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Kananaskis Country, Alberta

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COVID-19: The New Challenges

Christine M Bond

As the second and third COVID-19 waves hit globally, including in Canada, it is timely to reflect on the current situation. While both policy and medical approaches have in general been guided by the science, the science has continually been catching up with the emerging body of evidence, and the practice of evidence-based medicine has become more complex than ever before.[1] Recommendations on effective treatments, lockdown approaches, and epidemiological modelling are constantly being revised. However, decisions about COVID-19 have implications far beyond the disease itself. The toll associated with delayed cancer diagnoses or deferred cardiac surgery and the pressures on health care staff may never be fully known. Further, the risk-benefit balance also includes political and economic considerations. Lockdown measures have had unimaginable consequences on the world economy and, at an individual level, have exposed social inequities (such as loss of employment and mental health issues) and disrupted the education of a generation of children, with disproportionately high numbers of elderly people experiencing the most severe morbidity and mortality.[2] Given this complexity, it is not surprising that, at the time of writing (in early 2021) and despite many sacrifices, we still have not overcome the pandemic.

Yet there is hope. Health Canada has now approved several vaccines,[3] with assurance of delivery of a combined total of 6 million doses in the first quarter of 2021.[4] However, decisions remain such as who should get the first vaccines. In common with many other countries, Canada has prioritized those in care homes for seniors, those over 80 years of age followed by those over 70, and those working in health care settings. It has also included Indigenous communities. The maximum rate of vaccination would be best achieved by involving the widest range of qualified professionals, including community pharmacists, yet Canada has been slow to communicate any tangible plans confirming the role of these providers.

In the meantime, all pharmacists can play their part by maximizing vaccine uptake in other ways. Two-thirds of Canadians have reportedly said they would take the vaccine if offered,[5] but a third would either wait or not take it at all. The latter group includes extreme vaccine deniers, who perpetrate conspiracy stories, and those who are concerned about potential unknown adverse effects. A focus on reassuring the uncertain rather than converting the anti-vaxxers is the most efficient policy.[6] Pharmacists, as trusted professionals, must reassure the public that the vaccines are safe and must dispel myths and misinformation. Convincing people may not be easy, but there are tools to help.[7] Pharmacists can also encourage people who have had the disease to still take the vaccine.[8] Further, once vaccinated, people must be advised to adhere to COVID-19 secure behaviour, including wearing a mask and social distancing. These measures must continue because immunity takes time to develop and because of the uncertainty of virus transmission after vaccination. Until everyone has been vaccinated, infections will continue to spread, and worries about "long COVID" and its effect on the younger working population cannot be ignored.[9]

Despite the optimism engendered by the vaccine program, we cannot expect to return to normality anytime soon. Unsurprisingly, the virus is already fighting back, and new variants or lineages are emerging. The effect of these on disease severity and the effectiveness of the vaccine itself are two more as-yet-unknown pieces of the COVID-19 jigsaw. These developments reinforce the need for our profession to play its part in controlling the virus spread by encouraging vaccine uptake and public health messaging.

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ON THE FRONT COVER

Gap and Elpoca Mountains, Kananaskis Country, Alberta

This photograph of Gap and Elpoca Mountains was captured by June Chen with a Canon PowerShot SD1100 IS digital camera. What started off as a snowy fall hike on Pocaterra Ridge ended up as a mild one under rays of sunshine!

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

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COVID-19 : Les nouveaux défis

par Christine M. Bond

Alors que les deuxième et troisième vagues de COVID-19 frappent le monde entier, y compris le Canada, il est temps de réfléchir à la situation actuelle. Bien que la science ait généralement guidé les approches politiques et médicales, elle a continuellement dû rattraper le retard par rapport à l'émergence de preuves, si bien que la pratique de la médecine factuelle est devenue plus complexe que jamais[1]. Les recommandations relatives à l'efficacité des traitements, aux approches portant sur le confinement et la modélisation épidémiologique sont constamment révisées. Cependant, les décisions portant sur la COVID-19 ont des conséquences bien au-delà de la maladie elle-même. On ne connaîtra peut-être jamais le bilan associé aux retards de diagnostics de cancer, aux chirurgies cardiaques différées ou aux pressions exercées sur le personnel de la santé. En outre, le rapport avantages-risques comprend également des considérations politiques et économiques. Les mesures de confinement ont eu des conséquences inimaginables sur l'économie mondiale et, sur le plan individuel, ont révélé les inégalités sociales, telles que la perte d'emploi et les problèmes de santé mentale, et perturbé l'éducation d'une génération d'enfants, avec un nombre disproportionnellement élevé de personnes âgées connaissant des morbidités et une mortalité très importantes[2]. Compte tenu de cette complexité, il n'est pas surprenant qu'au moment de la rédaction de cet article, au début de 2021, et malgré de nombreux sacrifices, nous n'ayons pas encore surmonté la pandémie.

Pourtant, il y a de l'espoir. Santé Canada a maintenant approuvé plusieurs vaccins[3], et promet la livraison de six millions de doses au total au courant du premier trimestre de 2021[4]. Cependant, des décisions restent à prendre, comme celles portant sur les personnes qui devraient recevoir les premiers vaccins. À l'instar de nombreux autres pays, le Canada a accordé la priorité aux personnes vivant dans les établissements de soins pour personnes âgées, à celles de plus de 80 ans, suivies de celles de plus de 70 ans et celles qui travaillent dans les environnements de soins de santé. Le gouvernement a également inclus les communautés autochtones dans les personnes prioritaires. Il serait plus facile d'atteindre le taux maximal de vaccination si un plus large éventail de professionnels qualifiés administraient le vaccin, les pharmaciens communautaires par exemple, mais le Canada a tardé à communiquer un plan concret confirmant le rôle de ces fournisseurs de services.

