

Résultats : La recherche a permis de trouver 560 citations distinctes et ainsi de repérer sept articles qui répondaient aux critères d'inclusion. Un article supplémentaire signalé par un expert du domaine a été inclus à l'analyse. Quatre de ces articles se limitaient aux allergies à la pénicilline ou à d'autres ß-lactamines. Six études ont noté des différences dans le choix des antibiotiques entre les patients ayant une mention d'allergie à leur dossier et ceux n'en ayant pas. Des antibiotiques à plus large spectre ou des médicaments de deuxième intention (comme la vancomycine, la clindamycine et les fluoroquinolones) étaient plus souvent prescrits pour les patients ayant une mention d'allergie à la pénicilline. Les coûts des antibiothérapies étaient significativement plus élevés pour les patients ayant une mention d'allergie que pour ceux n'en ayant pas à leur dossier. L'effet des mentions d'allergie sur les résultats cliniques était inégal. Une étude indiquait un séjour plus long à l'hôpital, deux études indiquaient des taux de réadmission plus élevés et une étude indiquait un taux plus élevé d'organismes résistants aux antibiotiques pour les patients ayant une mention d'allergie comparativement à ceux n'en ayant pas.

Conclusions : La majeure partie des articles disponibles se limitent aux allergies à la pénicilline ou à d'autres ß-lactamines. De plus en plus, le savoir vient appuyer le concept voulant que les mentions d'allergies aux ß-lactamines ne soient pas bénignes et que leur emploi en l'absence d'une allergie réelle ait un effet négatif sur les soins aux patients. Les mentions d'allergie semblent être associées à un choix sous-optimal d'antibiotiques, des coûts de traitement plus élevés, des séjours plus longs, des taux de réadmission plus élevés et une plus grande prévalence d'organismes résistants aux antibiotiques. Or, les programmes de gérance des antimicrobiens pourraient permettre de mettre

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en œuvre des procédures de vérification systématique des allergies afin d'optimiser l'antibiothérapie et d'améliorer les soins aux patients.

Mots clés : mentions d'allergie aux antimicrobiens, allergie aux antibiotiques, gérance des antimicrobiens, gérance des antibiotiques

INTRODUCTION

Antibiotic resistance is a growing public health problem, with substantial burden throughout the health care system.[1] It is generally recognized that inappropriate antibiotic prescribing and unnecessary use of broad-spectrum antibiotics contribute to antibiotic resistance. Both inappropriate antibiotic prescribing and antibiotic resistance are associated with increased morbidity and mortality.[2,3]

Although many patients report or have a medical record of antimicrobial allergies, referred to as "allergy labels", not all of these allergy labels are accurate. Inaccurate antimicrobial allergy labelling contributes to inappropriate antibiotic selection through prescribers' avoidance of first-line or narrow-spectrum antibiotics. This can result in the use of broader-spectrum antibiotics, suboptimal therapy, and increased risks of antibiotic resistance and adverse events, as well as increased costs.[4] Reporting of antibiotic allergies is common. Trubiano and others[5] stated that 25% of patients admitted to hospital had documentation of an antimicrobial allergy, with 70% of these allergies involving ß-lactams. Although the prevalence of reported ß-lactam allergies is high, confirmed (true) allergic reactions are less common. For example, Park and others[6] showed that 96% of patients with a self-reported penicillin allergy did not have a true immunoglobulin E (IgE)-mediated allergy based on penicillin skin testing.[6] Reporting rates of true allergies to classes of antimicrobials other than ß-lactams are scarce.

Antimicrobial stewardship programs aim to optimize antimicrobial use, thereby improving patient outcomes, minimizing adverse effects, and reducing *Clostridium difficile* infections and the development of antimicrobial resistance.[7] A greater understanding of the impact of antimicrobial allergy labels can provide an impetus for improved allergy verification strategies, aimed at optimizing selection of antimicrobial therapy and patient outcomes.

This systematic review was performed to answer the following 3 separate but related questions: What is the impact of antimicrobial allergy labels on antimicrobial prescribing (e.g., choice and duration of therapy)? Do antimicrobial allergy labels increase health care costs and resource utilization? What is the effect of antimicrobial allergy labels on clinical outcomes (e.g., hospital length of stay, readmission rates, and mortality)?

METHODS

Searches for English-language articles published since 1990 were conducted in 4 databases (initially performed in MEDLINE and adapted into Embase, CINAHL, and Scopus) on January 18 and 21, 2016, by Public Health Ontario Library Services. The search concepts were "antimicrobial/antibiotic allergy label", "antimicrobial/antibiotic", and "patient/prescribing/utilization outcomes". Both primary literature and review articles were included. The full search strategy is available in Appendix 1 (see https://www.cjhp-online.ca/index.php/cjhp/issue/view/125/showToc).

English-language articles retrieved by the searches were assessed for eligibility. To ensure that the review would be comprehensive, there were no restrictions on study design, population, antimicrobial allergy, health care setting, or outcomes. Articles were included if the objective of the research was to assess the impact of antimicrobial allergy labels, relative to a control group, on antimicrobial prescribing, resource utilization, and/or clinical outcomes. Case reports and studies involving non-antimicrobial allergies, the efficacy or safety of antimicrobial allergy testing, or drug intolerance were excluded. Title and abstract screening, as well as full-text screening, was performed individually in duplicate by 2 reviewers (J.H.C.W. and B.J.L.). Data for overall results (e.g., allergy label versus control) were extracted by one of these reviewers (J.H.C.W.), with extraction verified by the second reviewer (B.J.L.) for 20% of the articles. Any disagreements regarding inclusion or data abstraction were resolved by consensus. Subgroup analyses, such as female versus male, were excluded. Results that did not reach statistical significance were recorded as not different from the control group. Because the inclusion criteria were broad (with inclusion of studies examining any allergy label, population, age, setting, and outcome), a descriptive analysis was performed.

RESULTS

The search identified 560 unique citations, with 7 articles meeting the inclusion criteria. During the review process, 1 additional article was identified by an expert in the field and was included. No reviews were found. Therefore, a total of 8 articles were included in the analysis[5,8-14] (Table 1).

The publication year of the included articles ranged from 2000 to 2015. Four studies were conducted in the United States,[8-10,14] 2 in Australia,[5,12] 1 in Canada,[13] and 1 in Israel.[11] The studies varied with respect to population (e.g., patients with penicillin allergy or any antimicrobial allergy), comparator (e.g., matched controls, patients with no antimicrobial allergies), methodology, and outcomes assessed (see Table 1).

Table 1 (part 1 of 2). Summary of Studies Included in a Systematic Review of Antimicrobial Allergy Labelling

Reference	Study Objective(s)	Study Design	Country and Setting	Population and Sample Size	Outcome Type Reported
Charneski et al. 2011[8]	To determine the impact of an antimicrobial allergy label in the medical record on clinical outcomes in hospitalized patients	Retrospective cohort study	United States: urban academic teaching hospital; nonsurgical patient care ward	Age ≥ 20 years, received at least 1 antimicrobial prescription (*n* = 11 872)	*Clinical* • Length of stay • ICU admission rate • Death • Readmission within 4 weeks of discharge *Prescribing* • Received > 1 antimicrobial
Lutomski et al. 2008[14]	To determine the frequency with which reported antibiotic allergies alter drug selection and to assess the validity of these allergies	Retrospective cohort study	United States: tertiary care teaching hospital; inpatients	Age ≥ 18 years, at least 1 documented antibiotic allergy, and received antibiotic during hospital admission (*n* = 300)	*Prescribing* • Antibacterial regimen • Most frequently selected alternative agents
MacLaughlin et al. 2000[9]	To evaluate effects of reported ß-lactam allergies on antibiotic selection and cost	Retrospective cohort study	United States: university-based family medicine clinic; ambulatory patients	Patients of any age who received antibiotic for upper respiratory tract infection, otitis media, sinusitis (acute or chronic), and/or urinary tract infection (*n* = 660)	*Prescribing* • Antibiotic selection (cephalosporin, macrolide) *Utilization* • Antibiotic costs
Macy and Contreras 2014[10]	To determine total hospital days, antibiotic exposure, and prevalence rates of *Clostridium difficile*, MRSA, and VRE in patients with and without penicillin allergy labels upon admission	Retrospective matched-control cohort study	United States: multiple hospitals (hospital type not specified); any admitted patient	Age not specified (*n* = 154 746)	*Clinical* • Length of stay • *C. difficile* prevalence • MRSA prevalence • VRE prevalence *Prescribing* • Antibiotic selection (fluoroquinolones, ciprofloxacin, vancomycin, clindamycin, cephalosporin) *Utilization* • Total hospital costs
Picard et al. 2013[13]	To determine how physicians at a large Canadian tertiary care academic hospital without allergists on staff treat patients with a history of penicillin allergy	Retrospective cohort study	Canada: tertiary care academic hospital; ICU, coronary care unit, internal medicine wards	Age not specified; penicillin allergy labelled (*n* = 172)	*Utilization* • Cost (additional cost of alternative antibiotics in place of ß-lactam standard of care) *Prescibing* • Antibiotic selection (fluoroquinolones, vancomycin)
Sade et al. 2003[11]	To examine the difference in cost and antibiotic usage between patients with and without penicillin allergy labels	Retrospective matched-control cohort study	Israel: tertiary level teaching hospital; internal medicine ward	Age not specified; penicillin allergy labelled by physician (*n* = 236)	*Clinical* • Death • Length of stay *Prescribing* • Antibiotic selection (cephalosporin, macrolide, vancomycin) • No. of antibiotics used during treatment • Route of antibiotic administration • Frequency of drug administration • Duration of therapy *Utilization* • Antibiotic costs during hospitalization • Antibiotic costs after hospitalization

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Table 1 (part 2 of 2). Summary of Studies Included in a Systematic Review of Antimicrobial Allergy Labelling

Reference	Study Objective(s)	Study Design	Country and Setting	Population and Sample Size	Outcome Type Reported
Trubiano et al. 2015[5]	To examine the rate of antimicrobial allergy labelling at a tertiary referral centre and impacts on antimicrobial usage and appropriateness	Two inpatient antimicrobial prevalence surveys	Australia: tertiary referral centre; inpatients	Inclusion criteria not specified (n = 509)	*Prescribing* • Antibiotic selection (cephalosporin, ß-lactams) • Duration of antimicrobial therapy • Inappropriate antimicrobial prescribing • Route of antimicrobial administration • Antimicrobial exposure days
Trubiano et al. 2015[12]	To (1) determine the prevalence of antimicrobial allergy labels in patients with cancer; (2) provide a description of reported antibiotic allergies; and (3) describe the impacts of an antimicrobial allergy label on antimicrobial choice, usage, and clinical outcomes	Retrospective cohort study	Australia: tertiary referral centre for cancer patients; oncology, hematology	Age not specified; patients coded as having an infective diagnosis who received antimicrobial agent for treatment of infection, with inpatient admission > 24 h (n = 198)	*Clinical* • 30-day or 60-day mortality • Length of stay • Overall readmissions • Readmissions with infectious disease diagnosis requiring antimicrobial therapy *Prescribing* • Antibiotic selection (fluoroquinolone) • Antibiotics used per admission • Antibiotic duration • Concordance with first-line therapy • No. of antibiotics employed

ICU = intensive care unit, MRSA = multidrug-resistant *Staphylococcus aureus*, VRE = vancomycin-resistant *Enterococcus*.

Two studies included only adult patients.[8,14] Seven of the 8 studies focused on inpatients,[5,8,10-14] and the other study focused on outpatients.[9] Four studies included patients labelled as having any type of antimicrobial allergy,[5,8,12,14] 3 studies focused on penicillin allergy,[10,11,13] and 1 study included any ß-lactam allergy.[9] None of the studies reported the source of the allergy labels (e.g., patient self-report or documented reaction). Three of the 4 studies that were not limited to ß-lactam allergies reported the prevalence of allergies to specific agents. Although allergies to penicillin and other ß-lactams were most common, 11%–21% of reported allergies were to sulfonamides, 7% to vancomycin, and less than 6% to each of fluoroquinolones, metronidazole, macrolides, and doxycycline.[5,12,14]

Prescribing Outcomes

Prescribing outcomes were reported in all 8 of the included studies. The prescribing outcomes considered were antimicrobial selection, duration of therapy, and appropriateness. Seven of the 8 studies reported differences in antibiotic selection between patients with allergy labels and controls.[5,9-14]

Alternative antibiotics were significantly more likely to be used for patients with penicillin allergy labels than for those without (38% versus 15%, $p < 0.0001$), as well as for those with cephalosporin allergy labels than for those without (55% versus 27%, $p = 0.0007$).[14] Patients with allergy labels were more likely to receive cephalosporins[9,11,12] (including first- to fourth-generation cephalosporins, $p < 0.001$[11,12]) and non-ß-lactam antibiotics.[5,9,10,12-14] Non-ß-lactam antibiotics that were used more frequently for patients with an allergy label were clindamycin,[10,14] vancomycin,[10,11,13,14] macrolides,[9,11] and fluoroquinolones.[10-14] In contrast, significantly lower cephalosporin use was noted for patients reported to have penicillin allergy relative to controls in 2 studies (24% versus 43%, $p = 0.05$[5]; 32% versus 50%, $p < 0.0001$[10]), including first-generation cephalosporins (16% versus 33%, $p < 0.0001$) and third-generation or higher cephalosporins (20% versus 23%, $p < 0.0001$).[10]

In the study by Sade and others,[11] a penicillin allergy label had no effect on the number of antibiotics prescribed, the number of antibiotics given parenterally, the duration of antibiotic therapy, or the frequency of administration. However, other studies identified significantly higher numbers of antibiotics employed (odds ratio [OR] 1.51, 95% confidence interval [CI] 1.33–1.70[8]) among patients with allergy labels than among those without allergy (average of 3 versus 2 antibiotics per admission, $p = 0.01$).[12]

Trubiano and others[12] reported that the presence of an allergy label was associated with a longer course of antibiotic therapy in hospitalized cancer patients after multivariable adjustment (p = 0.03). In another study, Trubiano and others[5] observed a significantly longer antibiotic duration for patients admitted to a tertiary care hospital (median duration 6 versus 4 days, p = 0.018) and a significantly higher use of IV relative to oral antibiotics in patients with an allergy label (60% versus 46%, p = 0.0001).

Trubiano and others[5] found no statistically significant difference between patients with allergy labels and those without in terms of appropriate antibiotic selection (using criteria from the National Antimicrobial Prescribing Survey of Australia; 29% versus 23%, p = 0.22) or the use of restricted antimicrobials (25% versus 24%, p = 0.44). However, in a different study, Trubiano and others[12] observed significantly less concordance with prescribing guidelines for patients with an antimicrobial allergy label (47% versus 91%, p < 0.001); Lutomski and others[14] also observed 30% deviation from standard of care (no statistical analysis reported).

Utilization Outcomes

Four studies reported on costs as a utilization outcome. Three of these reported antibiotic costs[9,11,13] and 1 translated hospital length of stay and total hospital use into financial costs.[10]

MacLaughlin and others[9] examined patients for whom antibiotics were prescribed in a family medicine clinic and observed a significantly higher mean antibiotic cost for individuals with a ß-lactam allergy label than for those without (65% higher). Similarly, if a penicillin allergy label was present, there were significantly higher costs for antibiotic therapy during hospital admission (56% higher) and after discharge (38% higher).[11] A Canadian study conducted in 2009 by Picard and others[13] found that the use of alternative antibiotics in place of standard-of-care ß-lactam regimens carried an additional cost of Can$326.50 per patient. Finally, the observed average increase in length of stay—0.59 days per penicillin-allergic patient—in a US hospital translated to an estimated total of US$64 626 630 over the study period (2010–2012).[10] This increased expenditure was reported to be approximately 9.5 times greater than the cost of conducting penicillin allergy testing in those patients.[10]

Clinical Outcomes

Clinical outcomes, reported by 4 studies, included length of stay,[8,10-12] readmission,[8,12] and death.[8,11,12] Overall, the effects of allergy labels on the various clinical outcomes were mixed.

Of the 4 studies assessing hospital length of stay, 2 studies indicated an increase among those with allergy labels (by 0.59 days [95% CI 0.47–0.71][10] and by 1.16 days[8]), whereas the other 2 studies reported no significant difference[11,12] Two studies reported admission and readmission rates.[8,12] One of these studies reported a significantly higher ICU admission rate (adjusted OR 1.42, 95% CI 1.21–1.67),[8] and the other reported a higher readmission rate due to diagnosis of an infectious disease requiring antimicrobial therapy in patients labelled as having an antimicrobial allergy (adjusted OR 3.27, 95% CI 1.55–6.88).[12] However, presence of an allergy label was not significantly associated with an increased overall risk of readmission (adjusted OR 1.99, 95% CI 0.95–4.15)[12] or the readmission rate within 4 weeks of discharge (adjusted OR 0.71, 95% CI 0.63–0.80).[8] Mixed results were also observed for the mortality outcome. Two studies found no difference in 30- and 60-day mortality[12] or in-hospital mortality,[11] whereas Charneski and others[8] indicated that patients with an antimicrobial allergy label had a significantly higher risk of in-hospital death (adjusted OR 1.56, 95% CI 1.20–2.04) relative to those with no reported allergy. The presence of a penicillin allergy label was associated with significantly higher prevalences of infection with *C. difficile* (OR 1.23, 95% CI 1.16–1.32), methicillin-resistant *Staphylococcus aureus* (OR 1.14, 95% CI 1.07–1.32), and vancomycin-resistant *Enterococcus* (OR 1.30, 95% CI 1.13–1.50).[10]

DISCUSSION

This systematic review assessed the potential negative impact of antimicrobial allergy labels on patient care. Although results varied, the studies included in this review found that reported antimicrobial allergies may be associated with worse clinical outcomes, including longer hospital stay,[8,10] higher readmission rates,[8,12] and higher mortality,[8] with increased treatment costs relative to those without allergies.[9-11,13] Given that antimicrobial allergy labels are common at the time of hospital admission, at a frequency ranging from 6%[11] to as high as 25%,[5] these negative clinical consequences have the potential to affect a large population.

In addition to their association with negative clinical outcomes, antimicrobial allergy labels may also lead to potentially unnecessary use of broad-spectrum antibiotics. ß-Lactams are frequently considered as first-line agents for many infections, given their proven clinical efficacy, safety, tolerability, and low propensity for drug interactions.[15-17] Use of alternative agents (e.g., vancomycin for serious infections due to methicillin-susceptible *S. aureus*) can compromise clinical efficacy.[18,19] Furthermore, alternative agents such as clindamycin and fluoroquinolones, which are frequently used for patients with allergy to penicillin or cephalosporin, have been associated with an increase in frequency of *C. difficile* infection.[10,20,21] In addition, the use of broader-spectrum agents and a greater number of antibiotics for a longer treatment course increases costs and the risk of antimicrobial resistance.[4,9]

Many of the studies included in this review described differences in antibiotic selection between patients with and without allergy labels, but few commented on the appropriateness of the chosen therapy. This may be because appropriateness of therapy is more difficult to assess, despite it being a key component of antimicrobial stewardship. Notably, most of the studies involved hospital inpatients. As a result, less insight is available regarding the outcomes of allergy labels in community practice.

Accurately assessing reported allergies to provide the best antimicrobial therapy is an important antimicrobial stewardship initiative.[7] Studies assessing allergy verification procedures have found that 84% to 99% of those with self-reported penicillin allergy are found to not have a true allergy and thus can be "de-labelled".[6,22-27] Hence, it is important for clinicians to carefully evaluate allergy status before prescribing alternative antimicrobial therapy. Allergy labels should be assessed through a detailed clinical history characterizing the type and timing of previous reactions. Many ß-lactams are well tolerated by patients with a history of penicillin allergy. For instance, cephalosporins can be safely administered to patients with a self-reported history of penicillin allergic reaction that occurred more than 10 years ago or if prior reactions did not include features of an IgE-mediated response, such as hives or anaphylaxis.[28,29]

Antibiotic allergy testing, in the form of a skin test, can be performed by trained health care professionals to help optimize antimicrobial use.[30] A recent systematic review and meta-analysis of penicillin allergy verification interventions found that penicillin skin testing was the most commonly reported method of allergy verification.[31] Allergy consultation before skin testing and pharmacy-driven interviews were other approaches.[31] In particular, penicillin skin testing was found to be a safe and effective way to clarify allergy status in inpatient settings. In addition, ruling out penicillin allergy was shown to decrease health care costs and influence antibiotic selection, with increased prescribing of penicillin and cephalosporin and reduced prescribing of vancomycin and fluoroquinolone.[31] Antimicrobial stewardship teams are encouraged to incorporate antibiotic allergy evaluation and testing into their programs.[32]

This review had some limitations. All relevant articles identified in the search were included in the analysis, because only a limited number of published studies were found. A quality assessment was not conducted, and therefore no exclusion criteria based on study quality were applied. There was substantial heterogeneity in the population and outcomes reported, which made it difficult to draw generalizable conclusions. All studies were retrospective in nature, introducing the possibility of unmeasured confounding factors. Many studies reported on differences in antibiotic selection between patients with and without antimicrobial allergies, but less frequently reported on appropriateness or clinical outcomes. As a result, definitive conclusions about the clinical impact of allergy labels will require further studies. Additionally, outcomes related to resolution of infection and adverse events were not reported in any of the studies, although these are important considerations when first-line antibiotics are not selected. Finally, most of the studies were hospital-based and focused on ß-lactam antibiotics; therefore, this review may not be generalizable to non-ß-lactam allergy labels or to patients in settings other than acute care hospitals.

The lack of review articles and the presence of only a handful of primary studies addressing the impact of antimicrobial allergy labels indicate a shortage of research in this area. However, it is evident from the data reported in this review and recent publications[33-36] that inaccurate antimicrobial allergy labels are associated with several important negative impacts on antimicrobial prescribing, patient care, and hospital resources. For example, one prospective study conducted in 3 academic hospitals in Toronto, and published after this review was completed, also identified an increased rate of adverse outcomes (particularly readmission to hospital and adverse drug reactions) among patients who received non-preferred therapy as a result of reported ß-lactam allergy.[36] A multicentre prospective evaluation of point-of-care ß-lactam allergy skin testing by antimicrobial stewardship teams demonstrated the feasibility of systematic allergy verification as well as increased use of preferred ß-lactam therapy in acute care hospitals without any increase in the risk of adverse drug reactions.[30] A growing body of antimicrobial stewardship initiatives targeted toward patients with reported ß-lactam allergies further emphasizes the benefit of allergy verification in this population.[31,37] The impact of non-ß-lactam allergy labels is not as well documented and may require further study.

CONCLUSION

This systematic review provides data to support antimicrobial stewardship programs in improving the appropriateness of antimicrobial therapy for patients labelled as having antimicrobial allergies. Policies and procedures to ensure systematic verification of allergies and selection of optimal antimicrobial therapy should be employed.

References

1. Davey PG, Marwick C. Appropriate vs. inappropriate antimicrobial therapy. *Clin Microbiol Infec*t. 2008;14 Suppl 3:15-21.
2. Kumar A, Ellis P, Arabi Y, Roberts D, Light B, Parrillo JE, et al. Initiation of inappropriate antimicrobial therapy results in a fivefold reduction of survival in human septic shock. *Chest*. 2009;136(5):1237-48.
3. De Kraker MEA, Davey PG, Grundmann H; BURDEN study group. Mortality and hospital stay associated with resistant *Staphylococcus aureus* and *Escherichia coli* bacteremia: estimating the burden of antibiotic resistance in Europe. *PLoS Med*. 2011;8(10):e1001104.
4. Joint Task Force on Practice Parameters; American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology. Drug allergy: an updated practice parameter. *Ann Allergy Asthma Immunol.* 2010; 105(4):259-73.

5. Trubiano JA, Cairns KA, Evans JA, Ding A, Nguyen T, Dooley MJ, et al. The prevalence and impact of antimicrobial allergies and adverse drug reactions at an Australian tertiary centre. *BMC Infect Dis.* 2015;15:572.
6. Park M, Markus P, Matesic D, Li JTC. Safety and effectiveness of a preoperative allergy clinic in decreasing vancomycin use in patients with a history of penicillin allergy. *Ann Allergy Asthma Immunol.* 2006;97(5):681-7.
7. Barlam TF, Cosgrove SE, Abbo LM, MacDougall C, Schuetz AN, Septimus EJ, et al. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis*. 2016;62(10):e51-77.
8. Charneski L, Deshpande G, Smith SW. Impact of an antimicrobial allergy label in the medical record on clinical outcomes in hospitalized patients. *Pharmacotherapy.* 2011;31(8):742-7.
9. MacLaughlin EJ, Saseen JJ, Malone DC. Costs of ß-lactam allergies: selection and costs of antibiotics for patients with a reported ß-lactam allergy. *Arch Fam Med*. 2000;9(8):722-6.
10. Macy E, Contreras R. Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: a cohort study. *J Allergy Clin Immunol.* 2014;133(3):790-6.
11. Sade K, Holtzer I, Levo Y, Kivity S. The economic burden of antibiotic treatment of penicillin-allergic patients in internal medicine wards of a general tertiary care hospital. *Clin Exp Allergy.* 2003;33:501-6.
12. Trubiano JA, Leung VK, Chu MY, Worth LJ, Slavin MA, Thursky KA. The impact of antimicrobial allergy labels on antimicrobial usage in cancer patients. *Antimicrob Resist Infect Control.* 2015;4:23.
13. Picard M, Bégin P, Bouchard H, Cloutier J, Lacombe-Barrios J, Paradis J, et al. Treatment of patients with a history of penicillin allergy in a large tertiary-care academic hospital. *J Allergy Clin Immunol Pract*. 2013;1(3):252-7.
14. Lutomski DM, LaFollette JA, Biaglow MA, Haglund LA. Antibiotic allergies in the medical record: effect on drug selection and assessment of validity. *Pharmacotherapy.* 2008;28(11):1348-53.
15. Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJC, Gorbach SL, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2014;59(2):e10-52.
16. Solomkin JS, Mazuski JE, Bradley JS, Rodvold KA, Goldstein EJC, Baron EJ, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clin Infect Dis.* 2010;50(2):133-64.
17. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis.* 2007;44 Suppl 2:S27-72.
18. Bull AL, Worth LJ, Richards MJ. Impact of vancomycin surgical antibiotic prophylaxis on the development of methicillin-sensitive *Staphylococcus aureus* surgical site infections: report from Australian Surveillance Data (VICNISS). *Ann Surg.* 2012;256(6):1089-92.
19. Kim SH, Kim KH, Kim HB, Kim NJ, Kim EC, Oh MD, et al. Outcome of vancomycin treatment in patients with methicillin-susceptible *Staphylococcus aureus* bacteremia. *Antimicrob Agents Chemother.* 2008;52(1):192-7.
20. Deshpande A, Pasupuleti V, Thota P, Pant C, Rolston DDK, Sferra TJ, et al. Community-associated *Clostridium difficile* infection and antibiotics: a meta-analysis. *J Antimicrob Chemother.* 2013;68(9):1951-61.
21. Wieczorkiewicz JT, Lopansri BK, Cheknis A, Osmolski JR, Hecht DW, Gerding DN, et al. Fluoroquinolone and macrolide exposure predict *Clostridium difficile* infection with the highly fluoroquinolone- and macrolide-resistant epidemic *C. difficile* strain BI/NAP1/027. *Antimicrob Agents Chemother.* 2015;60(1):418-23.
22. Arroliga ME, Wagner W, Bobek MB, Hoffman-Hogg L, Gordon SM, Arroliga AC. A pilot study of penicillin skin testing in patients with a history of penicillin allergy admitted to a medical ICU. *Chest.* 2000;118(4):1106-8.
23. Arroliga ME, Radojicic C, Gordon SM, Popovich MJ, Bashour CA, Melton AL, et al. A prospective observational study of the effect of penicillin skin testing on antibiotic use in the intensive care unit. *Infect Control Hosp Epidemiol.* 2003;24(5):347-50.
24. Li JTC, Markus PJ, Osmon DR, Estes L, Gosselin VA, Hanssen AD. Reduction of vancomycin use in orthopedic patients with a history of antibiotic allergy. *Mayo Clin Proc*. 2000;75(9):902-6.
25. Macy E. Elective penicillin skin testing and amoxicillin challenge: effect on outpatient antibiotic use, cost, and clinical outcomes. *J Allergy Clin Immunol.* 1998;102(2):281-5.
26. Park MA, McClimon BJ, Ferguson B, Markus PJ, Odell L, Swanson A, et al. Collaboration between allergists and pharmacists increases ß-lactam antibiotic prescriptions in patients with a history of penicillin allergy. *Int Arch Allergy Immunol*. 2011;154(1):57-62.
27. Nadarajah K, Green GR, Naglak M. Clinical outcomes of penicillin skin testing. *Ann Allergy Asthma Immunol.* 2005;95(6):541-5.
28. Daulat S, Solensky R, Earl HS, Casey W, Gruchalla RS. Safety of cephalosporin administration to patients with histories of penicillin allergy. *J Allergy Clin Immunol*. 2004;113(6):1220-2.
29. Goodman EJ, Morgan MJ, Johnson PA, Nichols BA, Denk N, Gold BB. Cephalosporins can be given to penicillin-allergic patients who do not exhibit an anaphylactic response. *J Clin Anesth*. 2001;13(8):561-4.
30. Leis JA, Palmay L, Ho G, Raybardhan S, Gill S, Kan T, et al. Point-of-care ß-lactam allergy skin testing by antimicrobial stewardship programs: a pragmatic multicenter prospective evaluation. *Clin Infect Dis.* 2017; 65(7): 1059-65.
31. Sacco KA, Bates A, Brigham TJ, Imam JS, Burton MC. Clinical outcomes following inpatient penicillin allergy testing: a systematic review and meta-analysis. *Allergy.* 2017;72(9):1288-96.
32. Trubiano JA, Beekmann SE, Worth LJ, Polgreen PM, Thursky KA, Slavin MA, et al. Improving antimicrobial stewardship by antibiotic allergy delabeling: evaluation of knowledge, attitude, and practices throughout the emerging infections network. *Open Forum Infect Dis.* 2016;3(3):ofw153.
33. Trubiano JA, Chen C, Cheng AC, Grayson ML, Slavin MA, Thursky KA; National Antimicrobial Prescribing Survey. Antimicrobial allergy 'labels' drive inappropriate antimicrobial prescribing: lessons for stewardship. *J Antimicrob Chemother.* 2016;71(6):1715-22.
34. van Dijk SM, Gardarsdottir H, Wassenberg MWM, Oosterheert JJ, de Groot MCH, Rockmann H. The high impact of penicillin allergy registration in hospitalized patients. *J Allergy Clin Immunol Pract.* 2016;4(5):926-31.
35. Su T, Broekhuizen BDL, Verheij TJM, Rockmann H. The impact of penicillin allergy labels on antibiotic and health care use in primary care: a retrospective cohort study. *Clin Transl Allergy.* 2017;7:18.
36. MacFadden DR, LaDelfa A, Leen J, Gold WL, Daneman N, Weber E, et al. Impact of reported beta-lactam allergy on inpatient outcomes: a multicenter prospective cohort study. *Clin Infect Dis.* 2016;63(7):904-10.
37. Vaisman A, McCready J, Hicks S, Powis J. Optimizing preoperative prophylaxis in patients with reported ß-lactam allergy: a novel extension of antimicrobial stewardship. *J Antimicrob Chemother*. 2017;72(9):2657-60.

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CASE REPORT

Rivaroxaban for a Patient with Class III Obesity: Case Report with Literature Review

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INTRODUCTION

Between 1985 and 2011, the prevalence of obesity, defined as body mass index (BMI) of 30 kg/m^2 or higher, increased from 6.1% to 18.3% in Canada.[1] It is estimated that by 2019, more than 55% of the adult Canadian population will be overweight or obese.[1] Obesity is associated with an approximately 2-fold increased risk of venous thromboembolism (VTE).[2] The major mechanisms proposed as being responsible for obesity-associated thrombosis are chronic inflammation, impaired fibrinolysis, and clinical factors such as immobility, obstructive sleep apnea, heart failure, and venous stasis.[2] Direct oral anticoagulants (DOACs) are indicated for the prevention of acute VTE in patients who have undergone elective hip or knee replacement, for the treatment of acute VTE, for the prevention of recurrent VTE, and for the prevention of stroke or systemic embolism in patients with atrial fibrillation. The Canadian rivaroxaban product monograph states that for patients with extremes of body weight (< 50 kg or > 120 kg), a 10-mg tablet caused less than a 25% change in the plasma concentration of rivaroxaban, and thus no dosage adjustment is required.[3] The 2016 guidelines of the International Society on Thrombosis and Haemostasis (ISTH) suggest that DOACs not be used in patients with weight greater than 120 kg or BMI greater than 40 kg/m^2 because of the lack of clinical data for this population.[4] We present here a case of rivaroxaban use in a patient with class III obesity and review the evidence for use of this medication in obese patients.

CASE REPORT

A 67-year-old woman with class III obesity (height 160 cm, weight 186.6 kg, BMI 73 kg/m^2) was admitted to hospital for hypoxia secondary to a viral illness and heart failure. Her medical history included diabetes mellitus, hypertension, atrial fibrillation, heart failure, chronic kidney disease, dyslipidemia, hypothyroidism, anemia, over-active bladder, chronic back pain, and gastroesophageal reflux disease. Medications before admission included candesartan 8 mg daily, diltiazem ER 180 mg daily, furosemide 40 mg daily, rivaroxaban 20 mg daily, rosuvastatin 10 mg daily, levothyroxine 212 µg daily, insulin glargine 24 units at bedtime, insulin lispro 4 units 3 times daily before meals, metformin 500 mg at breakfast and 1000 mg at lunch and supper, pantoprazole 40 mg daily, tolterodine ER 4 mg daily, cholecalciferol 3000 units daily, and tramadol 37.5 mg/acetaminophen 325 mg 2 tabs 3 times daily as needed. The patient denied use of other over-the-counter or herbal medications.

The patient had no known drug allergies and stated that she was intolerant of warfarin. More specifically, she reported that she had been given warfarin (for atrial fibrillation) more than 10 years before the current admission but had stopped this medication because her international normalized ratio (INR) was labile and the medication made her feel unwell; however, she could not remember the specific intolerance. The patient stated that acetylsalicylic acid 81 mg daily was then prescribed. A review of prescription records showed that 3.6 years before the current admission, this therapy had been changed to rivaroxaban ($CHADS_2$ score 3 and HAS-BLED score 1).

Transthoracic echocardiography 30 days before the admission showed mild concentric left ventricular hypertrophy with normal left ventricular systolic function. Right ventricular systolic function was mildly reduced. Fibrocalcific degenerative changes of the mitral valve leaflets and mild mitral stenosis were noted. The left and right atria were of normal size. No other evidence of valvular disease was noted.

Vital signs upon admission were blood pressure 115/85 mm Hg, heart rate 94 beats/min, temperature 36.7°C, respiratory rate 24 breaths/min, and oxygen saturation 93% on 10 L/min of oxygen. The physical examination showed mild pedal edema, and the respiratory examination showed wheezing and diffuse crackles bilaterally through all fields. Other physical

findings were unremarkable. Electrocardiography revealed atrial fibrillation, with a rapid ventricular rate of 156 beats/min. Chest radiography showed bilateral pulmonary edema.

Laboratory test results included serum creatinine 143 µmol/L (normal range 35–100 µmol/L) and estimated creatinine clearance (CrCl) 52 mL/min based on the Cockcroft–Gault calculation with adjustment for body weight (baseline serum creatinine 130–140 µmol/L). On admission, liver enzymes were normal, except for slight elevation of Ɣ-glutamyl transferase to 63 units/L (normal range 0–35 units/L). Pneumonia, influenza, and thrombosis were ruled out as the cause of the patient's shortness of breath. All home medications were continued during the admission.

The clinical team had a discussion with the patient about the lack of evidence to support the use of rivaroxaban in patients with obesity. The patient was made aware that rivaroxaban might not be reducing her risk of stroke or systemic embolism, but she declined switching to warfarin or any other anticoagulant. The patient gave informed consent to have samples drawn for determination of peak and trough anti–factor Xa levels and for publication of this case report.

During the admission, all doses of rivaroxaban were administered at 0800 with breakfast. Rivaroxaban anti-Xa levels were measured with a chromogenic anti-Xa assay using STA-Liquid Anti-Xa (competitive chromogenic assay for factor Xa inhibition) and STA-Rivaroxaban Calibrator (high-performance liquid chromatography–referenced calibration plasmas for rivaroxaban) on the STA-r Evolution analyzer (analyzer and calibrator: Diagnostica Stago S.A.S., Asnières-sur-Seine, France). The rivaroxaban concentration was reported in nanograms per millilitre (ng/mL), according to calibration of anti-Xa level using the rivaroxaban calibrator. There is no anti-Xa reference range defining the efficacy and safety of rivaroxaban. On day 10 of the admission, peak rivaroxaban concentration measured 3.5 h after a dose was 465 ng/mL. On day 15, trough rivaroxaban concentration measured 23.5 h after the previous dose was 92 ng/mL. The patient was discharged on day 15, with continuation of rivaroxaban 20 mg daily. Four months after discharge the patient continued to take rivaroxaban with no evidence of stroke or systemic embolism.

DISCUSSION

To understand the implications of rivaroxaban therapy in this patient, certain aspects of the drug's pharmacokinetics must be reviewed. According to Mueck and others,[5] rivaroxaban is absorbed rapidly, with peak plasma concentrations (C_{max}) occurring within 2–4 h. The bioavailability of a 20-mg tablet is 66% under conditions of fasting, and the area under the curve (AUC) increases by 39% when rivaroxaban is taken with food. There is no influence on pharmacokinetics by type of food (high-fat versus high-carbohydrate meal). The volume of distribution is about 0.62 L/kg, which indicates low-to-moderate affinity for the peripheral tissues.[5] One-third of each dose of rivaroxaban is excreted unchanged in the urine, with the remaining two-thirds of each dose being subject to metabolic degradation. The resulting metabolites are eliminated both renally and via the hepatobiliary route.[5] In the case reported here, rivaroxaban was administered once daily with breakfast to maximize absorption. The sample for determination of peak concentration was drawn within the 2- to 4-h window in which rivaroxaban peaks in the blood. As noted above, the drug does not have a high volume of distribution, which suggests that it is not extensively distributed into fat. The patient did not require a reduction in rivaroxaban dose because of renal function.

Our literature search identified only one pharmacokinetic study evaluating rivaroxaban in patients with obesity. This small (48 healthy participants), single-centre, randomized, single-blind, placebo-controlled study was conducted to study the influence of body weight on rivaroxaban pharmacokinetics.[6] Patients were classified by weight (≤ 50 kg, 70–80 kg, > 120 kg). The average BMI among patients weighing more than 120 kg was 43.5 kg/m^2 (standard deviation [SD] 4.2 kg/m^2). Twelve participants in each study arm received a single dose of rivaroxaban 10 mg, and 4 patients in each arm received placebo. The bioavailability, time to C_{max}, and AUC were similar in all weight groups. Rivaroxaban inhibited factor Xa activity to a similar extent in all 3 weight groups.[6] On the basis of these results, the authors proposed that rivaroxaban is unlikely to require dose adjustment according to body weight. The dose of rivaroxaban used in this study,[6] 10 mg daily, is typically used to prevent VTE after total hip or total knee replacement or as thromboprophylaxis in medically ill patients.[3,7] At BMI 73 kg/m^2, the patient in our case was much larger than the healthy participants studied by Kubitza and others,[6] and she was receiving a higher dose of rivaroxaban (20 mg daily) for a different indication (stroke prevention secondary to atrial fibrillation).

Randomized controlled trials of DOACs including a total of more than 71 000 patients have shown that fixed-dose, unmonitored therapy is at least as effective as dose-adjusted warfarin for stroke prevention and is associated with less major bleeding, particularly decreased intracranial bleeding.[8] Routine monitoring and dose adjustments of DOACs cannot be recommended on the basis of available information. Measurement of drug concentration or anticoagulant effect might be useful in certain clinical scenarios, such as major bleeding or thrombotic events, to establish the optimal timing of surgery or other invasive procedures, and to detect drug accumulation in patients with renal or hepatic insufficiency or suspected overdose.[8,9] Other indications for monitoring may include subtherapeutic or supratherapeutic levels secondary to extremes of body weight, to identify candidates for specific reversal agents, and to assist

in the management of drug interactions with DOACs.[8,9] Median trough levels of DOACs may vary by a factor of 6 to 11 among individual patients.[8] Within-patient variability, expressed as the coefficient of variation, ranges between 20% and 50%, depending on the population and whether sampling is done at peak or trough.[8] Measurement of drug concentration or anticoagulant effect is problematic because there are no defined therapeutic ranges for DOACs, and very few laboratories have anti-Xa assays calibrated for rivaroxaban, apixaban, and edoxaban.[4,9]

The ISTH recommends that DOACs not be used in patients with BMI above 40 kg/m^2 or body weight above 120 kg, because of the limited clinical pharmacokinetic and pharmacodynamic data suggesting possible decreased drug exposures, reduced C_{max}, and shorter half-life with increasing weight. This recommendation raises the concern of underdosing in obese patients.[4] If DOACs *are* used for patients with BMI above 40 kg/m^2 or body weight above 120 kg, determination of peak and trough anti-Xa levels for rivaroxaban, apixaban, and edoxaban or measurement of drug concentration by mass spectrometry is suggested. If either falls within the expected range (based on the literature), then the DOAC may be continued. However, if either falls below the expected range, then a switch to an oral vitamin K antagonist should be considered, rather than adjustment of the DOAC dose.[4] Review of the literature suggests average reported ranges for rivaroxaban concentrations are peak 173–467 ng/mL and trough 17–94 ng/mL, with wide interpatient variation.[5,10-18] The range in concentration is similar whether measured by mass spectrometry or anti-Xa. These concentrations have not been correlated with clinical outcomes such as VTE or bleeding. The patient in our case had rivaroxaban peak and trough concentrations at the higher end of these ranges, and the rivaroxaban was therefore continued upon discharge.

A search of PubMed, Embase, and Google Scholar from inception to August 2017 using the search terms "rivaroxaban" and "obesity" yielded 2 case reports of rivaroxaban use in patients with class III obesity. The first case involved a 27-year-old woman who received the anticoagulant phenprocoumon for recurrent deep vein thrombosis with subsequent labile INRs.[19] No other medications were reported. The peak BMI was 61 kg/m^2, which led to bariatric surgery. Two months after the surgery, the patient was admitted to hospital with INR above 9. The phenprocoumon was discontinued, and rivaroxaban 20 mg daily was initiated. Anti-Xa levels were measured at 3, 6, 12, and 24 h after the first dose, and again 3 h after the second dose. The rivaroxaban concentrations at 3 h after the first and second doses were 224.22 ng/mL and 262.46 ng/mL, respectively. The trough concentration 24 h after the first dose was 35.54 ng/mL. Serum creatinine, liver enzymes, and other medications were not reported.[19] The effect of rivaroxaban could have been diminished because of potential erratic absorption of the drug after the bariatric surgery and low caloric intake in the immediate postoperative period.[20,21] There is limited evidence concerning the use of DOACs in patients who have undergone major gastrointestinal tract surgery.[22]

The second case involved a 67-year-old man with ischemic stroke, BMI 40 kg/m^2, and CrCl 132 mL/min.[23] The patient was started on dabigatran 150 mg twice daily. The patient's other medications included bisoprolol and atorvastatin. Seven days after initiation, dabigatran concentration was measured with a thrombin inhibitor assay immediately before and 2, 4, and 6 h after the morning dose. The authors noted that the drug concentration never reached the interquartile range for C_{max} and was below the quartile range for trough level. The patient's anticoagulation was changed to rivaroxaban 20 mg daily. Five days after initiation, peak and trough rivaroxaban concentrations were 200 ng/mL and 30 ng/mL, respectively.[23] In both of these cases,[19,23] the patients were not followed over the long term to evaluate the safety and efficacy of rivaroxaban therapy. In the case reported here, the peak concentration was about 2-fold higher and the trough concentration 3-fold higher than the 2 cases summarized above.

Mass spectrometry and anti-Xa determination show high interpatient variability for a given dose, as well as high variability among populations with different indications for anticoagulation (see Table 1).[5,10-18] In the case reported here, rivaroxaban peak concentration was measured 3.5 h after a dose (465 ng/mL) and trough concentration 23.5 h after the previous dose (92 ng/mL). The case series by Martin and Moll[13] most closely relates to the case presented here, but it lacks certain pertinent information. In that series, 15 patients received rivaroxaban: 20 mg daily for 12 patients (summarized in Table 1), 15 mg twice daily for 2 patients, and 15 mg daily for 1 patient. All but 4 of the patients had estimated glomerular filtration rate (eGFR) above 60 mL min^{-1} 1.73 m^{-2}; of the remaining 4 patients, 3 had eGFR between 30 and 60 mL min^{-1} 1.73 m^{-2} and 1 had eGFR of 11 mL min^{-1} 1.73 m^{-2} (eGFR values were not reported for individual patients). The main reason for determining anti-Xa levels was extremes of body weight: obesity in 7 patients and low body weight in 1 patient. The mean age was 42.6 years (SD 13.4), with weight ranging from 44.5 kg to 203.9 kg (median 106.2 kg). Peak and trough anti-Xa levels were determined for only some of the patients, and the timing of anti-Xa levels in relation to rivaroxaban administration was not consistently reported. Of the 2 patients who received rivaroxaban 15 mg twice daily, one had a trough rivaroxaban concentration of 0 at 17 h after dosing, and the other had peak rivaroxaban concentration of 161.6 ng/mL. The patient who received rivaroxaban 15 mg daily had 3 samples drawn for determination of peak concentrations, with values reported as 5.8 ng/mL, 116 ng/mL, and 155.5 ng/mL. There

Table 1 (part 1 of 2). Study Design, Patient Population, and Plasma Rivaroxaban Concentrations Derived from Mass Spectrometry and Anti–Factor Xa Determination*

Reference	Study Design†	Characteristics of Study Sample (Indication, Body Weight, and BMI)	Drug Dose and Frequency	Rivaroxaban Concentration (ng/mL)		Additional Details
				Peak	Trough	
DRUG CONCENTRATIONS DERIVED FROM MASS SPECTROMETRY						
Kubitz et al.[15]	R, SB, PC	7 healthy patients Weight 81.2 ± 11 kg BMI 24.9 ± 3 kg/m^2	20 mg × 1 dose	Mean 173 (range 111–294)	Not reported	Median age 33 years CrCl not reported Rivaroxaban administered on empty stomach Rivaroxaban peak plasma concentration measured 2 h after administration Rivaroxaban dose escalation study 1.25 mg to 80 mg (time between doses not defined) Concomitant medications not reported
Mueck et al.[16]	DB, OL	131 patients with total hip replacement Weight median 74 (range 45–120) kg BMI not reported	20 mg daily	Median 222.6 (range 159.6–359.8)	Median 22.3 (range 4.3–95.7)	Median age 65 years Median CrCl 81 mL/min Rivaroxaban administered with food Rivaroxaban plasma concentration measured after 5 days of therapy: peak at 2–3 h after dose and trough 0.5 h before next dose Concomitant medications not reported
Francart et al.[17]	Controlled	29 patients with VTE or atrial fibrillation Weight 91.7 ± 18 kg BMI 31.8 ± 7 kg/m^2	20 mg daily	Range 103–660	Range 8.9–92	Mean age 60 years Mean CrCl 106 mL/min Rivaroxaban administration with food not reported Duration of rivaroxaban therapy not reported Rivaroxaban peak plasma concentration measured 2.5 h after dose and trough concentration measured immediately before next dose Concomitant medications not reported
Mueck et al.[5,14]	R, DB	870 patients with DVT Weight for men 85 ± 17 kg Weight for women 73 ± 16 kg BMI not reported	20 mg daily	Mean 270 (range 189–419)	Mean 26 (range 6–87)	Mean age 61 years Mean CrCl 87 mL/min Rivaroxaban administration with food not reported Duration of rivaroxaban ≥ 21 days Rivaroxaban peak plasma concentration measured 2–4 h after dose and trough measured 20–28 h after dose Concomitant medications not reported
Martin and Moll[13]	RR, O	12 patients, indication not reported Weight 121.7 ± 34.7 kg BMI 39.4 ± 11.5 kg/m^2	20 mg daily	Mean 202 (range 123.7–459.8)	Mean 17.6 (range 0–37.8)‡	Rivaroxaban administration with food not reported Duration of rivaroxaban therapy not reported Concomitant medications not reported

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Table 1 (part 2 of 2). Study Design, Patient Population, and Plasma Rivaroxaban Concentrations Derived from Mass Spectrometry and Anti–Factor Xa Determination*

Reference	Study Design†	Characteristics of Study Sample (Indication, Body Weight, and BMI)	Drug Dose and Frequency	Rivaroxaban Concentration (ng/mL)		Additional Details
				Peak	Trough	
DRUG CONCENTRATIONS DERIVED FROM ANTI-Xa						
Lang et al.[10]	OL	Sample size and indication not reported (373 blood samples analyzed) Weight and BMI not reported	15 mg daily	196.6 ± 117	93.8 ± 70	No documentation of patient demographics CrCl not reported Rivaroxaban administration with food not reported Duration of rivaroxaban therapy not reported Rivaroxaban anti-Xa measured at < 3 h, 3–12 h, 12–19 h, and > 19 h after dose Concomitant medications not reported
			20 mg daily	213.8 ± 138	64.2 ± 64	
Ikeda and Tachibana[11]	P	36 patients with atrial fibrillation Weight 60.3 ± 11.7 kg BMI 23.6 ± 2.5 kg/m^2	10 mg or 15 mg daily	Mean 467.3 (range 99–821.3)	Mean 62.5 (range 0–290.3)	Mean age 74 years Mean CrCl 69 mL/min Mean $CHADS_2$ score 2.1 Rivaroxaban administration with food not reported Rivaroxaban anti-Xa measured after 7–911 days: peak 2–5 h after dose and trough 20–26 h after dose Concomitant medication classes reported
Testa et al.[12]	P, O	71 patients with atrial fibrillation (at 3 clinics) Weight 74 ± 16.5 kg BMI 25.4 ± 5.6 kg/m^2	15 mg daily	Clinic A: mean 190 (range 77–355) Clinic B: mean 229 (range 149–365) Clinic C: mean 205 (range 85–39)	Clinic A: mean 25 (range 17–49) Clinic B: mean 26 (range 19–34) Clinic C: mean 32 (range 0–88)	Mean age 74 years CrCl not reported Mean $CHADS_2$ score 2.4 Rivaroxaban administered with food Rivaroxaban anti-Xa measured after 15–25 days: peak 2 h after dose and trough 24 h after dose Concomitant medications not reported
			20 mg daily	Clinic A: mean 247 (range 61–449) Clinic B: mean 229 (range 65–370) Clinic C: mean 231 (range 138–341)	Clinic A: mean 39 (range 16–74) Clinic B: mean 41 (range 16–106) Clinic C: mean 43 (range 5–119)	
Jayakody Arachchillage et al.[18]	OL	167 patients with VTE Weight < 50 kg, 50–120 kg, or> 120 kg§ BMI not reported	20 mg daily	Weight < 50 kg: median 460 (95% CI 380–601) Weight 50–120 kg: median 308 (95% CI 308–381) Weight > 120 kg: median 281 (95% CI 242–327)¶	Not reported	Mean age 59 years CrCl > 30 mL/min Rivaroxaban administration with food not reported Duration of rivaroxaban therapy not reported Rivaroxaban peak anti-Xa measured 2–4 h after dose Concomitant medications not reported

AF = atrial fibrillation, CI = confidence interval, CrCl = creatinine clearance, DVT = deep vein thrombosis, NR = not reported, VTE = venous thromboembolism.
*All data are reported as mean ± standard deviation, except where indicated otherwise.
†Abbreviations used for aspects of study design: DB = double-blind, O = observational, OL = open label, P = prospective, PC = placebo-controlled, R = randomized, RR = retrospective review, SB = single-blind.
‡Five of the 12 patients had trough rivaroxaban determined by anti-Xa.
§For 18 patients, weight < 50 kg (mean 43 kg, range 38–49 kg); for 105 patients, weight 50–120 kg (mean 86 kg, range 50–120 kg); for 44 patients, weight > 120 kg (mean 135 kg, range 121–186 kg).
¶Patients weighing < 50 kg had significantly higher rivaroxaban concentrations than patients weighing 50–120 kg or > 120 kg ($p = 0.005$).

Table 2. Summary of Landmark Clinical Trials of Rivaroxaban According to BMI of Patients

Reference	Study Design*	Study Population	Distribution of Patients by BMI (kg/m²) and No. (%) of Patients				Treatment	Treatment Duration	Follow-Up	Outcome
Freidman et al.[24]	R, DB	12 355 patients with total hip or knee arthroplasty	BMI < 25 *n* = 3008 (24.3)	BMI 25–29 *n* = 4916 (39.8)	BMI 30–39 *n* = 3986 (32.3)	BMI ≥ 40 *n* = 445 (3.6)	Riv 10 mg PO daily or Enox 40 mg SC daily or Enox 30 mg SC bid	31–39 or 10–14 days	30–35 days	No significant differences in VTE or major bleeding in relation to BMI
Di Nisio et al.[25]	OL, R	8282 patients† with deep vein thrombosis or pulmonary embolism	BMI < 25 *n* = 2481 (30.0)	BMI ≥ 25 to < 30 *n* = 3258 (39.3)	BMI ≥ 30 to < 35 *n* = 1630 (19.7)	BMI ≥ 35 *n* = 861 (10.4)	Riv 15 mg bid × 21 days, then 20 mg daily or dose-adjusted Enox (according to body weight), followed by VKA, with target INR of 2–3	Median 182 days	30 days	No association between body weight or BMI and VTE or major bleeding
Patel et al.[26]	R, DB	14 264 patients‡ with atrial fibrillation	BMI ≤ 25 *n* = 3445 (24.2)	BMI 25 to ≤ 35 *n* = 8826 (61.9)		BMI > 35 *n* = 1891 (13.3)	Riv 20 mg daily (15 mg daily if CrCl 30–49 mL/min) or dose-adjusted warfarin, with target INR of 2–3	Median 590 days	Median 707 days	No association between body weight or BMI and risk of stroke or systemic embolism or bleeding events

BMI = body mass index, Enox = enoxaparin, INR = international normalized ratio, NS = nonsignificant, Riv = rivaroxaban, VKA = vitamin K antagonist, VTE = venous thromboembolism.
*Abbreviations used for aspects of study design: DB = double-blind, OL = open label, R = randomized.
†BMI was missing for 52 patients (0.6% of the sample): 1 patient did not provide informed consent, 10 patients did not report body weight, and 41 patients did not report height.
‡BMI data were taken from Figure 3 in the ROCKET AF supplementary appendix, which did not account for all patients.

was no change to rivaroxaban therapy in the 15 patients. Overall, the trough concentrations were 5-fold lower and peak concentrations 2-fold lower than in the patient described in our case report.

Patients with obesity have been underrepresented in landmark rivaroxaban clinical trials (Table 2).[24-26] There were no significant differences in VTE or major bleeding in relation to BMI, but these trials were not powered to consider efficacy and safety outcomes between patients with and without obesity. Of these trials, ROCKET AF[26] was the one most similar to our case. The median BMI in ROCKET AF was 28.2 kg/m^2 (interquartile range 25.2–32 kg/m^2), whereas the patient in our case had BMI 73 kg/m^2. A subgroup analysis in ROCKET AF showed no significant difference (p = 0.537) in stroke or systemic embolism among patients with BMI above 35 kg/m^2 relative to patients with lower BMI.[26]

A post hoc analysis of the ROCKET AF trial by Balla and others[27] compared the incidence of stroke and systemic embolism in normal-weight patients (BMI 18.5–24.99 kg/m^2), overweight patients (BMI 25.00–29.99 kg/m^2), and obese patients (BMI ≥ 30 kg/m^2). Over 2 years, the rate of stroke and systemic embolism per 100 patient-years was 3.05 in normal-weight patients (n = 3289), 2.34 in overweight patients (n = 5535; hazard ratio [HR] 0.77, 95% confidence interval [CI] 0.62–0.95, p = 0.013), and 1.90 in obese patients (n = 5206; HR 0.62, 95% CI 0.50–0.78, p < 0.001).[27] Overweight and obese patients had significantly lower risk of stroke than normal-weight patients, even after adjustment for hypertension, diabetes, congestive heart failure, prior stroke or transient ischemic attack, age, sex, and serum creatinine (overweight patients, HR 0.79, 95% CI 0.64–0.98, p = 0.029; obese patients, HR 0.66, 95% CI 0.53–0.84, p < 0.001).[27] There is no clear explanation for this observation; it is possible that patients with higher body weight might receive optimal cardiac medications more often than those without high body weight, resulting in a lower risk of thromboembolic and cardiovascular outcomes.[28]

CONCLUSION

There is very little evidence to guide clinicians on the use of rivaroxaban in patients with class III obesity. To the authors' knowledge, this is the first published case reporting use of rivaroxaban in a patient with BMI over 70 kg/m^2. In this case, the peak and trough rivaroxaban concentrations were at the higher end of the ranges reported in the literature. The patient remained on rivaroxaban 20 mg daily for about 4 years with no clinical evidence of stroke or systemic embolism. In the previous literature, use of rivaroxaban in obese patients with hip or knee arthroplasty, VTE, and atrial fibrillation did not suggest decreased efficacy or increased bleeding. However, these conclusions were based on subgroup analyses; the trials were not powered to compare outcomes in patients with and without obesity. Current ISTH guidelines suggest that DOACs not be used in patients with BMI above 40 kg/m^2 or weight greater than 120 kg; however, if rivaroxaban, apixaban, or edoxaban *are* used, measurement of peak and trough anti-Xa levels or determining drug concentration by mass spectrometry may be considered. If the levels are within the average ranges reported in the literature, therapy may be continued. Randomized controlled trials evaluating the efficacy and safety of rivaroxaban use in obese patients are needed.

References

1. Twells LK, Gregory DM, Reddigan J, Midodzi WK. Current and predicted prevalence of obesity in Canada: a trend analysis. *CMAJ Open.* 2014; 2(1):E18-26.
2. Lentz SR. Thrombosis in the setting of obesity or inflammatory bowel disease. *Blood*. 2016;128(20):2388-94.
3. Xarelto [product monograph]. Mississauga (ON): Bayer Inc; 2015 Jul 20.
4. Martin K, Beyer-Westendorf J, Davidson BL, Huisman MV, Sanset PM, Moll S. Use of direct oral anticoagulants in obese patients: guidance from the SSC of the ISTH. *J Thromb Haemost*. 2016;14(6):1308-13.
5. Mueck W, Stampfuss J, Kubitza D, Becka M. Clinical pharmacokinetic and pharmacodynamics profile of rivaroxaban. *Clin Pharmaokinet*. 2014; 53(1):1-16.
6. Kubitza D, Becka M, Zuehlsdorf M, Mueck W. Body weight has limited influence on the safety, tolerability, pharmacokinetics, or pharmacodynamics of rivaroxaban (BAY 59-7939) in healthy subjects. *J Clin Pharmacol.* 2007; 47(2):218-26.
7. Cohen AT, Spiro TE, Büller HR, Haskell L, Hu D, Hull R, et al. Rivaroxaban for thromboprophylaxis in acutely ill medical patients. *N Engl J Med.* 2013; 368(6):513-23.
8. Eikelboom JW, Quinlan DJ, Hirsh J, Connolly SJ, Weitz JI. Laboratory monitoring of non-vitamin K antagonist oral anticoagulant use in patients with atrial fibrillation: a review. *JAMA Cardiol.* 2017;2(5):566-74.
9. Conway SE, Hwang AY, Ponte CD, Gums JG. Laboratory and clinical monitoring of direct oral anticoagulants: what clinicians need to know. *Pharmacotherapy*. 2017;37(2):236-48.
10. Lang K, Patel J, Chitongo P, Czuprynska J, Roberts L, Patel R, et al. Real-world rivaroxaban levels from King's College Hospital [abstract]. *J Thromb Haemost.* 2015;13 Suppl 2:117-8.
11. Ikeda K, Tachibana H. Clinical implication of monitoring rivaroxaban and apixaban by using anti-factor Xa assay in patients with non-valvular atrial fibrillation. *J Arrhythm.* 2016;32(1):42-50.
12. Testa S, Tripodi A, Legnani C, Pengo V, Abbate R, Dellanoce C, et al. Plasma levels of direct oral anticoagulants in real life patients with atrial fibrillation: results observed in four anticoagulation clinics. *Thromb Res*. 2016;137: 178-83.
13. Martin K, Moll S. Direct oral anticoagulant drug level testing in clinical practice: a single institution experience. *Thromb Res*. 2016;143:40-4.
14. Mueck W, Lensing AWA, Agnelli G, Décousus H, Prandomi P, Misselwitz F. Rivaroxaban: population pharmacokinetic analysis in patients treated for acute deep-vein thrombosis and exposure simulations inpatients with atrial fibrillation treated for stroke prevention. *Clin Pharmacokinet.* 2011;50(10): 675-86.
15. Kubitz D, Becka M, Voith B, Zuehlsdorf M, Wensing G. Safety, pharmacodynamics, and pharmacokinetics of single doses of BAY 59-7939, an oral, direct factor Xa inhibitor. *Clin Pharmacol Ther*. 2005;78(4):412-21.
16. Mueck W, Borris LC, Dahl OE, Haas S, Huisman MV, Kakkar AK, et al. Population pharmacokinetics and pharmacodynamics of once and twice-daily rivaroxaban for the prevention of venous thromboembolism in patients undergoing total hip replacement. *Thromb Haemost.* 2008;100(3):453-61.
17. Francart SJ, Hawes EM, Deal AM, Adcock DM, Gosselin R, Jeanneret C, et al. Performance of coagulation tests in patients on therapeutic dose of rivaroxaban. *Thromb Haemost*. 2014;111(6):1133-40.

18. Jayakody Arachchillage D, Reynolds R, Devey T, Maclean R, Kitchen S, Van Veen J. Effect of extremes of body weight on efficacy and safety of rivaroxaban in the treatment of venous thromboembolism: real life experience [abstract]. *J Thromb Haemost.* 2016;14 Suppl 1:8.
19. Mahlmann A, Gehrisch S, Beyer-Westendorf J. Pharmacokinetics of rivaroxaban after bariatric surgery: a case report. *J Thromb Thrombolysis.* 2013; 36(4):533-5.
20. Thomas Z, Bareket Y, Bennett W. Rivaroxaban use following bariatric surgery [letter]. *J Thromb Thrombolysis.* 2014;38(1):90-1.
21. Bland CM, Quidley AM, Love BL, Yeager C, McMichael B, Bookstaver PB. Long-term pharmacotherapy considerations in the bariatric surgery patient. *Am J Health Syst Pharm*. 2016;73(16):1230-42.
22. Hakeam HA, Al-Sanea N. Effect of major gastrointestinal tract surgery on the absorption and efficacy of direct oral acting anticoagulants (DOACs). *J Thromb Thrombolysis*. 2017;43(3):343-51.
23. Safouris A, Demulder A, Triantafyllou N, Tsivgoulis G. Rivaroxaban presents a better pharmacokinetic profile than dabigatran in an obese non-diabetic stroke patient [letter]. *J Neurol Sci.* 2014;346(1-2):366-7.
24. Freidman RJ, Hess S, Berkowitz SD, Homering M. Complication rates after hip or knee arthroplasty in morbidly obese patients. *Clin Orthop Relat Res.* 2013;471(10):3358-66.
25. Di Nisio M, Vedovati MC, Riera-Mestre A, Prins MH, Mueller K, Cohen AT, et al. Treatment of venous thromboembolism with rivaroxaban in relation to body weight: a sub-analysis of the EINSTEIN DVT/PE studies. *Thromb Haemost*. 2016;116(4):739-46.
26. Patel MR, Mahaffey KW, Garg J, Pan G, Singer DE, Hacke W, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med.* 2011;365(10):883-91.
27. Balla SR, Cyr D, Lokhnygina Y, Becker R, Berkowitz S, Breithardt G, et al. Obesity paradox for stroke in patients with atrial fibrillation treated with rivaroxaban and warfarin in the ROCKET AF trial [abstract]. *J Am Coll Cardiol.* 2014;63(12):A371.
28. Boonyawat K, Caron F, Li A, Chai-Adisaksopha C, Lim W, Iorio A, et al. Association of body weight with efficacy and safety outcomes in phase III randomized controlled trials of direct oral anticoagulants: a systematic review and meta-analysis. *J Thromb Haemost*. 2017;15(7):1322-33.

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Do the Benefits of Electronic Cigarettes Outweigh the Risks?

THE "PRO" SIDE

Smoking is a dangerous lifestyle choice that results in increased risk of premature death or serious morbidities, such as cancer and coronary heart disease for the smoker and adverse health outcomes for the unborn children of pregnant women who smoke.[1] Passive smoking also has serious health implications for both children and adults. The corollary of this situation is that smoking cessation is one of the most important, effective, and efficient health care interventions that can be undertaken. Within a year of quitting smoking, a former smoker's chance of developing heart disease drops to half that of a continuing smoker.[2] Between 5 and 15 years after quitting, the chance of lung cancer decreases by almost half, and the risk of dying from cancer becomes similar to that of a nonsmoker.[3] However, smoking is a particularly addictive behaviour, and stopping is not easy. While it is possible to stop smoking with just a behavioural intervention, the introduction of complementary pharmacological treatments, such as nicotine replacement therapy and varenicline, has increased rates of smoking cessation. The pharmacy profession has played its part by providing behavioural support and supplying therapies. Societal recognition of the dangers of smoking and support for a smoke-free environment have also contributed to the overall reduction of smoking prevalence in the Western world. For example, in Canada the prevalence of smoking has declined from about 26% in 2001 to 20% in 2011[4] and to 13% in 2015.[5]

Despite these developments, quitting is still not possible for many current smokers, and alternative approaches are required. The introduction of e-cigarettes is one such alternative approach. The e-cigarette was first developed by a pharmacist in China in the early 2000s. It is a device that produces a nicotine aerosol by using a battery to heat a solution (typically based on propylene glycol or glycerol) of nicotine and flavouring agents. The device is cylindrical and has a mouthpiece for inhaling the vapour. In contrast to other forms of nicotine replacement, e-cigarettes allow the user to mimic the hand-to-mouth ritual of smoking a cigarette but deliver the vapourized nicotine to the lungs without the toxic by-products that accompany the smoking of tobacco. Thus, they intuitively feel more natural and acceptable to the habituated smoker.

A recent Cochrane review of the evidence for the effectiveness of e-cigarettes[6] has suggested that e-cigarettes may increase the chance of a long-term quit. The review included 24 completed studies: 21 cohort studies; 2 RCTs comparing e-cigarettes with placebo e-cigarettes (i.e., without nicotine), with a combined sample of 662 participants, in which the 6-month quit rates were 9% with e-cigarettes and 5% with the placebo device; and a third RCT, which compared e-cigarettes with a nicotine patch and found no difference in quit rates at 6 months. None of the included studies reported serious adverse effects from e-cigarettes, although it was acknowledged that the quality of the evidence was weak because of the small number of trials, the low event rates, and the wide confidence intervals around the estimates; furthermore, there is limited evidence of the long-term safety of e-cigarettes for either the user or those exposed passively to the vapours.[7] Concerns have been expressed repeatedly that e-cigarettes represent a gateway to smoking cigarettes for young people, that they have toxic effects, and that they produce carcinogens. It is unclear the extent to which e-cigarettes are being used as aids to smoking cessation, for smoking reduction, or just as a new nicotine-related habit. It is generally acknowledged that all of this deserves thorough exploration.

Internationally, there is great variation in the extent to which countries support or restrict the use of e-cigarettes. A survey of different countries' regulatory approaches reported that 26 countries have banned all use of e-cigarettes and 21 have imposed restrictions on their sale.[8] In Canada, e-cigarettes containing nicotine cannot be legally manufactured, sold, or imported, yet despite these prohibitions, the devices are available online and in some retail outlets. In the United States, an increasing number of states are banning indoor use of e-cigarettes.[9] Among countries of the Western world, England has adopted a more liberal approach to e-cigarettes, prioritizing the importance of helping people to quit smoking over any safety concerns. Public Health England has claimed that e-cigarettes are 95% safer than smoked tobacco and has expressed concern that increasing numbers of people think e-cigarettes are more harmful than smoking.[10] In a recent commissioned report, the same agency presented data confirming that the vast majority of e-cigarette users are current or ex-smokers and that the number of people using e-cigarettes who have never smoked is very small.[11] The report also suggested that nicotine release into the environment is negligible and that there is no indication that e-cigarette users are exposed to dangerous levels of toxic chemicals, such as aldehydes. A recently published cross-sectional survey involving 5863 adults who smoked concluded

that continued abstinence was more likely for those using e-cigarettes than for those who bought over-the-counter nicotine replacement therapy.[12] In a later analysis, the same authors estimated that in 2015 e-cigarettes helped about 18 000 people to give up smoking in England, and suggested that these data justify use of these devices.[13] There are also indications that the UK National Institute for Health and Care Excellence will soon endorse use of e-cigarettes as a smoking cessation aid.

No medicine is completely safe, and the decision on whether or not to use a medicine must balance the risks and the benefits. Although e-cigarettes are not classified as a medicine, similar principles should arguably be adopted when deciding on whether to support their use. This is the basis upon which Public Health England strongly supports the use of e-cigarettes, justifying this stance by highlighting the known negative health implications of smoked tobacco relative to the lesser risks of e-cigarettes. At present, e-cigarettes are largely unregulated, and there is little quality control over different components of e-cigarettes (the solvent, the additives such as flavour enhancers, or even the concentration of active ingredient). This lack of quality control is a valid cause for concern that needs to be addressed if e-cigarettes are to become an established part of the health care professional's armamentarium. However, recent European guidance, effective from 2017, has introduced rules to ensure minimum safety standards for the safety and quality of e-cigarettes,[14] thus removing some of the potential for harm. Guidance on the product information leaflet and restrictions on advertising are also included in the European document. Supporting the wider adoption of such standards and recommending only licensed products for smoking cessation should allow patients to experience the benefits of e-cigarettes while minimizing the risks.

In summary, a quality-controlled e-cigarette, used as part of a structured smoking cessation program, could provide an effective additional option for smokers for whom other approaches have failed.

References

1. Schane RE, Ling PM, Glantz SA. Health effects of light and intermittent smoking: a review. *Circulation*. 2010;121(13):1512-22.
2. Ghadirian P. *Sleeping with a killer: the effect of smoking on human health.* Ottawa (ON): Health Canada; 2004.
3. *The health benefits of smoking cessation: a report of the Surgeon General.* Rockville (MD): US Department of Health and Human Services; 1990.
4. Janz T. *Health at a glance. Current smoking trends*. Ottawa (ON): Statistics Canada; 2015 [cited 2017 Nov 29]. Catalogue no. 82-624-X. Available from: https://www.statcan.gc.ca/pub/82-624-x/2012001/article/11676-eng.htm
5. Reid JL, Hammond D, Rynard VL, Madill CL, Burkhalter R. *Tobacco use in Canada: adult tobacco use.* Waterloo (ON): University of Waterloo, Propel Centre for Population Health Impact; 2017 [cited 2017 Nov 29]. Available from: https://uwaterloo.ca/tobacco-use-canada/adult-tobacco-use
6. Hartmann-Boyce J, McRobbie H, Bullen C, Begh R, Stead LF, Hajek P. Electronic cigarettes for smoking cessation. *Cochrane Database Syst Rev.* 2016;9:CD010216.
7. Jensen RP, Luo W, Pankow JF, Strongin RM, Peyton DH. Hidden formaldehyde in e-cigarette aerosols [letter]. *N Engl J Med.* 2015;372(4):392-4.
8. Country laws regulating e-cigarettes: a policy scan. Baltimore (MD): Johns Hopkins Bloomberg School of Public Health, Institute for Global Tobacco Control; 2017 [cited 2017 Nov 29]. Available from: http://globaltobaccocontrol.org/e-cigarette/country-laws-regulating-e-cigarettes
9. Glenza J. E-cigarette bans highlight public health divide between US and UK researchers. *The Guardian*. 2017 Oct 24 [cited 2017 Nov 30]. Available from: https://www.theguardian.com/society/2017/oct/24/e-cigarette-bans-highlight-public-health-divide-between-us-and-uk-researchers
10. McNeill A, Hajek P. Underpinning evidence for the estimate that e-cigarette use is around 95% safer than smoking: authors' note. London (UK): Public Health England; 2015 [cited 2017 Nov 29]. Available from: https://www.gov.uk/government/publications/e-cigarettes-an-evidence-update
11. McNeill A, Brose LS, Calder R, Hitchman SC, Hajek P, McRobbie H. *E-cigarettes: an evidence update. A report commissioned by Public Health England.* London (UK): Public Health England; 2015 [cited 2017 Nov 29]. Available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/457102/Ecigarettes_an_evidence_update_A_report_commissioned_by_Public_Health_England_FINAL.pdf
12. Brown J, Beard E, Kotz D, Michie S, West R. Real-world effectiveness of e-cigarettes when used to aid smoking cessation: a cross-sectional population study. *Addiction*. 2014;109(9):1531-40.
13. Beard E, West R, Michie S, Brown J. Association between electronic cigarette use and changes in quit attempts, success of quit attempts, use of smoking cessation pharmacotherapy, and use of stop smoking services in England: time series analysis of population trends. *BMJ.* 2016;354:i4645.
14. Directive 2014/40/EU of the European Parliament and of the Council of 3 April 2014 on the approximation of the laws, regulations and administrative provisions of the Member States concerning the manufacture, presentation and sale of tobacco and related products and repealing Directive 2001/37/EC. *Off J Eur Union.* 2014 [cited 2017 Nov 29];57(L127):1-38. Available from: https://ec.europa.eu/health//sites/health/files/tobacco/docs/dir_201440_en.pdf.