En attendant, tous les pharmaciens peuvent jouer un rôle en maximisant l'utilisation du vaccin par d'autres moyens. Les deux tiers des Canadiens auraient déclaré qu'ils se feraient vacciner si le vaccin leur était offert[5], mais un tiers attendrait ou ne le prendrait pas du tout. Ce dernier groupe comprend les opposants extrêmes aux vaccins, qui échafaudent des théories de complot, et ceux qui sont préoccupés par les potentiels effets indésirables inconnus. La politique la plus efficace consiste à mettre l'accent sur le besoin des indécis d'être rassurés plutôt que sur la conversion des opposants aux vaccins[6]. Les pharmaciens, en tant que professionnels de confiance, doivent rassurer le public sur la sécurité des vaccins et dissiper les mythes et la désinformation. Il n'est peut-être pas facile de convaincre les gens, mais des outils existent pour faciliter les choses[7]. Les pharmaciens peuvent également conseiller aux personnes qui ont eu la maladie de se faire vacciner[8]. De plus, une fois que les gens sont vaccinés, il faut les inciter à adhérer à un comportement responsable contre la COVID-19, soit porter un masque et respecter les mesures de distanciation physique. Ces mesures doivent se poursuivre en raison de l'immunité qui prend du temps à se développer et de l'incertitude de la transmission du virus après la vaccination. Tant que tout le monde n'aura pas été vacciné, on ne peut faire fi des infections qui continueront de se propager et des inquiétudes concernant la « durée de la COVID » et ses effets sur la population active plus jeune[9].

Malgré l'optimisme engendré par le programme de vaccination, nous ne pouvons pas nous attendre à un retour rapide à la normale. Comme on pouvait s'y attendre, le virus riposte déjà par l'apparition de nouveaux variants ou de nouvelles lignées. Leur effet sur la gravité de la maladie et l'efficacité du vaccin lui-même sont deux autres aspects encore inconnus du casse-tête que représente la COVID-19. Ces développements renforcent la nécessité pour notre profession de jouer un rôle dans le contrôle de la propagation du virus en encourageant le recours au vaccin et la diffusion de messages de santé publique.

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Soins plus — mise en place d'une intervention à trois volets visant à accroître la visibilité et la disponibilité du pharmacien dans un hôpital pédiatrique : une étude randomisée contrôlée

par Flaviu Mosora, Myriam Guèvremont, Gabriel Vézina, Karine Côté, Marianne Boulé, Denis Lebel, Jean-François Bussières et Marie-Élaine Métras

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RÉSUMÉ

Contexte : Le rôle du pharmacien au sein de l'équipe multidisciplinaire est souvent méconnu. Diverses interventions peuvent être mises en place pour promouvoir le rôle du pharmacien en milieu hospitalier auprès des familles, des patients et des autres professionnels de la santé. Peu d'études décrivent la faisabilité et évaluent l'impact de ces interventions, particulièrement en pédiatrie.

Objectifs : Décrire l'implantation d'une intervention à trois volets visant à accroître la visibilité du pharmacien et de son rôle dans l'équipe traitante, pour permettre d'optimiser les soins pharmaceutiques des patients hospitalisés dans les unités de pédiatrie générale du CHU Sainte-Justine, à Montréal (Québec). Comparer la perception et la satisfaction des parents de patients hospitalisés et des soignants recevant soit des soins pharmaceutiques usuels, ou soit des soins pharmaceutiques intégrant l'intervention.

Méthode : Étude expérimentale randomisée contrôlée à simple aveugle portant sur des patients admis dans les unités de pédiatrie générale entre le 5 mars et le 8 août 2019. Outre des soins usuels, l'intervention comporte la remise d'une brochure d'information sur les services et soins pharmaceutiques, l'accès à une ligne téléphonique permettant aux familles et aux patients de prendre contact avec un résident en pharmacie pendant leur séjour à l'hôpital et jusqu'à un mois après le congé et le remplissage par le pharmacien responsable du patient d'un formulaire de congé standardisé. Un sondage de perception et de satisfaction a aussi été réalisé auprès des participants et des professionnels de la santé concernés.

Résultats : Six cent quarante et un (641) participants ont été inclus dans l'étude, 321 dans le groupe intervention et 320 dans le groupe témoin. La brochure a été remise à tous les parents du groupe intervention. Douze appels téléphoniques ont été faits au moyen d'une ligne téléphonique spéciale. Le formulaire de congé standardisé de 46,7 % (150/321) des participants du groupe intervention a été rempli. Une majorité des parents et des patients ayant répondu au sondage (81,2 %, 298/367) se disent satisfaits des services et des soins pharmaceutiques reçus dans les deux groupes. Une proportion de 83,9 % des participants du groupe intervention se disent satisfaits des soins et services pharmaceutiques reçus comparativement à 78,5 % du groupe témoin ($p = 0,18$). De plus, 60,3 % (111/184) des participants du groupe intervention disent que l'information transmise pendant l'hospitalisation concernant les médicaments leur a apporté de nouvelles connaissances, contre 48,1 % (87/181) des participants du groupe témoin ($p = 0,019$). Les résultats du sondage montrent que les soignants sont en accord avec l'intervention.