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THE "CON" SIDE

The 21st century has given rise to a novel method of commercializing public nicotine dependence, in the form of electronic nicotine delivery systems (ENDS), such as electronic cigarettes (e-cigarettes). Smoking combustible tobacco is now passé, and "vaping", as it is termed, has become the latest popular trend among the fashionable, including A-listers such as Leonardo DiCaprio and Katy Perry. If history has taught us anything, it is not to rely on celebrities for sound health advice. The vapour trail is nothing more than a smokescreen.

E-cigarettes use a battery to heat a solution that is vapourized and inhaled.[1] This "e-liquid" typically comprises propylene glycol (i.e., antifreeze) and/or glycerol, nicotine, and flavours (e.g., tobacco, menthol, fruit, candy).[2] To be blunt, using an e-cigarette is not unlike inhaling vapourized, berry-flavoured aircraft de-icing fluid. As of this

writing (in late 2017), Health Canada does not permit or regulate the sale of ENDS. In other words, none of the currently available forms of nicotine-containing e-cigarettes are legal in Canada, and this lack of oversight means that an e-liquid could contain pretty much anything. Furthermore, e-liquids are available in various strengths of nicotine, ranging from 6 to 36 mg/mL,[3] which could result in toxic effects if the specified concentration is misinterpreted or the amount is incorrectly measured. Additionally, some bottles of flavoured e-liquid are adorned with brightly coloured pictures of fruit, which means they could be mistaken for juice or candy. Accidental ingestion of e-liquid by children is particularly concerning—a nicotine dose of about 1 mg/kg could be lethal, and this amount could be delivered in a few drops of a concentrated solution.[4]

No data are available regarding the long-term safety of ENDS, but there is rapidly evolving evidence that links vaping with pulmonary toxicity.[5] Use of an ENDS has been associated with respiratory symptoms (e.g., wheezing, coughing), increased airway hypersensitivity, increased airway resistance, decreased host immunity, and increased alveolar cytotoxicity.[5,6] Furthermore, ENDS may produce a variety of carcinogenic compounds, such as formaldehyde, acetaldehyde, and acrolein.[7,8] Exposure to diacetyl, a common e-cigarette flavouring with a buttery or creamy taste, has been associated with acute-onset bronchiolitis obliterans or "popcorn lung", a severe and irreversible obstructive pulmonary condition.[9] A new study estimated that a frequent user of an e-cigarette (defined by the authors as ≥ 250 puffs/day) would be exposed to levels of formaldehyde, acrolein, and diacetyl that exceed occupational limits in the United States.[7] As well, ENDS may produce heavy metals, such as chromium, lead, and nickel.[10] Nicotine itself is not without risk: a retrospective cohort study conducted in Sweden showed that individuals who continued to use smokeless tobacco after myocardial infarction, as opposed to those who quit smoking, had an approximately 2-fold higher mortality rate over 2 years.[11] Finally, the safety of exposure to the ostentatious plume of vapour created by an e-cigarette user ("second-hand vape") is completely unknown.

Other hazards are becoming known. Traditional cigarettes may burn your fingers, but ENDS may explode. This rare but serious occurrence, caused by overheating of the battery, should give pause to even the most fervent e-cigarette advocate. A series of images of ENDS explosion injuries was recently published; these included flame and chemical burns, tooth loss, and extensive soft-tissue damage.[12] Dramatic visuals can be useful prompts; for example, images of diseased lungs on cigarette packages may motivate some individuals to quit smoking. Perhaps ENDS packages should feature pictures of explosion injuries.

I concede that, at present, ENDS appear to be safer than traditional cigarettes, and they may have a role in harm reduction.[2] However, cessation of both smoking and vaping is preferred. Evidence for using e-cigarettes for smoking cessation, though promising, is not sufficiently robust to recommend them for this indication,[13] a position that is supported by a policy statement from the American Heart Association.[3]

The ENDS industry has employed aggressive marketing to normalize vaping and subvert the social stigma associated with smoking.[14] Such marketing is particularly concerning when directed toward adolescents, especially those who would not have otherwise tried smoking but who may start using e-cigarettes as a result. A report from the US Centers for Disease Control and Prevention (CDC) estimated that approximately 70% of middle and high school students were exposed to ENDS advertisements in 2014.[15] E-cigarettes are perceived as safer than traditional cigarettes (particularly among youth) and are portrayed as more socially acceptable in popular culture. Advertisements depict e-cigarettes as sexy, rebellious, independent, and trendy—I would even venture to say that if the film *Rebel Without a Cause* were remade today, the poster would feature James Dean's character with an e-cigarette. ENDS may also be more accessible for young people and easier to hide from authority figures.

To be pragmatic, e-liquid flavouring is an unequivocally blatant strategy to target youth. Candy flavours, such as cotton candy, gummy bears, Skittles, and Froot Loops (all of which exist), are created largely to appeal to young people.[16] A survey of US adolescents aged 13–17 years found that they were more likely to try an e-cigarette offered by a friend if it were fruit-flavoured than if it were tobacco-flavoured.[17] As well, respondents believed that fruit-flavoured e-cigarettes were less harmful than those flavoured like tobacco, and about one-fifth stated that they believed e-cigarettes did not contain nicotine or they were uncertain about nicotine content. A CDC report using data from the 2016 National Youth Tobacco Survey showed that e-cigarettes were the most commonly used tobacco product among teenaged students—4.3% and 11.3% of middle and high school students, respectively, had used an e-cigarette within the past 30 days.[18] There is also evidence that ENDS may be a gateway to smoking traditional cigarettes.[19,20] A recent meta-analysis demonstrated that ever e-cigarette users had 3.6-fold greater adjusted odds of becoming a smoker relative to never-users.[20]

E-cigarettes may prove useful as a harm reduction strategy, but they are far from safe, and at this point the overall potential benefits do not outweigh the risks. This conclusion is affirmed by emerging evidence of ENDS-associated pulmonary toxicity and exposure to carcinogens, and the lack of long-term data. Oh, and they may explode. Meanwhile, industry is unabashedly recruiting a whole new generation of nicotine-addicted youth with little to no regulatory oversight. They say hindsight is 20/20, which is of particular relevance in medicine. Seventy years ago, tobacco cigarettes were not only considered safe, but were also purported to have positive health effects, and we all know how that turned out.

References

1. Dinakar C, O'Connor GT. The health effects of electronic cigarettes. *N Engl J Med.* 2016;375(14):1372-81.
2. Hajek P, Etter JF, Benowitz N, Eissenberg T, McRobbie H. Electronic cigarettes: review of use, content, safety, effects on smokers and potential for harm and benefit. *Addiction*. 2014;109(11):1801-10.
3. Bhatnagar A, Whitsel LP, Ribisl KM, Bullen C, Chaloupka F, Piano MR, et al. Electronic cigarettes: a policy statement from the American Heart Association. *Circulation*. 2014;130(16):1418-36.

4. Gupta S, Gandhi A, Manikonda R. Accidental nicotine liquid ingestion: emerging paediatric problem. *Arch Dis Child.* 2014;99(12):1149.
5. Chun LF, Moazed F, Calfee CS, Matthay MA, Gotts JE. Pulmonary toxicity of e-cigarettes. *Am J Physiol Lung Cell Mol Physiol.* 2017;313(2):L193-L206.
6. Wang MP, Ho SY, Leung LT, Lam TH. Electronic cigarette use and respiratory symptoms in Chinese adolescents in Hong Kong. *JAMA Pediatr.* 2016;170(1):89-91.
7. Logue JM, Sleiman M, Montesinos VN, Russell ML, Litter MI, Benowitz NL, et al. Emissions from electronic cigarettes: assessing vapers' intake of toxic compounds, secondhand exposures, and the associated health impacts. *Environ Sci Technol.* 2017;51(16):9271-9.
8. Jensen RP, Luo W, Pankow JF, Strongin RM, Peyton DH. Hidden formaldehyde in e-cigarette aerosols [letter]. *N Engl J Med.* 2015;372(4):392-4.
9. Barrington-Trimis JL, Samet JM, McConnell R. Flavorings in electronic cigarettes: an unrecognized respiratory health hazard? *JAMA.* 2014;312(23): 2493-4.
10. Hess CA, Olmedo P, Navas-Acien A, Goessler W, Cohen JE, Rule AM. E-cigarettes as a source of toxic and potentially carcinogenic metals. *Environ Res*. 2017;152:221-5.
11. Arefalk G, Hambraeus K, Lind L, Michaëlsson K, Lindahl B, Sundström J. Discontinuation of smokeless tobacco and mortality risk after myocardial infarction. *Circulation*. 2014;130(4):325-32.
12. Brownson EG, Thompson CM, Goldsberry S, Chong HJ, Friedrich JB, Pham TN, et al. Explosion injuries from e-cigarettes [letter]. *N Engl J Med.* 2016;375(14):1400-2.
13. Hartmann-Boyce J, McRobbie H, Bullen C, Begh R, Stead LF, Hajek P. Electronic cigarettes for smoking cessation. *Cochrane Database Syst Rev.* 2016;9:CD010216.
14. Gostin LO, Glasner AY. E-cigarettes, vaping, and youth. *JAMA.* 2014; 312(6):595-6.
15. E-cigarettes ads and youth. Atlanta (GA): Centers for Disease Control and Prevention; 2017 Mar [cited 30 Nov 2017]. Available from: https://www.cdc.gov/vitalsigns/ecigarette-ads/index.html
16. Nine e-juice flavors that sound just like kids' favorite treats. Washington (DC): Campaign for Tobacco-Free Kids; 2014 Jun 11 [cited 30 Nov 2017]. Available from: https://www.tobaccofreekids.org/blog/2014_06_11_ecigarettes
17. Pepper JK, Ribisl KM, Brewer NT. Adolescents' interest in trying flavoured e-cigarettes. *Tob Control.* 2016;25(Suppl 2):ii62-ii66.
18. Jamal A, Gentzke A, Hu SS, Cullen KA, Apelberg BJ, Homa DM, et al. Tobacco use among middle and high school students – United States, 2011-2016. *MMWR Morb Mortal Wkly Rep*. 2017;66(23):597-603.
19. Leventhal AM, Strong DR, Kirkpatrick MG, Unger JB, Sussman S, Riggs NR, et al. Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. *JAMA.* 2015;314(7):700-7.
20. Soneji S, Barrington-Trimis JL, Wills TA, Leventhal AM, Unger JB, Gibson LA, et al. Association between initial use of e-cigarettes and subsequent cigarette smoking among adolescents and young adults: a systematic review and meta-analysis. *JAMA Pediatr.* 2017;171(8):788-97.

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Path to the Canadian Antidote Registry

Antidotes play an essential role in the treatment of many poisonings and must be readily available for timely administration. Although there is expert consensus concerning guidelines on stocking of antidotes (e.g., Dart and others[1]), studies have consistently shown insufficient inventory of antidotes in Canadian emergency care hospitals.[2-5] This letter describes some of the initiatives that have emerged across Canada to ensure adequate stocking of antidotes, which have ultimately led to development of the Canadian Antidote Registry.

For many decades, the British Columbia Drug and Poison Information Centre (DPIC) operated a clinical antidote program for digoxin immune Fab (starting in 1986) and fomepizole (starting in 2002).[6,7] Upon consultation, the DPIC would provide free antidote replacement to the treating hospital. This approach ensured that patients received the antidotes after consultation with a toxicology expert, which minimized costs and allowed DPIC to collect province-wide usage data. The program was discontinued in April 2017. Now, BC hospitals must purchase their own stock of antidotes, which makes it easier for each hospital to control its inventory.

Between 2002 and 2004, the West Parry Sound Health Centre began to operate the Massasauga Rattlesnake Antivenom Depot (https://www.wpshc.com/index.php/ontario-antivenom-depot-117), which now manages antivenom supplies for depot sites across Ontario (about 150–200 vials total). An advisory group meets twice a year, and protocols are reviewed by the depot's medical director. The antivenom depot rotates stock across provincial depot sites to avoid expiration of unused vials and to reimburse hospitals that ask for clinical consultations. In the Toronto region, hospital pharmacy directors have, since 2004, signed an annual agreement for the Toronto and Area Hospital Pharmacy Departments Antidote Sharing Strategy. This strategy includes procedures and policies for sharing and borrowing antidotes. Following the death by poisoning of a 25-year-old man,[8] the Patient Safety Review Committee of the Office of the Chief Coroner recommended in 2013 that "[h]ospitals should review the antidotes they stock on a regular basis, and at least annually. If a given antidote is not stocked by a hospital, a plan should be in place and readily available to staff in order to ensure that this antidote can be obtained rapidly from another institution or source, on a 24/7 basis."[9]

In May 2005, the IWK Regional Poison Centre introduced the Nova Scotia Provincial Antidote Kit Program, through which hospital administrators manage antidote purchases. All tertiary care centres and regional hospital emergency departments stock full kits, whereas community hospitals may stock full or modified kits. Because the province has a small number of hospitals (n = 37), this initiative appears to be viable and provides usage data. In 2016, overall hospital compliance was 89%.[10]

In 2012, the Institut national de santé publique du Québec (the Quebec National Institute of Public Health) created the Quebec Antidote Registry to assist health care professionals.[5] This registry is now hosted by the Portail Toxicologie Clinique (Clinical Toxicology Portal; https://www.inspq.qc.ca/toxicologie-clinique/registre-provincial-des-antidotes). It includes all available formulations of antidotes, as selected by a group of experts, and hospital participation is voluntary. An analysis of data from this registry was undertaken recently as part of the background to the Canadian Antidote Registry. The analysis showed that from 2012 to 2016, an average of 85% (93/109) of hospitals providing emergency care services in the province participated in the registry. Over the same period, for many antidotes the percentage of hospitals stocking the first dose or the minimum recommended amount increased (Table 1), although a few antidotes remain unavailable. This small study is the first to report a substantial increase in hospitals' adherence to the recommendations of the Centre antipoison du Québec (Quebec Poison Centre) for antidote stockpiling in the province.

In March 2012, the New Brunswick Drugs and Therapeutics Committee adopted its Antidote Policy.[11] All 19 NB hospitals with an emergency department must stock and maintain a quota of antidotes, with 8 of these hospitals being defined as depot sites. The provincial Antidote Committee reviews the antidote list and associated drug monographs every 12–18 months.

In 2014, Alberta Health Services Pharmacy Services developed the Alberta Antidote Stocking Recommendations, which are reviewed every 1–2 years. Unlike typical poison centre recommendations, these have been approved by the Provincial Drugs and Therapeutics Committee, which makes them mandatory for all hospitals in the province. However, no data are available on hospitals' compliance with the recommendations.

According to the successful model already in place in Quebec, a preliminary version of the Canadian Antidote Registry was developed, following recommendations made by the experts

Table 1. Stocking of Minimum Recommended Amount of First Dose of Selected Antidotes by Quebec Hospitals Providing Emergency Services (2016 versus 2012)

Antidote	No. (%) of Hospitals Stocking Minimum Recommended Amount*			No. (%) of Hospitals Stocking a First Dose		
	2012 (*n* = 78)	2016 (*n* = 100)	Increase†	2012 (*n* = 78)	2016 (*n* = 100)	Increase†
Fomepizole	23 (29)	58 (58)	+29	30 (38)	92 (92)	+54
Digoxin immune Fab	29 (37)	62 (62)	+25	67 (86)	93 (93)	+7
Hydroxocobalamin	25 (32)	60 (60)	+28	54 (69)	89 (89)	+20
Pralidoxime	19 (24)	42 (42)	+18	44 (56)	69 (69)	+13
Pyridoxine	24 (31)	58 (58)	+27	68 (87)	91 (91)	+4
Black widow antivenom	0 (0)	0 (0)	NA	0 (0)	0 (0)	NA
Rattlesnake antivenom	0 (0)	0 (0)	NA	0 (0)	0 (0)	NA
Prussian blue	0 (0)	0 (0)	NA	0 (0)	0 (0)	NA

NA = not applicable.
*Amount necessary to treat a 70 kg patient for 24 h.
†Increases are presented in percentage points (obtained by subtraction).

involved in the programs and initiatives described above. The application will be hosted on the Canadian Network for Public Health Intelligence platform (https://www.cnphi-rcrsp.ca/cnphi/index.jsp) and will include a Web-based formulary to more effectively collect the data. Eventually, hospitals will be asked to report their inventories of antidotes to the national registry, at least twice a year and following any changes in their quotas. In the coming months, one Provincial Antidote Registry (PAR) Coordinator will be appointed by each province or territory. Also, within each jurisdiction, a Local Antidote Registry (LAR) Coordinator will be appointed for each hospital or health establishment that stocks antidotes. The experts working on the national registry have agreed that all PAR and LAR Coordinators should be hospital pharmacists.

A pilot project will be conducted by March 31, 2018, in selected hospitals. Depending on the adjustments that need to be carried out, the Canadian Antidote Registry should be operational by fall 2018. Meanwhile, the "Canadian Antidote Guide in Acute Care Toxicology" should be available online and on mobile apps by summer 2018. This guide will complement the registry and will help health care professionals in managing proper antidote administration to their patients. It can be concluded that the expertise of hospital pharmacists will be required in the coming months and years to improve the quality of care provided to patients who experience poisoning.

References

1. Dart RC, Goldfrank LR, Erstad BL, Huang DT, Todd KH, Weitz J, et al. Expert consensus guidelines for stocking of antidotes in hospitals that provide emergency care. *Ann Emerg Med*. 2017. Available from: http://dx.doi.org/10.1016/j.annemergmed.2017.05.021 [Epub ahead of print].
2. Bailey B, Bussières JF. Antidote availability in Quebec hospital pharmacies: impact of *N*-acetylcysteine and naloxone consumption. *Can J Clin Pharmacol*. 2000;7(4):198-204.
3. Wiens MO, Zed PJ, Lepik KJ, Abu-Laban RB, Brubacher JR, Gorman SK, et al. Adequacy of antidote stocking in British Columbia hospitals: the 2005 Antidote Stocking Study. *CJEM*. 2006;8(6):409-16.
4. Gorman SK, Zed PJ, Purssell RA, Brubacher J, Willis GA. Antidote stocking in British Columbia hospitals. *CJEM*. 2003;5(1):12-7.
5. Dubé PA, Lord MC, Bussières JF, Courteau M. Conformité des établissements de santé du Québec aux recommandations de stockage des antidotes. *Pharmactuel*. 2013;46(3):221-7. Article in French, with English abstract.
6. Gair R, Kent DA, Purssell R, Copland M. Chronic digoxin toxicity in elderly British Columbians. *BC Med J*. 2011;53(9):490-1.
7. Gair R. Antidote program in British Columbia [letter]. *Am J Health Syst Pharm*. 2012;69(13):1108.
8. File no. 2012-7219 (PSRC-201 3-01) [case report of Patient Safety Review Committee]. Toronto (ON): Office of the Chief Coroner for Ontario, Patient Safety Review Committee; 2013 [cited 2018 Jan 16]. Available from: http://www.justiceforjosh.com/patientsafetya.PDF
9. *Patient Safety Review Committee 2013-2014 annual report*. Toronto (ON): Office of the Chief Coroner Province of Ontario; 2015 Nov [cited 2016 Oct 12]. Available from: https://www.oha.com/Documents/2013-14%20PSRC%20Annual%20Report%20-%20English.pdf
10. Murphy NG, Bona DR, Hurley TA. A system-wide solution to antidote stocking in emergency departments: the Nova Scotia antidote program. *CJEM*. 2017. doi: 10.1017/cem.2017.400. [Epub ahead of print].
11. Provincial Drugs and Therapeutics Committee. Antidotes policy. New Brunswick Regional Health Authorities; 2015 Jun.

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Funding for Antimicrobial Stewardship Programs: A Customizable Business Case Template

Antimicrobials are a societal resource, and their future utility requires appropriate usage in the present. Successful antimicrobial stewardship programs (ASPs) in Canada and elsewhere have led to decreases in the incidence of *Clostridium difficile* infections and in the prevalence of colonization with resistant bacteria.[1,2] Moreover, in institutions with an ASP, appropriate utilization of antimicrobials increases, which leads to cost savings.[3-7] Although establishment of an ASP is a Required Organizational Practice of Accreditation Canada,[8] antimicrobial stewardship is a poorly filled niche in health care in Canada. Challenging aspects of establishing an ASP relate to funding and long-term support from the hospital or health region administration. One of the biggest stumbling blocks to obtaining funding is the need to write a cogent, understandable business case for health care administrators.

Pharmacists are recognized by the International Pharmaceutical Federation[9] and Accreditation Canada[8] as key players in the management of antimicrobial resistance. Not only do hospital pharmacists play a central role in recognizing the need for antimicrobial stewardship at the facility level, but the pharmacy system is often the only service that can provide data on antimicrobial use before and after establishment of an ASP. In most primary care and long-term care facilities, pharmacists also play a central role in carrying out stewardship activities, with the support of physicians knowledgeable about infectious diseases. Pharmacy directors and clinical pharmacists often create the impetus to initiate and write the business cases for ASPs, because the budgets for antimicrobials and personnel to administer the programs will be affected by the content of the proposals. To this end, the Antimicrobial Stewardship and Resistance Committee of the Association of Medical Microbiology and Infectious Disease Canada (AMMI Canada) has developed a business case template for use by individual institutions that are intent on establishing an institutional ASP and acquiring funding for the required personnel.

The authors of this article, all of whom are current or former members of the AMMI Canada Antimicrobial Stewardship and Resistance Committee, represent a group of experts who have built and maintained ASPs, and the template reflects the required elements of a business case. The intent of the business case itself is to secure necessary resources from health care administrators to support ASPs in a meaningful and long-term fashion at health care institutions. The document supporting the business case template consists of an executive summary, 3 textual sections providing detailed background information to support the request, and a spreadsheet-based template for a business case analysis.

The first section of the document provides details on both the benefits of antimicrobials and the unintended consequences of these medications. For example, most executives will likely not be aware of the unique aspects of antimicrobials and their broader long-term impact on society through the spread of drug resistance.

The second section elaborates on the issues of the burden and costs of antimicrobial-resistant organisms and *C. difficile* illness. Many of the data in this section come from the 2016 report of the Public Health Agency of Canada outlining the burden of antimicrobial-resistant organisms in Canada.[10] Bacteria specifically described in that report include methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, Enterobacteriaceae that are resistant to cephalosporins, and *C. difficile*. The language in this section is scientific and factual, but concepts such as "increased length of stay" should be readily understood by hospital administrators. Institution-specific data obtained from an institution's microbiology laboratory or from local infection prevention and control programs can be inserted within this section of the template.

The third section explores evidence linking the existence of robust ASPs with the control of antimicrobial use.[2] For example, the use of antimicrobials usually drops by one-fifth following implementation of an ASP. The third section also addresses the issue of staffing, drawing from the staffing model for infection prevention and control and from provincial working groups. On the basis of these sources, the business case recommends 1.0 physician, 3.0 pharmacist, 0.5 administrative support, and 0.4 data analyst full-time equivalents per 1000 acute care beds.

A subsection also deals with the ethical responsibility of health care personnel toward their patients.[11,12] More specifically, if antimicrobial use continues without restraint, many patients will experience failure of empiric therapy and perhaps suffer consequences.

The fourth (stand-alone) section is the spreadsheet-based template for a business case analysis in Microsoft Excel 2013 (Microsoft Corp, Redmond, Washington), which allows users to insert the costs and benefits of the proposed business case for their local institution. The spreadsheet file includes instructions for using the template and suggestions for determining operating budgets, estimating the costs of personnel and antimicrobials, and performing a return-on-investment analysis. Although primarily

targeted to acute care institutions, the AMMI Canada business case for an ASP can be modified for cancer care, rehabilitation, and complex continuing care institutions.

Both the supporting Word document and the Excel business case template are available as open access resources from the AMMI Canada website (https://www.ammi.ca/?ID=126).

The need and hence the justification for antimicrobial stewardship in Canadian health care institutions is undeniable and pressing. The AMMI Canada business case for stewardship provides an easily customizable tool that individual institutions can use in seeking funding for and establishing successful ASPs. More generally, it is also intended as a call to action to promote appropriate use of antimicrobials in Canadian facilities and institutions.

References

1. Valiquette L, Cossette B, Garant MP, Diab H, Pépin J. Impact of a reduction in the use of high-risk antibiotics on the course of an epidemic of *Clostridium difficile*-associated disease caused by the hypervirulent NAP1/027 strain. *Clin Infect Dis*. 2007;45 Suppl 2:S112-21.
2. Baur D, Gladstone BP, Burkert F, Carrara E, Foschi F, Döbele S, et al. Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and *Clostridium difficile* infection: a systematic review and meta-analysis. *Lancet Infect Dis*. 2017;17(9):990-1001.
3. Campbell TJ, Decloe M, Gill S, Ho G, McCready J, Powis J. Every antibiotic, every day: maximizing the impact of prospective audit and feedback on total antibiotic use. *PLoS One*. 2017;12(5):e0178434.
4. Nault V, Pepin J, Beaudoin M, Perron J, Moutquin JM, Valiquette L. Sustained impact of a computer-assisted antimicrobial stewardship intervention on antimicrobial use and length of stay. *J Antimicrob Chemother*. 2017; 72(3):933-40.
5. Morris AM. Antimicrobial stewardship programs: appropriate measures and metrics to study their impact. *Curr Treat Options Infect Dis*. 2014;6(2):101-12.
6. Lowe CF, Payne M, Puddicombe D, Mah A, Wong D, Kirkwood A, et al. Antimicrobial stewardship for hospitalized patients with viral respiratory tract infections. *Am J Infect Control*. 2017;45(8):872-5.
7. Vaisman A, McCready J, Hicks S, Powis J. Optimizing preoperative prophylaxis in patients with reported ß-lactam allergy: a novel extension of antimicrobial stewardship. *J Antimicrob Chemother*. 2017;72(9):2657-60.
8. Antimicrobial stewardship. In: *Required organizational practices handbook 2017*. Ottawa (ON): Accrediation Canada; 2016. p. 40-1.
9. Countries should have AMR plans in place by May 2017. The Hague (Netherlands): International Pharmaceutical Federation; 2017 [cited 2017 May 5]. Available from: www.fip.org/www/index.php?page=news_publications&news=newsitem&newsitem=202
10. *Canadian antimicrobial resistance surveillance system. Report 2016*. Ottawa (ON): Public Health Agency of Canada; 2016.
11. Rushton CH. Creating a culture of ethical practice in health care delivery systems. *Hastings Cent Rep*. 2016;46 Suppl 1:S28-31.
12. Spellberg B, Srinivasan A, Chambers HF. New societal approaches to empowering antibiotic stewardship. *JAMA*. 2016;315(12):1229-30.

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Tribute to the Reviewers of the *Canadian Journal of Hospital Pharmacy*

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If you are interested in becoming a reviewer for the *CJHP*, please register online at http://cjhp.msubmit.net.

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Programme national des prix 2018 de la SCPH : lauréats et lauréates

The winner of the **Distinguished Service Award** (sponsored by Johnson & Johnson, Family of Companies) is **Mary H H Ensom** (Vancouver, BC).

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Note: The **New Hospital Pharmacy Practitioner Award** was not awarded in 2018.

Management and Leadership Best Practice Award
Sponsored by **Apotex Inc.**
Health Authority Pharmacists' Perceptions of Independent Pharmacist Prescribing (completed at Lower Mainland Pharmacy Services)
Mitch Prasad, Peter Loewen, Stephen Shalansky, Arden Barry

Patient Care Enhancement Award
Sponsored by **Teva Canada Limited**
A Cohort Study to Identify Risk Factors for Drug-Related Emergency Department Visits in Older Adults (completed at Nova Scotia Health Authority and Dalhousie University)
Shanna Trenaman

Pharmacotherapy Best Practices Award
Sponsored by **Pfizer Canada Inc.**
Point-of-Care Beta-lactam Allergy Skin Testing by Anti-microbial Stewardship Programs: A Pragmatic Multicenter Prospective Evaluation (completed at Sunnybrook Health Sciences Centre)
Lesley Palmay, Tiffany Kan

Safe Medication Practices Award
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Vancomycin Trough Concentrations and Outcomes in Non-deep Seated Infections: A Retrospective Cohort Study (completed at Sunnybrook Health Sciences Centre)
Michael Wan, Sandra A N Walker, Marion Elligsen, Lesley Palmay

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The award-winning abstracts are published exactly as submitted by the authors and have not undergone any copyediting by the Canadian Journal of Hospital Pharmacy.

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Health Authority Pharmacists' Perceptions of Independent Pharmacist Prescribing

Management and Leadership Best Practice Award, sponsored by Apotex Inc.

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Background: The role of the pharmacist has evolved to include independent prescribing in some jurisdictions. To date, there has been no formal assessment of health authority-based pharmacists' perceptions of independent pharmacist prescribing (IPP) in British Columbia (BC).

Objectives: To assess health authority-based pharmacists' attitudes, beliefs, and perceptions of IPP, how it might affect their practice, and perceived barriers and enablers to incorporating IPP into their practice.

Methods: This was a cross-sectional evaluation of health authority-based pharmacists that utilized a prospective, anonymous online survey. All pharmacists employed by Lower Mainland Pharmacy Services in BC, Canada were invited via email to participate. A multivariate regression analysis was performed to identify factors associated with IPP.

Results: Two hundred and sixty-six pharmacists (39%) responded. Pharmacists agreed IPP is important to the profession, relevant to their practice, and may enhance job satisfaction. As well, many respondents felt that they have the expertise to prescribe. Activities identified where IPP could positively affect behaviour include deprescribing, prescribing on discharge or transfer, and renewing medications. Enablers to applying for IPP included perceived impact on patient care and the profession, level of support from management and coworkers, and personal ability. Most pharmacists indicated they would be likely to apply for IPP if this authority were to be granted. Those with <10 years of experience or a clinical practice or research role were significantly more likely to apply for IPP.

Conclusions: Heath authority-based pharmacists believed IPP is relevant and of significance to the profession, and that it would aid in various aspects of their practice to maintain patient safety and improve patient outcomes. There were no perceived barriers identified to applying for or incorporating IPP into their practice. Most respondents stated they are likely to apply for IPP if it is granted in BC.

Keywords: pharmacists, drug prescriptions, delivery of health care, hospital pharmacy service

A Cohort Study to Identify Risk Factors for Drug-Related Emergency Department Visits in Older Adults

Patient Care Enhancement Award, sponsored by Teva Canada Limited

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Background: Polypharmacy and inappropriate medications increase the risk of drug-related emergency department (ED) visits. Prior research has focused on the number of medications used or specific problematic medications.

Objective: The goal of the present study was to examine the medication appropriateness index (MAI), specific medications, medical, social and economic factors as predictors of drug-related ED visits in older adults.

Methods: The retrospective cohort study included subjects 65 years of age or older who were assessed by geriatric medicine in the ED at a tertiary care center. ED visits were assessed on both Hepler and Strand and Naranjo criteria for drug-related events. Risk factors for drug-related ED visits in older adults were assessed using backward stepwise multivariate logistic regression. Potential risk factors included information from each subject's comprehensive geriatric assessment and included medical history, medication use, MAI, function, cognition, demographics, frailty and social supports.

Results: Of 201 patients, 53.2% were women. Mean age was 81.1±8.1 years. Patients took an average of 9.0±5.6 medications. There were 40 drug-related ED visits based on the Hepler and Strand criteria and only seven events were deemed drug-related using the Naranjo criteria. The mean MAI was 12.5±13.0. Logistic regression based on Hepler and Strand definition of a drug-related event identified narcotic use (p=0.035), any anticholinergic drug use (p=0.042) and the absence of social supports (p=0.013) as being statistically significant risk factors for a drug-related ED visits. Logistic regression based on Naranjo score identified MAI as being a statistically significant risk factor (p=0.007).

Conclusions: Avoidance of anticholinergic medications, narcotics and inappropriate medications as well as the presence of adequate social support are important in the prevention of drug-related ED visits in older adults.

Point-of-Care Beta-lactam Allergy Skin Testing by Antimicrobial Stewardship Programs: A Pragmatic Multicenter Prospective Evaluation

Pharmacotherapy Best Practices Award, sponsored by Pfizer Canada Inc.

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Background: Beta-lactam allergy skin testing (BLAST) is recommended by antimicrobial stewardship program (ASP) guidelines, yet few studies have systematically evaluated its impact when delivered at point-of-care.

Objectives: to determine the feasibility of implementing a pharmacist-led beta-lactam allergy skin testing service to optimize first-line beta-lactam therapy for the treatment of clinically-documented infections

Methods: s multicenter prospective evaluation of the use of point-of-care beta-lactam allergy BLAST by Infectious Diseases (ID) and ASP pharmacists at three hospital sites in Toronto, Ontario (Sunnybrook Health Sciences Centre, North York General Hospital and Michael Garron Hospital) over a 15 month period. Patients with a reported beta-lactam allergy were identified by the ASPs through their routine audit-and-feedback programs or by the ID consultation service. During both the baseline and intervention periods, patients receiving alternate second-line therapy because of an allergy history were assessed and switched to preferred beta-lactam therapy, when it was deemed that the benefit outweighed the risk. During the intervention period, bedside BLAST was offered to and performed on eligible patients reporting immediate hypersensitivity reactions that precluded the prescription of a beta-lactam on history alone.

Results: a total of 827 patients were identified with reported penicillin allergies, of whom 76% required beta-lactam therapy. During the baseline period (when BLAST was not offered) only 50% received preferred beta-lactam therapy based on history, which increased to 60% (p= 0.02) during the intervention period. This proportion was further increased to 81% (p< 0.001) upon the provision of BLAST, without any increases in adverse events. BLAST was found to be associated with a 4.5-fold greater odds of receiving preferred beta-lactam therapy (p<0.001).

Conclusions: This project demonstrated the feasibility of trained ID/ASP pharmacists providing inpatient BLAST at the point- of-care to safely increase the use of preferred beta-lactam therapy in patients with reported penicillin allergies.

Keywords: beta-lactam allergy, skin testing, penicillin allergy evaluation, penicillin allergy

Vancomycin Trough Concentrations and Outcomes in Non-deep Seated Infections: A Retrospective Cohort Study

Safe Medication Practices Award, sponsored by HealthPRO Procurement Services Inc.

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Background: Vancomycin guidelines recommend dosing to attain trough concentrations >10mg/L in non-deep seated infections. However, no studies have evaluated the risk of poor clinical or microbiological outcomes associated with vancomycin troughs ≤10mg/L (low) versus >10mg/L (high) when vancomycin is used to treat non-deep seated infections for ≤14 days.

Objective: The primary objective was to evaluate patients with non-deep seated infections treated with vancomycin for ≤14 days to determine whether there were differences in clinical or microbiological outcomes with serum trough concentrations of vancomycin ≤10 mg/L versus >10 mg/L.

Methods: A retrospective cohort study of patients hospitalized between March 10, 2010 and December 31, 2015 who received ≤14 days of vancomycin to treat a non-deep seated infection and had at least one steady state trough concentration was completed. Patient cohort data were compared using appropriate statistical tests (t-test, Fisher's exact, or Mann-Whitney) and binary logistic regression was used to identify factors associated with clinical outcome.

Results: Of 2098 patients screened, 103 (5%) met inclusion criteria. Baseline characteristics between cohorts were not different. Clinical cure was not different between the low (42/48 [88%]) and high trough (48/55 [87%]) cohorts (p>0.99) and vancomycin trough concentration was not associated with clinical outcome (p=0.973). More patients in the high trough group had dosing changes (7/48 [15%] vs. 22/55 [40%], p=0.0046), with approximately three times more dose adjustments per patient (0.17 vs. 0.55, p=0.0193). No signal for increased vancomycin resistance associated with vancomycin troughs was identified.

Conclusions: No difference in clinical or microbiological outcomes based on vancomycin trough concentrations were observed in patients with non-deep seated infections treated with vancomycin for ≤14 days. Targeting higher vancomycin trough concentrations may be associated with increased workload with no corresponding benefit in clinical or microbiological outcomes in these patients.

Keywords: vancomycin; non-deep seated infections; trough concentrations; levels; therapeutic drug monitoring

Optimizing Patient Education of Oncology Medications: A Patient Perspective

Teaching, Learning and Education Award, sponsored by Pfizer Canada Inc.