Conclusion : Les trois volets de l'intervention ont été implantés dans les unités de pédiatrie sur une période de cinq mois. Cette intervention est perçue comme étant positive par les parents et les soignants concernés et les répondants ont été majoritairement satisfaits des services et des soins pharmaceutiques offerts.

Mots-clés : pharmacien, ligne téléphonique, formulaire de congé standardisé, brochure d'information

ABSTRACT

Background: The pharmacist's role within the multidisciplinary team is often poorly understood. Various interventions can be put into place to promote the role of the pharmacist in the hospital setting with families, patients, and other health care professionals. Few studies have described the feasibility and assessed the impact of such interventions, particularly in pediatrics.

Objectives: To describe the implementation of a 3-part intervention aimed at increasing the visibility of pharmacists and their role on the treatment team, with the goal of optimizing the pharmaceutical care of hospitalized patients in the general pediatric units of CHU Sainte-Justine, in Montréal, Quebec, and to compare the perceptions and satisfaction of patients' parents and of health care professionals with exposure to either usual pharmaceutical care or to pharmaceutical care incorporating the intervention.

Methods: This single-blind, randomized, controlled experimental study involved patients admitted to general pediatric units between March 5 and August 8, 2019. In addition to usual care, the intervention included delivery of an information brochure about pharmaceutical services and care, access to a telephone line (which allowed families and patients to contact a pharmacy resident during their stay in hospital and up to 1 month after discharge), and completion of a standardized discharge form by the pharmacist responsible for the patient. The participants and health professionals concerned were surveyed to determine their perceptions and level of satisfaction.

Results: A total of 641 participants were included in the study, 321 in the intervention group and 320 in the control group. The brochure was given to all parents in the intervention group. Twelve phone calls were made through the dedicated telephone line. The standardized discharge form was completed for 46.7% (150/321) of the participants in the intervention group. Most of the parents and patients who responded to the survey, in either group (81.2%, 298/367), reported satisfaction with the pharmaceutical services and care received. Of participants in the intervention group, 83.9% were satisfied with the pharmaceutical care and services received, compared with 78.5% of those in the control group ($p = 0.18$). In addition, 60.3% (111/184) of participants in the intervention group said that the information about medications that was provided during the hospital stay gave them new knowledge, compared with 48.1% (87/181) of those in the control group ($p = 0.019$). The results of the survey showed that care providers were in agreement with the intervention.

Conclusions: The 3 components of the intervention were implemented in the pediatric units over a period of 5 months. The intervention was perceived as positive by the parents and care providers concerned, and the respondents were mostly satisfied with the services and pharmaceutical care offered.

Keywords: pharmacist, telephone line, standardized discharge form, information brochure

INTRODUCTION

Les soins pharmaceutiques ont beaucoup évolué au cours des dernières décennies[1]. Bien que la plupart des patients hospitalisés soient en contact avec des pharmaciens, une méconnaissance du rôle de ces derniers persiste au sein de l'équipe multidisciplinaire[2-6]. Les patients ne sont pas toujours conscients qu'il existe des pharmaciens à l'hôpital et qu'il est possible de recourir à leurs services. Dans le même ordre d'idées, le pharmacien a un rôle important en pédiatrie pour gérer des enjeux spécifiques à la population pédiatrique, tels que l'administration des médicaments ou la disponibilité de formes pharmaceutiques particulières après le congé. Plusieurs auteurs ont mis en évidence quelques interventions visant à rendre davantage visibles la présence et le rôle du pharmacien auprès des soignants et des patients [4,7,8]. Parmi ces interventions, on retrouve notamment la remise d'information sur le rôle du pharmacien, le bon usage des médicaments ainsi que l'utilisation d'outils contribuant à une meilleure planification du congé[4,7]. Dans l'optique d'une amélioration continuelle des soins pharmaceutiques offerts aux patients, nous nous sommes donc questionnés sur la possibilité de développer une intervention à visée informative et collaborative. Toutefois, il existe peu d'études évaluant la faisabilité et l'impact de ces interventions, particulièrement en pédiatrie. Nous voulons décrire l'implantation d'une intervention à trois volets et son ajout aux soins usuels dans les unités de pédiatrie générale. Notre hypothèse postule que l'implantation de cette intervention est réaliste et que la satisfaction des parents concernés par l'intervention sera supérieure à celle des parents du groupe contrôle.

MÉTHODE

Protocole de l'étude

Il s'agit d'une étude descriptive, randomisée, contrôlée, à simple aveugle. L'étude a été approuvée par le comité d'éthique de la recherche du CHU Sainte-Justine.

Population à l'étude

L'étude cible tous les patients hospitalisés dans les unités de pédiatrie générale du CHU Sainte-Justine, un hôpital mère-enfant de soins tertiaires de 500 lits, situé à Montréal (Québec), entre le 5 mars et le 8 août 2019. Étant donné que l'étude portait sur une population pédiatrique, l'intervention en trois volets est davantage destinée aux parents et aux patients plus âgés (adolescents ≥ 14 ans). Ainsi, dans ce texte, le terme « parent » inclut les patients. Les adolescents de plus de 14 ans recevaient la même information que leurs parents.