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Introduction: The provision of oncology medication education is becoming progressively more important due to increasing complexity of cancer treatments, an aging population and improved prognoses. To optimize patient education, it is important to explore the patient perspective, as this is associated with a number of potential benefits. However, reports of oncology patients' dissatisfaction with the amount and type of information provided are being increasingly recognized. The information needs of patients with cancer have been primarily studied using quantitative methods and little qualitative research on this topic exists. It is currently unknown what oncology medication education patients at the Nova Scotia Health Authority (NSHA) wish to receive.

Objective: To explore patients' perspectives of optimal oncology medication education provided to patients at NSHA.

Methods: Adult (≥ 18 years) outpatients in medical oncology and hematology at NSHA were invited to participate in focus groups, which were audio-recorded, transcribed and analyzed thematically.

Results: Three focus groups, including 21 outpatients, were conducted. Four major themes were identified. *Preparing for what lies ahead* consisted of: readiness to receive information, anxiety over the unknown, setting expectations and patients supporting one another. *Bridging the information gaps* was made up of: gap in provision of patient education, gap in continuity of patient education and gap in trustworthy information. *Understanding the education needs of the patients* was comprised of: sources of information, education timing and setting, prioritizing information needs and individuality. *Experience within the health care system* encompassed: interactions with health care professionals, willingness to ask questions, patient satisfaction and financial implications.

Conclusions: This study identified previously unknown patient education needs and also supported ideas reported in the literature. This data will guide the strategies that will be used to optimize the delivery of oncology medication education at our facility and possibly other health care institutions.

Keywords: oncology, medication, education, patient perspective, focus group

CSHP Professional Practice Conference 2018: Poster Abstracts / Conférence sur la pratique professionnelle 2018 de la SCPH : résumés des affiches

Facilitated Poster Sessions: Discussions of original research and pharmacy practice projects

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

Sunday, February 4, 2018 • Dimanche 4 février 2018

Infectious Diseases / Antimicrobial Stewardship

1. Falsely Elevated Vancomycin Concentrations in a Patient Not Receiving Vancomycin
2. A Case of Vancomycin-Induced Thrombocytopenia
3. Successful Treatment of Chronic Spinal Osteomyelitis Caused by Multidrug Resistant *Pseudomonas aeruginosa* with Ceftolozane-Tazobactam and Surgical Intervention
4. Clinical Burden of Antibiotic Resistance Following Implementation of a Multidisciplinary Antimicrobial Stewardship Initiative in a Major Tertiary Care Center: A Controlled Interrupted Time Series Analysis Over 14 Years
5. Antibiotic Utilization Feedback Reports on General Medicine: A Qualitative Assessment

Pharmacy Practice / Patient-Centred Care / Pharmacy Education #1

1. A Descriptive Analysis of an Alternate-Level-of-Care Patient Cohort: Comprehensive Medication Overview
2. Pharmacist Actual and Perceived Priority Interventions in the Emergency Department: An Observational Study and Survey Questionnaire
3. Patient Preferences for Atrial Fibrillation Stroke Prevention Therapy Using an Individualized Risks and Preferences-Based Decision Aid
4. Optimizing Patient Education of Oncology Medications: A Patient Perspective (award—see page 55)
5. Informing Patients and Families about Storage and Disposal of Opioids

Medication Utilization, Effectiveness, and Safety

1. Pan-Canadian Trends in the Prescribing of Opioids, 2012 to 2016
2. Cardiac Arrest after Acute on Chronic Colchicine Toxicity
3. Mandatory Quality Related Events Reporting in Canada: A Province-wide Review over 7 Years
4. Analysis of Smart Pump Continuous Quality Improvement Data across Multiple Organizations
5. Comparison of Weight-Based versus Fixed-Dose Norepinephrine Dosing in Patients with Septic Shock

Drug Stability, Drug Shortages, Pharmacokinetics, and Occupational Exposure

1. Varying Ammonia Levels with Two Formulations of Sodium Phenylbutyrate
2. Stability of 8.4% Injectable Sodium Bicarbonate When Stored at Room Temperature
3. Stability of Ropivacaine 2.7 mg/mL, Morphine 0.091 mg/mL and Ketorolac 0.27 mg/mL in Polyvinyl Chloride Bags at 4°C
4. Étude descriptive de la contamination urinaire de travailleurs exposés au cyclophosphamide, à l'ifosfamide, au méthotrexate et au fluorouracile
5. Stability of 10, 40 and 200 mcg/mL Hydromorphone Solutions Stored in Syringes at Room Temperature (23°C)

Pharmacy Practice / Patient-Centred Care / Pharmacy Education #2

1. Atrial Fibrillation Patient Knowledge Gaps: A Systematic Review
2. A Feasibility Study: Implementing a Medication Adherence Contract in Kidney Transplant Recipients Followed by an Outpatient Transplant Clinic
3. An Emerging Challenge: Pharmacists' Ability to Counsel a Growing Immigrant Population
4. Toxicology Education Needs of Emergency Department Pharmacists
5. Implementation of an Overnight Pharmacist Mode

Medication Utilization, Effectiveness, and Safety / Drug Stability and Shortages

1. A Literature-Based Algorithm for the Assessment, Management and Monitoring of Drug-Induced QTc Prolongation in the Psychiatric Population
2. Provincial Smart Pump Program Improves Patient Safety
3. A Multi-Incident Analysis on Medication Incidents Associated with Patient Harm
4. Insourcing High-Risk Sterile Compounded Injectables: Development of In-House Capacity to Produce High-Quality Injectables during the Sodium Bicarbonate Shortage
5. Coordinating a Response to a Critical Drug Shortage: Experience with Sodium Bicarbonate

Monday, February 5, 2018 • Lundi 5 février 2018

Infectious Diseases / Antimicrobial Stewardship

1. Development and Implementation of a Mobile Antimicrobial Handbook App at a Tertiary Teaching Hospital
2. Retrospective Multicentre Cohort Study Comparing Safety and Efficacy Outcomes with Intermittent Infusion versus Continuous Infusion Vancomycin
3. Evaluation of Dosing Strategies with Meropenem using Monte Carlo Simulations against Bacteria with Raised MIC
4. Development of an HIV National Clinical Observership Program for Pharmacists
5. An Innovative In-House Developed Access® Database to Capture and Analyze Antimicrobial Stewardship Interventions

Pharmacy Practice / Patient-Centred Care / Pharmacy Education

1. Performance of an Innovative Patient Decision Aid for Atrial Fibrillation Stroke Prevention Therapy
2. Novel Student-Preceptor Models in Pharmacy Education: A Qualitative Analysis of the PharmD Student Experience
3. Evaluation of Physical Assessment Education for Practicing Pharmacists: A Cross-Sectional Study
4. International Normalized Ratio Point of Care Testing in an Outpatient Anticoagulation Clinic and the Impact on the Patient Experience: A Quality Improvement Study

Medication Utilization, Effectiveness, and Safety #1

1. Case Report: Fatal Arrhythmia in a Patient Receiving an Aconite Herbal Product
2. A Survey of the Use of Cannabis in Children at a Tertiary Teaching Hospital
3. Current Identification and Management Practices of Steroid-Induced Hyperglycemia in Brain and Spinal Tumour Patients on a Neurosurgical Unit
4. Clonidine for Sedation in Critically Ill Adults: A Retrospective Chart Review
5. The Effect of Preoperative Cannabis Use on Opioid Consumption Following Surgery: A Cohort Analysis

Drug Stability, Drug Shortages, Pharmacokinetics, and Occupational Exposure

1. Stability of Extemporaneously-Compounded Temozolomide 10 mg/mL Suspension in Oral Mix SF in Glass and Plastic Bottles and Plastic Syringes
2. Stability of 20, 40 and 50 mcg/mL Fentanyl Solutions Stored in Syringes at Room Temperature (23°C)
3. Stability of Generic Formulations of Bortezomib 1.0 and 2.5 mg/mL in Vials and Syringes Stored 4°C and Room Temperature (23°C)
4. Stability of 4 and 10 mcg/mL Remifentanil Solutions Stored in Syringes at Room Temperature (23°C)
5. Satisfaction des établissements de santé suite à la mise en place d'une plateforme web de surveillance environnementale

Medication Utilization, Effectiveness, and Safety #2

1. Medication Fluids in the Intensive Care Unit
2. Drug Use Evaluation of Oxycodone at a Canadian Teaching Hospital
3. Inpatient Insulin Stewardship Program: A Baseline Needs Assessment
4. Long-Term Beta-Blockers after Myocardial Infarction in the Contemporary Era: A Systematic Review
5. Clinical Guide for Pharmacists to Evaluate Risks and Manage QTc Prolongation Drug-Drug Interactions

Infectious Diseases / Antimicrobial Stewardship/ Pharmacy Practice

1. Trickle-Down Antimicrobial Stewardship: Reduction in Long-Term Care Resistance Rates Following Implementation of a Prospective Audit and Feedback Intervention in the Adjacent Acute Care Hospital
2. Enhancing Mental Health Services through Hospital Outpatient Pharmacy and Assertive Community Treatment Team Collaboration
3. Vancomycin Every 4 hours in Paediatric Patients: A Case Series
4. Comparison of Clinical Pharmacy Services in General Medicine and Surgery Patients: A Workload Measurement Study

Tuesday, February 6, 2018 • Mardi 6 février 2018

Infectious Diseases / Antimicrobial Stewardship

1. Validation of a Screening Tool to Assist in the Early Identification of Bloodstream Infection in Older Patients
2. Patterns of Antimicrobial Use in an Outpatient Hemodialysis Unit
3. Impact of an Antimicrobial Stewardship Bloodstream Infection Surveillance Program in Hospitalized Patients
4. Epidemiology of Carbapenemase-Producing Enterobacteriaceae Bacteremia and Evaluation of Antimicrobial Prescribing Practices in a Community . Hospital Setting
5. Development and Implementation of a Provincial Beta-Lactam Allergy Management Initiative

Pharmacy Practice / Patient-Centred Care/ Pharmacy Education #1

1. Factors Affecting Time to Fill Antiplatelet Therapy for Patients Discharged from Hospital
2. Evaluation of the Impact of Pharmacist-Led Penicillin Allergy Assessments on Antibiotic Utilization in a Large Community Teaching Hospital
3. Pharmacy Technician Continuing Education Program at a Large Teaching Hospital
4. 5 Questions to Ask about Your Medications
5. A Pharmacy-Led Interdisciplinary Teaching Model in Specialized Pharmacotherapy: An HIV Pharmacy Rotation for Medical Residents

Medication Utilization, Effectiveness, and Safety / Drug Stability

1. Influence of Manufacturer on Cefazolin Stability
2. Opioid Selection in the Neonatal Intensive Care Unit: Morphine versus Fentanyl: Impact on Total Opioid Exposure and Time to Enteral Feeds
3. The Prevalence of Mortality due to Rebound Toxicity after "Treat and Release" Practices In Prehospital Opiate Overdose Care: A Systematic Review
4. A Pan-Canadian Study on the Compounded Medicines Most in Need of Commercialized Oral Pediatric Formulations
5. A Comparison of Intravenous Iron Dosing Regimens for Anemia Management in Patients Undergoing Hemodialysis

Pharmacy Practice / Patient-Centred Care / Pharmacy Education #2

1. User Satisfaction Regarding Standard Assessment Tool for Field-Based Pharmacy Training
2. Pharmacy Student-Led Best Possible Medication History Quality Audit
3. A Work-Sampling Study of Clinical Pharmacists
4. Development and Evaluation of an Anticoagulation Education Program for Pharmacists
5. Évaluation de l'oculométrie comme outil de rétroaction en validation pharmaceutique : étude pilote

Pharmacy Practice / Patient-Centred Care / Pharmacy Education #3

1. Qualitative Thematic Analysis of Interprofessional Perspectives on Clinical Pharmacy Key Performance Indicators
2. Enabling Expanded Scope in Hospital Practice: Implementation of a Pharmacist Modification Orders Protocol
3. Design, Implementation, and Evaluation of a Clinical Pharmacy Key Performance Indicator Tracker: DIE−cpKPI Study
4. Assessing the Perception and Implementation of Continuous Quality Improvement in Pharmacy Professionals: A Pre-Safety IQ Initiative
5. From "Dot" to "Dot Com": Navigating Pharmacist Handoff in a Digital Era

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

Falsely Elevated Vancomycin Concentrations in a Patient Not Receiving Vancomycin

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Background: Therapeutic drug monitoring (TDM) of vancomycin is recommended by the Infectious Diseases Society of America for efficacy and toxicity. Immunoassays are commonly used in diagnostic laboratories to determine serum vancomycin concentrations. A case of falsely elevated vancomycin serum concentrations, in a patient not receiving vancomycin therapy, is described.

Case Description: An elderly female was prescribed vancomycin and imipenem for a suspected septic knee. A blood sample was inadvertently collected prior to her receiving vancomycin, and the concentration reported as 36.10mg/L (Roche Modular P analyzer). Repeated serum sampling over the subsequent 48 hours, despite not receiving vancomycin, yielded similar concentrations (33.10-35.30mg/L). Eight months later, she was again found to have an elevated vancomycin concentration (32.9mg/L) in the absence of therapy.

Assessment of Causality: The patient sample was tested for vancomycin using liquid chromatography-tandem mass spectrometry (LC-MS/MS) as the gold-standard, and by four alternate commercial immunoassay platforms. Vancomycin was undetectable by LC-MS/MS. The immunoassays showed undetectable to high (35mg/L) concentrations. The falsely elevated concentration observed by our Roche method was investigated for interference by concurrent medications and endogenous substances, such as paraproteins and human anti-mouse antibodies. Polyethylene glycol precipitation and heat inactivation resulted in the removal of the interference responsible for the falsely elevated concentration.

Literature Review: A single case of a spuriously high vancomycin concentration before receiving the drug, secondary to suspected endogenous interference, has been reported. However, to our knowledge, this is the first report of falsely elevated vancomycin concentrations on the Roche Modular P analyzer in a patient not receiving vancomycin.

Importance to Practitioners: Vancomycin immunoassays are robust in facilitating TDM, but are susceptible to cross-reactivity. Spurious concentrations may lead to unnecessary dose adjustments, impacting efficacy or toxicity. Assay interference should be considered and laboratory professionals contacted when vancomycin levels do not correlate with clinical expectations.

A Case of Vancomycin-Induced Thrombocytopenia

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Background: Vancomycin has been implicated in causing cytopenias. While neutropenia is well described, vancomycin-induced thrombocytopenia is rare and may be overlooked in an initial thrombocytopenia workup, increasing the risk of potentially life-threatening bleeding.

Case Description: A 41 year-old female underwent revision of a previous spinal decompression surgery. Irrigation and debridement 15 days later found complications of dural leaks, pseudomeningocele and necrotic bone. She was empirically started on vancomycin and meropenem. Her baseline platelet count was 349 (reference range: 150-400x109/L). Between days 4 and 9 from vancomycin initiation her platelets decreased from 300 to 62, reaching a nadir of 15 on day 12. Antibiotics were discontinued. The platelets rebounded to 68 the following day and meropenem was resumed for a total of 6 weeks. The patient was transferred to another institution where vancomycin was restarted on day 19 with a platelet count of 372, which decreased to 78 by the following morning. Vancomycin was discontinued and the platelets rebounded to 120 by day 23.

Assessment of Causality: The Naranjo scale score of 10 identified vancomycin as a definite cause of the thrombocytopenia. The reaction resolved with drug withdrawal and recurred within 24 hours of rechallenge. Flow cytometry testing for drug-induced thrombocytopenia was positive with vancomycin-dependent immunoglobulin G binding to platelets detected in the post-exposure but not in the pre-exposure serum.

Literature Review: A retrospective review published in 2017 identified 30 case reports of vancomycin-induced thrombocytopenia. A study investigating a case series of patients receiving vancomycin detected vancomycin-dependent antiplatelet antibodies only in those in whom thrombocytopenia developed.

Importance to Practitioners: Although vancomycin-induced thrombocytopenia is a rare side effect, prompt recognition and drug discontinuation may minimize the risk of a life-threatening bleed. At least weekly monitoring of platelets has been recommended and patient counseling regarding risks of future exposure is important.

Successful Treatment of Chronic Spinal Osteomyelitis Caused by Multidrug Resistant *Pseudomonas aeruginosa* with Ceftolozane-Tazobactam and Surgical Intervention

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Background: Ceftolozane-tazobactam is a novel intravenous antibiotic combining an anti-pseudomonal cephalosporin with a beta-lactamase inhibitor. It is indicated for complicated intra-abdominal and urinary tract infections. Information on the use of ceftolozane-tazobactam in osteomyelitis is limited and is the focus of this case report.

Case Description: A 67 year-old morbidly obese female with chronic draining wounds, refractory to multiple courses of antibiotics after spinal deformity correction three years prior, was admitted for surgical irrigation and debridement. Existing rods and hardware were removed and pockets of purulent material were found throughout the spinal exposure. Intraoperative cultures grew *Streptococcus anginosus* and multidrug resistant (MDR) *Pseudomonas aeruginosa* sensitive only to aminoglycosides. A clinical diagnosis of chronic osteomyelitis was made. Treatment with tobramycin and meropenem was initiated. Additional testing by disk diffusion demonstrated susceptibility to ceftolozane-tazobactam. Treatment with a 6 week course of ceftolozane-tazobactam 3g intravenously every 8 hours was well tolerated.

Assessment of Causality: At days 4 and 31 after the start of ceftolozane-tazobactam, intraoperative cultures were negative for the previously identified organisms. At last follow up, 6 months after the initial surgery, the patient's wounds had healed completely. She was clinically well and not receiving antibiotic therapy.

Literature Review: The 5 published case reports using ceftolozane-tazobactam for osteomyelitis have involvedMDR *Pseudomonas* (4) and MDR *Stenotrophomonas* (1). Doses varied from 750mg (adjusted for renal impairment) to 3g intravenously every 8 hours for at least 6 weeks. Three

cases reported clinical success at 3 to 18 months of follow-up while two reports did not include outcome information.

Importance to Practitioners: MDR organisms remain challenging to treat, particularly when involving deep seated infections such as osteomyelitis. Sharing this experience of using ceftolozane-tazobactam combined with surgical intervention is a valuable addition to the existing literature for clinicians faced with similar clinical scenarios.

Clinical Burden of Antibiotic Resistance Following Implementation of a Multidisciplinary Antimicrobial Stewardship Initiative in a Major Tertiary Care Center: A Controlled Interrupted Time Series Analysis Over 14 Years

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Background: Our institution launched a multidisciplinary prospective audit-and-feedback (PAF) Antimicrobial Stewardship program (ASP) in October 2009. Although reducing antimicrobial resistance (AMR) is a major incentive for ASPs, a paucity of high quality data evaluating the impact of ASPs on microbial outcomes remains.

Objective: The objective was to evaluate changes in institutional AMR and antimicrobial use (AMU) in the 7 years following PAF-ASP implementation.

Methods: Patient-level microbiologic data (clinical isolates of aerobic gram-negative bacteria, *Staphylococcus aureus*, and *Enterococcus spp*.) and antibiotic-use data were obtained over the 14 year study period. Program impact was assessed by evaluating changes in institutional AMR and AMU trends (Δ slope) between the pre- (October 2002 – September 2009) and post-intervention (October 2009 – September 2016) periods using interrupted time-series analyses with segmented regression. Incidence of hospital-acquired isolates resistant to at least one therapeutically active antibiotic agent per month standardized to 10,000 patient days (PD) was assessed as the primary outcome. Change in the incidence of antibiotic-resistant community-acquired isolates was evaluated as an AMR control. Changes in inpatient AMU were quantified using antibiotic days of therapy (DOT) (all patients, all antibiotic agents)/10,000 PD per month.

Results: A significant reduction in nosocomial AMR (Δ slope =-0.7 resistant hospital-acquired isolates/10,000 PD/month, $p<0.001$) and inpatient AMU (Δ slope =-36 antibiotic DOT/10,000 PD/month, $p<0.001$) was found. Conversely, community-acquired AMR increased significantly over the same period (Δ slope =+0.2 resistant community-acquired isolates/10,000PD/month, $p=0.03$).

Conclusions: Time series modelling revealed that implementation of a PAF-ASP was associated with a significant reduction in nosocomial AMR and inpatient AMU. The identified increase in community acquired AMR further strengthens the causal inference of our findings, since an institutional ASP would not be expected to impact community AMR and the observed significant rise in community AMR is in keeping with the known global crisis of rising AMR in the community.

Antibiotic Utilization Feedback Reports on General Medicine: A Qualitative Assessment

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Background: Between 30 to 50% of antibiotic prescriptions are potentially unnecessary and these inappropriate prescriptions drive antimicrobial resistance. Evidence suggests that despite treating similar patient populations, antibiotic prescribing practices can vary dramatically among prescribers. Peer comparison is an increasingly recognized behavioural intervention to improve physician prescribing practices.

Objectives: We sought to measure prescriber-level antibiotic utilization among general internal medicine (GIM) attending physicians to provide peer comparison reports, and assess any impact on physician practices.

Methods: Antibiotic Days of Therapy (DOT) per 1000 patient days under the care of each GIM physician was calculated using our antimicrobial stewardship database. We included all attending physicians with at least 3 weeks of inpatient service during the study period (January 2nd 2015 to June 27th 2016). Readmission or death within 30 days for patients who received at least one antibiotic was used as a balancing measure. Anonymous, personalized feedback reports were emailed to GIM physicians describing their antibiotic prescribing practices compared to their peers. An electronic survey was conducted 2 months later to assess perceptions regarding feedback and any contemplated changes in practice as a result of the report.

Results: Among 17 GIM physicians, DOT per 1000 patient days varied from 316 to 569. Despite these differences, there was no difference in 30 day readmission or death among patients receiving antibiotics. Of the 10 physicians that completed the feedback survey (response rate 63%), 9 prescribers (90%) found the report represented their practice while 4 (40%) contemplated changes in practice.

Conclusions: Provider-level antibiotic utilization at our institution confirmed wide variation in prescribing practices without an obvious difference in patient outcomes. The majority of physicians surveyed felt that antibiotic prescribing feedback reports were useful, but longer term follow up is needed to evaluate impact on antibiotic prescribing practices.

A Descriptive Analysis of an Alternate-Level-of-Care Patient Cohort: Comprehensive Medication Overview

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Background: Alternate Level of Care (ALC) patients are hospitalized, not receiving active medical care waiting to be transferred to another facility. Many older patients are on complex, often inappropriate

medications. To our knowledge, there has been no analysis of ALC medication regimens. We conducted an audit of all ALC patients within a tertiary institution.

Objectives: (1) to analyze health-related parameters and obtain a descriptive representation of ALC patients currently admitted at our institution; (2) to cross-reference medications to 3 existing literature references for potentially inappropriate medications (PIMs) (Beer's list, STOPP/START and ISMP high alert medications); and (3) to assess the appropriateness of medication regimens.

Methods: We conducted a cross-sectional audit of ALC patients in June 2017 as a phase I quality improvement project. Data was collected with a standardized case report form to obtain a descriptive representation of ALC patients. Medications were categorized and coded based on the 3 PIM lists. Data was analyzed by calculating mean, median and IQR where appropriate.

Results: Eighty-two ALC patients were included in this study. The mean age of patients was 75.6 (±15) years. Female patients accounted for 52.4% of our population. Patients had 6.4 (SD±3) chronic conditions, and were prescribed 12.8 (SD±7) medications; 28.9% of patients were prescribed ≥ 1 drug from 7 different classes of medications concurrently. PIMs were most frequent on the Beer's list with an average of 3.9 (SD±3) medications/patient. One patient had zero medications flagged as PIM from any of the 3 PIM lists.

Conclusions: ALC patients at our institution have 6 chronic conditions managed with at least 12 medications, many of which are PIMs. This data will inform next steps to make recommendations to simplify, reduce or discontinue medications in which there is an unclear indication, lack of effectiveness or evidence of potential harm.

Pharmacist Actual and Perceived Priority Interventions in the Emergency Department: An Observational Study and Survey Questionnaire

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Background: Emergency Department (ED) pharmacists are a finite resource and activities with higher value should be prioritized. Literature shows that clinical pharmacists who resolve drug therapy problems, called pharmacist interventions (PI), improve patient outcomes and reduce health-resource utilization. Tracking high quality PI and surveying pharmacists to understand their perceptions of their practice will help us establish baseline ED pharmacist practice behaviour and identify potential gaps in ED pharmacist services delivery.

Objectives: To describe the number of PI completed by ED pharmacists in a Canadian health authority, to describe the proportion of interventions that were priority disease PI (PD-PI) and quality indicator PI (QI-PI), and to identify ED pharmacist perceptions of which patients they felt they should be providing prioritized care to and which activities they felt they should be completing.

Methods: This study consisted of two parts; a retrospective PI tracking review and an internet-based survey. PI tracking data was captured from three EDs with dedicated clinical pharmacist coverage over a one year period. An electronic survey was distributed to a convenience sample of Canadian ED pharmacists. Data was analyzed using descriptive statistics.

Results: A total of 2043 PI were completed. Of these, 1127 (54.4%) were PD-PI and 473 (22.9%) were QI-PI. Survey participants agreed that many priority diseases and high-value activities (QI-PI and clinical pharmacist key performance indicators [cpKPI]) previously established in a general medicine population should be prioritized in the ED, but not all. Several potential new ED-specific priority diseases were identified.

Conclusions: ED pharmacists in a Canadian health authority are performing impactful, high quality interventions for patients with priority diseases. Surveyed pharmacists identified gaps in current definitions of priority diseases and high value pharmacist activities specific to the ED. Our findings support the presence of unique opportunities for ED clinical pharmacists to provide prioritized, impactful care.

Patient Preferences for Atrial Fibrillation Stroke Prevention Therapy Using an Individualized Risks and Preferences-Based Decision Aid

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Background: Many antithrombotic therapies are effective for atrial fibrillation (AF) stroke prevention, but choosing is complex because patients must make trade-offs based on their values and preferences. To address this, we have developed a decision aid (DA) that integrates AF education, individualized stroke and bleeding risk estimates, clinical trial evidence, a best-worst scaling discrete choice experiment (BWS-DCE), and quantification of the alignment between therapy options and patient preferences.

Objective: To assess the preferences of AF patients and their consequent stroke prevention therapy choices.

Methods: Prospective observational study of patients with AF or at risk of AF (age>50 y/o). Participants completed a pre-DA questionnaire, the DA, and a post-DA questionnaire. The DA integrated each participant's stroke and major bleed risk with the results of a 9-attribute BWS-DCE to generate individualized preference scores for each therapy option. Participants made therapy choices based on the results presented.

Results: 38 participants (mean age 71) completed the study. 61% had CHA2DS2-VASc score >1 and 32% had HAS-BLED score >2. 70% were on OAC. Stroke and intracranial hemorrhage were the highest and daily doses and cost were the lowest-weighted attributes. 54% of participants changed their preferred treatment after using the DA. 68% and 12% chose the highest-scored therapy option on decision 1 (no therapy, ASA, or OAC) and decision 2 (choice of OAC), respectively. In 54%, the direction of therapy change was to de-intensify (OAC to ASA or ASA to no therapy). 47% of OAC users preferred a different OAC than current.

Conclusions: Using a DA that included individualized risk estimates, values clarification, and scoring of therapy options, most AF patients decided they preferred a different therapy than the one currently prescribed. The DA requires refinement for choice of OAC. Using the DA could be a valuable facilitator of shared decision-making in AF patients.

Informing Patients and Families about Storage and Disposal of Opioids

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Background: Unsafe storage or disposal of medications including opioids has resulted in accidental poisonings, inappropriate use, and theft in patient's homes. Increasing demand for home-based end-of-life care underscores the opportunity to provide guidance to patients and families.

Objectives: The project objectives were to 1) identify preferred practices for safe home-based opioid storage and disposal, and 2) develop and refine educational materials to support patients, families, and healthcare providers.

Methods: Preferred practices regarding home-based opioid storage and disposal were identified via thematic analysis of 155 out of 1285 articles screened for inclusion and 20 multi-disciplinary stakeholder interviews. An information card (English version below) was developed using usability testing with research ethics board approval.

Results: Thematic analysis revealed that patient/family education was not consistently provided by the healthcare system, nor reliably supported with educational tools.

Complementary preferred practices were identified:

1. Homecare service providers pick up unused medications
2. Pharmacists providing in-home medication reviews pick up unused medications
3. Patients/families return medications to a pharmacy; they can contact the XXX to identify Canadian pharmacies participating in 'returns programs'

Given variability in clinical practices, an information card was developed to support preferred practice #3 above. Usability testing revealed opportunities for improvement; the information card was refined to integrate feedback.

Conclusions: The information card can be used by healthcare providers providing counselling to end-of-life care patients and families, including by hospital pharmacists providing discharge counselling.

Project partners have committed to supporting its dissemination.

For the image that goes with this abstract, please see Abstract Appendix, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/125/showToc

Pan-Canadian Trends in the Prescribing of Opioids, 2012 to 2016

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Background: Canada is in the midst of a worsening opioid crisis. Several studies have identified an association between the dispensing of opioids and opioid-related harms. The ongoing monitoring of opioid prescribing trends is needed to support urgent public health surveillance needs to address the crisis.

Objective: To characterize the pan-Canadian and provincial opioid prescribing trends from 2012 to 2016.

Methods: Opioid prescribing trends were characterized by the quantity dispensed as measured by defined daily doses (DDDs), the number of prescriptions dispensed and the number of people who were prescribed opioids. Pan-Canadian aggregate drug claims data were used to examine the number of DDDs and prescriptions dispensed. Additionally, record-level drug claims data from three provinces were used to determine the number of people prescribed opioids.

Results: Between 2012 and 2016, the rate of DDDs declined by 9% from 6,858 to 6,246 DDDs per 1,000 population; while the rate of opioid prescriptions increased by just over 2%, from 582 to 595 prescriptions per 1,000 population. With respect to the number of people prescribed opioids, for the three provinces included in this analysis, the rate decreased from 132 people per 1,000 population to 125 per 1,000 population during the study period. Seniors were prescribed opioids most often with more than 1 in 5 seniors receiving a prescription for an opioid. Among the seniors prescribed an opioid, about 1 in 8 were prescribed a strong opioid on a chronic basis.

Conclusions: The overall quantity of opioids dispensed in Canada declined between 2012 and 2016 despite a steady increase in the number of prescriptions. Moreover, the number of people prescribed an opioid per 1,000 population steadily declined. The results of this study highlight the importance of developing pan-Canadian strategies to reduce the harms associated with the use of prescription opioids.

Cardiac Arrest after Acute on Chronic Colchicine Toxicity

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Background: Colchicine is an antimitotic agent with a long history of use in gout and familial Mediterranean fever. For this reason, clinicians may overlook the potentially detrimental effects of colchicine toxicity. Therapeutic, toxic and lethal dose are not well defined and there is no available antidote. We report a case of colchicine use at 0.6-1.2mg/day in a renally compromised patient which may have contributed to cardiac arrest.

Case Description: An 80-year-old male with renal dysfunction received colchicine 0.6mg daily as needed and in 2016, increased to twice daily for 3 days. He decreased back to 0.6mg daily; however the prescription was not updated. On multiple admissions to hospital over a 1 month period, colchicine was mistakenly increased to twice daily during the medication reconciliation process. On his last admission he presented with diarrhea, nausea, and malaise. His leukocyte count was $0.7x10^9$/L, he was afebrile, and culture negative. Four days later, he was transferred for management of elevated troponin thought to be uremic pericarditis and consideration for intermittent hemodialysis. He was found pulseless and unresponsive while undergoing peritoneal dialysis. Return of spontaneous circulation was achieved after 15 minutes of downtime and he was transferred to intensive care where he later succumbed to his condition.

Assessment of Causality: A Naranjo score of 3 categorized this event as a possible colchicine toxicity owing to increased colchicine dose and subsequent sequelae such as diarrhea, nausea, leukopenia and eventual cardiac arrest.

Literature Review: Documented risk factors for colchicine toxicity include increased age, renal and/or hepatic dysfunction, chronic use, intravenous use, loading doses, and drug interactions. Clinical stages of toxicity including gastrointestinal, multi-organ failure and recovery phase are also well documented.

Importance to Practitioners: Practitioners should be vigilant with colchicine use and obtaining accurate medication histories due to unpredictable individual dose response and potentially fatal consequences.

Mandatory Quality Related Events Reporting in Canada: A Province-wide Review over 7 Years

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Background: There has been limited research that quantitatively analyzes quality related events (QREs) in pharmacies. Recognizing the importance of quality improvement and management to patient safety, several Canadian provinces have moved towards mandatory reporting of QREs in pharmacies to an independent third party.

Description: The objective of this project is to quantify and characterize medication-related QREs that were anonymously reported to a third-party national error-reporting database by pharmacies in a Canadian province over 7 years.

Action: A retrospective analysis was conducted on medication-related QREs from pharmacies occurring between October 1, 2010 and June 30, 2017. Descriptive analysis was performed on all medication-related QREs with respect to type of incident, discoverer, medication system stages, medications, and outcome.

Evaluation: A total of 131, 031 QREs were anonymously reported by 301 pharmacies in Nova Scotia to a third-party national medication safety organization. 74.87% (98, 097) was medication-related QREs. Overall, 82.05% (80, 488) of reported medication-related QREs did not reach the patient (i.e. near misses) and only 0.95% (928) resulted in harm. Reports of incorrect dose/frequency (25.58%; 25, 089), incorrect quantity (20.00%; 19, 619), and incorrect drug (14.22%; 13, 951) were most common. Pharmacists discovered the majority of medication-related QREs (75.17%; 73, 739). Order entry was the most frequently reported medication system stage for error occurrence, followed by prescription preparation/dispensing, and prescribing. The most reported medications were levothyroxine sodium, amoxicillin, and rosuvastatin. Medications with the highest proportion of QREs with harm were methadone, risperidone, and warfarin.

Implications: Pharmacists play a significant role in patient safety and preventing medication incidents. The most frequently reported medications were among the top dispensed medications in Canada, but we also identified new high-alert medications. Our findings suggested the need for medication system stage-specific and medication-focused interventions to mitigate harm and improve patient safety.

Analysis of Smart Pump Continuous Quality Improvement Data across Multiple Organizations

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Background: Smart pump technology can generate Continuous Quality Improvement (CQI) data to provide objective information on IV infusion practices and identify potential safety gaps. However, this valuable data is not frequently shared between organizations.

Objectives: The project's aim was to identify opportunities for increased infusion safety by analyzing smart pump data across organizations nationally.

Methods: A pooled, observational analysis was conducted by pooling smart pump CQI data from five organizations across Canada in November 2016. Data from 7430 pumps was weighted according to the number of pumps per organization and analyzed, by evaluating average drug library compliance, frequency of alerts due to soft or hard limit events and the top 5 drugs with soft and hard limit events. Soft limit alert events consist of overriding the exceeded soft limit or modification of the dose to within soft limits. Hard limit alert events occurred when the set hard limit was exceeded.

Results: An average drug library compliance of 97 percent was found across organizations. No significant variance across patient care areas was noted. Soft limit exceeded alert ranged from 3.6 percent to 11.2 percent of all infusion starts. Hard limit attempted ranged from 1.2 percent to 6.5 percent of all infusion starts. The top five drugs with soft limit events resulting in an override were propofol, hydromorphone, heparin, vancomycin and norepinephrine. The top five drugs with soft limit events resulting in a modification of the dose were morphine, propofol, ondansetron, vancomycin and heparin. The top five drugs with hard limit attempted events were heparin, IV fluids, vancomycin, piperacillin/tazobactam and amiodarone.

Conclusions: Using smart pump data from multiple organizations nationally provides the opportunity to improve drug safety by focusing on common results, and providing benchmarking information. Changes in drug libraries can also be made to reduce alert fatigue and increase infusion safety.

Comparison of Weight-Based versus Fixed-Dose Norepinephrine Dosing in Patients with Septic Shock

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Background: Norepinephrine is the first line vasopressor recommended by the 2016 Surviving Sepsis guidelines. There is limited data with respect to superiority of commonly used dosing strategies (fixed versus weight based).

Objective: The primary objective was to compare the two dosing strategies in maintaining target mean arterial pressure (MAP) of 65 mm Hg at six hours after initiation of norepinephrine. The secondary objectives were to assess the need for add-on vasopressors, need for hydrocortisone, ICU length of stay, mortality, and treatment side effects.

Method: This was a retrospective, pre-post intervention cohort study. On March 1st 2016, the smart pump programming at this institution changed from fixed-dose (mcg/min) to weight-based (mcg/kg/min). All patients who received norepinephrine six months before and after implementation of this change were screened. Patients who were started

on norepinephrine and met the 2016 Surviving Sepsis Campaign definition of severe sepsis were included. The primary outcome was analyzed using logistic regression analysis and secondary using descriptive statistics.

Results: Overall 110 patients were included: 54 in the weight-based arm and 56 in the fixed-dose arm. All the baseline characteristics were similar between the two groups. There was a greater proportion of patients at MAP of 65 mm Hg or greater at six hours in the weight-based arm compared to the fixed-dose arm (94.4% vs. 75.0%). This corresponded to an odds ratio of 3.5 (95 confidence interval 1.01 to 12.13). There was no statistically significant difference comparing weight-based to fixed-dose regimens in: mortality (50% vs. 55%; P=0.71), need for additional vasopressors (28% vs. 45%; P=0.18), need for hydrocortisone (15% vs. 20%; P=0.67), and days spent in ICU (9 days vs. 10 days; P=0.26).

Conclusion: Weight-based dosing of norepinephrine is more likely to maintain a MAP of 65 mm Hg or greater at six hours compared to a fixed-dose strategy.

Varying Ammonia Levels with Two Formulations of Sodium Phenylbutyrate

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Background: Ornithine transcarbamylase (OTC) deficiency is a urea cycle disorder treated with ammonia scavenging drugs to prevent hyperammonemic morbidity and mortality. Sodium phenylbutyrate (NaPB) is commercially available as Pheburane® and Buphenyl®. This is the first case describing significant variation in ammonia levels with two formulations of NaPB. Pheburane® coated granules can be compounded into a 200mg/mL suspension, while Buphenyl® powder is compounded into a 50 mg/mL suspension.

Case Description: A 3-day-old male was diagnosed with OTC deficiency after ammonia >400 µmol/L was detected (reference range <50 µmol/L). After the initial hyperammonemic crisis was treated, the patient was started on maintenance Pheburane®, which was compounded into a suspension. The patient's ammonia remained consistently >100 µmol/L while on Pheburane®. Pheburane® was switched to Buphenyl® after ammonia peaked at 180 µmol/L 2 weeks into therapy. The following day, the patient's ammonia drastically declined and remained within normal range for the remainder of therapy.

Assessment of Causality: Although a daily dose of 2.4 g NaPB was used with both products, the Pheburane® suspension had a larger volume and was compounded by crushing the coated granules. After reaching peak ammonia levels of 180 µmol/L on Pheburane®, the patient was switched to Buphenyl®. Upon the next blood draw fifteen hours later, his ammonia level dropped to 39 µmol/L.

Literature Review: A bioequivalence study of subjects aged 19-50 demonstrated that Pheburane® coated granules displayed bioequivalence to Buphenyl®. Moreover, a follow-up study found a reduction in vomiting and hyperammonemic crises when patients switched nitrogen-scavenging treatment to Pheburane®. Despite this promising evidence, no studies have been published on Pheburane® in neonates.

Importance to Practitioners: Failure to treat neonatal OTC deficiency can lead to coma and death. Clinicians should consider the use of Buphenyl® over Pheburane® when treating neonates and infants.

Stability of 8.4% Injectable Sodium Bicarbonate When Stored at Room Temperature

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Background: Shortage of sodium bicarbonate injection required the evaluation of alternatives.

Objective: To evaluate the stability of 8.4% injectable sodium bicarbonate solution in glass vials, compounded in-house and stored at room temperature unprotected from ambient room fluorescent light for 91 days.

Methods: On days 0,2,5,7,9,12,14,16,21,23,28,42,56,70 and 91, a 50mL volume (52.8g) of sodium bicarbonate solution was withdrawn from each glass vial and titrated against 2M HCl to determine buffer capacity. Sodium bicarbonate samples were also delivered to the biochemistry lab for determination of initial pH, sodium, and bicarbonate levels.

Results: Evaluation of titrations of 2M HCL against 50mL volumes of bicarbonate indicated the method was reproducible. Within day reproducibility for buffer capacity as determined by the standard deviation of regression averaged 0.11% for pH 5. Similarly, between days variability for sodium and bicarbonate analysis averaged 1.24% and 1.87%, respectively. The initial pH, before any 2M HCl was added, indicates that solutions stored at room temperature increase in pH by less than 0.05 pH units over the 91 day study period. Analysis of sodium and bicarbonate concentrations indicates less than a 3% change occurred during the study period and that it would take more than 91 days before a 10% change was observed, with 95% confidence. Similarly, analysis of buffer capacity, based on the volume of 2M HCl to achieve a pH of 5, indicates that it would take more than 10,238 days before a 10% change was observed and with 95% confidence this would not occur sooner than 1873 days.

Discussion: We observed that sodium bicarbonate solution, compounded in-house, is stable for at least 91 days, with 95% confidence, when stored at room temperature. A beyond-use date of 91 days should be used only after due consideration of institutional capability, applicable standards, sterility verification and completion of required quality tests.

Stability of Ropivacaine 2.7 mg/mL, Morphine 0.091 mg/mL and Ketorolac 0.27 mg/mL in Polyvinyl Chloride Bags at 4°C

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Background: The National Association of Pharmacy Regulatory Authorities (NAPRA) Model Standards for Pharmacy Compounding of Non-Hazardous Sterile Preparations indicates that stability data from peer reviewed literature or appropriate experimental studies are required, to assign a beyond use date (BUD) to a given compound.

Objective(s): To determine the stability of ropivacaine 2.7 mg/mL, morphine 0.091 mg/mL and ketorolac 0.27 mg/mL in sodium chloride 0.9% stored in polyvinyl chloride (PVC) plastic bags packaged in an Ultra-Violet Light Inhibiting (UVLI) bag at 4°C over 9 days.

Methods: An arthroplasty infiltration solution was prepared and stored in the dark at 4°C. From day 0 to 9, samples were taken and frozen at -85°C, until analysed by purity-indicating gas chromatography mass spectrometry (GC/MS). In each GC/MS run, chromatographic peaks were generated for the drug and its internal standard. Drug/internal standard peak area ratios were calculated for each analytical run. Peak

area ratios from quintuplicate test day samples were then calculated as a percentage of the corresponding peak area ratios of quintuplicate day zero samples analysed in the same GC/MS batch. 95% confidence limits were calculated from these data. Daily physical inspections and pH measurements were also performed.

Results: The 95% confidence limits for each measured drug remained above 90% for the entire study indicating acceptable stability throughout. The arthroplasty infiltration solution remained clear and colourless and the pH remained essentially constant at a mean of 6.3 with a standard deviation of 0.11. The mass spectra of the day 9 drug peaks were identical to the corresponding mass spectra of the drug day 0 peaks, demonstrating drug purity to the end of the study.

Conclusion(s): The ropivacaine, morphine and ketorolac arthroplasty mixture in saline prepared in PVC bags stored in the dark at 4°C is stable for at least 9 days.

Étude descriptive de la contamination urinaire de travailleurs exposés au cyclophosphamide, à l'ifosfamide, au méthotrexate et au fluorouracile

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Contexte : Certains professionnels de la santé sont exposés aux médicaments dangereux et une absorption systémique de ces médicaments est possible.

Objectif : Déterminer la faisabilité d'un programme de surveillance biologique par détection de médicaments dangereux.

Méthodologie : Étude descriptive observationnelle. Cohorte d'infirmiers, pharmaciens et assistants-technique manipulant des médicaments dangereux au sein de deux centres d'oncologie adultes (A (750 lits) et B (700 lits)). Ont été mesurés : cyclophosphamide (limite de détection: 0,009ng/mL), ifosfamide (0,0097ng/mL), méthotrexate (0,075ng/mL) et FBAL, métabolite urinaire du fluorouracile (0,120ng/mL) par UPLC/MS-MS. Chaque participant volontaire a fourni un échantillon d'urine en fin de journée et complété un journal.

Résultats : Ont été recrutés 56 participants ayant au moins une activité liée à la manipulation de médicaments dangereux ciblés soit 27/28 (A) et 24/28 (B). En centre A, l'utilisation des gants était conforme pour 77/89(86,5%) des activités réalisées par 13 infirmiers. Deux infirmiers (2/13) portaient une blouse et aucun (0/13) le masque pendant l'administration. Tout le personnel de la pharmacie (15/15) portait les protections recommandées pour l'ensemble des activités (34/34). En centre B, l'utilisation des gants était conforme pour 49/68(72%) des activités réalisées par 10 infirmiers. Neuf infirmiers (9/10) portaient une blouse et quatre (4/10) portaient un masque pendant l'administration. Les assistants techniques portaient l'équipement recommandé pour la préparation et manipulation des médicaments dangereux en salle blanche (3/3). Seulement deux pharmaciens (2/8) et deux assistants techniques (2/9) portaient l'ensemble de l'équipement recommandé pendant leurs activités. Aucun échantillon (0/56) ne comportait de trace détectable des quatre médicaments dangereux.

Conclusion : Il est faisable de mettre en place un programme de surveillance biologique en établissement de santé. Un tel programme doit comprendre un profil des mesures de protection appliquées par travailleur exposé. Cette étude confirme l'absence de traces de quatre médicaments dangereux dans l'urine de 56 travailleurs en oncologie adulte.

Stability of 10, 40 and 200 mcg/mL Hydromorphone Solutions Stored in Syringes at Room Temperature (23°C)

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Background: Inpatient hospital pharmacies must compound intravenous products and assign an appropriate beyond-use-date (BUD) as per NAPRA standards, because products are not commercially available. Having opioid infusions available as ready-to-administer (RTA) products on nursing units is important for safe and timely administration of pain control. Paediatric patients require lower concentrations of opioid continuous infusions than adults and previous publications have demonstrated the stability of hydromorphone, but not at lower concentrations and not in syringes.

Objective: We sought to evaluate the chemical stability of lower concentrations of hydromorphone, prepared in syringes

Methods: On study day 0, 50mL solutions of 0.2mg/mL and 10mg/mL concentrations of hydromorphone were prepared in BD syringes. 3 units of each container and concentration were stored at room temperature. Concentration analysis was completed on study days 0,1,3,7,14,24, 38,51,78 and 90. Hydromorphone concentrations were determined by a validated stability-indicating liquid chromatographic method with UV detection. Chemical stability was based on the intersection of the lower limit of the 95% confidence interval of the observed degradation rate and the time to achieve 90% of the initial concentration.

Results: The analytical method separated degradation products from hydromorphone such that the concentration was measured specifically, accurately (deviations from known averaged 2.1%) and reproducibly (replicate error was less than 0.6%(CV(%)). During the study period all solutions retained more than 98% of the initial concentration. Analysis of variance revealed significant differences in percent remaining due to concentration ($p<0.001$), but not study day ($p=0.339$). The study was capable of detecting a 0.81% difference in concentration due to study day or concentration. The calculated beyond-use-date exceeded the 90-day study period for all concentrations.

Conclusions: We conclude that 10, 40 and 200mcg/mL solutions of hydromorphone diluted in saline and stored in BD polypropylene syringes are physically and chemically stable for at least 90 days at room temperature (23°C)

Atrial Fibrillation Patient Knowledge Gaps: A Systematic Review

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Background: Atrial fibrillation (AF) patients frequently do not adhere to their medication. Poor patient understanding of their disease has been associated with poor adherence. Identifying patients' knowledge gaps is the first step towards improving patient education strategies, adherence

and health outcomes. To date, there are no systematic reviews of AF patient knowledge gaps.

Objective: To characterize the published literature about AF patients' knowledge of their condition and medications, and to identify knowledge gaps.

Methods: Systematic review following PRISMA guidelines. We systematically searched PubMed, Embase, CINAHL and PSYCHINFO for quantitative and qualitative studies that measured people's knowledge about AF, stroke, rate/rhythm control and stroke prevention medications using "AF patient knowledge" and closely-related terms. Qualitative data was summarized narratively. We grouped quantitative data from related questions into "knowledge categories", calculating the median and IQR of the % correct responses for each category. A category with median ≤50% was classified as a "knowledge gap". Quality was assessed using standard design-specific quality of reporting appraisal instruments.

Results: We included 19 studies involving 4,582 participants, with 89% being of high quality. Less than half of the studied patients were aware that AF can be asymptomatic, can recur, or predispose to heart failure and stroke. Other knowledge gaps included: AF causes, symptoms, the rationale for oral anti-thrombotic (OAT) therapy, and OAT- related dietary restrictions. AF patients' knowledge of stroke signs/symptoms, and rate/rhythm medications could not be assessed due to paucity of data.

Conclusions: Majority of patients lack knowledge of AF causes, symptoms, risk of stroke, the rationale for anti-thrombotic therapy and drug and food interactions. Our results highlight the need for more widespread and better-quality patient education strategies.

A Feasibility Study: Implementing a Medication Adherence Contract in Kidney Transplant Recipients Followed by an Outpatient Transplant Clinic

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Background: Medication adherence contracts have been more effective in improving adherence compared to providing educational pamphlets, pillboxes and medication refill reminders alone.

Objectives: Primary objective was to determine patient enrollment. Secondary objectives investigated patient retention, time required for encounters, interventions by pharmacists, patient satisfaction, health care professional acceptability and perception of patient adherence to immunosuppressants.

Methods: Kidney transplant recipients transplanted within 0-6 months, followed by the Outpatient Transplant Clinic, with access to a telephone that could be communicated to in English were approached for consent. The Contract was administered in clinic or Inpatient Transplant unit using semi-structured discussions and reviewed in 3 to 9 weeks with patients via phone.

Results: Seventeen of 47 eligible patients (36%) were enrolled over 3.3 weeks in the clinic (n=11) and on the inpatient unit (n=6). Patient enrollment was 52% (17 of 33 patients) considering only 33 of 47 eligible patients were approached. Barriers to enrollment were back to back clinic appointments, lack of designated clinic space and prioritizing non-research related responsibilities during the last 1-2 weeks of data collection. Median time for administration and review of the Contract was 21 and 12 minutes respectively. Interventions provided include discussion of adherence tools (n=13); education on immunosuppressants (n=6), consequences of non-adherence (n=5) and anti-infective medications (n=4) as well as medication regimen simplification (n=5). Most patients found their encounters with pharmacists valuable (n=6) or extremely valuable (n=6). More than half of health care professionals were very likely to identify and refer patients that may benefit from a Medication Adherence Contract (n=8).

Conclusion: Medication Adherence Contracts are feasible in practice provided there is dedicated space and time for encounters. Majority of patients and professionals were satisfied with and accepting of the Contract respectively. This study provides recommendations for those considering adopting such contracts in practice.

An Emerging Challenge: Pharmacists' Ability to Counsel a Growing Immigrant Population

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Background: Counselling provided by pharmacists is a critical component for the safe and effective use of medications, which is particularly important given the serious consequences of errors. In the case of new international migrants, however, cultural barriers might be limiting pharmacists' ability to counsel effectively.

Objectives: The study aimed to identify: cultural factors noted in the literature to influence interactions between pharmacists and immigrants during counselling sessions; and potential solutions to cultural barriers in pharmacy counselling.

Methods: A scoping review was conducted, which consists of the following 5 stages: (1) identifying the research questions, (2) identifying the relevant studies, (3) identifying criteria for study selection, (4) charting the data, and (5) collating the results. The quality of selected studies was also assessed.

Results: Only 7 studies were found, but revealed 4 important factors: preconceived beliefs about drugs and healthcare, language barriers, use of informal interpreters, and nonverbal communication. Several solutions for reducing medication errors and increasing patient safety were also identified. One solution is to work towards achieving a certain level of understanding about ethnic minority patients. This involves increasing cultural sensitivity among pharmacists and learning about immigrant patients' culture and illness perception.

Conclusion: The literature is sparse, but confirms that assessment and redress of cultural disparities is important to improve medication use and the quality of encounters with patients of all cultural backgrounds.

Toxicology Education Needs of Emergency Department Pharmacists

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Background: Emergency department (ED) pharmacists are routinely consulted on the care of poisoned patients. Toxicology training varies by country and the learning needs of pharmacists have not been explored.

Objective: To survey and compare subjective toxicology knowledge and learning needs of ED pharmacists in Canada and the United States (US).

Methods: Pharmacists were surveyed via online emergency medicine speciality networks hosted by the Canadian Society of Hospital Pharmacy and American College of Clinical Pharmacy. Pharmacists rated their knowledge and interest for future learning regarding 29 toxicology topics using a 5-point Likert scale. Preferred learning formats were also surveyed. Paired T-tests were conducted to assess knowledge and interest differences between US and Canadian pharmacists.

Results: Two-hundred ED pharmacists (response rate 16%) responded to the survey. Pharmacists rated their knowledge highest on analgesics and communicating with poison centres. Chloroquine, metals and bioterrorism were rated as the least knowledgeable subjects. Pharmacists identified drugs of abuse, blood gas and ECG interpretation as the most desired topics for future learning. Respondents were least interested in learning to communicate with poison centres, and about chloroquine and theophylline poisonings. Webinars and podcasts were the preferred learning formats for pharmacists. Online discussion forums, YouTube videos and toxicology rotations were the least popular. US pharmacists consistently rated their knowledge higher than Canadian pharmacists (Mean Difference in Likert Scores 0.58, 95% CI: 0.48-0.69). No significant difference was noted in interest levels between the two groups.

Conclusions: Future education for ED pharmacists should focus on diagnostic assessment of the poisoned patient and drugs of abuse. Delivery should be in webinar format. Toxicology residencies and fellowships are available in the US and may reflect differences in knowledge assessment scores.

Implementation of an Overnight Pharmacist Model

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Background: The Pharmacy Department at a tertiary care academic centre initiated overnight pharmacist services in 2014 in response to computerized physician order entry.

Description: One of the hospital sites developed an overnight model in which 2 pharmacists rotate every 2 weeks through weeknight shifts (2230 to 0630 hours) and weekday clinical services to a surgical unit. The pharmacists cross cover each other for vacations. Comprehensive overnight services include order verification, therapeutic interventions and drug information. Daytime pharmacists are scheduled to cover weekend overnight services.

Action: After surveying 24 hour operations at select Ontario hospitals a site-specific model was created through a consensus process. The goal was to create a role that optimized professional satisfaction, recruitment and retention. This was accomplished by ensuring opportunities similar to those of daytime pharmacists with respect to direct patient care, education, teaching and research with comparable scheduling percentages for distribution and clinical time. Two pharmacists were recruited and intensively trained over 3 months.

Evaluation: During a weeknight shift the pharmacist on average verifies 500 medication orders for 650 patients, of which 25 are new admissions, thus alleviating the morning workload and alerting daytime pharmacists to patients needing prioritized pharmaceutical care. The pharmacists are clinically integrated into a surgical service, which previously had high pharmacist turnover, with excellent feedback regarding the consistent quality of service. Weekly discussions take place with the clinical practice leader regarding patient cases and role feedback. Job satisfaction and retention have been positive with approximate 3 year tenure for the current team. A third pharmacist has been successfully recruited into the role.

Implications: This successful service model, as evidenced from operational and clinical perspectives, can be used as a template for other hospitals seeking to implement or modify an overnight pharmacist role, particularly if retention has been challenging.

A Literature-Based Algorithm for the Assessment, Management and Monitoring of Drug-Induced QTc Prolongation in the Psychiatric Population

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Background: Certain psychotropics and a number of other medications used to treat medical conditions in psychiatric patients can increase the risk of prolonging the corrected QT (QTc) interval on the electrocardiogram which poses patients at risk of life-threatening ventricular arrhythmias such as *Torsades de Pointes*. Pharmacists are often consulted about medications which are known to prolong the QTc interval. Although this information is often accessible, advising how to identify, assess, manage and refer psychiatric patients at risk for drug-induced QTc prolongation is more challenging.

Objectives: The objective of this project was first to review the literature which describe guidelines and recommendations for the assessment and management of drug-induced QTc prolongation, and then to design an algorithm to be used by pharmacists working closely with mental health professionals or who provide care to psychiatric patients.

Methods: A review of the literature was undertaken. Predefined keywords were used to perform the database search in MEDLINE, EMBASE, and International Pharmaceutical Abstracts to identify reviews, reports and guidelines on the assessment, prevention or monitoring of drug-induced QTc prolongation emphasizing on psychotropic medications and management in the psychiatric population.

Results: A total of 560 relevant citations were retrieved from the electronic database search, of which a total of 22 relevant articles were selected. Of these, only 8 articles provided recommendations for the assessment and management of drug-induced QTc prolongation in psychiatric patients. Although the remainder 14 articles did not discuss strategies specifically for the psychiatric population, they were still reviewed and some relevant recommendations adapted in the development of the algorithm and related guide.

Conclusion: The literature-based algorithm developed provides a stepped based approach for the assessment, management and monitoring of drug-induced QTc prolongation in the psychiatric population. After this developmental phase, feedback on the algorithm and related guide by pharmacists will be undertaken.

Provincial Smart Pump Program Improves Patient Safety

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Background: The use of Dose Error Reduction Software to inform pump programmers of potential keystroke, entry errors or potentially harmful doses reduces patient harm. The creation of a single province-wide drug library ensures the same level of safety across the province and facilitates patient movement between sites.

Description: A multi-disciplinary team from all Regional Health Authorities and the Cancer Agency developed the drug library and implemented SMART pumps throughout the entire province. A provincial program team was created to: maintain and update the drug library, maintain provincial parenteral monographs, and report on regional and provincial use of smart pumps.

Action: Once the smart pump was implemented in all health regions, the Provincial Smart Pump Program was established to maintain, update and report on the use of smart pumps. A monthly drug library update cycle was established during the first year. Updates from the Program are delivered to regional servers where local staff update their smart pumps with the newest drug library.

Evaluation: Six percent of 2,351,379 program attempts created an alert; 2% of programs were edited based on the alert resulting in 46,213 program changes. Each program change may have avoided harm if infused as originally programmed. The 10 Medication lines were responsible for 34,699 alerts in 315,158 program attempts. Of these, 11,296 alerts resulted in a programming change.

Implications: Province-wide standardization of the drug library, medication preparation and parenteral monographs facilitates the safe transfer of patient throughout the continuum of care across the province without wastefully re-preparing infusions for local protocols. Work standards ensure regions continue to utilize the most current drug library. The Smart Pump Program evaluates the drug library and alerts, with feedback from users, for appropriateness. Reporting can highlight regional practice variation for investigation. Dose limit notifications reduce potential patient harm from infusions.

A Multi-Incident Analysis on Medication Incidents Associated with Patient Harm

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Background: Medication incidents associated with patient harm can either result in sub-optimal disease management or expose patients to unnecessary life-threatening situations, calling for attention to such incidents and the need to adopt strategies to improve overall patient and medication safety.

Description: The objective of this multi-incident analysis was to gain a deeper understanding of the possible contributing factors to incidents associated with patient harm, and to develop potential recommendations to prevent error recurrences.

Action: A total of 971 medication incidents associated with patient harm were extracted from a national incident reporting database from 2009 to 2017, with the subsequent performance of a qualitative and thematic analysis on 909 incidents that met the inclusion criteria.

Evaluation: Three main themes were identified from the multi-incident analysis, which included (1) high-risk processes in pharmacy practice, (2) communication gaps, and (3) preventable adverse drug reactions. Subthemes were further developed for each theme, which included (1) methadone maintenance therapy, (2) multi-medication compliance aids, and (3) compounding; (1) patient-provider engagement and (2) interprofessional collaboration; and lastly, (1) drug-drug interactions and (2) documented drug allergies.

Implications: Independent double checks can be considered as a gate-keeping strategy for high-risk processes that are involved in the medication-use system. Clear communication within the circle of care is crucial for safe and effective patient-centered care. Technology can serve as clinical decision support for healthcare practitioners in mitigating preventable adverse drug reactions. It is hoped that findings from this analysis and potential solutions presented can aid with the adoption of error reduction strategies and safe medication practices. Sharing lessons learned from medication incidents will contribute to overall patient and medication safety.

Insourcing High-Risk Sterile Compounded Injectables: Development of In-House Capacity to Produce High-Quality Injectables during the Sodium Bicarbonate Shortage

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Background: High-risk sterile compounding appears to have decreased considerably in recent years given perceived risk and regulatory/media attention. When commercial supplies are lacking and where alternatives are inadequate, Pharmacies need to weigh patient risk from lack of access against their ability to prepare a high quality compounded sterile product (CSP).

Description: Formulation of a CSP - Sodium Bicarbonate 8.4% Injection (SBI) was undertaken during disruption of commercial supply and used to develop the infrastructure to extend this capability to other future CSPs.

Action: Specifications utilizing USP were developed for our SBI formulation. Multiple test iterations were prepared until the desired elements were attained. A "Quality by Design" (QBD) approach was utilized in the formulation process which attempts to mitigate against foreseeable risk elements during production. Validation and testing of the finished product for endotoxin level and sterility were completed through an outside laboratory and in-house quality testing for particulates, pH, sodium and bicarbonate concentrations were completed for each batch.

Evaluation: Development of the SBI and the QBD approach required approximately 0.25 FTE each of Pharmacist and Pharmacy Technician time. Time to implementation of a patient-ready CSP was approximately 3 months from inception. Batch production quantity models for best economic return were developed based on expected monthly use and batch costs. The final SBI prepared lots met all USP specifications for Sodium/Bicarbonate content, pH, endotoxin levels and sterility.

Implications: By following a QBD approach, Pharmacies can prepare a high-quality injectable from raw non-sterile starting ingredients. Appropriate final product quality testing should be undertaken. Up-front investments and effort are required in order to safely develop the required resources for safe compounding, but enhances patient access to necessary products in the event of commercial supply disruption or inadequate therapeutic alternatives.

Coordinating a Response to a Critical Drug Shortage: Experience with Sodium Bicarbonate

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Background: In June 2017, a critical shortage of intravenous sodium bicarbonate occurred across Canada. Our health authority needed to act rapidly to ensure availability of a drug used in critically ill patients.

Description: Sodium bicarbonate as an intravenous solution is provided by a single supplier with important therapeutic value in critically ill patients. When production issues, compounded by a voluntary recall, rapidly depleted the stock on hand and hampered any ability to procure more, our heath authority faced a situation of having less than one week's stock on hand. At the time, usage patterns were approximately 2000 vials per week. No commercially produced or compounded product was available and Health Canada would not rapidly commit to allowing importation of foreign supply.

Action: Our senior pharmacy leadership team ran a virtual Emergency Operations Centre (EOC) to coordinate efforts across our sites and report up to senior organizational leadership. EOC members met with clinical stakeholders to determine restrictions on sodium bicarbonate use, coordinated communication to all sites and impacted departments, validated and tested a recipe for compounding, worked out a process for sterile filtration of potentially contaminated product, and worked with senior organizational leadership to prioritize the various strategies developed to manage the crisis.

Evaluation: Weekly stock counts and utilization reporting at all sites demonstrated that restricting product use resulted in an approximate 75% reduction in overall consumption. This rate was maintained for the duration of the shortage and may point to potential ongoing cost savings. Follow-up with clinical stakeholders suggested minimal negative patient impact from the restrictions.

Implications: By leveraging our central governance and coordination efforts, our pharmacy team was able to overt a potentially critical situation. Lessons learned for future shortages include exploration of our internal compounding resources and ability to identify inappropriate use of drugs in our health authority.

Development and Implementation of a Mobile Antimicrobial Handbook App at a Tertiary Teaching Hospital

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Background: Institutional antimicrobial guidelines were previously available as printed and electronic format handbooks. With the ever increasing use of technology to improve direct patient care, our hospital's Antimicrobial Stewardship Team (AST) recognized the need to optimize the accessibility and usability of our current guidelines.

Description: In June 2015, our AST began developing an Antimicrobial Handbook app for mobile devices and desktop computers. This electronic tool includes treatment and prophylaxis guidelines, annual hospital antibiograms, renal dosing guidelines, and safety guidelines for pregnancy and breastfeeding.

Action: The mobile site was launched in November 2015, and promoted to pharmacists and physicians at our institution and other practice sites. The app content and format are continuously reviewed and updated based on advances in clinical evidence and feedback from its users. Quantitative user data is electronically provided monthly from Google Analytics Solutions.

Evaluation: Between January 1, 2017 and June 30, 2017, there have been over 10,000 page views of our app, by over 2,000 unique users. There has been a 73% increase in usage, with an average of 1,720 visits per month to the homepage in 2017, compared to 995 visits per month in 2016. Similarly, the number of total users and new users has increased by 100% and 84%, respectively. The majority of our users are located in the Greater Toronto Area (75%), but our app also has frequent users from Hamilton, Ottawa, Montreal, and other Canadian cities. The most visited sections are the treatment guidelines (37%), antimicrobials (27%), and renal dosing guidelines (14%).

Implications: The Antimicrobial Handbook app is an extremely innovative tool that has provided widespread access to clinically relevant information, enabled efficient information updates, and allowed for timely, accurate evaluation to assess the need for ongoing modifications. Evaluation of the clinical impact of this app on antimicrobial prescribing practices is planned.

Retrospective Multicentre Cohort Study Comparing Safety and Efficacy Outcomes with Intermittent Infusion versus Continuous Infusion Vancomycin

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Background: Patients with good renal function receiving intermittent infusion vancomycin (IIV) may require total daily doses ≥4g to achieve trough concentrations of 15-20mg/L, increasing the risk of vancomycin associated nephrotoxicity (VAN). Continuous infusion vancomycin (CIV) may enable attainment of concentrations between 15-20mg/L with a lower daily vancomycin dose, potentially reducing the risk of VAN.

Objectives: The primary objective was to compare VAN risk (serum creatinine (sCr) increase ≥50% from baseline) and renal damage (sCr increase ≥100% from baseline) in patients receiving IIV versus CIV. The secondary objective was to compare clinical cure between IIV and CIV in patients who achieved vancomycin trough or steady state concentrations of ≥15mg/L, respectively.

Methods: Retrospective chart reviews for eligible patients admitted to Sunnybrook Health Sciences Centre or Holland Orthopaedic and Arthritic Centre between January 1, 2010 and December 31, 2016 were completed. Adult inpatients who received at least 48 hours vancomycin for a documented gram positive infection and had at least one steady state vancomycin concentration were eligible. Baseline patient characteristics, safety and efficacy outcomes for the IIV and CIV cohorts were compared using appropriate statistical tests (Fisher's exact, Student's t-test, or Mann-Whitney), with significance defined as $P<0.05$.

Results: Of 2134 patients identified, 1104 (52%) met inclusion criteria. Chart review has been completed for 89 patients (113 courses of vancomycin). Patients receiving courses of IIV were more likely to be at risk of VAN (15/62 [24.2%] versus 4/51[7.8%]; P=0.02) and experience renal damage (9/62 [14.5%] versus 1/51 [2.0%]; P=0.02). There was no difference in clinical cure between IIV (19/27 [70.4%]) and CIV patients (13/17 [76.5%]; P=0.74).

Conclusion: Patients in the IIV cohort were more likely to experience increases in sCr resulting in VAN risk and renal damage. The results indicate there is no difference in clinical cure between patients who received IIV versus CIV.

Evaluation of Dosing Strategies with Meropenem using Monte Carlo Simulations against Bacteria with Raised MIC

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Background: The worldwide increased prevalence of gram negative bacterial (GNB) resistance coupled with few therapeutically appropriate available antibiotics (TAAAs) necessitates evaluation of dosing strategies to optimize the use of TAAAs against more resistant pathogens. Burn patients are a unique population, having altered pharmacokinetics for many antibiotics and high risk of infection with resistant GNB, to add increased complexity to their care.

Objective: The objective of this study was to identify optimal dosing of meropenem in burn patients using pharmacokinetic and pharmacodynamic (PK-PD) targets for meropenem against bacteria with an elevated minimum inhibitory concentration (MIC).

Methods: Weighted mean pharmacokinetic parameters for meropenem in burn patients and healthy volunteers were determined from the published literature. Monte Carlo simulations (MCS) with 1,000,000 iterations were completed to determine the probability of target attainment (PTA) for several intermittent infusion (IIV) and continuous infusion (CIV) meropenem dosing regimens using weighted mean pharmacokinetic parameters and MICs ranging from 0.5 to 32 *mg/L* for burn patients and healthy subjects (HS). PK-PD targets evaluated were % time above MIC (%T>MIC) of 30%, 50% and 80%.

Results: Compared to HS, burn patients had an increased meropenem volume of distribution (V), and decreased elimination rate constant (k), resulting in a calculated clearance (Cl) that was comparable to HS (Cl=kV). PTA in burn patients was different than in HS with different meropenem dosing regimens due to differences in V and k between these patient populations. At higher MICs, CIV regimens had a better PTA than IIV in HS and burn patients. Both meropenem CIV 1g IV q4h and 2g IV q8h provided optimal PTA with a high MIC of up to 8mg/L.

Conclusion: In burn patients with resistant GNB up to an MIC of 8mg/L, the optimal PTA is achieved with continuous infusion meropenem of 1g IV q4h or 2g IV q8h.

Development of an HIV National Clinical Observership Program for Pharmacists

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Background: Pharmacists play a significant role in optimizing care for HIV patients, managing challenges of adherence, resistance, comorbidities, polypharmacy and drug interactions. HIV residency programs or electives provide specialized training but may not be ideal for practicing pharmacists. A national observership program was developed to meet the learning needs of working pharmacists.

Description: The observership program was launched in 2017 by a national network of HIV pharmacists. Program objectives were to improve pharmacists' confidence in HIV therapy management, to increase awareness of different practice sites and subspecialties, and to promote collaboration. All pharmacists wishing to gain clinical experience or specialized knowledge through shadowing/teaching with another HIV pharmacist were eligible to apply. Observerships of 1 to 5 days in duration were offered.

Action: A working group developed terms of reference and application criteria. Funding was secured for one year via an unrestricted industry educational grant. Calls for applications were issued through the network, with priority given to new practitioners or those from rural/ underserviced areas.

Evaluation: To date, 4 observerships have been completed with all participants completing surveys on their experience. On average, observers had worked for 4 years, with less than 6 months of experience providing HIV care in a hospital (50%) or clinic/community (50%) setting; 75% were practicing in a small urban centre. Overall, pharmacists found the observership to be extremely beneficial, and resulted in increased confidence in therapeutic knowledge and ability to provide care and enhanced professional networking with potential for future collaboration. All preceptors felt the workload was reasonable and were willing to offer future observerships.

Implications: A national clinical observership program has been successful in providing learning and mentorship opportunities for HIV pharmacists. Continued program funding is being pursued. This program may serve as a model for implementation in other countries or in other therapeutic areas.

An Innovative In-House Developed Access® Database to Capture and Analyze Antimicrobial Stewardship Interventions

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Background: Antimicrobial stewardship programs are responsible for optimizing use of antimicrobials. Our program focuses on reviewing antimicrobials on Day 3. Infectious disease physician and pharmacist are responsible to review antimicrobials on clinical care areas. We utilize a Meditech system, which provides antimicrobial utilization data; however, it is currently not used to capture patient-specific antimicrobial stewardship interventions. It is imperative to capture these interventions and analyze them to improve the program and patient outcomes.

Description: We developed an in-house database using Microsoft Access® to capture antimicrobial stewardship interventions at the patient-specific level. The database captures information under 3-categories: patient, visit, and intervention as shown below.

Action: For the image that goes with the "Action" section of this abstract, please see Abstract Appendix, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/125/showToc

Evaluation: We evaluated 6-months of data from September 2016 - February 2017. We were able to categorized types of interventions by frequency and identify which clinical care areas had the highest number of interventions. We found that the majority of IV-to-PO conversions were from piperacillin/tazobactam to amoxicillin-clavulanate. Meropenem to ertapenem was the leading IV-to-IV conversion. It took about 3-3.5

days to convert from either IV-to-PO or IV-to-IV. Piperacillin/tazobactam was the leading antimicrobial for dose optimization. Finally, we were able to demonstrate saving of $15,000 in direct antimicrobial costs during the first 6-months.

Implications: The database allows us to capture and analyze stewardship patient-specific interventions, which can be used to improve the program and share results with stakeholders. We can also utilize the database to calculate cost savings, acceptance rates, and benchmark physicians among peers.

Performance of an Innovative Patient Decision Aid for Atrial Fibrillation Stroke Prevention Therapy

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Background: Choosing stroke prevention therapy in atrial fibrillation (SPAF) is complicated because it requires patients to make trade-offs and individual patient preferences are unpredictable. Misalignment between prescribed therapy and patient preferences is associated with poor therapy adherence and persistence and SPAF failure. To help address this misalignment, we have developed a unique online decision aid (DA), SPARC-DT, which integrates patients' stroke and bleeding risk, their values and preferences for key therapy attributes, and best evidence to identify which options are best matched with their preferences. Using SPARC-DT could be a basis for shared decision-making (SDM).

Objective: To evaluate the performance of SPARC-DT in patients with AF or at risk of AF.

Methods: Design: Prospective observational study. Participants were AF patients or patients at risk of AF based on age>50 y/o recruited from AF clinics and community centers. Consenting participants completed a pre-DA questionnaire, the SPARC-DT decision aid, and a post-DA questionnaire, either self-guided or by study personnel based on participant preference. Study outcomes were pre- vs. post-SPARC-DT AF knowledge assessment (AFKA), decisional conflict scale (DCS), System Usability Scale (SUS), and qualitative user feedback.