Pour être inclus dans l'étude, le patient devait avoir entre 0 et 20 ans et être admis ou transféré d'une autre unité au nom d'un pédiatre, d'un infectiologue, d'un neurologue, d'un généticien ou d'un immunologue dans l'une des quatre unités de pédiatrie que ciblait le projet. Il devait également avoir obtenu son congé durant la période d'étude. Les parents devaient détenir une adresse courriel et consentir à remplir le sondage d'évaluation des soins et services pharmaceutiques.

Les parents ne comprenant pas le français écrit, les patients réadmis durant la période de l'étude et ayant déjà participé à l'étude ou refusé d'y participer lors d'une hospitalisation antérieure, les patients ayant obtenu leur congé le même jour que leur admission, ceux transférés à une autre spécialité et ceux prenant part à une autre étude interagissant avec la présente étude étaient exclus. Les patients pour qui le contexte clinique et social était jugé inapproprié n'ont pas été recrutés.

Interventions

Les participants du groupe témoin ont reçu les soins pharmaceutiques usuels prodigués par le pharmacien responsable du patient, soit une revue quotidienne de leur dossier, la participation à la tournée médicale, une rencontre avec les patients si nécessaire et des interventions liées à leur pharmacothérapie. Les soins pharmaceutiques usuels sont donc adaptés aux patients présents aux unités et priorisés selon la charge de travail quotidienne.

Les participants du groupe intervention ont été exposés aux soins pharmaceutiques usuels ainsi qu'à l'intervention comportant trois volets : la remise d'une brochure d'information sur les services et soins pharmaceutiques, l'accès à une ligne téléphonique et le remplissage par le pharmacien d'un formulaire de congé standardisé.

La brochure d'information a été conçue par les pharmaciens du CHU Sainte-Justine (la brochure est disponible aux lecteurs, sur demande à l'auteure correspondante). Elle était remise aux parents du groupe intervention en format papier lors du recrutement, après la randomisation. Cette brochure de 16 pages (3250 mots) porte sur la pratique de la pharmacie hospitalière, le rôle du pharmacien hospitalier, la gestion des médicaments à l'hôpital, l'observance aux médicaments et propose quelques astuces pratiques pour la gestion et l'administration des médicaments à domicile.

La ligne téléphonique consacrée à la réalisation du protocole permettait aux parents de joindre directement un résident en pharmacie, de 8 heures à 18 heures en semaine et jusqu'à 28 jours après le congé. Le numéro remis aux participants était lié à un téléphone intelligent destiné à l'étude. Une boîte vocale recevait les appels reçus à l'extérieur des heures d'ouverture et à un moment où le résident n'était pas disponible. Un délai de 24 heures ouvrables était prévu pour donner une réponse verbale aux parents. Le résident en pharmacie validait systématiquement les réponses auprès du pharmacien responsable du patient.

Le résident en pharmacie déposait le formulaire de congé standardisé au dossier du patient dans la section des ordonnances (Annexe 1, publiée au https://www.cjhp-online.ca/index.php/cjhp/issue/view/204). Une fois le formulaire déposé, le résident informait le pharmacien responsable du patient par courriel, par message texte ou en personne selon le moyen convenu. Le pharmacien responsable du patient

devait remplir le formulaire afin de décrire les interventions pharmaceutiques envisagées avant le congé et faciliter la planification du congé. Le document était destiné aux autres intervenants participant aux soins du patient durant son hospitalisation, dont le médecin traitant et les infirmières présentes aux unités de soins.

Objectifs

L'objectif primaire était de décrire l'implantation d'une intervention à trois volets visant à accroître la visibilité du pharmacien et son rôle auprès des familles et de l'équipe traitante, afin d'optimiser les soins pharmaceutiques.

L'objectif secondaire était de comparer la perception et la satisfaction des parents de patients hospitalisés et des soignants relatives aux soins pharmaceutiques usuels et aux soins pharmaceutiques intégrant l'intervention.

Les données disponibles sur les caractéristiques des patients étaient recueillies auprès du parent lors du recrutement ainsi qu'à l'aide du dossier du patient.

Concernant la brochure d'information, nous avons documenté la remise ou non de la brochure aux patients du groupe intervention. Quant à la ligne téléphonique, le nombre d'appels reçus, le délai de réponse aux questions posées par téléphone, les heures des appels avec le parent ainsi que la durée de chaque communication ont été colligés. À la suite de la colligation de ces données, une rencontre entre tous les pharmaciens de l'équipe a eu lieu pour déterminer si l'implantation de cette intervention n'alourdissait pas trop la charge de travail. Pour ce qui est du formulaire de congé standardisé, nous avons évalué le dépôt ou non du formulaire de congé dans le dossier du patient. Le journal de bord des pharmaciens, un outil préexistant de documentation quotidienne des activités pharmaceutiques, a servi à comptabiliser le nombre d'interventions faites par le pharmacien pour chaque patient de l'étude.

L'évaluation de la perception et de la satisfaction des parents et des soignants ayant participé à l'étude, liées aux services et aux soins pharmaceutiques, s'est déroulée à l'aide de sondages. Sept jours après le congé du patient, chaque parent a reçu un courriel affichant un hyperlien vers le sondage. Ceux qui n'avaient pas répondu recevaient entre un et trois rappels hebdomadaires. Le sondage visait à évaluer leurs connaissances du rôle du pharmacien, les soins et services qu'ils avaient reçus du Département de pharmacie, leur perception et leur satisfaction quant aux soins pharmaceutiques dont ils avaient bénéficié. Une section était aussi disponible pour les commentaires des répondants. Quant aux soignants (c.-à-d. médecins et infirmières), ils ont reçu à la fin de l'expérience une version électronique ou papier de leurs connaissances, de leur perception et de leur satisfaction relativement aux services et aux soins pharmaceutiques dispensés. Le sondage auprès des professionnels visait un objectif exploratoire servant à vérifier l'impact de ces interventions sur le personnel soignant. Une échelle de Likert à quatre choix a permis de mesurer la satisfaction (TA = très en accord, PA = partiellement en accord, PD = partiellement en désaccord, TD = totalement en désaccord) dans les deux sondages. Ceux-ci pouvaient être remplis en ligne, mais des versions papier ont été distribuées aux unités de soins pour faciliter le remplissage (Google Forms, Google LLC).

Taille échantillonnale

Un échantillon de 700 patients (soit, 350 dans chaque groupe) a été ciblé initialement. Une grande taille d'échantillon semblait adéquate pour représenter le roulement rapide des patients aux unités de pédiatrie générale et refléter les circonstances réelles d'implantation. À partir de cet échantillon de 700 patients et avec une estimation du taux de réponses des parents de 70 %, nous étions en mesure de détecter une différence de satisfaction de 6,5 % d'un taux de satisfaction estimé à 90 % pour l'objectif secondaire. Ce taux de 90 % provient d'une étude menée sur la satisfaction des patients dans une autre unité du même centre hospitalier[9].

Randomisation

Les populations présentes dans chacune des quatre unités de pédiatrie générale peuvent comporter des spécificités en termes de diagnostics. Afin d'assurer une distribution adéquate de chaque population dans le groupe témoin et intervention, les investigateurs ont fait une randomisation stratifiée par unité de soins choisie. Chaque patient, dont le résident en pharmacie et le pharmacien responsable ont vérifié l'admissibilité, a reçu un numéro au hasard afin de déterminer son ordre de randomisation. Après une vérification des critères d'inclusion et d'exclusion les chercheurs ont attribué le patient à son groupe selon une randomisation par blocs de quatre, selon un ratio d'allocation 1:1, stratifiée par unité de soins (effectuée avec RANDOM.ORG, Randomness and Integrity Services Ltd, Dublin, Irlande). Ensuite, un résident en pharmacie a procédé au recrutement et à l'enrôlement dans l'étude. Les participants ne connaissaient pas le groupe auquel ils appartenaient, ce qui assurait le simple aveugle de cette étude.

Analyses statistiques

Les données recueillies ont été saisies dans une base de données (Access, Microsoft Corporation). Elles ont été transférées dans un chiffrier (Excel, Microsoft Corporation), puis analysées avec Excel et GraphPad (version en ligne) (GraphPad Inc).

L'évaluation de l'objectif primaire a fait appel aux seules statistiques descriptives.

Quant à l'objectif secondaire, les chercheurs ont commencé par diviser les réponses concernant la perception et la satisfaction des participants et des soignants en réponses positives (totalement en accord et partiellement en accord) et négatives (totalement en désaccord et partiellement en désaccord). Pour ce qui est du sondage visant les participants, un test du chi-carré a permis de comparer les proportions

recueillies dans les deux groupes. Lorsque l'échantillon était inférieur à 30 participants pour une variable, les investigateurs ont eu recours au test exact de Fisher. Quand les variables du sondage étaient évaluées par une moyenne, un test de *t* de Student a permis de comparer les moyennes entre les deux groupes. Quant au sondage pour les soignants, seules des statistiques descriptives ont été utilisées. Une valeur de *p* inférieure à 0,05 est considérée comme statistiquement significative.

RÉSULTATS

Caractéristiques des participants

Sur les 924 patients admissibles, 283 ont été exclus en raison des critères d'exclusion ou parce qu'ils ont obtenu leur congé avant le recrutement par le résident en pharmacie. Six cent quarante et un (641) participants ont été inclus dans l'étude (Figure 1). Les résultats concernant les caractéristiques des participants démontrent que la randomisation ainsi que la stratification par unité de soins ont bien fonctionné et que les groupes sont comparables autant sur le plan des caractéristiques que des classes diagnostiques.

Le tableau 1 présente les caractéristiques des patients inclus dans l'étude.

Description de l'intervention

Les trois volets de l'intervention ont été mis en place pour les 321 participants du groupe intervention.

Après la randomisation, tous les participants du groupe intervention (n = 321) ont reçu la brochure d'information remise par le résident en pharmacie lors du recrutement.

Douze appels ont été reçus par la ligne téléphonique spéciale; six de ces appels ont été pris en charge en direct et les six autres par la boîte vocale. Les parents et un pharmacien communautaire ont pris l'initiative de faire onze appels. Le tiers (4/12) des questions posées lors des appels portaient sur l'innocuité. Les autres questions concernaient les allergies, le remboursement d'un médicament, l'efficacité d'un traitement, la prise concomitante de plusieurs médicaments, le diagnostic, une dose omise ou vomie ou encore la stabilité des médicaments. Les participants pour lesquels la ligne téléphonique a été utilisée avaient en moyenne 3,2 ans et prenaient en moyenne 3,1 médicaments au congé. Le délai de réponse moyen était de 4,2 heures (médiane : 1,4 heure) entre le moment où la question était posée et le retour d'appel. Ce dernier a duré en moyenne neuf minutes.