Results: 38 patients (mean age 71) completed the study. Using SPARC-DT improved AFKA scores (7.93 vs. 8.61/10; p=0.02), reduced overall decisional conflict (DCS Δ -21/100; p<0.01), and improved all DCS subscales (all p<0.05). Those "unsure" about their preferred therapy was reduced by 50%. On the SUS and from qualitative feedback, most participants found SPARC-DT easy to use and learn, expressed willingness to use and confidence in using it, and found it to be well integrated.

Conclusion: SPARCT-DT performed well on all conventional measures of decision aid performance, reducing decisional conflict, increasing knowledge, and was deemed highly usable by participants. With refinement, SPARC-DT could be a valuable facilitator of SDM.

Novel Student-Preceptor Models in Pharmacy Education: A Qualitative Analysis of the PharmD Student Experience

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Background: Experiential rotation requirements in the Entry-to-Practice PharmD program have increased. To accommodate significantly more pharmacy learners on-site, institutions have explored novel student-preceptor teaching models. These include peer-assisted-learning (PAL; 2 or more students of same educational level), near-peer-teaching (NPT; 1 or more junior students with 1 or more senior students), and co-preceptorship (CoP; 2 or more preceptors).

Objective: To describe students' experiences and perceptions of novel teaching models and evaluate the effectiveness of these models on students' learning using Kirkpatrick's levels.

Methods: Pharmacy students from the class of 2015, 2016, and 2017 were invited to participate in semi-structure interviews. Interviews were transcribed, coded, and analyzed for themes. Themes were mapped according to the Kirkpatrick model for appraising educational training.

Results: Twenty semi-structured interviews were conducted with 10 pharmacy students from the class of 2017, and 5 each from the classes of 2016 and 2015. Forty-three experiences (19 CoP, 14 PAL, 10 NPT) were described from 14 institutions. Many themes overlapped between the three novel teaching models. In CoP, students described increased preceptor availability and exposure to different patient care approaches. Challenges arose when preceptors had different student expectations. Students overwhelmingly endorsed a multi-learner environment. Both PAL and NPT students felt well supported as collaboration with other learners was readily fostered. Potential challenges in PAL and NPT included student competitiveness and difficulties when personalities conflicted. All three models allowed for the development of skills including communication, collaboration, and teamwork. Because of their experiences, students reported an improvement in their approach to patient care. They also described a positive impact on their professional practice and approaches to teaching as new preceptors.

Conclusion: Pharmacy students enjoyed their experiences in novel student-preceptor models. These opportunities had a positive impact on overall learning during the rotations and as new practitioners.

Evaluation of Physical Assessment Education for Practicing Pharmacists: A Cross-Sectional Study

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Background: Pharmacists are now seeking to incorporate physical assessment (PA) into their practice. This prompted the creation of a 30-hour PA course for practicing pharmacists developed by a Canadian Society of Hospital Pharmacists branch.

Objectives: To evaluate pharmacists' knowledge, skills, and confidence with performing PA after completion of the course.

Methods: We invited all course participants via email to complete online surveys immediately and 6 months after completion of the course.

Results: Of 218 pharmacists who completed the course, 102 (46.8%) completed the immediate post-course survey. Two-thirds of respondents did not use PA in their practice prior to the course. A lack of formal training and comfort were the most frequently selected barriers to performing PA prior to the course. All participants agreed the course improved their knowledge of PA and 96% agreed it improved their skills. Most respondents (90%) agreed the course improved their ability to care for patients. After the course, 60% and 67%, respectively, agreed they felt confident performing PA or intervening on a patient's drug therapy based on their PA findings. The most common suggestion for course improvement was more hands-on practice. Twenty-five of 158 eligible participants (15.8%) completed the 6-month post-course survey, of which 79% had performed PA in practice. Only 60% agreed they felt confident performing PA, whereas 84% now agreed they would intervene on a patient's drug therapy based on their PA findings. The most frequently selected barrier to performing PA was now lack of time. The primary limitation of this study was potential responder bias.

Conclusions: The course improved pharmacists' knowledge and skills with performing PA. Six months after the course, most respondents used PA in practice. While the proportion of participants that felt confident performing PA had not increased, more were willing to use their PA findings to change drug therapy.

International Normalized Ratio Point of Care Testing in an Outpatient Anticoagulation Clinic and the Impact on the Patient Experience: A Quality Improvement Study

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Background: Patients who are receiving warfarin therapy require ongoing blood testing to monitor their international normalized ratio (INR). In Canada, the standard for INR testing is by laboratory venipuncture. Point-of-care testing (POCT) is an alternative method, and previous studies have shown that it may enhance patient convenience and comfort. However, there is little information on the impact of INR POCT on the patient experience in a pharmacist-led, outpatient anticoagulation clinic.

Objective: To evaluate how the implementation of an INR POCT device for the initiation and stabilization of warfarin therapy in a pharmacist-led, outpatient anticoagulation clinic impacts the patient experience compared to laboratory testing.

Methods: We performed a prospective, before-and-after, quality improvement study of patients attending an outpatient anticoagulation clinic in Victoria BC, Canada. Using an anonymous patient survey, we evaluated outcomes measured before and after the implementation of an INR POCT device. Outcomes included patient time spent and number of visits to the hospital for anticoagulation-related care in one day, patient satisfaction with their blood testing experience, cost to patient, missed activities, and pain and discomfort. A one-month cost analysis was completed to compare health care cost of INR POCT and laboratory testing.

Results: Fifty-eight patients completed the survey. Patients undergoing POCT spent less time receiving anticoagulation-related care compared to laboratory testing (59.7 min vs 144.5 min; $p<0.05$). Using a 10-point scale to quantify satisfaction with their blood testing experience, patients expressed higher satisfaction with POCT (9.6 vs. 7.8; $p=0.001$). There were no differences in number of visits to the hospital, cost to patient, missed activities, or patient pain and discomfort. Health care cost was similar for both testing strategies when comparing one month of testing.

Conclusions: Our findings support the continued use of INR POCT for the initiation and stabilization of warfarin therapy in a pharmacist-led, outpatient anticoagulation clinic.

Case Report: Fatal Arrhythmia in a Patient Receiving an Aconite Herbal Product

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Background: Aconite is commonly used in traditional Chinese medicine. Aconite poisoning can lead to serious cardiac toxicity such as ventricular arrhythmias.

Case Description: A 44 year old male was found unconscious for an unknown duration. His rhythm showed ventricular tachycardia and fibrillation, requiring defibrillation and an amiodarone infusion. Arrhythmias subsided after 24 hours, however brain imaging was consistent with brain death. The family noted that he had ingested a large quantity of an herbal medication "Aconite". The patient had previously been boiling the medication prior to ingestion, but on the morning of presentation, he consumed a large handful without boiling.

Assessment of Causality: Based on the Naranjo scale, there is a "probable" chance of an adverse drug reaction (total score 6):
There are previous reports on this reaction (+1)
The event appeared after administration (+2)
There are no alternative causes that could have on their own caused the reaction (+2)
The reaction was confirmed by objective evidence (+1)

Literature Review: Aconite poisoning has been well documented in the Chinese literature. Patients may present with gastrointestinal (nausea and vomiting), neurologic (paresthesias), and cardiac symptoms (arrhythmias). Cardiac toxicity is thought to be related to the binding of fast voltage gated sodium channels, resulting in persistent depolarization. Processing (boiling) is recommended to hydrolyze the contents into less toxic derivatives. Amiodarone and flecainide have been used with some success, but no single agent have been shown to be of consistent benefit.

Importance to Practitioners: This case report is unique as it describes a fatal arrhythmia after ingestion of an herbal medication. With the increasing use of herbal products and the prevalence of Chinese immigrants in Canada, pharmacists can play an important role in identifying and assessing their potential harmful effects.

A Survey of the Use of Cannabis in Children at a Tertiary Teaching Hospital

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Background: There has recently been an increase use of cannabis for medical purposes in the pediatric population. However, limited data on the efficacy and safety of cannabis in children has been published. A comprehensive characterization of cannabis use in this population can further contribute to a better understanding under which circumstances cannabis is being used and the observed outcomes.

Objectives: To perform a retrospective drug use evaluation to describe all inpatient and outpatient medical uses of cannabis in a tertiary teaching hospital over the last 3 years.

Methods: A retrospective medical record review was completed of inpatients and outpatients <18 years of age prescribed medical cannabis between May 1st, 2014 and May 1st, 2017. Patients using cannabis recreationally were excluded.

Results: There were a total of 300 unique patients identified and 37 children were included in this study. Of these, 30 patients were using medical cannabis and most were using it for seizures (93%) where 82% were described as having intractable/ refractory seizures. Among these, 78% reported a decrease in seizures and of those 76% had a transient effect where a decrease was noted for 130.38 days (±99.14), but then seizures increased once again. Additionally, a subgroup of 7 patients were self-medicating with cannabis. They obtained cannabis without proper authorization as a dried flower and were using it for chronic pain (71%) and/or anxiety (71%).

Conclusions: Cannabis use is reported more often for childhood refractory epilepsy compared to other chronic conditions. The use of cannabis in children with medication-refractory epilepsy may be warranted after trying first line anticonvulsant medications and after discussing non-pharmacological options. Based on our data, decrease in seizures may only be transient.

Current Identification and Management Practices of Steroid-Induced Hyperglycemia in Brain and Spinal Tumour Patients on a Neurosurgical Unit

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Background: Brain and spinal tumor (BST) patients often receive dexamethasone to alleviate neurological symptoms. Steroid-induced hyperglycemia (SIH) has been reported in 5-72% of Brain tumour patients. Hyperglycemia has been associated with worsened clinical outcomes, including shortened survival in brain tumour patients. We hypothesize that a gap exists in identifying and managing SIH in BST patients at our institution.

Objectives: We aim to describe the current identification and management practices of SIH in BST patients at our institution.

Methods: A retrospective chart review of adult BST patients admitted to the neurosurgical unit at a tertiary care hospital between January and December 2016, and received dexamethasone as well as diabetic medication(s), was performed. The primary endpoints included the average proportion of blood glucose (BG) readings above 10 mmol/L per admission and the percentage of patients with: 1) BG monitoring for 48 hours after dexamethasone start; 2) incidences of hypoglycemia; 3) a start on corrective insulin scale for initial glycemic control; 4) an appropriate corrective insulin scale; 5) "STAT" dose of insulin; 6) change(s) to diabetic medication(s) at discharge; and 7) endocrine or medicine consult

Results: Thirty-six patients over 41 admissions were reviewed. The primary endpoints were: 61.7% was the average proportion of BG readings above 10mmol/L, 92.7% of patients had BG monitoring for 48 hours after dexamethasone start, 4 incidences of hypoglycemia, 56% started on corrective insulin scale for initial glycemic control, 43.9% received appropriate corrective insulin scale, 26.8% received "STAT" dose insulin, 74% had change(s) to diabetic medication(s) at discharge, and 36.5 % had endocrine or medicine consult.

Conclusion: While screening for SIH seems reasonable, the management of SIH at our institution appears to be sub-optimal and highly variable. These results will enable us to design a quality improvement project that optimizes SIH identification and management in BST patients.

Clonidine for Sedation in Critically Ill Adults: A Retrospective Chart Review

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Background: The alpha2 agonist clonidine may be used as an adjunct for Intensive Care Unit (ICU) sedation and analgesia to decrease traditional sedative and opioid requirements. However, use has been associated with hypotension and bradycardia.

Objectives: 1) To describe clonidine dosing regimens used for sedation in a mixed medical surgical ICU, as well as adverse events associated with use (i.e., hypotension, bradycardia, rebound withdrawal), and 2) to determine if clonidine has sparing effects on traditional drugs used for pain, sedation and agitation.

Methods: We conducted a retrospective chart review of all critically ill adult patients admitted who had received at least one dose of clonidine for sedation during a five-year study period. Patients were categorized for the analysis into low dose (LD ≤ 0.4 mg/day) versus high dose (HD > 0.4 mg/day) based on the maximum total daily clonidine dose. Data was analyzed using the Mann Whitney U test and Chi squared test for continuous and binary variables, respectively. A p value < 0.05 was considered statistically significant.

Results: Of the 166 patients that met inclusion criteria, seventy-eight patients (47%) had clonidine titrated to HD. There were no statistically significant differences in hypotension, bradycardia or withdrawal symptoms between the LD and HD clonidine groups. There was a greater reduction in mean daily opioid dose for HD clonidine versus LD (mean -218.8 mcg vs. -42.5 mcg of fentanyl equivalents, p = 0.049). The decrease in sedative usage post-clonidine initiation was not significant. Antipsychotic doses increased for HD compared to LD (5.7 mg olanzapine equivalents vs 0 mg, p = 0.04).

Conclusions: Clonidine doses titrated beyond 0.4 mg/day may decrease patients' opioid but not sedative requirements without causing statistically significant adverse effects. Antipsychotic doses increased as clonidine was titrated.

The Effect of Preoperative Cannabis Use on Opioid Consumption Following Surgery: A Cohort Analysis

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Background: Anecdotally, healthcare professionals on the Acute Pain Service have observed that individuals consuming cannabis preoperatively had higher opioid requirements in the postoperative period.

Objective: This study examined whether preoperative cannabis use impacted opioid consumption in the first 24 postoperative hours, in individuals undergoing abdominal surgery for inflammatory bowel disease (IBD).

Methods: We conducted a chart review of patients who underwent surgery for IBD at a tertiary, university affiliated hospital between January 2014 and December 2015. Patients were excluded if they used methadone preoperatively, used synthetic forms of delta-9-tetrahydrocannabinol preoperatively or received neuraxial analgesia. Demographic data, cannabis use, as well as data on perioperative analgesia was collected. Linear regression analysis was used to correct for potential confounding factors in order to compare the opioid consumption in the first 24 hours postoperatively between cannabis users (C) and non-users (NC).

Results: Of the 354 charts included, 42 (11.9%) were classified in the C group and 312 (88.1%) in the NC group. The C group was significantly ($p<0.05$) younger, with a higher percentage of males but did not differ with respect to type of surgery, length of surgery, preoperative opioid use or intraoperative opioid use compared with the NC group. Linear regression analysis demonstrated an increase in postoperative opioid consumption proportional to the amount of cannabis consumed preoperatively. The cannabis group required an additional 1.13 mg (95% CI: 1.02-1.25) morphine equivalent per gram of daily cannabis used ($p=0.015$).

Conclusions: Our results demonstrated that cannabis use increased the postoperative opioid consumption in patients undergoing IBD surgery. This could influence postoperative pain management and increase the risk of opioid side effects. Future prospective studies should expand beyond the IBD population and look at the role of synthetic cannabinoids as adjuncts for pain management.

Stability of Extemporaneously-Compounded Temozolomide 10 mg/mL Suspension in Oral Mix SF in Glass and Plastic Bottles and Plastic Syringes

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Background: Temozolomide oral suspension is not commercially available. Colour changes and crystal formation have been observed with previously published extemporaneous temozolomide suspension formulations.

Objective: To evaluate the stability of 3 temozolomide 10mg/mL suspensions prepared in Oral Mix SF stored in 3 types of containers (amber glass, amber polyethylene terephthalate (PET) and polypropylene oral syringes) at 4°C and 25°C.

Methods: Three separate batches of 3 different formulations in Oral Mix SF with (i) povidone K-30; (ii) povidone K-30 and citric acid and (iii) neither povidone K-30 nor citric acid were made and were stored in 3 container types (amber glass, amber PET and oral syringes). Half of the aliquots in each container type was stored at 25°C, the other half at 4°C, protected from light. On study days 0, 5, 8, 14, 21, 28, 35, 42, 56, physical stability was assessed and the temozolomide concentration was determined using a stability-indicating method for samples drawn from each container type stored at each temperature. Chemical stability was based on the intersection of the lower limit of the 95% confidence interval (CI) of the observed degradation rate and the time to achieve 90% of the initial concentration (T-90[95%]).

Results: The stability-indicating analytical method was accurate (deviation <1.5%) and reproducible (CV%<1.5%). Samples stored at 25°C turned from white to orange. Temozolomide concentrations in all refrigerated samples in all container types remained above 90% of the initial concentration for 56-days, resulting in a T-90[95%] exceeding 56-days. Analysis of variance demonstrated changes in concentration due to study day and temperature ($p<0.001$) but not container ($p=0.991$) or formulation ($p=0.987$).

Conclusions: Temozolomide 10mg/mL oral suspension in Oral Mix SF with and without povidone K-30 or citric acid was chemically stable when stored at 4°C and 25°C in in glass, PET, or oral syringes for 56 and 6-days, respectively.

Stability of 20, 40 and 50 mcg/mL Fentanyl Solutions Stored in Syringes at Room Temperature (23°C)

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Background: Inpatient hospital pharmacies must compound intravenous products and assign an appropriate beyond-use-date (BUD) as per NAPRA standards, because products are not commercially available. Furthermore, having medications in a Ready-To-Administer format on nursing units is important for safe and timely administration. Paediatric patients require lower concentrations of opioid continuous infusions than adults and while previous publications have demonstrated the stability of fentanyl, data for lower concentrations stored in syringes is not available.

Objective: We sought to evaluate the chemical stability fentanyl, prepared in syringes.

Methods: On study day 0, 50mL solutions of 20mcg/mL, 40mcg/mL and 50mcg/mL concentrations of fentanyl were prepared in BD syringes. 3 units of each container and concentration were stored at room temperature. Concentration analysis was completed on study days 0,1,3,7,14,24,38,57,77 and 90. Fentanyl concentrations were determined by a validated stability-indicating liquid chromatographic method with UV detection. Chemical stability was based on the intersection of the lower limit of the 95% confidence interval of the observed degradation rate and the time to achieve 90% of the initial concentration.

Results: The analytical method separated degradation products from fentanyl such that the concentration was measured specifically, accurately (deviations from known averaged 2.5%) and reproducibly (replicate error was less than 1.4%(CV(%)). During the study period all solutions retained more than 96.7% of the initial concentration. Analysis of variance revealed significant differences in percent remaining due to concentration ($p< 0.001$), and study day ($p< 0.001$) although the study was capable of detecting less than a 0.51% difference in percent remaining. The calculated beyond-use-date was greater than 235days, exceeding the 90-day study period for all concentrations.

Conclusions: We conclude that 20 and 40mcg/mL solutions of fentanyl diluted in saline and 50mcg/mL undiluted solutions of fentanyl, stored in polypropylene BD syringes are physically and chemically stable for 90 days at room temperature (23°C).

Stability of Generic Formulations of Bortezomib 1.0 and 2.5 mg/mL in Vials and Syringes Stored 4°C and Room Temperature (23°C)

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Background: Generic versions of bortezomib raise questions about the reliability of extending stability study data from brand to brand.

Objective: To evaluate the stability of Janssen, Teva, Actavis and Dr.Reddy's bortezomib formulations reconstituted to produce either 1.0 or 2.5mg/mL, during storage over at least 21-days at room temperature (23°C), and under refrigeration (4°C) in plastic syringes and manufacturer vials.

Methods: On study day 0, 2.5mg/mL and 1.0mg/mL concentrations of the Janssen, Teva, Actavis and Dr.Reddy's formulations were prepared. Three units of each container were stored at 23°C and 3 at 4°C. Concentration and physical inspection were completed on at least 8-study days over a 21-42 day study period. Bortezomib concentrations were determined by a validated stability-indicating liquid chromatographic method with UV detection. The end point of these studies is the time to achieve 90% of the initial concentration (T-90). This was completed with confidence determining the intersection of the lower limit of the 95% confidence interval of the observed degradation rate and 90% of the initial concentration (T-90[95%]).

Results: The analytical method separated degradation products from bortezomib during all studies such that the concentration was measured specifically, accurately (deviations less than 2.5%) and reproducibly (replicate error averaged 2.5%). During all studies, all solutions retained more than 94% of the initial concentration. The T-90[95%] exceeded the study period for all formulations at all temperatures, concentrations and container combinations. Analysis of variance failed to detect significant differences between manufacturers (p=0.970).

Conclusions: We conclude that formulations of bortezomib currently marketed in Canada by Janssen, Teva, Actavis or Dr.Reddy's, reconstituted with 1.4mL or 3.5mL of 0.9% sodium chloride to create solutions containing 2.5mg/mL or 1.0mg/mL, respectively, are physically and chemically stable for more than 21-days at 4°C or 23°C in both syringes and the manufacturer's glass vial.

Stability of 4 and 10 mcg/mL Remifentanil Solutions Stored in Syringes at Room Temperature (23°C)

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Background: Inpatient hospital pharmacies must compound intravenous products and assign an appropriate beyond-use-date (BUD) as per NAPRA standards, because products are not commercially available. Furthermore, having medications in a Ready-To-Administer format on nursing units is important for safe and timely administration. Paediatric patients require lower concentrations of opioid continuous infusions than adults and while previous publications have demonstrated the stability of remifentanil, data for lower concentrations stored in syringes is not available.

Objective: We sought to evaluate the chemical stability remifentanil, prepared in syringes.

Methods: On study day 0, 5mL solutions of 4mcg/mL and 10mcg/mL concentrations of remifentanil were prepared in 5mL BD syringes. 3 units of each container and concentration were stored at room temperature. Concentration analysis was completed on study days 0,1,3,7,14,24, 38,56,76 and 90. Remifentanil concentrations were determined by a validated stability-indicating liquid chromatographic method with UV detection. Chemical stability was based on the intersection of the lower limit of the 95% confidence interval of the observed degradation rate and the time to achieve 90% of the initial concentration (T-90).

Results: The analytical method separated degradation products from remifentanil such that the concentration was measured specifically, accurately (deviations from known averaged 2.65%) and reproducibly (replicate error averaged 0.82%(CV(%)). During the study period all solutions retained more than 96.96% of the initial concentration. Analysis of variance revealed significant differences in percent remaining due to study day ($p= 0.002$) but not concentration ($p= 0.203$). The study was capable of detecting a difference of more than a 0.76%. The difference due to concentration was less than 0.5%. The calculated T-90, with 95% confidence, exceeded 156 days for both concentrations.

Conclusions: We conclude that 4 and 10mcg/mL solutions of remifentanil diluted in saline stored in polypropylene BD syringes are physically and chemically stable for 90 days at room temperature (23°C).

Satisfaction des établissements de santé suite à la mise en place d'une plateforme web de surveillance environnementale

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Contexte : Une étude annuelle de surveillance environnementale de traces de médicaments dangereux est menée au Canada depuis 2008 auprès des établissements de santé participant. Jusqu'à maintenant, la communication des rapports individualisés se faisaient par courriel.

Objectif : Évaluer la satisfaction des établissements de santé à la mise en place d'une plate-forme web contenant le rapport surveillance environnementale.

Méthodologie: Étude descriptive transversale. Une plate-forme web sur un serveur Linux (PHP) a été développée avec une base de données MySQL sur un domaine sécurisé par une connexion SSL (HTTPS). La plate-forme inclut les données actuelles et historiques de tous les établisse-

ments et permet l'affichage et l'impression en temps réel des données d'un établissement comparées aux données agrégées de tous les établissements. La personne contact de chaque établissement a été invitée à répondre à un questionnaire en ligne (14 questions) visant à évaluer leur satisfaction.

Résultats : La plate-forme a été lancée le 1er octobre 2017 auprès des 83 établissements ayant participé à l'étude 2017. Quarante-trois répondants (taux de participation de 51,8%) ont complété le sondage. Quinze répondants (35%) avaient plus de 15 civières en oncologie. Trente (70%) ont participé à plus de deux études jusqu'à maintenant. Quarante-et-un (95%) ont dit préféré avoir un accès en ligne en temps réel par rapport aux rapports papier, 43 (100%) se sont dit satisfaits de la présentation visuelle des données et 38 (88%) ont apprécié le format d'impression. Douze (28%) ont rencontré des difficultés d'accès au départ compte tenu de la nécessité de recopier un hyperlien et de blocages liés à certains pare-feu. Ces problèmes ont été résolus.

Conclusion : Cette étude décrit le déploiement réussi d'une plateforme web d'accès aux rapports de surveillance environnementale. Cet accès facilité pourrait encourager le partage des données avec les équipes de chaque établissement.

Medication Fluids in the Intensive Care Unit

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Background: Fluid administration is essential to the care of critically ill patients; however fluid overload is associated with increased morbidity and mortality. Strategies to reduce fluid administration in this patient population must consider the contribution of medications, but this has not been well characterized.

Objectives: Our primary objective was to determine the contribution of medications to overall fluid administered in the intensive care unit (ICU). Secondary objectives include describing how fluid administration changes over time, and whether medication fluid volume can be reduced.

Methods: This retrospective observational study included patients admitted for >24h to either of two adult tertiary care ICUs between July 1 and October 31, 2016. We selected a random sample of 50 patients. We collected baseline demographics, daily fluid intake categorized by fluid type, and medication dose, concentration, and the associated fluid. We identified the maximum concentrations of medications using Micromedex, Pediatric Injectable Drugs and the Ottawa Manual.

Results: The median total volume of fluid administered is highest on day 1 at 3910 mL/day and decreases over time. Medications contribute 20% of fluids administered in the ICU. Throughout patients' stay in ICU, medication fluids maintain a proportional contribution of 20%. Antimicrobials are the largest contributor of medication fluid. Among the top five antimicrobials used, medication fluid could be reduced by up to 71%.

Conclusions: We identified opportunities to dramatically reduce the fluid from medications. Future studies should identify which patient populations would most benefit from limiting fluid volume. Any interventions to reduce fluid intake should include assessing the feasibility of further concentrating intravenous medications.

Drug Use Evaluation of Oxycodone at a Canadian Teaching Hospital

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Background: Harms associated with prescription opioids are of increasing public concern. Oxycodone lacks superiority compared to other opioids, with an increased abuse potential. Since oxycodone's removal from the formulary at a Canadian hospital in 2012, its usage has not been characterized. We hypothesized that oxycodone was over-utilized and that opportunities exist for use optimization.

Objectives: This study was designed to characterize oxycodone use in concordance with evidence-based assessment criteria.

Methods: A retrospective observational drug use evaluation (DUE) was conducted for a four month period (April 1 to July 31, 2016) at a Canadian, urban, university-affiliated, tertiary care centre. Inpatients who received at least one dose of oxycodone immediate (IR) or controlled released (CR) were included. The primary measure of the evidence-based assessment criteria was the proportion of patients who received oxycodone CR in hospital, and were also stabilized on a CR formulation prior to admission. Patients were identified using the pharmacy computer system. Patients' electronic charts were reviewed using a standardized data collection form. Descriptive statistical analyses were performed.

Results: A total of 147 patient encounters with 248 orders for oxycodone were identified. Of oxycodone CR orders, 74/91 (81%) were deemed appropriate as per the primary measure. Most oxycodone (IR and CR) orders (52/248 [21%]) were initiated on the orthopedic ward. Four of the five top oxycodone prescribers were acute pain service physicians. Patient controlled analgesia (PCA) use was observed in 46% (67/147) of all patient encounters. Of the patients prescribed oxycodone CR on discharge, the majority (17/20 [85%]) were taking a CR formulation prior to admission.

Conclusions: The majority of oxycodone utilized at our institution was deemed appropriate according to the DUE assessment criteria. Opportunities to further optimize its use may be explored through order set modification or prescriber education.

Inpatient Insulin Stewardship Program: A Baseline Needs Assessment

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Background: Inpatient insulin use often occurs in a non-standardized way, including use of sliding scales without basal-bolus treatment as recommended by Diabetes Canada Clinical Practice Guidelines. These practices lead to poor glycemic control, which is associated with increased infection and prolonged hospitalization. A previous study at our institution indicated that 35% of inpatients have hyperglycemia, suggesting a need for improvement.

Objective: With the overall goal of improving inpatient diabetes management, a baseline hospital-wide needs assessment regarding diabetes management was conducted in order to identify key barriers regarding inpatient diabetes management to inform the development of an insulin stewardship program, with the use of tailored interventions.

Methods: Surveys (online, hard-copy) and focus groups were conducted with medical trainees (residents, students), nurse practitioners, medical and surgical nurses, and clinical pharmacists. Surveys were analyzed using descriptive statistics. Focus group recordings were transcribed and analyzed thematically.

Results: Surveys (n=84) and focus groups (n=8) revealed provider-, patient- and systems-related barriers to inpatient diabetes management. Provider-related barriers included: 1) inconsistent insulin start education; 2) peri-operative insulin use; 3) hypoglycemia avoidance/ management; 4) converting between insulin regimens; 5) correctional insulin use; 6) blood glucose monitoring education; and 7) when to consult the endocrine service for diabetes management. Patient-related barriers included appropriate use of home insulin in the inpatient setting. System-related barriers included: 1) lack of knowledge and awareness of standardized insulin order sets; 2) lack of resources available to support diabetes management; and 3) lack of decision support for appropriate insulin ordering.

Conclusion: Based on survey and focus group data, an insulin stewardship program will be developed to target the above barriers. Interventions include revised insulin order sets coupled with decision support; development of cheat sheets, standardized care protocols and manuals; revision of professional roles (e.g. pharmacisits), and insulin ordering/ inpatient diabetes management education.

Long-Term Beta-Blockers after Myocardial Infarction in the Contemporary Era: A Systematic Review

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Background: Beta-blockers are currently recommended as standard of care for patients who experience a myocardial infarction (MI) primarily based on evidence from the pre-reperfusion era. The effect of long-term beta-blocker therapy in patients post-MI without left ventricular dysfunction in the modern era is unknown.

Objective: To review the evidence for long-term (≥1 year) beta-blockers as secondary cardiovascular preventive therapy on all-cause mortality and major adverse cardiovascular events (MACE), specifically cardiovascular mortality, nonfatal MI, and nonfatal stroke.

Methods: A systematic search of EMBASE, MEDLINE, and CENTRAL (to September 2017) for randomized controlled trials or propensity-matched cohort studies published within the last 10 years that compared beta-blockers to no beta-blockers on discharge in patients post-MI without heart failure or reduced left ventricular ejection fraction (<30%) was performed. Both authors independently completed the literature search, data extraction, and study analysis.

Results: Eight cohort studies were included. Median study population was 1838 and duration of beta-blocker use ranged from 1-5 years. Definition of left ventricular dysfunction and reperfusion strategies varied among studies. Two smaller studies showed a significant reduction in all-cause mortality, whereas no difference was observed in 5 studies. One study showed significantly reduced cardiovascular mortality at 1 year, but no difference at 5 years, and no difference in all-cause mortality at 1 and 5 years. None of the 4 studies that reported MACE showed a significant reduction with beta-blocker therapy. These data are limited by inherent limitations of observational studies.

Conclusions: Though heterogeneous, the majority of contemporary studies identified did not demonstrate a reduction in death or MACE with chronic beta-blocker therapy in patients post-MI without left ventricular dysfunction. In the absence of an appropriately designed randomized controlled trial, these data impart uncertainty regarding the current standard of practice. Consequently, beta-blocker therapy should be reassessed on a case-by-case basis in patients post-MI.

Clinical Guide for Pharmacists to Evaluate Risks and Manage QTc Prolongation Drug-Drug Interactions

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Background: There is an increasing number of medications with potential QTc prolongation risks and the subsequent degeneration into torsades de pointes (TdP), a devastatingly fatal ventricular tachyarrhythmia.

Description: Our primary objectives were to identify recommendations posed by clinicians in evaluating QTc prolongation risks and to create a clinical algorithm or thought process aimed to help pharmacists in assessing and managing these drug-drug interactions.

Action: We focused on three commonly prescribed medications that were known to be associated with QTc prolongation risks (citalopram, domperidone, and ciprofloxacin). We conducted an environmental scan of recommendations made by national regulatory bodies and clinical guidelines; and performed a systematic review of primary literature between 2006 and 2016, with a primary focus on randomized controlled trials, systematic reviews, and meta-analyses.

Evaluation: We reviewed 7 articles. The primary literature, current recommendations from national regulatory authorities, and clinical guidelines consensually state that the evaluation of QTc prolongation risks requires a risk-benefit analysis of the drug combination. This analysis should be based on the severity of the drug-drug interactions, the patient's modifiable risk factors, and the mechanism in which the drug interaction results. In cases where the necessary doses may exceed the maximum dosing recommendations, pharmacists should ensure that baseline and steady-state 12-lead electrocardiograms are performed. Patients should be made aware of the signs and symptoms of abnormal arrhythmias and precipitating factors that may result in TdP. We developed a clinical algorithm to guide pharmacists in assessing and managing drug-drug interactions that involve potential QTc prolongation risks associated with these 3 medications.

Implications: Until further large-scale risk assessment tests and scoring can be performed, our clinical algorithm derived from a comprehensive environmental scan and literature review suggests that pharmacists should utilize their medication therapy expertise and effectively communicate potential risks of QTc prolongation to patients.

Trickle-Down Antimicrobial Stewardship: Reduction in Long-Term Care Resistance Rates Following Implementation of a Prospective Audit and Feedback Intervention in the Adjacent Acute Care Hospital

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Background: The Sunnybrook Health Sciences Center Bayview Campus is a shared site, home to a 627-bed acute care hospital and a 475-bed long-term-care (LTC) facility. A multidisciplinary antimicrobial stewardship (AMS) intervention was implemented in the acute care facility in October 2009. No specific intervention was initiated in LTC.

Objective: This study explores the impact of the acute care intervention on the burden of resistance in the adjoining LTC facility in the 7 years following the acute care program implementation.

Methods: Patient level data for clinical isolates of aerobic gram negative bacteria, *Staphylococcus aureus*, and *Enterococcus spp*. were obtained over a 14 year time period. Changes in the trend (Δ slope) and level of resistance between the pre-intervention (October 2002 – September 2009) and post-intervention (October 2009 – September 2016) periods were assessed using interrupted time-series analyses with segmented regression. The primary outcome was the number of bacterial isolates exhibiting resistance to at least one therapeutically active antibiotic per month standardized to 10,000 patient days (PD) for all species collectively and all gram-negative species (GNs).

Results: A statistically significant reduction in resistance rate trend was found for all species collectively (Δ slope = -0.97 resistant isolates/10,000 PD/month, p=0.001) and all GNs (Δ slope = -0.82 resistant isolates/10,000 PD/month, p=0.001). A significant reduction in the level of resistance was found for all bacteria beginning at post-intervention month 18 (-3.24 resistant isolates, p=0.023) and at post-intervention month 30 for all GNs (-2.83 resistant isolates, p=0.046).

Conclusion: Time series modelling revealed that implementation of the acute care AMS program was associated with significant improvements in the adjoining LTC facility's antibiotic resistance rates, suggesting a trickle-down effect.

Enhancing Mental Health Services through Hospital Outpatient Pharmacy and Assertive Community Treatment Team Collaboration

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Background: The local Assertive Community Treatment (ACT) team is a multidisciplinary team working with chronic mental health patients in the community supported by the hospital. Outpatient community hospital pharmacy is ideal to resolve potential gaps in pharmaceutical care and further enhance services over traditional community pharmacy.

Description: Outpatient hospital pharmacy is able to provide individualized solutions for ACT team and their patients that will lead to outcomes that reduce workload, reduce amount of medication on site, improve storage conditions, increase clinical nursing time, implement educational initiatives and provide further support for both mental health inpatients and outpatients.

Action: The hospital outpatient pharmacy devised a business case to transition the medication distribution system for the local ACT team from a retail pharmacy outside the community in order to enhance workflow, increase medication monitoring, provide better transitional care and increase flexibility. The projected revenue enabled pharmacy to provide a full-time clinical pharmacist and pharmacy technician. Working closely with the ACT team, pharmacy was able to identify offsite ACT office clinical needs to ensure all necessary services, such as medication disposal, were improved to meet internal hospital standards.

Evaluation: Implementation increased nursing clinical availability and alleviated many technical aspects from their role. Pharmacy's involvement has been expanded to incorporate all facets of medication management to increase safety measures and reduce areas of risk, such as implementing improved storage and distribution solutions. Full-time access to a small clinical pharmacy team with the capacity for on call support has increased staff rapport and communication, reduced drug wastage, errors and improved transition of care in and out of hospital.

Implications: Outpatient pharmacy in a hospital setting is ideal to service hospital outpatient programs by providing the flexibility, availability, quality and understanding that a community pharmacy may not always be able to lend focus to.

Vancomycin Every 4 hours in Paediatric Patients: A Case Series

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Background: Vancomycin target concentrations of 10-20 mg/L can be difficult to attain in paediatric patients due to their developmental pharmacokinetics. The usual starting dose for vancomycin is 15 mg/kg IV every 6 hours in infants and children. In some cases, pharmacists have used every 4 hour dosing in an attempt to reach therapeutic vancomycin concentrations.

Objectives: To review cases of hospitalized paediatric patients who have received vancomycin every 4 hours, in order to determine if this dosing interval appears safe and effective.

Methods: For this quality assurance case series, patients who had received vancomycin every 4 hours for ≥24 hours were identified from a report of paediatric patients prescribed vancomycin from February 2014 until October 2017. Vancomycin trough levels, drawn within 30 minutes of the scheduled dose, were used as a surrogate marker for efficacy. Safety parameters included serum creatinine and urea, which were assessed at baseline and during vancomycin treatment. Descriptive statistics were used.