Le formulaire de congé standardisé a été versé au dossier de tous les patients du groupe intervention mais rempli pour seulement 46,7 % (150/321) de ces patients.

Sondage auprès des parents

Concernant l'objectif secondaire, 58,6 % (188/321) des parents du groupe intervention et 57,5 % (184/320) des parents du groupe témoin ont rempli le sondage (tableau 2). Puisque certains répondants n'ont pas complètement rempli le sondage, le dénominateur de chaque question est individualisé.

Une majorité des répondants (81,2 %, 298/367) se disent satisfaits des services et soins pharmaceutiques reçus, indépendamment du groupe dans lequel ils étaient intégrés. Dans le groupe intervention, 83,9 % se disent partiellement ou totalement satisfaits comparativement à 78,5 % dans le groupe témoin, mais cette différence n'était pas statistiquement significative (p = 0,18).

Des 57 répondants (15,3 %, 57/372) disant avoir reçu les services d'un pharmacien pendant l'hospitalisation, 49 (86 %, 49/57) se disent totalement satisfaits, six (10,5 %, 6/57) se disent partiellement satisfaits de leurs échanges avec le pharmacien. Dans le groupe intervention, 96,9 % (31/32) se

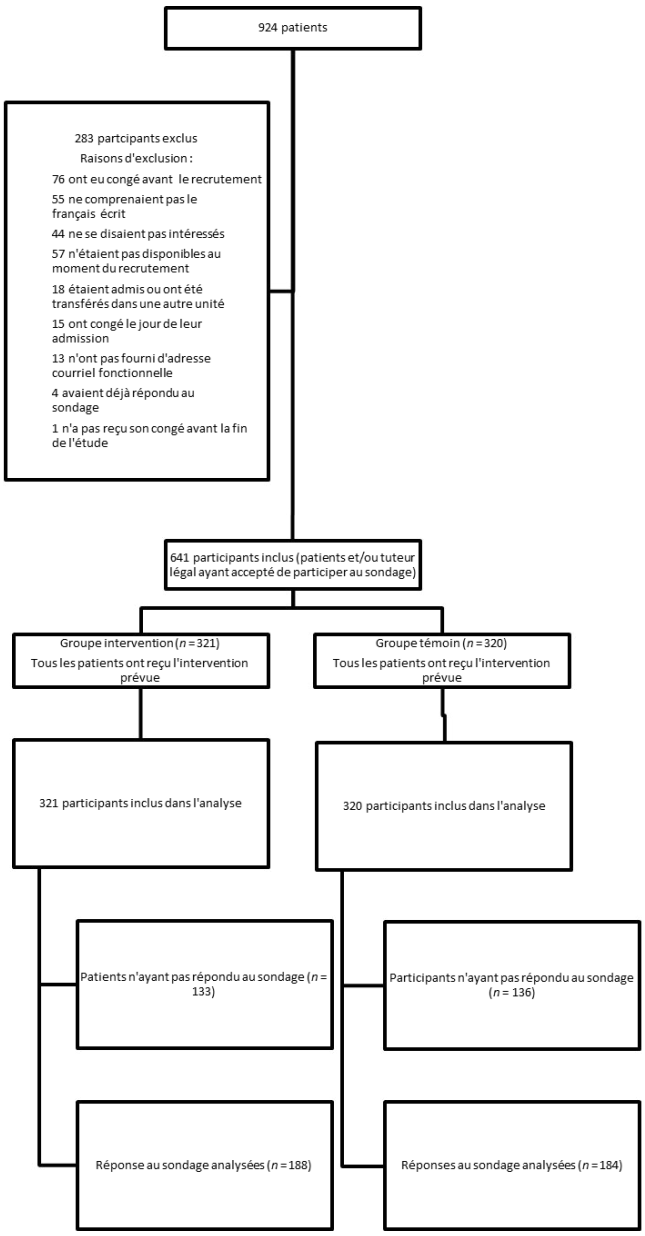

FIGURE 1. Diagramme de flux des participants.

disent partiellement ou totalement satisfaits comparativement à 96 % (24/25) du groupe témoin ($p = 0,86$).

À la suite de la remise de la brochure, une majorité (88 %, 161/183) des répondants sont partiellement ou totalement en accord avec le fait que le rôle du pharmacien est méconnu et qu'on devrait mieux informer les patients, contre 83,2 % (149/179) du groupe témoin ($p = 0,20$). Les parents ayant reçu la brochure ne démontraient pas une meilleure connaissance des rôles du pharmacien clinique (4,6 rôles mentionnés contre 4,3 dans le groupe témoin) ($p = 0,10$). Cependant, 60,3 % (111/184) des participants du groupe intervention disent être partiellement ou totalement d'accord que l'information transmise pendant l'hospitalisation concernant les médicaments leur a apporté de nouvelles connaissances, contre 48,1 % (87/181) de ceux du groupe témoin ($p = 0,019$), ce qui résulte en une différence statistiquement significative. Les commentaires des répondants reflètent aussi le fait que les parents sont mal informés de la disponibilité du pharmacien à l'unité de pédiatrie et qu'ils auraient aimé avoir un contact avec le pharmacien durant l'hospitalisation de leur enfant.

Il existe des incohérences dans les résultats du sondage. Une proportion de 75,7 % (78/103) des participants du groupe intervention qui ont affirmé avoir reçu de l'information de la part du pharmacien ont dit avoir reçu la brochure. Étonnamment, 27,1 % (13/48) des répondants du groupe témoin ont aussi répondu avoir reçu la brochure. Par ailleurs, 47,6 % (151/317) des participants ont répondu avoir reçu de l'information du pharmacien, mais 70,2 % (106/151) ont également répondu n'avoir eu aucun contact avec le pharmacien pendant leur séjour, ce qui semble contradictoire. Un seul des participants ayant utilisé les services de la ligne téléphonique a répondu avoir utilisé cet outil de communication. De plus, les trois autres répondants qui ont dit l'avoir utilisé n'ont aucun appel documenté associé à leur numéro de participant.

Sondage auprès des soignants

En ce qui concerne l'objectif secondaire, 23 sondages ont été remplis à la suite de l'intervention. Le tableau 3 présente la perception et la satisfaction des soignants vis-à-vis des soins et services pharmaceutiques offerts dans les deux groupes.

Les résultats du sondage montrent que les soignants sont en accord avec l'intervention. Une grande majorité des répondants ont répondu être totalement ou partiellement en accord avec le fait que les trois volets de l'intervention sont une excellente idée (tableau 3). Une proportion de 31,8 % (7/22) des professionnels ayant répondu au sondage disent avoir remarqué qu'à la suite à l'intervention, les notes pharmaceutiques relatives au congé étaient plus explicites.

TABLEAU 1. Caractéristiques des patients inclus dans l'étude

Caractéristiques	Groupe intervention ($n = 321$)	Groupe témoin ($n = 320$)
Âge au moment du recrutement (ans)		
Moyenne ± écart-type	4,0 ± 4,9	4,4 ± 5,1
Médiane	1,7	1,9
Assurance médicament privée, *n* (%)	220 (68,5)	228 (71,3)
Nombre moyen de médicaments par patient à l'admission, y compris les médicaments au besoin (moyenne ± écart-type)	1,7 ± 2,0	1,6 ± 2,0
Nombre moyen de médicaments prescrits au départ du CHU Sainte-Justine (moyenne ± écart-type)	2,5 ± 2,2	2,5 ± 2,3
Classes diagnostiques, *n* (%)		
Infectiologie	203 (63,2)	192 (60,0)
Gastroentérologie	45 (14,0)	38 (11,9)
Neurologie	21 (6,5)	23 (7,2)
Pneumologie	20 (6,2)	15 (4,7)
Rhumatologie / immunologie	11 (3,4)	13 (4,1)
Psychiatrie	4 (1,2)	6 (1,9)
Génétique	3 (0,9)	4 (1,3)
Hématologie	2 (0,6)	8 (2,5)
Autres	12 (3,7)	21 (6,6)
Nombre moyen de jours d'hospitalisation (moyenne ± écart-type)	5,0 ± 6,2	4,6 ± 5,0
Nombre moyen d'hospitalisations au CHU Sainte-Justine dans la dernière année (moyenne ± écart-type)	0,7 ± 1,7	0,5 ± 1,3
Nombre moyen d'interventions par patient, que les pharmaciens de l'équipe de pédiatrie ont documentées dans le journal de bord (moyenne ± écart-type)	2,4 ± 2,5	2,3 ± 2,6

TABLEAU 2. Perception et satisfaction des parents vis-à-vis des soins et services pharmaceutiques offerts dans les deux groupes

Issues	Groupe intervention	Groupe témoin	Valeur de *p*
Taux de réponse au sondage, *n*/*N* (%)	188/321 (58,6)	184/320 (57,5)	0,78
Satisfaction globale des parents vis-à-vis des services et soins pharmaceutiques reçus, *n*/*N* (%) satisfaits	156/186 (83,9)	142/181 (78,5)	0,18
Impact de la brochure d'information			
Nombre de rôles du pharmacien mentionnés par les répondants sur les sept rôles proposés (moyenne ± écart-type)	4,6 ± 1,9	4,3 ± 1,8	0,10
Répondants en accord avec l'énoncé : « L'information transmise concernant les médicaments m'a apporté de nouvelles connaissances » , *n*/*N* (%)	111/184 (60,3)	87/181 (48,1)	0,019
Satisfaction des parents vis-à-vis des échanges avec le pharmacien, *n*/*N* (%) satisfaits	31/32 (96,9)	24/25 (96,0)	0,86
Proportion des répondants disant avoir tenté d'entrer en contact avec le pharmacien pendant leur séjour ou celui de leur enfant, *n*/*N* (%)	17/188 (9,0)	9/184 (4,9)	0,12
Nombre (%) de parents ayant tenté d'entrer en contact avec le pharmacien pendant leur séjour ou celui de leur enfant			
En le rencontrant directement	5/17 (29,4)	6/9 (66,6)	0,10
En demandant au personnel médical	11/17 (64,7)	5/9 (55,6)	0,69
Par la ligne téléphonique	3/17 (17,6)	1/9 (11,1)	> 0,99
En posant la question au résident en pharmacie lors du recrutement	1/17 (5,9)	0/0 (0,0)	> 0,99
Nombre (%) des répondants disant avoir contacté le pharmacien pendant leur séjour ou celui de leur enfant	32/188 (17,0)	25/184 (13,6)	0,36
Nombre de fois où le répondant dit avoir joint le pharmacien pendant son séjour ou celui de son enfant (moyenne ± écart-type)	1,4 ± 0,6	1,5 ± 0,7	0,57

DISCUSSION

Pour ce qui est de l'objectif principal, cette étude a permis de décrire la mise en place de l'intervention concernant chacun des trois volets.