Results: A total of 18 paediatric patients, aged 6 months to 8 years old were included in the case series. All patients achieved therapeutic concentrations during their treatment. A total of 4 patients had supratherapeutic trough concentrations. Observations indicate that serum creatinine and urea trended upward as trough concentrations increased.

Conclusions: Our observations suggest that vancomycin dosing every 4 hours in the paediatric population correlates with a high frequency of supratherapeutic trough concentrations, along with increased urea and serum creatinine. Further investigation is required to identify which patients are most likely to benefit from every 4 hour vancomycin dosing and those more likely to experience supratherapeutic concentrations.

Comparison of Clinical Pharmacy Services in General Medicine and Surgery Patients: A Workload Measurement Study

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Background: Canadian data describing the clinical services provided by hospital pharmacists (clinical pharmacy services, CPS) is lacking. Moreover, no Canadian study has examined if CPS demand and provision times differ for general medicine (GM) and surgery (GS) inpatients.

Objective: To describe the clinical services that hospital pharmacists provide, determine the incidence and provision times for various CPS, and identify differences in pharmacist workload as a function CPS and patient partition (GM or GS).

Methods: A data collection form to capture patient characteristics and CPS frequency and service times was developed. CPS activities included best possible medication history (BPMH), medication reconciliation, pharmacotherapy care plan, medication order review, insurance inquiries, dose clarification, therapeutic drug monitoring, antibiotic follow-up, thromboprophylaxis assessment, health care team discussions, inpatient counselling, discharge preparation activities, and "other" clinical activities. Ward pharmacists were asked to complete one documentation form for each patient admitted to their care over a 1 month period. Differences in patient characteristics, CPS frequency, CPS service times, total-time-per-patient, and daily-time-per-patient between GM and GS patients were evaluated using chi-squared and Mann-Whitney tests.

Results: Workload data for 273 GM patients and 191 GS patients were obtained. Inpatient counselling (8% vs. 3%, $p<0.05$) and discharge preparation activities (19% vs. 9%, $p<0.05$) were reported more frequently for GM patients, while pharmacotherapy care plan (64% vs. 77%, $p<0.05$), medication order review (7% vs. 29%, $p<0.05$), "other" activities (9% vs. 25%, $p<0.05$) were reported less frequently. Median service times for BPMH (15m vs. 10m, $p<0.001$), pharmacotherapy care plan (15min vs. 10min, $p<0.001$), and "other" activities (10min vs. 5min, $p=0.019$) were higher for GM patients. No difference in total-time-per-patient was detected. Daily-time-per-patient was higher for GS patients (6min vs. 4min, $p<0.001$).

Conclusion: Significant differences in PCS frequency, PCS service times, and daily-time-per-patient were found between GM and GS patients.

Validation of a Screening Tool to Assist in the Early Identification of Bloodstream Infection in Older Patients

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Background: Delayed diagnosis of blood stream infection (BSI) occurs in >20% of older patients. A validated BSI screening tool (ST) to identify older patients with a high probability of BSI may improve early diagnosis and management.

Objective: The objective was to validate a BSI-ST in older patients.

Methods: Inpatients ≥65 years old admitted between March 12, 2010-December 2, 2013 were eligible. A retrospective chart review of a matched cohort of older patients with and without documented BSI was completed. Data analysis was done for two age cohorts (≥ 80 years old and 65-79 years old) and for all patients ≥ 65 years old. Bacteremia pre-test probability, sensitivity, specificity, accuracy, false positive and negative rates of bacteremia, and positive and negative predictive value, post-test probability, and likelihood ratios were determined.

Results: The BSI-ST was validated in 310 patients. Of 25942 patients ≥65 years old admitted during the study, 534 had BSI, corresponding to a period prevalence (PP) of BSI in older patients of 2.1%. At the 2.1% BSI PP, the negative predictive value is 100% with a 0.4% probability of missing a BSI in an older patient.

Conclusion: The BSI-ST has excellent predictive capability for identifying older patients in whom a blood culture should be obtained, with a positive predictive value of 92% and false positive rate of only 10%. Although the false negative rate was 20%, a negative test in a patient with a BSI would occur in only 0.4% of patients at the institutional PP of BSI in older patients. Therefore, the retrospective validation of the BSI screening tool supports its implementation and pragmatic prospective evaluation.

For the table that goes with this abstract, please see Abstract Appendix, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/125/showToc

Patterns of Antimicrobial Use in an Outpatient Hemodialysis Unit

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Background: Hemodialysis (HD) patients are at high risk for infections, including those caused by multi-drug resistant organisms (MDROs). Since antimicrobial exposure is the main risk factor for the emergence of MDROs, minimizing inappropriate antimicrobial use is imperative.

Objectives: To optimize antimicrobial use, it is first important to understand patterns of antimicrobial prescribing in the HD setting. The objectives of this study were to: (1) measure antimicrobial use, and (2) describe antimicrobial prescribing patterns, among patients receiving outpatient HD.

Methods: A retrospective observational cohort study was performed in an outpatient HD unit at an academic centre from February 1 – April 30, 2017. Eligible patients included adults who were prescribed at least one oral or intravenous (IV) antimicrobial by a hospital or community prescriber. Data were retrieved from the HD unit infection control database and analyzed using descriptive statistics. The primary outcome was total antimicrobial days of therapy (DOT) per 1000 patient-days. Secondary outcomes were antimicrobial prescriptions characterized by type of antimicrobial, purpose, indication, route, and prescriber type.

Results: A total of 53 patients were eligible for inclusion and 75 antimicrobial prescriptions were included for analysis. Antimicrobial use occurred in 53 (16%) of 330 total outpatient HD patients. Over the 3-month study

period, antimicrobial use was 27.5 DOTs/1000 patient-days. The most common indication for antimicrobial therapy was skin and soft tissue infection, followed by bloodstream infection and respiratory tract infection. Fluoroquinolones were the most frequently prescribed antimicrobials, accounting for 23% of prescriptions, while the second most prescribed were first-generation cephalosporins (21%).

Conclusion: Overall, this study indicates that antimicrobial use was common, with 1 in 6 HD patients receiving antimicrobials during the 3-month study period. This may be the first study to describe prescribing patterns for both oral and IV antimicrobials in an outpatient HD population.

Impact of an Antimicrobial Stewardship Bloodstream Infection Surveillance Program in Hospitalized Patients

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Background: Bloodstream infections (BSI) in hospitalized patients represent sentinel events characterized by increased mortality. These infections represent an attractive stewardship opportunity because they warrant rapid initiation of empiric antimicrobial therapy, deft transition to directed (gram stain guided) and definitive (susceptibility guided) therapy.

Objectives: To measure the impact of a bloodstream infection surveillance program (BISP) on the adequacy and timing of antimicrobial therapy in hospitalized patients and model factors impacting antimicrobial cost, length of stay, and mortality in BSI patients.

Methods: A pre-post study design by retrospective chart review was carried out 18 months before and 18 months after initiation of a hospital BISP. The hospital ward and attending physician were notified of all positive blood cultures pre-intervention. Post-intervention an infectious disease pharmacist collaborating with an infectious disease consultant was notified in addition to standard notifications. Pre- and post-groups were compared using t-tests and Fisher exact tests. Antimicrobial costs and mortality were analysed using log-linear and logistic models, respectively.

Results: BSI were identified in 226 patients pre-intervention and 195 patients post-intervention. The two cohorts were similar in baseline characteristics and source of infection. *E. coli, S. aureus*, other enterobacteriaceae and beta-hemolytic streptococci were the most common bloodstream isolates. The post-intervention cohort received directed therapy 4.36 hours earlier (p=0.003), were more

Epidemiology of Carbapenemase-Producing Enterobacteriaceae Bacteremia and Evaluation of Antimicrobial Prescribing Practices in a Community Hospital Setting

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Background: The increasing incidence of carbapenemase-producing Enterobacteriaceae (CPE) bacteremia is a growing concern. With mortality rates exceeding 50%, there remains no consensus surrounding optimal antimicrobial treatment. There is little literature pertaining to CPE in Canada. The majority of isolates submitted to our provincial Public Health Laboratory are from our health system's service area.

Objectives: This study aims to characterize our health system's CPE bacteremia population and evaluate the antimicrobials used for treatment, including the effect of monotherapy versus combination therapy on mortality.

Methods: A dual-centre retrospective chart review was conducted of adult CPE bacteremia patients admitted between January 1, 2010 and April 30, 2017. Baseline demographics included out-of-country hospitalization, causative organism, and susceptibilities. Measured outcomes included length of hospitalization, mortality within 30 days of index blood cultures, and re-admission within 30 days of discharge. Prescribing pattern data included antimicrobial agent, dosing regimen, and use of monotherapy or combination therapy.

Results: Thirteen cases of CPE bacteremia were reviewed. They most frequently occurred in patients with prior hospitalization outside of Canada, particularly in the Indian subcontinent (9/13, 69%). Ninety-two percent (12/13) of isolates produced New Delhi metallo-beta-lactamase. All isolates were susceptible or intermediate to tigecycline. Tigecyline and colistin were the most commonly prescribed antimicrobials, respectively used in 62% (8/13) and 54% (7/13) of cases. Thirty-day mortality and readmission rates were 54% (7/13) and 50% (3/6), respectively. Survivors were 4 times more likely to have received combination therapy versus monotherapy (Odds ratio: 4.0, 95% confidence interval: 0.36 – 41.11, $P = 0.26$).

Conclusions: This study highlights the largest Canadian CPE bacteremia cohort to date. Our results suggest that combination therapy is more effective than monotherapy in improving survival outcomes. The inclusion of tigecycline as part of empiric combination therapy should be considered when CPE bacteremia is being considered or confirmed within our health system.

Development and Implementation of a Provincial Beta-Lactam Allergy Management Initiative

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Background: Beta-lactam allergies are often over diagnosed and over reported. Up to 10% of the population will report a penicillin allergy; however, as many as 95% of these patients are not truly allergic. Healthcare providers are more likely to prescribe non beta-lactam alternatives to these patients, which may be: less effective, more toxic, broader spectrum, more expensive and more likely to lead to infection or colonization with resistant organisms.

Description: The Provincial Anti-Infective Stewardship Committee (ASC) includes members from the two regional health authorities. Among its delegated tasks, the ASC develops educational resources and guidelines to improve the appropriateness, safety and cost-effectiveness of anti-infective use.

Action: The ASC developed the "Management of Penicillin and Beta-Lactam Allergy" guideline along with an executive summary document that condensed the main recommendations into a pocket sized booklet. A month-long educational and communication initiative was executed for their launch. The implementation initiative included announcement memos, educational bulletins, e-learning and live educational sessions. PRE/POST surveys were also sent to all health professionals of the target audience within both regional health authorities to assess the impact of the targeted educational program paired with the implementation of the guideline.

Evaluation: Response rates for the PRE and POST surveys were low at 7.8% and 3.9% respectively. The table summarizes key results from the surveys.

Implications: Results showed that there was a significant degree of interest in the guidelines and a trend in improvement in antibiotic related knowledge and feelings of preparedness; however, response rates were poor and 54% felt their practice had not changed. Results highlight the importance of active interventions to engage practice change in antimicrobial stewardship.

For the table that goes with this abstract, please see Abstract Appendix, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/125/showToc

Factors Affecting Time to Fill Antiplatelet Therapy for Patients Discharged from Hospital

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Background: Delays in filling antiplatelet therapy following hospital discharge have been identified in other parts of North America for patients who have undergone percutaneous coronary intervention (PCI) to treat acute coronary syndrome (ACS). These delays have been associated with an increased risk of recurrent myocardial infarction and all-cause mortality. It is unknown if delays exist for patients at the study site and what factors may affect this.

Objectives: The purpose of this study was to determine if delays exist for patients in the study area, and if so, the impact on hospital readmission rates. The secondary objective was to assess the impact of medication attitude, distance to home from site of discharge, site of discharge and medication insurance status on the time to fill antiplatelet therapy.

Methods: Prospective, observational, single-centre pilot project; conducted between January-April 2017. Patients 19 years of age and older, admitted to undergo PCI to treat ACS and discharged on clopidogrel, prasugrel or ticagrelor were eligible for enrolment during the index hospitalization. At 7-10 days post-discharge, prescription filling data was collected by telephone survey with participant and participant's community pharmacy. The Merck Adherence Estimator was administered at this time to gauge participant medication attitudes. Readmission to hospital data was collected from the provincial Electronic Health Record (EHR) 30-45 days post-discharge.

Results: Nineteen participants (79.2%) reported filling a prescription for their antiplatelet agent on the day of discharge. No statistically significant delay was identified. Merck Adherence Estimator score (p=0.0463) and distance to home from site of discharge (p=0.0062) were identified as factors impacting time to fill.

Conclusions: Delays in filling antiplatelet therapy may not be an issue for our patients. This should be confirmed with further investigation. The Merck Adherence Estimator may be an appropriate tool to screen patients who may be at risk of experiencing delays.

Evaluation of the Impact of Pharmacist-Led Penicillin Allergy Assessments on Antibiotic Utilization in a Large Community Teaching Hospital

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Background: Penicillins are the most common cause of allergic drug reactions with a prevalence of up to 20% in hospitalized patients. To date, there are limited Canadian publications describing pharmacist involvement in penicillin skin-testing. The purpose of this study is to evaluate the impact of a pharmacist-led initiative in a community hospital on de-labelling penicillin allergies and reducing the use of two broad spectrum antibiotics, meropenem and vancomycin.

Objectives: To determine the proportion of patients in whom an antibiotic change was made as a result of a penicillin allergy assessment and identify barriers for not de-escalating therapy in patients deemed non penicillin allergic. Potential drug cost savings were also examined for skin-tested patients.

Methods: This is an observational cohort study conducted in a community teaching hospital between October 1st 2016 and May 31st 2017, following the implementation of a policy allowing pharmacists to refer patients to an inpatient allergist for skin testing.

Results: Pharmacists recommended a penicillin skin test (PST) for 15 of 32 identified patients (46.9%) with a penicillin allergy who were prescribed meropenem or vancomycin. Nine of 15 eligible patients (60%) underwent a PST, with five patients having their antimicrobial therapy de-escalated to a beta-lactam antibiotic. Four patients had their therapy modified based only on the pharmacist assessment. De-escalation of therapy led to an average cost saving of was $137.89 for patients switched to a beta-lactam after PST.

Conclusion: A minimal-cost, pharmacist-led initiative to reduce broad-spectrum antibiotic use in penicillin allergic patients resulted in antimicrobial de-escalation in nine patients, demonstrating another opportunity for pharmacist involvement in antimicrobial stewardship.

Pharmacy Technician Continuing Education Program at a Large Teaching Hospital

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Background: Provincial College of Pharmacists mandates that its members maintain professional knowledge and skills appropriate for their scope of practice. At a large, teaching hospital, pharmacists have multiple opportunities to receive continuing education (CE) in an organized process; however, technician CE was not yet established.

Description: To describe the design and delivery of a structured, CE program for pharmacy technicians.

Action: A pilot was initiated in 2012 based on the structure of an existing pharmacist CE. It consisted of 30 minute, monthly presentations delivered at each site by pharmacy students. In 2013, an anonymous, needs assessment survey was sent for feedback. Comments were analyzed and incorporated into developing the final program launched in 2013.

Evaluation: Data from January 2014 to June 2017 was collected from 2 main sources; needs assessment surveys in 2013 and 2015 (total 33 respondents) and written feedback collected after presentations. Results showed that presentation topics were initially predominated by clinical therapeutic foci. However, over time, there was increase in the numbers of non-therapeutic topics reflecting real-time incorporation of technicians'

feedback. There was equal interest for therapeutic and non-therapeutic topics. Pharmacy students comprised majority of presenters (90%), pharmacists and technicians represented 5% each. Forty-one percent of respondents expressed most interest in receiving education from peers (other technicians). Ninety percent felt more knowledgeable about the topic presented and 71% found the sessions were meeting their educational needs. Some common challenges to attending CE was workload, presentation time of day, location, and lack of interest in the topic.

Implications: A pharmacy technician CE program has been a sustainable initiative at our institution. A lead facilitator is necessary to coordinate the schedule and recruit presenters. Future directions include standardization of feedback survey to capture timely feedback, leverage digital media to increase access and explore opportunities to enable more peer-technician presenters.

5 Questions to Ask about Your Medications

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Background: Patients are the constant in every transition of care and can be at high risk of adverse drug events, particularly at discharge from hospital to home. Knowing the right questions to ask can empower patients to be an active partner in their health and can help to mitigate risk of harm from medications.

Description: "5 Questions to Ask" is a national campaign to help patients and hospital pharmacists engage in a conversation about medication safety.

Action: The intervention was to develop, test, evaluate and disseminate a medication safety 'checklist' for use by patients and healthcare providers. Through small tests of change the 'checklist' was re-designed to the '5 Questions'.

Evaluation: A national online survey of patients and healthcare providers (n=291) revealed that 85% of patients would feel comfortable asking their healthcare provider the '5 Questions', 84% of healthcare providers would be willing to answer their patient's '5 Questions' and 75% of patients responded that the answers to these '5 Questions' would be very useful to help them understand their medications. A key performance measure was the extent of collaboration and use of the '5 Questions' among healthcare organizations. More than 150 Canadian organizations, at local, provincial and national levels have formally endorsed the '5 Questions' and implemented programs to increase reach and dissemination. Collective evaluation results demonstrate a commitment to a shared aim of empowering patients with questions to ask about their medications. There have been over 30,000 downloads of the poster since launch. The YouTube video has been viewed over 4000 times since its launch September 2016. Social media measures are also being collected.

Implications: The '5 Questions' with visible organization endorsements and translation in over 22 languages has demonstrated a shared interest in empowering patients. These questions may be a useful counselling framework or teach-back tool to help hospital pharmacists communicate more effectively with patients so they can better understand how to safely use their medications before they leave the hospital.

A Pharmacy-Led Interdisciplinary Teaching Model in Specialized Pharmacotherapy: An HIV Pharmacy Rotation for Medical Residents.

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Background: The medical training model has traditionally been physician-to-physician, contrasting the current interdisciplinary healthcare practice environment. Pharmacists with specialized drug knowledge are well-positioned to provide expert training in complex antiretroviral therapy. We developed a collaborative teaching model, incorporating a pharmacist-led rotation for medical residents to learn specialized HIV pharmacotherapy.

Description: In 2010 a postgraduate residency program was inaugurated in which family practice medical residents could receive focused training in the delivery of HIV care. The provision of HIV care, however, is multifaceted and drug treatment can be complex. Thus, in 2013, a specialized HIV pharmacy rotation at our university-affiliated ambulatory clinic was created and offered to these family practice residents as an elective, with the primary goal to augment HIV drug knowledge and better equip physicians to providing exemplary HIV care. The concept was for the medical trainee to "become the pharmacist", learning to recognize and manage common drug-therapy issues in HIV-infected persons.

Action: A formalized curriculum was developed, including rotation goals to foster key competencies in family medicine while addressing gaps in pharmacology training and HIV care. The rotation could be tailored to the resident but generally consists of a core set of one-on-one teaching, case-based learning, and application of pharmacotherapeutics in a busy specialized ambulatory HIV clinic.

Evaluation: A pre- and post-rotation survey was developed to assess whether the pharmacy rotation improved the resident's confidence in their knowledge of HIV pharmacotherapy. This survey also gathered feedback and recommendations to enhance future rotations. Thus far, 5 medical residents have completed this residency with the elective pharmacy rotation and have strongly endorsed the rotation as valuable to their future practice.

Implications: This collaborative teaching model appears to be extremely valuable to enhance patient care and should be considered in other highly-specialized pharmacotherapeutic areas.

Influence of Manufacturer on Cefazolin Stability

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Background: Some Canadian institutions have interpreted NAPRA and USP 797 guidance as requiring unique stability data for each manufacturer's brand to determine the beyond-use-date for sterile products. However, no studies have been done to validate the effect of manufacturer variations on cefazolin stability.

Objective: To evaluate if variations in drug manufacturer contributes to variations in cefazolin admixture stability.

Methods: We conducted a systematic review and meta-analysis of studies assessing the stability of cefazolin sodium in sterile preparations. We searched the PubMed, Scopus, and EMBASE for all studies (in English) from January 1950 to October 2017 and extracted data pertaining to

the lab performing the study, study days, percent of drug remaining, drug manufacturer, temperature of storage (refrigerated or room temperature), container (polyvinylchloride minibags, glass, or polypropylene syringe), diluent (dextrose 5%, normal saline or sterile water) and drug concentration. Eligibility criteria included: stability quantified using high pressure liquid chromatography, absence of freezing and thawing, single drug admixtures, and full text availability. We performed multiple linear regression on the percent remaining reported in cefazolin stability studies.

Results: Our search revealed 3449 studies. Duplicates were removed, and a total of 8 studies met our inclusion criteria resulting in 172 data points. Six different manufacturers were recorded for cefazolin (Eli Lilly, Smith Kline, Bristol-Myers, Apothecon, Novopharm, Apotex). Multiple linear regression demonstrated that manufacturers, container, diluent and concentration do not significantly impact cefazolin stability, while study day, temperature and lab did significantly impact stability (Table).

Conclusions: Our evidence suggests that manufacturer differences do not significantly contribute to variations in stability. Future research is needed to investigate the role of other contributing factors identified.

For the table that goes with this abstract, please see Abstract Appendix, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/125/showToc

Opioid Selection in the Neonatal Intensive Care Unit: Morphine versus Fentanyl: Impact on Total Opioid Exposure and Time to Enteral Feeds

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Background: Opioids are often used to treat neonatal pain. However, there is limited information to guide initial opioid selection in the neonatal intensive care unit (NICU).

Objective: The objective of this study is to determine if there is an association between initial opioid selection and time to full enteral feeds or total opioid exposure.

Methods: A retrospective chart review was conducted of neonates who were admitted to a level 3 academic perinatal critical care unit and received morphine or fentanyl continuous infusions between October 1, 2015 and April 1, 2017. Primary outcomes were time to enteral feed volume of 120 mg/kg/day and total duration of opioid exposure. Secondary outcomes included cumulative opioid dose. Cumulative doses were compared between groups using a conversion factor of 1:60 to convert fentanyl to morphine equivalents. Outcomes were compared between neonates who received morphine and those that received fentanyl using appropriate statistical tests (t-test, Wilcoxon-Mann-Whitney test or chi-square test).

Results: There were no significant differences in primary outcomes between groups. The median time to enteral feed volume of 120 mL/kg/day was 13 days in the morphine group (n=19) and 15 days in the fentanyl group (n=19). The median duration of opioid exposure was 11 days in the morphine group and seven days in the fentanyl group. Neonates in the fentanyl group received significantly more cumulative opioid (median: 6015 mcg/kg morphine equivalents) compared to neonates in the morphine group (median: 1646 mcg/kg) ($p<0.0001$).

Conclusions: Initial opioid selection was not associated with a difference in primary outcomes of time to achieve feed volume of 120mL/kg/day or duration of opioid exposure. Neonates in the fentanyl group received significantly larger cumulative opioid doses compared to morphine. The clinical significance of larger cumulative opioid doses is currently unclear. Future neurobehavioural outcome studies will be performed in this patient population.

The Prevalence of Mortality due to Rebound Toxicity after "Treat and Release" Practices In Prehospital Opiate Overdose Care: A Systematic Review

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Background: Traditionally, patients who have overdosed on opiated that are managed by emergency medical services (EMS) are treated with naloxone, provided ventilatory support and transported to hospital. However, some EMS agencies have allowed paramedics to not transport if patients have the capacity to refuse transport.

Objectives: The safety of this practice has not been examined by a systematic review. Therefore, we aimed to determine the prevalence of mortality and serious adverse events within 48 hours of EMS treat and release due to suspected rebound opiate toxicity after naloxone administration.

Methods: A systematic search was performed on May 11th 2017 in PubMed, Cochrane Central, Embase and CIHAL using search strategies developed with the aide of a health sciences librarian. No search limits were applied. Included studies were hand searched. Two authors conducted the screening, selection and data extraction process. Discrepancies were resolved via discussion. A modified QUIPs tool was used to evaluate risk of bias. Analysis for prevalence of outcomes were preformed.

Results: 1401 records were screened after duplicate removal. Eighteen full text studies were reviewed with 8 selected for inclusion. Included studies had a low risk of bias. The prevalence of mortality within 48 hours was so infrequent that it could not be quantitatively meta-analyzed. There were 4/4912 (0.00081%) total reported deaths of suspected rebound etiology from included patients across all studies. Only one study reported on adverse events of patients released on scene. This study found no incidence of adverse events from their sample of 71 released patients.

Conclusion: The prevalence rate of mortality or serious adverse events due to suspected rebound toxicity was very low. Therefore, we conclude this practice may be considered as an alternative to traditional transport. Additional prospective studies need to be performed to strengthen knowledge around adverse events.

A Pan-Canadian Study on the Compounded Medicines Most in Need of Commercialized Oral Pediatric Formulations

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Background: A large number of drugs administered to children have no commercially available formulations. As a result, health care providers and parents manipulate dosage forms designed for adults. Although compounding is essential to increase access to medicines for children, it can result in adverse events or therapeutic failure. There is an urgent need to undertake a mapping of the needs for child-friendly medicines in Canada.

Objectives: To determine: 1) the most frequently compounded medicines in Canadian pediatric hospitals; 2) the challenges associated with drug compounding; and 3) medicines most in need of commercialized oral pediatric formulations.

Methods: Sixteen Canadian pediatric academic hospitals were contacted to participate in a telephone survey including 12 open-, close-ended or Likert-scale questions.

Results: Thirteen centers participated in the survey (81.3%). Fifty-three drugs were identified as most in need of a commercialized oral pediatric formulation. Of those, 12 were reported by ≥4 hospitals as a priority (Table). The most frequently reported compounding challenges were: lack of standardization, bad taste, lack of awareness of prescribers, stability of the formulation, and availability of compounding pharmacies.

Conclusions: This study highlights which drugs are most in need for pediatric oral formulations in Canada. For compounded medicines with pediatric formulations available in other countries, we are currently assessing their adequacy and partnering with pharmaceutical industry to bring them to the Canadian market. As for those medicines without pediatric formulations in Canada or abroad, we are looking for pharmaceutical partners interested in developing such formulations. Furthermore, harmonized regulations and data-sharing should be pursued to facilitate access to child-friendly medicines for the largest number of children across borders.

A Comparison of Intravenous Iron Dosing Regimens for Anemia Management in Patients Undergoing Hemodialysis

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Background: Anemia is common in patients undergoing hemodialysis and can result in decreased quality of life, cardiovascular events, and need for blood transfusions. Guidelines recommend the use of intravenous (IV) iron and erythropoietin stimulating agents (ESAs) for anemia management. Optimization of doses used for IV iron and ESAs is warranted, as both are associated with adverse reactions and significant costs.

Objective: The objective of this study was to compare the efficacy of a lower once weekly dose (62.5mg) of IV sodium ferric gluconate versus the standard dosing regimen (125mg of IV sodium ferric gluconate) utilized at our institution.

Methods: A retrospective, observational, cohort study was conducted on patients receiving hemodialysis. Primary outcome was hemoglobin level (g/L) at 3 months. Secondary outcomes included mean weekly ESA use (units), need for blood transfusions (%), and mean cumulative iron dose (mg) over the 3-month intervention period.

Results: Of the 102 eligible patients, 52 patients received the once weekly low-dose regimen and 50 patients received the once weekly standard-dose regimen. Multiple linear regression analysis demonstrated that IV iron-dosing regimen was not a significant predictor of hemoglobin level at 3 months (p=0.859). Mean hemoglobin levels (g/L) in the once weekly low-dose and once weekly standard-dose regimens were 112.58 ± 12.63 and 114.68 ± 10.32, respectively. Mean weekly ESA use (units) was significantly higher in the once weekly low-dose regimen (12 686.81 ± 6774.07 vs. 7040 ± 7392.66; p<0.001). Number of patients requiring transfusions did not differ significantly between the two dosing regimens (11.32% vs. 20%; p=0.367).

Conclusion: Neither of the two IV iron-dosing regimens was associated with lower hemoglobin levels. Analysis suggests this may be due to the higher ESA use in the once weekly low-dose regimen. Based on these results, it may be more optimal to continue with the standard once weekly dosing regimen.

User Satisfaction Regarding Standard Assessment Tool for Field-Based Pharmacy Training

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Background: A province-wide standard competency-based assessment tool with companion glossary was collaboratively developed and implemented by schools of pharmacy, residency training sites and provincial licensing body within the last year in order to improve consistency of learner performance assessments.

Description: A user (preceptor/assessor, learner) satisfaction survey was conducted post-implementation of the province-wide assessment tool in order to assess user opinions regarding its usability and overall satisfaction.

Action: The survey questions were derived through a collaborative process including review by assessment experts and typical assessment tool users. After completion of each field-based final assessment utilizing the tool, preceptors/assessors and learners (students/residents) were invited via email to participate in the survey. A reminder email was sent at a scheduled follow-up time to encourage survey completion.

Evaluation: Preliminary survey results (n=236) showed the following: the layout of the tool was easy to follow (87% preceptors/assessors, 94% learners), the tool's accompanying glossary was seen as helpful (83% preceptors/assessors, 59% learners), the tool accurately captures learner's performance (75% preceptors/assessors, 53% learners), the tool does not have redundant areas of assessment (80% preceptors/assessors, 73% learners), and the tool is not missing important content areas of assessment (73% preceptors/assessors, 83% learners). Seventy-two percent of preceptors/assessors were satisfied with the tool while 54% of learners were satisfied with the tool. The majority of comments indicated the tool was well designed, comprehensive and fair. A suggestion was to review the length.

Implications: Users indicated that the province-wide assessment tool is usable. The tool's measurement domains were generally seen to be appropriate. Preceptors were more satisfied overall with the tool versus learners. Work continues to determine details around these results and to further validate the province-wide assessment tool.

Pharmacy Student-Led Best Possible Medication History Quality Audit

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Background: In May of 2016, our hospital implemented a change in practice and reconciliation of the Best Possible Medication History (BPMH) resulted in physician orders. The majority of BPMH are collected and documented by a registered nurse (RN) in our hospital and although the rate of BPMH documentation was good, reconciliation by

physicians was below target. There was a perception that the quality of BPMH by an RN differed based on the unit where it was completed. A BMH quality audit was undertaken to explore this perception.

Description: Quality audits are not part of our regular pharmacy operations therefore, a second-year pharmacy student intern was hired to lead the BPMH audit under the supervision of a staff pharmacist.

Action: The pharmacy student completed site-specific BPMH training and had their skills validated by a staff pharmacist. Convenience sampling was used to identify eligible patients. The pharmacy student obtained verbal consent to conduct a second BPMH and quality was determined by comparing the two independent BPMH (nurse and pharmacy student) to identify discrepancies. Discrepancies were reviewed, classified, and reconciled by a staff pharmacist. Discrepancy rates were calculated based on number of home medications and descriptive statistics were used to report total discrepancies, and to compare results between units.

Evaluation: Twenty BPMH interviews were repeated for 2 clinical programs; 10 from each program. Ninety–five discrepancies were evaluated; 83 documented by nursing staff, and 12 by the pharmacy student. Discrepancy rate for BPMH by an RN 38.8% in one program and 38.7% in the other.

Implications: A pharmacy student successfully conducted a BPMH quality audit. The audit demonstrated that there was an opportunity to improve BPMH by RNs and that there was no difference in BPMH quality between programs. Audit results will be shared within our facility and used to inform our interventions.

A Work-Sampling Study of Clinical Pharmacists

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Background: As Canadian pharmacists have gradually expanded their scope of practice, this has also increased the demand on pharmacists' time. There is a current lack of literature examining the tasks that clinical pharmacists perform in Canada and how much time each task typically consumes. It is unclear whether there are indirect patient care activities that may be reassigned to support staff or regulated technicians in order to allow more time for direct patient care activities.

Objective: To quantify the total amount of time that clinical pharmacists spend on direct and indirect patient care activities and determine which activities require the most time.

Methods: An observational work-sampling study was conducted at two urban hospitals. Trained observers followed clinical pharmacists individually for 1.5-4 hours in a variety of different wards and recorded their activities in 1-minute intervals and sorted each activity as a direct or indirect patient care activity. Simple descriptive statistics were used to analyze the time consumed by each activity.

Results: 2044 minutes of activity from 11 pharmacists were recorded. 82.8% of their time was spent on direct clinical activities, such as: 40.9% assessment and evaluation (includes 9.9% and 17.0% on reviewing paper charts and computer systems, respectively), 23.3% rounds, 9.5% therapeutic interventions. Only 17.2% of their time was spent on indirect clinical activities, such as: 4.6% walking, 2.7% looking for something.

Conclusions: Although it was an excellent finding that pharmacists spend minimal time on indirect activities (17.2%), the majority of the time they spent on direct clinical activities was assessment and evaluation – namely, review of paper charts and computer systems. An electronic medical record as well as technicians may be beneficial in organizing pertinent patient data for quicker chart reviews and workups.

Development and Evaluation of an Anticoagulation Education Program for Pharmacists

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Background: As part of a broader practice standardization project, an education program was developed. A series of therapeutic topics with focus on high risk medications were identified for practice standardization. Anticoagulants are high risk medications that require pharmacists to have minimal baseline knowledge of in order to identify and resolve related drug therapy problems (DTPs).

Description: To ensure pharmacists possess the required knowledge and skills, an anticoagulation education module was developed, implemented and evaluated.

Action: The anticoagulation education module consisted of a voiced-over slideshow presentation, which included supporting institutional policies and procedures. The education module underwent review and feedback from expert and typical pharmacist users prior to deployment. Assessment of the pharmacist's knowledge and skills consisted of a 20-question multiple choice test that was administered both at baseline and after review of the module. Point-biserial (p-bis) and p-values were used to ensure test question validity and reliability. Pharmacists were required to score at least 80% on the post-module test. Program evaluation consisted of a questionnaire asking about the pharmacist's own confidence and that of their colleagues to identify and resolve anticoagulation related DTPs, and the perceived value of the program.

Evaluation: Fifty-one pharmacists completed the pre- and post-module tests. Post-module completion, the average test score increased from 76% to 90%. The majority of the pharmacists (49/51 [96%]) passed the test. Responses from the post-module questionnaire indicated that pharmacists were overall confident in their own and colleagues' ability to identify and resolve anticoagulation DTPs, and perceived the program as beneficial to improve patient care and safety.

Implications: The results suggest that pharmacists benefitted from an anticoagulation education program. Completion of the education module and post-module test are now mandatory for all new staff. Based on the program's success, future modules on different therapeutic topics are in development.

Évaluation de l'oculométrie comme outil de rétroaction en validation pharmaceutique : étude pilote

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Contexte : L'oculométrie regroupe un ensemble de techniques permettant d'enregistrer les mouvements oculaires.

Objectif : Évaluer la concordance des données recueillies par oculométrie selon deux méthodes d'analyse de données.

Méthodologie : Étude descriptive. Une simulation de validation pharmaceutique du dossier pharmacologique avec interactions en personne et au téléphone (< 15 minutes, 12 ordonnances de médicaments) a été menée auprès de 16 participants. Les données recueillies par l'oculomètre (Redn, Sensomotoric Instruments, Teltow, Allemagne) ont été couplées par le logiciel utilisé à une captation de l'écran de validation vu par les participants et ces vidéos ont été analysées et recodées manuellement par deux assistantes de recherche afin d'identifier les champs d'intérêt

regardés par les participants. Nous avons évalué la concordance (Kappa) de périodes de validation active de champs d'intérêt du dossier pharmacologique entre les données issues de l'analyse de la captation vidéo et les données brutes de l'oculomètre. Une valeur de p inférieure à 0,05 est considérée statistiquement significative.

Résultats : Seulement 13 des 16 captations vidéos ont permis de générer des données exploitables pour un total de 903 paires de périodes de validation active. La concordance est partielle entre la captation vidéo et les données brutes de l'oculomètre soit, en ordre décroissant de champs d'intérêt du dossier pharmacologique: posologie (0,633), équivalence (0,499), date d'ordonnance (0,490), dose (0,469), dosage (0,171), médecin prescripteur (0,079), trame (0,066).

Conclusion : Il existe une faible concordance entre les données issues de l'analyse de la captation vidéo et les données brutes de l'oculomètre. Nous pensons que l'oculométrie représente un outil potentiellement très utile pour offrir une rétroaction en temps réel à un pharmacien ou un assistant-technique en pharmacie lors de la validation des ordonnances. Toutefois, il est nécessaire d'identifier une plate-forme logicielle mieux adaptée aux besoins de recherche.

Qualitative Thematic Analysis of Interprofessional Perspectives on Clinical Pharmacy Key Performance Indicators

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Background: Eight national clinical pharmacy key performance indicators (cpKPIs) were developed by hospital pharmacists to advance pharmacy practice and improve the quality of patient care. Six of the eight cpKPIs have been adopted by the CSHP Excellence program. Interprofessional feedback is essential to optimize, refine and effectively communicate the importance and meaning of the cpKPIs.

Description: To identify, on a national scale, qualitative themes related to interprofessional perspectives on cpKPIs and specific areas for improved cpKPI description.

Action: This was a prospective, multi-centre, multi-province, qualitative descriptive study. Stakeholders were defined as a healthcare professional or administrator who interacts with a hospital pharmacist regularly and/or is involved in the measurement of quality/performance indicators. Focus group and individual interviews were conducted to gather interprofessional stakeholder feedback about the cpKPIs with a semi-structured interview guide. All discussions were audio-recorded and transcribed. Two investigators conducted the qualitative thematic analysis using NVivo software.

Evaluation: Thematic analysis using feedback provided by 92 participants across 4 Canadian provinces revealed 8 major themes and 13 sub-themes related to interprofessional perceptions of cpKPIs (See Table 1). Study participants included a wide variety of stakeholders including physicians, nurses, allied health professionals, hospital administrators, and non-hospital pharmacists.

Implications: Thematic analysis of interprofessional cpKPI perspectives revealed valuable opportunities to refine the cpKPIs with a focus on their importance to support the need for pharmacists and their patient care role. The analysis also identified specific description enhancements to improve comprehension of the cpKPIs by an interprofessional audience. These perspectives can serve to inform implementation of cpKPIs nationally.

For the table that goes with this abstract, please see Abstract Appendix, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/125/showToc

Enabling Expanded Scope in Hospital Practice: Implementation of a Pharmacist Modification Orders Protocol

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Background: The revised Pharmacy Act and Pharmacy Act Regulations expanded pharmacists' scope of practice in Ontario to include prescribing. Pharmacists are not listed as prescribers in the Public Hospitals Act Regulations which currently restricts pharmacists from exercising their expanded scope in the hospital setting.

Description: A protocol was developed at our institution to provide a mechanism for pharmacists to modify medication orders for inpatients. Pharmacists use "pharmacist modification" heading to write an order in the patient chart that the pharmacist is authorized to write, based on their clinical judgment and scope of practice. Pharmacist modification orders may include: change in dose, dosage form, directions for use, route of administration, concentration, diluent or rate of administration through a parenteral route, administration time or medication hold. Pharmacists use "pharmacist suggests" heading to make a suggestion to the medical team when the pharmacist is not authorized to independently write an order.

Action: The Pharmacist Scope of Practice working group reviewed practice at other hospitals within and outside of Ontario. Building on current collaborations with physicians, pharmacists and nurses, the working group ensured organization readiness for the protocol through stakeholder discussions and meetings. Approval and endorsements were obtained from appropriate pharmacy, interprofessional, and medical advisory committees followed by education sessions for pharmacists and clinical teams and subsequent implementation in July 2017.

Evaluation: A one-day audit of pharmacist orders was completed approximately one month after protocol implementation. Pharmacists wrote 188 orders: 47 modifications, 102 suggestions, 22 automatic substitutions and 17 others. Interventions included: 32% initiations, 23% dose adjustments, 16% medication management and 12% discontinuations. Pharmacist feedback has been positive with respect to patient care and workflow.

Implications: This protocol has enabled pharmacists to expand their scope of practice in order to improve effectiveness, safety, efficiency and cost-effectiveness of patient care.

Design, Implementation, and Evaluation of a Clinical Pharmacy Key Performance Indicator Tracker: DIE–cpKPI Study

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Background: High-quality evidence shows clinical pharmacists providing Canadian consensus clinical pharmacy key performance indicator (cpKPI) activities with their inter-professional team improve health and economic outcomes. A cpKPI tracker is required to measure health service delivery, advance pharmacy practice, and improve patient care.

Objective: To design, implement, and evaluate a theory-informed and evidence-based professional behavior change intervention (BCI) used to implement a cpKPI tracker.

Methods: Prospective, quasi-experimental, one group, PRE/POST study at three hospitals from January 30th to June 30th, 2017. The primary outcome was the mean difference in scores of a 45-item PRE and POST BCI questionnaire scores. Secondary outcomes included the mean difference in PRE and POST BCI questionnaire scores across each of the 14 domains of the Theoretical Domains Framework (TDF), percentage of clinical pharmacists "satisfied" with the BCI, and percentage of discharged patients receiving cpKPI interventions during 2-month pilot period.

Results: Twenty four (80%) of representative pharmacists participated in the study. The mean (95% confidence interval) difference in PRE and POST BCI questionnaire scores was -0.75 (-0.65 to -0.84). Scores were significantly reduced across all TDF domains except "intentions". Overall, 71% of the participants were "satisfied" with the intervention provided. Overall, 634 of 7264 (8.7%) of discharged patients received at least one cpKPI intervention. Participation in interprofessional patient care rounds, implementing a PC plan, resolving DTPs, and providing inpatient education and counseling were provided most frequently. Admission and discharge medication reconciliation and discharge education and counselling were provided less frequently.

Conclusions: An evidence-based BCI was systematically designed, efficiently implemented, and successfully evaluated. The BCI reduced perceived barriers to cpKPI tracking, and pharmacists were satisfied with the BCI used to implement the cpKPI tracker. Pilot data captured was successfully retrieved and reported. Several hypotheses may explain the frequency of cpKPI activities reported, which will guide additional pre-implementation work.

Assessing the Perception and Implementation of Continuous Quality Improvement in Pharmacy Professionals: A Pre-Safety IQ Initiative

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Background: Safety IQ is a standardized continuous quality improvement (CQI) program in Manitoba designed to prevent medication incidents from happening in pharmacies.

Description: The objective of this project was to explore the current perceptions, benefits, barriers, and experience of CQI programs in pharmacy professionals prior to the launch of the province-wide Safety IQ initiative.

Action: We administered a 28-item online questionnaire over a two-week period to all registered pharmacists and pharmacy technicians in Manitoba. We conducted descriptive statistics and qualitative thematic analysis, accordingly, on the responses collected.

Evaluation: We collected 125 responses, with 32% pharmacy managers, 56.80% staff pharmacists, and 11.20% pharmacy technicians. Pharmacy professionals had a fairly positive perception of CQI program and its associated benefits to patient care and safety. They viewed CQI program as a platform for communication and shared leaning with the ultimate goal of preventing medication incidents. There were concerns regarding CQI program implementation, such as the potential requirement for additional financial and human resources, as well as fear of reporting and discussing incidents. Time was considered to be the greatest challenge in CQI program implementation. Pharmacy professionals preferred a simple, efficient CQI program, and perceived that support from management would be required for its sustainability. They shared a wide range of experiences with current CQI programs in their practice.

Implications: Implementation of CQI programs vary widely in Manitoba and most seem to be generally informal and internally focused. Despite concerns in increased resource requirements, pharmacy professionals appeared to be open and supportive of a standardized CQI program. They expect such a program will provide benefits including a more positive work environment, increased public trust, and a reduction in medication errors. This project provides support for the implementation of Safety IQ as a standardized CQI program to improve patient and medication

From "Dot" to "Dot Com": Navigating Pharmacist Handoff in a Digital Era

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Background: Effective communication is an important aspect of providing exceptional patient-centered care. During transition of care points, a requirement for timely, accurate and important information to the receiving provider is necessary. Referred to as a 'handoff', transfer of care occurs when two or more health care professionals exchange information pertinent to a patient's care. The shift to computerized provider order entry (CPOE) and a vision of "Lean, Green and Digital" for our new hospital provided an opportunity to evaluate and standardize our pharmacist handoff processes.

Description: Our previous pharmacist handoff processes involved various methods, dependent on the pharmacist at the initial point of care. A "sticker dot" on the original paper order was the most common (greater than 50%) method of communication. The dot would be accompanied with handwritten notes. The aim of our intervention was to provide congruency between pharmacists at handoff; ensuring communication was clear, concise, timely, and inclusive.

Action: A group of key stakeholders including the pharmacy managers, director, pharmacists, drug utilization, and informatics pharmacists led this project. A baseline documentation survey was sent to all pharmacists to address the needs and concerns. Utilizing these results, we were able to facilitate automated reports that were customizable; allowing for prioritization of handoff interventions. Extensive educational sessions were held for pharmacists to ensure uptake of the new handoff tool.

Evaluation: The Plan-Do-Study-Act (PDSA) cycle was used to ensure the tool was relevant and useful. Follow up educational sessions were required for front line pharmacists to use the handoff tool appropriately and effectively. Our pharmacists utilize the automated tool on a daily basis and have implemented it into their daily workflow processes.

Implications: The success of standardizing the electronic handoff processes has allowed for seamless transfer of care between pharmacists. Future enhancements may focus on documentation standardization for pharmacists.

cshp47

Myrella Roy

To be a man is, precisely, to be responsible. It is to feel, when setting one's stone, that one is contributing to the building of the world.
—Antoine de Saint-Exupéry, *Wind, Sand and Stars* (1939)

In 2017, the Canadian Society of Hospital Pharmacists (CSHP) celebrated its 70th anniversary; Canada, the centennial year of its Confederation; and Montréal, the 50th anniversary of Expo 67, the 1967 International and Universal Exposition. I still vividly remember 1967: it was the year my parents converted our home on Montréal's South Shore into a bed and breakfast for 6 months, during which my family welcomed our share of the 50 million visitors from around the world. I am ever so grateful to my parents for allowing me plenty of spare time from housekeeping to spend most of that summer on the exhibition archipelago, passport in hand, travelling the world within 3.65 km^2 in the middle of the St. Lawrence River.

Logo

The basic unit of Expo 67's logo is an ancient pictogram of a human figure with outstretched arms, linked in pairs and arranged in a circle to symbolize friendship around the world. As for CSHP, it adopted a new logo on the occasion of its 70th anniversary. The broken, overlapping aspect of the stylized cross and mortar and the different colours are meant to portray the interconnection among the various facets of pharmacy practice—patient care, drug distribution, education, research, informatics, etc.—as well as the diversity of CSHP's members, their practice areas, and the patient populations they serve.

Theme

The theme of Expo 67 was "Man and His World", based on the 1939 book entitled *Terre des hommes* (translated as *Wind, Sand and Stars*) by the French aviator-writer Antoine de Saint-Exupéry. The Expo 67 directors likened their vision of the event to the celebration of friendship, mutual assistance, and humanistic values emanating from the book. CSHP also embraces these principles and exemplified them through its collaboration with other healthcare organizations on a number of salient enterprises in 2017.

After 7 years of relentless advocacy to Health Canada's Office of Controlled Substances, CSHP was ecstatic when a class exemption to section 56 of the *Controlled Drugs and Substances Act* was issued last March for practitioners prescribing methadone to inpatients in a hospital setting. Since then, practitioners have no longer had to obtain a temporary methadone s.56 exemption to continue treating inpatients who were taking methadone before their hospital admission.

CSHP made 7 commitments toward the Joint Statement of Action to Address the Opioid Crisis, led by the Government of Canada (https://www.canada.ca/en/health-canada/services/substance-abuse/opioid-conference/joint-statement-action-address-opioid-crisis.html). CSHP submitted a further 2 commitments through its participation in the Pharmacy Opioid Summit convened by the Canadian Pharmacists Association, which brought together 38 pharmacy and partner organizations in June 2017 (https://www.pharmacists.ca/news-events/news/cpha-statement-on-canadian-pharmacists-conference-opioid-summit/).

As a member of the Surgical Care Safety Best Practices Partners Group, CSHP endorsed the Enhanced Recovery Canada position statement. A leadership and dissemination strategy has been planned to support implementation of relevant best practices for Enhanced Recovery After Surgery, within the framework of the Canadian Patient Safety Institute's Surgical Care Safety Action Plan (www.patientsafetyinstitute.ca/en/toolsResources/Enhanced-Recovery-after-Surgery/Pages/Additional-Information.aspx).

Pavilions

Expo 67 featured 90 national, provincial and state, theme, and privately sponsored pavilions. To visit the most popular ones (Canada, Czechoslovakia, France, Soviet Union, and United States of America), I would get to the grounds bright and early with my folding chair and my packed lunch to line up before the pavilions opened. Even so, and much to my chagrin, 3 pavilion visas were missing from my passport when Expo 67 closed.

CSHP also had to get up bright and early throughout the year to answer some 35 calls from external stakeholders for consultation and assistance. Responses on the following issues stand out as the most captivating for CSHP members: to the Association of Faculties of Pharmacy of Canada, on the draft revised *Educational Outcomes for First Professional Degree Programs in Pharmacy* (*Entry-to-Practice Pharmacy Programs*) *in Canada*; to the Canadian Council for the Accreditation of Pharmacy Programs, on the draft revised *Accreditation Standards for Canadian Pharmacy Technician Programs*; to Health Canada, on an inquiry about medical cannabis ordering and handling in hospital pharmacies, on proposed regulations amending the Food and Drug Regulations to allow the importation of drugs for an urgent public health need (such as the opioid crisis) that are authorized for sale by a trusted foreign regulatory authority (namely, authorities in the United States, the European Union, and Switzerland), on draft guidance documents on the handling and destruction of unserviceable stock and postconsumer returns (specifically those containing a narcotic, targeted substance, or controlled drug), on proposed regulations amending the Food and Drug Regulations to strengthen postmarket oversight of opioids and to require a warning sticker and patient information handout be provided with prescription opioids at time of dispensing, on a consultation paper and technical discussions on the mandatory reporting of serious adverse drug reactions and medical device incidents by healthcare institutions, and on the renewal of the Special Access Programme; and to the Public Health Agency of Canada, on the draft *Tackling Antimicrobial Resistance and Antimicrobial Use: A Pan-Canadian Framework for Action*.

Theme Pavilions

Expo 67's theme pavilions were built on variations of its overarching theme, "Man and His World". They explored humanity from various universal thematic perspectives, such as agriculture, environment, health, technology, urban life, and visual arts.

The official launch of CSHP's Excellence in Hospital Pharmacy program in February 2017 unveiled 3 priority themes: patient engagement/patient centredness, best practice (including patient safety), and effective communication and collaborative practice. The program's success will be gauged against 6 principles and 15 attendant measures of performance (https://www.cshp.ca/excellence).

Thanks to the generous sole sponsorship of Eli Lilly Canada for more than 30 years, the Hospital Pharmacy in Canada (HPC) Report has become a leading reference and benchmarking tool for hospital pharmacy services across Canada and around the world. In 2017, the CSHP Board accepted the HPC Editorial Board's request to become one of its "thematic" affiliated boards. The CSHP HPC Survey Board, as it is now known, conducted its 2016/2017 survey under this new affiliation, with sponsorship from AstraZeneca Canada, Eli Lilly Canada, and Pfizer Canada. The results will be published shortly at www.hospitalpharmacysurvey.ca.

CSHP also introduced a new publication, the *Canadian Medication Optimization Briefing* (*CMOB*), a series of 2-page, peer-reviewed quick references on specific themes in clinical pharmacy practice. With the permission of the Royal Pharmaceutical Society and the Centre for Pharmacy Postgraduate Education in Great Britain, the layout was adapted from their *Medicines Optimisation Briefing*. The inaugural issue of the *CMOB* focused on antimicrobial stewardship and was released in time for World Antibiotic Awareness Week 2017.

Telephone Pavilion

The pavilion sponsored by the Telephone Association of Canada captured visitors' imagination. To this day, I can still remember its feature attraction, *Canada '67*, a documentary film by The Walt Disney Company projected on a huge panoramic screen (Circle-Vision 360°), as well as its display of futuristic technological marvels, including touch-tone and cordless phones, telephone banking, and AT&T's Picturephone. Realm of fancy?

Technology was very much on CSHP's mind as well last year. First, its website underwent a much-needed facelift. When the website was launched, CSHP also introduced its new ".pharmacy" domain name, which was granted in 2016 by the National Association of Boards of Pharmacy in the United States; this domain name assures netizens that a pharmacy-related website is safe and legitimate. Furthermore, CSHP's Canadian Pharmacy Residency Board upgraded its residency matching service and enhanced it with a centralized application process. Lastly, CSHP introduced the Assessment Tool for Aseptic Compounding, which draws on the best and leading practices articulated in its publication *Compounding: Guidelines for Pharmacies* (learn more at https://www.cshp.ca/assessment-tool-aseptic-compounding-0).

Hostesses and Hosts

Just as the hostesses and hosts were deemed ambassadors of the highly successful Expo 67, CSHP's gracious employees played a pivotal role in these impressive achievements. What's more, with the hiring of Sarah Jennings as part-time Professional Affairs Associate, the Society's pharmacist complement grew to 2.5 full-time equivalents. Other causes for celebration in the course of CSHP's 70th year were the birth of Amanda Iannaccio's daughter, the hiring of Christopher Doody and Julie Sobowale to jointly fulfil the role of Publications Administrator during Amanda's maternity leave, and the 5-year employment anniversary of Pamela Saunders (General Program Administrator).

Legacy

Just as Expo 67 left indelible memories, may CSHP continue its unfailing and unforgettable contributions to the building of pharmacists' practice in hospitals and other collaborative healthcare settings.

Myrella Roy, BScPhm, PharmD, FCCP, is Executive Director of the CSHP.

scph47

par Myrella Roy

Être un homme, c'est sentir, en posant sa pierre,
que l'on contribue à bâtir le monde.
—Antoine de Saint-Exupéry, *Terre des hommes* (1939)

En 2017, la Société canadienne des pharmaciens d'hôpitaux célébrait son 70e anniversaire; le Canada, le centenaire de la Confédération; et Montréal, le 50e anniversaire de l'Expo 67, l'exposition universelle de 1967. Je me souviens toujours de 1967 comme si c'était hier; c'était l'année où mes parents ont transformé notre chez-nous sur la Rive-Sud dans la région de Montréal en couette et café afin d'y accueillir notre part des 50 millions de visiteurs du monde entier durant 6 mois. Je serai éternellement reconnaissante envers mes parents de m'avoir grandement libérée de l'entretien ménager pour que je puisse passer la majeure partie de cet été-là dans l'archipel de l'exposition, passeport en main, à la découverte du monde sur moins de 3,65 km2 au milieu du fleuve Saint-Laurent.

Logo

Le motif du logo de l'Expo 67 s'inspire d'un ancien pictogramme représentant une silhouette humaine debout, les bras tendus, et est disposé par paires, en cercle, pour symboliser l'amitié universelle. Quant à la SCPH, elle a adopté un nouveau logo à l'occasion de son 70e anniversaire. L'aspect discontinu et chevauchant de la croix et du mortier stylisés ainsi que les différentes couleurs tentent d'évoquer le lien entre les multiples facettes de la pratique de la pharmacie — soins des patients, distribution des médicaments, formation, recherche, informatique, etc. — et de traduire la diversité des membres de la SCPH, de leurs domaines de pratique et des populations de patients qu'ils servent.

Thème

Le thème de l'Expo 67, « Terre des Hommes », reprend le titre d'un ouvrage par l'écrivain-aviateur français Antoine de Saint-Exupéry, publié en 1939. Les dirigeants d'Expo 67 ont assimilé leur vision de l'événement à la célébration de l'amitié, de l'assistance mutuelle et des valeurs humanistes émanant du livre. La SCPH souscrit aussi à ces principes, ce qu'elle a démontré en collaborant avec d'autres organismes de la santé à maintes affaires saillantes en 2017.

La SCPH était absolument ravie que son acharnement depuis sept ans à faire valoir les préoccupations des pharmaciens d'hôpitaux auprès du Bureau des substances contrôlées de Santé Canada ait enfin été récompensé par une exemption en vertu de l'article 56 de la *Loi réglementant certaines drogues et autres substances* pour les praticiens qui prescrivent de la méthadone à des patients hospitalisés. Depuis mars dernier, les praticiens n'ont plus à demander d'exemption temporaire pour poursuivre le traitement à la méthadone d'un patient la recevant déjà avant son hospitalisation.

La SCPH a pris sept engagements à l'égard de la Déclaration conjointe sur les mesures visant à remédier à la crise des opioïdes, une initiative menée par le Gouvernement du Canada (https://www.canada.ca/fr/sante-canada/services/toxicomanie/conference-opioides/declaration-conjointe-mesures-visant-remedier-crise-opioides.html). La SCPH a présenté deux autres engagements lors de sa participation au Sommet pharmaceutique sur les opioïdes auquel l'Association des pharmaciens du Canada avait convoqué 38 organismes et partenaires du secteur de la pharmacie en juin 2017 (https://www.pharmacists.ca/news-events/news/cpha-statement-on-canadian-pharmacists-conference-opioid-summit/).

Comme membre du Groupe de partenaires soucieux des pratiques exemplaires en matière de sécurité des soins chirurgicaux, la SCPH a sanctionné l'énoncé de position canadien sur le rétablissement amélioré après la chirurgie. Une stratégie de leadership et de dissémination a été élaborée pour soutenir la mise en œuvre des pratiques exemplaires pertinentes au rétablissement amélioré après la chirurgie, dans le cadre du Plan d'action sur la sécurité chirurgicale de l'Institut canadien pour la sécurité des patients (http://www.patientsafetyinstitute.ca/fr/toolsresources/enhanced-recovery-after-surgery/pages/additional-information.aspx).

Pavillons

L'Expo 67 présentait 90 pavillons nationaux, provinciaux et d'états, thématiques et commandités par le secteur privé. Afin d'arriver à visiter les plus populaires (Canada, États-Unis, France, Tchécoslovaquie et Union soviétique), je me rendais sur le site de bon matin avec ma chaise pliante et mon sac à lunch pour faire la queue avant l'ouverture des pavillons. Malgré cela, et à mon grand regret, les visas de trois pavillons manquaient toujours dans mon passeport à la clôture de l'Expo 67.

Tout au long de l'année, la SCPH a également dû se lever de bon matin pour parvenir à répondre à quelque 35 demandes de consultation et de collaboration formulées par maintes parties prenantes. Les réponses sur les sujets suivants intéresseront tout particulièrement les membres de la SCPH : à l'Association des facultés de pharmacie du Canada, sur l'ébauche de la version révisée des *Compétences visées par les programmes de formation de premier cycle en pharmacie* (*programmes d'entrée dans la profession*) *au Canada*; au Conseil canadien de l'agrément des programmes

de pharmacie, sur l'ébauche de la version révisée des *Normes d'agrément des programmes canadiens de formation des techniciens en pharmacie*; à Santé Canada, sur une demande de renseignements touchant l'approvisionnement en cannabis à des fins médicales et la gestion de ce produit dans les pharmacies hospitalières, sur un projet de règlement modifiant le *Règlement sur les aliments et drogues* pour permettre l'importation de drogues pour des besoins urgents en matière de santé publique (comme dans le cas de la crise des opioïdes) dont la vente est autorisée par une autorité réglementaire étrangère digne de confiance (à savoir une autorité appartenant aux États-Unis, à la Suisse ou à l'Union européenne), sur l'ébauche des documents d'orientation traitant de la manipulation et de la destruction des stocks inutilisables et des produits postconsommation (précisément ceux contenant des stupéfiants, des drogues contrôlées et des substances ciblées), sur un projet de règlement modifiant le *Règlement sur les aliments et drogues* pour renforcer la surveillance des opioïdes après leur mise en marché et exiger l'apposition d'un autocollant d'avertissement et la remise d'une fiche d'information à l'intention du patient lors de la dispensation des opioïdes d'ordonnance, sur un document de consultation et des discussions techniques en matière de déclaration obligatoire des réactions indésirables graves à un médicament et des incidents relatifs aux instruments médicaux par les établissements de santé, et sur le renouvellement du Programme d'accès spécial; et à l'Agence de santé publique du Canada, sur l'ébauche du *Cadre d'action pancanadien relatif à la résistance aux antimicrobiens et à l'utilisation des antimicrobiens.*

Pavillons thématiques

Les pavillons thématiques de l'Expo 67 étaient déclinés en variantes du thème prédominant « Terre des Hommes ». Ils exploraient l'humanité sous différents angles thématiques universels tels que l'agriculture, l'environnement, la santé, la technologie, la vie urbaine et les arts visuels.

Le lancement officiel en février 2017 du programme Excellence en pharmacie hospitalière constituait l'occasion propice au dévoilement de ses trois thèmes centraux : participation du patient/approche centrée sur le patient; meilleures pratiques (dont la sécurité des patients); communication efficace et pratique en collaboration. Le succès du programme sera évalué au regard de six principes et de quinze mesures de rendement (https://www.cshp.ca/excellence).

Grâce à la générosité de la compagnie Eli Lilly Canada, commanditaire unique depuis plus de 30 ans, le *Rapport sur les pharmacies hospitalières canadiennes* s'est taillé une réputation enviable comme référence et outil d'étalonnage pour les services de pharmacie hospitalière à l'échelle du Canada et même du monde. En 2017, le Conseil de la SCPH a accepté la demande du comité de rédaction du Rapport de l'admettre parmi ses conseils affiliés « thématiques ». Le Conseil de la SCPH chargé du sondage sur les pharmacies hospitalières, comme il s'appelle dorénavant, a réalisé le sondage 2016-2017 sous cette nouvelle affiliation, avec l'appui financier d'AstraZeneca Canada, d'Eli Lilly Canada et de Pfizer Canada. Les résultats paraîtront sous peu au www.hospitalpharmacysurvey.ca.

La SCPH a aussi mis en circulation une nouvelle publication, la *Synthèse canadienne sur l'optimisation de la médication* (c.-à-d. *Canadian Medication Optimization Briefing* [*CMOB*] en anglais), une série d'articles de consultation rapide, évalués par les pairs, sur des thèmes précis afférents à la pratique de la pharmacie clinique et traités chacun en deux pages. Avec la permission de la Royal Pharmaceutical Society et le Centre for Pharmacy Postgraduate Education en Grande-Bretagne, la mise en page s'est inspirée de leur *Medicines Optimisation Briefing*. Le premier numéro de la Synthèse portait sur la gérance des antimicrobiens et sa parution en version anglaise a coïncidé avec la Semaine mondiale pour un bon usage des antibiotiques 2017.

Pavillon du téléphone

Le pavillon commandité par l'Association du téléphone du Canada a captivé l'imagination des visiteurs. Aujourd'hui encore, je me souviens de son attraction vedette, *Canada '67* — un film documentaire produit par la compagnie Walt Disney et projeté sur un écran panoramique géant (*Circle-Vision 360°*) — ainsi que de son étalage de technologiques futuristes prodigieuses, comme les téléphones à clavier et sans fil, les services bancaires par téléphone et le Picturephone d'AT&T. Domaine de l'imaginaire?

La technologie a également été une préoccupation omniprésente pour la SCPH l'an dernier. D'abord, son site Web a profité d'une cure de jouvence bien méritée. Lorsque le site Web a été lancé, la SCPH a adopté simultanément le nouveau nom de domaine « .pharmacy » qui lui avait été octroyé en 2016 par la National Association of Boards of Pharmacy des États-Unis; un tel nom de domaine rassure les internautes quant à la sécurité et à la légitimité d'un site Web ayant trait à la pharmacie. En outre, le Conseil canadien de la résidence en pharmacie a mis à niveau son service d'appariement pour la résidence et l'a doté d'un processus centralisé de demande d'admission. Enfin, la SCPH a conçu un outil d'évaluation pour la préparation aseptique qui s'appuie sur les pratiques exemplaires exposées dans sa publication *Préparation pharmaceutique : Lignes directrices pour les pharmacies* (pour en savoir davantage, visitez le https://www.cshp.ca/assessment-tool-aseptic-compounding-0).

Hôtesses et hôtes

Sans contredit, les hôtesses et les hôtes ont contribué comme ambassadeurs et ambassadrices au succès retentissant de l'Expo 67. De même, les employés serviables de la SCPH ont joué un rôle clé dans ces réalisations impressionnantes. Qui plus est, avec l'embauche de Sarah Jennings à titre d'associée aux affaires professionnelles, l'effectif des pharmaciens à l'emploi de la Société a atteint 2,5 équivalents temps plein. La SCPH a eu d'autres raisons de célébrer au cours de sa 70e année : la naissance de la fille d'Amanda Iannaccio, l'embauche de Christopher Doody et de Julie Sobowale pour combler ensemble le poste d'agent aux publications durant le congé de maternité d'Amanda et le cinquième anniversaire d'embauche de Pamela Saunders (agente générale de programmes).

Héritage

À l'instar de l'Expo 67 qui a laissé des souvenirs indélébiles, puisse la SCPH façonner assidûment la pratique des pharmaciens dans les hôpitaux et les autres établissements de santé misant sur la collaboration par ses contributions inépuisables et inoubliables!

Myrella Roy, B. Sc. Phm., Pharm. D., FCCP, est directrice générale de la SCPH.

S'unir autour de valeurs fondamentales

par Lauza Saulnier

L'automne dernier, à Fredericton, au Nouveau-Brunswick, s'est tenu la 70e assemblée générale annuelle de la Société canadienne des pharmaciens d'hôpitaux (SCPH). Les membres du conseil de la SCPH et des représentants des conseils des sections de partout au pays ont tenu des réunions, ils ont participé au programme éducatif et ils ont célébré le 50e anniversaire de la section du Nouveau-Brunswick.

Être témoin du travail acharné et du dévouement des bénévoles et du personnel de la SCPH ainsi que de la camaraderie des membres m'a poussée à me demander ce que signifie être membre de la SCPH.

Grâce aux valeurs de la SCPH, les membres ont des liens en commun. La SCPH leur offre des occasions de réseautage avec des collègues d'autres régions, ce qui leur permet d'entendre parler de pratiques novatrices, de découvrir de nouveaux domaines d'intérêt, de vivre des expériences enrichissantes et de contribuer à l'évolution de la profession tout en faisant partie d'une communauté de pratique dynamique. Voici quelques exemples où les valeurs de la SCPH se manifestent par des actions qui aident les membres à tendre vers l'excellence d'une pratique de la pharmacie indispensable aux soins centrés sur le patient.

- *L'excellence et l'innovation dans le domaine des soins aux patients :* par la publication du document *Pratique de la pharmacie dans les hôpitaux et les autres milieux de soins de santé misant sur la collaboration : déclarations de principes*, qui décrivent la position de la SCPH ainsi que le niveau de performance souhaité et réalisable qu'on peut attendre de la pratique de la pharmacie; par la mise sur pied de programmes comme celui de l'Excellence en pharmacie hospitalière qui oriente le travail des membres vers l'amélioration des résultats cliniques en s'appuyant sur la participation du patient, les meilleures pratiques, la communication efficace et la pratique en collaboration; par des normes d'agrément pour les programmes postuniversitaires de résidence en pharmacie mises en place par le Conseil canadien de la résidence en pharmacie.
- *La collaboration interprofessionnelle :* par de solides partenariats avec des parties prenantes externes et une valorisation efficace d'une excellente pratique de la pharmacie en répondant à des demandes de consultation pertinentes et en collaborant avec des organisations nationales.
- *Le perfectionnement professionnel et le mentorat :* par des services et des activités qui inspirent aux membres l'excellence de leur pratique de la pharmacie, comme le *Journal canadien de la pharmacie hospitalière*, la Conférence sur la pratique professionnelle, le Séminaire de gestion en pharmacie Harrison et toute une gamme de programmes éducatifs offerts par les sections de la SCPH; par des réseaux de spécialistes en pharmacie qui facilitent le réseautage et la communication dans l'ensemble du pays entre les personnes ayant en commun des intérêts professionnels.
- *La reconnaissance de l'engagement des membres envers notre Société et la profession :* par l'intermédiaire du programme de prix qui récompense les membres s'étant distingués professionnellement ou ayant réalisé des projets importants pour la pratique de la pharmacie; par des gestes qui soulignent l'importance des bénévoles pour mener à bien les activités de la SCPH et de ses sections, des bénévoles qui offrent généreusement leur temps et partagent leurs connaissances et leurs expériences pour faire avancer la pratique de la pharmacie et aider la Société à atteindre ses objectifs.
- *L'obligation de rendre des comptes à nos membres :* par la publication du tableau de bord équilibré 2015–2020 de la SCPH qui met de l'avant les indicateurs clés de performance et les progrès réalisés vers l'atteinte des objectifs organisationnels; par des rapports semestriels produits par les sections provinciales, les conseils affiliés et les comités qui présentent la façon dont leurs objectifs et leurs actions sont intégrés dans les priorités stratégiques de la Société et qui indiquent les progrès réalisés.

Dans la dernière année, j'ai eu le privilège de rencontrer et de travailler avec des bénévoles enthousiastes et dévoués qui ont aidé à bâtir l'avenir et ont contribué à apporter des changements avec une incidence positive sur les résultats cliniques. Je suis fière d'être membre de la SCPH et de faire partie d'une société dynamique, en constante évolution, qui saura inspirer l'excellence d'une pratique de la pharmacie indispensable aux soins centrés sur le patient dans les hôpitaux et les autres milieux de soins de santé misant sur la collaboration.

[Traduction par l'éditeur]

Lauza Saulnier, B. Sc. (Pharm.), A.C.P.R., est présidente sortante et agente de liaison pour la vision de la Société canadienne des pharmaciens d'hôpitaux.

Becoming United through Core Values

Lauza Saulnier

Last fall, the 70th Annual General Meeting of the Canadian Society of Hospital Pharmacists (CSHP) was held in Fredericton, New Brunswick. Board members and branch council members from across the country conducted meetings, attended the educational program, and joined in the 50th anniversary celebration of the CSHP's New Brunswick Branch.

Witnessing the tireless work and dedication of CSHP volunteers and staff and the camaraderie among members made me ponder the question, "What does it mean to be a CSHP member?"

Members share common bonds through CSHP's values. CSHP provides opportunities to network with colleagues from other regions and learn about innovative practices, to discover new areas of interest, to participate in rewarding experiences, and to contribute to the advancement of the profession while belonging to a vibrant community of practice. Here are some tangible examples of how CSHP values support Society members in providing excellent pharmacy practice integral to patient-centred care:

- *Excellence and innovation in patient care*, through publications such as *Pharmacy Practice in Hospitals and Other Collaborative Healthcare Settings: Position Statements*, which express the CSHP's stance and describe a desired and achievable level of performance that is applicable to the practice of pharmacy; through programs such as Excellence in Hospital Pharmacy, an initiative that focuses members' efforts on improving patient health outcomes through patient engagement, best practice, effective communication, and collaborative practice; and through accreditation standards for postgraduate pharmacy residency training programs, established by the Canadian Pharmacy Residency Board.
- *Interprofessional collaboration,* through strong partnerships with external stakeholders and effective advocacy for excellent pharmacy practice, by responding to requests for relevant consultations and collaborating with national organizations.
- *Professional development and mentorship*, made available to members through services and events that lead and inspire excellent pharmacy practice, such as the *Canadian Journal of Hospital Pharmacy*, the Professional Practice Conference, the Harrison Pharmacy Management Seminar, and an array of educational programs offered by CSHP Branches; and through Pharmacy Specialty Networks, which facilitate nationwide networking and communication among individuals who share common professional practice interests.

- *Recognition of members' dedication to our Society and the profession* through the Awards Program, which acknowledges members who have distinguished themselves within the profession or have completed projects of importance to pharmacy practice; and through recognition of volunteers who contribute to CSHP activities at the national or branch level, generously giving time, sharing knowledge and life experiences to advance pharmacy practice, and helping the Society to achieve its goals and objectives.
- *Accountability to members*, through public reporting of the CSHP Balanced Scorecard 2015–2020, which highlights key performance indicators and progress toward achievement of organizational goals; and through semi-annual reporting by provincial branches, affiliated boards, and committees on how their objectives and actions are integrated within corporate strategic priorities and progress to date.

Over the past year, I have had the privilege of meeting and working with many enthusiastic and committed volunteers who help to shape the future and contribute to changes that will positively affect patient health outcomes. I am proud to be a CSHP member and to be part of a thriving, progressive Society, leading and inspiring excellent pharmacy practice integral to patient-centred care in hospitals and other collaborative healthcare settings.

Lauza Saulnier, BSc(Pharm), ACPR, is Past President and Vision Liaison for the Canadian Society of Hospital Pharmacists.

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

COMMUNAUTÉS DE PRATICIENS AYANT DES INTÉRÊTS SPÉCIAUX
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POUR AMÉLIORER LES SOINS AUX PATIENTS

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Les RSP :

- mettent les membres en contact avec d'autres personnes qui ont une passion pour un aspect particulier de la profession de pharmacien
- facilitent le partage rapide d'idées, de développements, de méthodes, d'expériences, de connaissances pour améliorer la pratique
- favorisent la collaboration à des projets, à des recherches et à des programmes éducatifs pour répondre aux besoins des membres des RSP
- proposent des occasions supplémentaires aux membres d'agir à titre de leaders d'opinion et de ressources clés pour le Conseil de la SCPH sur des questions de pratique spécialisée, dont la rédaction de déclarations de principes, de lignes directrices et des documents d'information pertinents

La participation aux RSP est gratuite pour les membres de la SCPH.

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