Quant à l'objectif secondaire, comme le degré de satisfaction des parents à l'endroit des soins et services pharmaceutiques usuels était déjà élevé, il n'a pas été possible de démontrer une augmentation de la satisfaction après la mise en place de notre intervention dans le groupe intervention par rapport au groupe témoin. Les soignants ayant participé aux interventions sont quant à eux en accord avec la mise en place de ces trois volets.

Brochure d'information

Notre étude révèle un intérêt réel pour la remise aux parents d'une brochure d'information sur les services et soins pharmaceutiques. Tous les patients du groupe intervention ont reçu la brochure. Ils ont été plus nombreux que ceux du groupe témoin à répondre qu'ils ont acquis de nouvelles connaissances sur les médicaments. Les commentaires recueillis lors du sondage reflètent également que les parents connaissaient peu le rôle du pharmacien et que plusieurs ignoraient sa présence dans l'hôpital et dans l'équipe de soins. Bajwa et collab. ont également remis à des parents une brochure décrivant le rôle du pharmacien dans une unité de soins intensifs néonataux pour augmenter la visibilité de ce professionnel de la santé[5]. La distribution de la brochure n'a pas permis d'augmenter le nombre de familles se souvenant d'avoir rencontré le pharmacien pendant leur séjour, mais les résultats indiquent que les patients aimeraient le rencontrer pendant leur hospitalisation[5]. Plusieurs répondants à notre sondage ont aussi manifesté de l'intérêt à rencontrer le pharmacien et pensent que les parents devraient être mieux informés de sa présence. Notre brochure a été produite en collaboration avec les éditions de l'Hôpital. Elle est donc disponible dans une section spéciale de leur site internet et le grand public peut y accéder en ligne. Certains pharmaciens travaillant dans des milieux externes ont même commencé à diffuser la brochure pour les conseils qu'elle contient et ils nous ont transmis des commentaires positifs.

À la lumière de ces résultats, la brochure d'information sera disponible à l'échelle de l'établissement. Il est probable qu'elle nécessite des adaptations en fonction de certaines patientèles (p. ex. oncologie, obstétrique-gynécologie, néonatologie). Des discussions sont en cours afin de déterminer le mode

TABLEAU 3. Perception et satisfaction des soignants vis-à-vis des soins et services pharmaceutiques offerts dans les deux groupes

Variables	Post-exposition	
Profession des répondants		
Médecins	8/23	(34,8)
Infirmières	13/23	(56,5)
Autre	2/23	(8,7)
Brochure : La remise systématique d'un guide d'accueil par les services et soins pharmaceutiques aux patients hospitalisés est une excellente idée [en accord]	20/23	(87,0)
Ligne téléphonique : La remise d'un numéro de téléphone permettant aux patients de joindre directement le pharmacien durant le séjour hospitalier est une excellente idée [en accord]	21/23	(91,3)
Formulaire de congé standardisé : La mention explicite des attentes du pharmacien à l'égard du congé du patient est une excellente idée [en accord]	22/23	(95,7)
Réponse à l'énoncé : J'ai remarqué la présence de notes plus explicites des pharmaciens concernant le congé [Oui]	7/22	(31,8)

optimal de diffusion qui tienne compte de nos préoccupations environnementales (possibilité d'inscrire le code QR sur une carte d'affaires ou documentation remise aux patients).

Ligne téléphonique

En ce qui concerne la ligne téléphonique, le nombre d'appels reçus était limité, ce qui laisse penser que cette mesure ne devrait pas affecter de façon importante la charge de travail des pharmaciens. En effet, il semble réaliste d'intégrer le temps nécessaire à la gestion des appels dans l'horaire du pharmacien, puisqu'on s'attend à moins de deux appels par semaine et que le nombre d'appels pourrait même augmenter légèrement. Toutefois, le faible nombre d'appels (taux d'utilisation de la ligne téléphonique : 3,1 %) peut être lié au fait que le recrutement était effectué par un résident en pharmacie ne participant pas aux soins plutôt que par le pharmacien lui-même responsable du patient. De plus, les parents ont la possibilité de prendre contact avec un pharmacien de différentes façons lors de l'hospitalisation. En effet, parmi les parents qui ont tenté de contacter un pharmacien, certains l'ont fait en le rencontrant directement ou en demandant à l'équipe médicale de le rencontrer. La ligne téléphonique peut donc avoir servi à répondre à quelques questions supplémentaires, surtout après le congé du patient. Au total, la ligne téléphonique a permis de répondre à 12 questions. La plupart des appelants ont téléphoné après le congé (11/12). En l'absence de ligne téléphonique, le pharmacien communautaire du patient aurait probablement pu répondre à la majorité des questions. Cependant, la connaissance du dossier hospitalier est un avantage pour répondre aux questions, comme en témoignent les résultats de Badiani et collab. qui ont observé que l'accès aux données locales, y compris au dossier du patient, aux procédures locales ou à l'accès à un professionnel connaissant le dossier du patient, était nécessaire dans 74,8 % des appels[10]. Des sondages évaluant l'expérience avec des lignes téléphoniques destinées aux patients et prises en charge par les pharmaciens d'hôpitaux démontrent que cet outil augmente la satisfaction des patients, les rassure et permet la résolution de problèmes[10-12]. Quant au délai de réponse, il est probablement surestimé en raison de la nécessité de valider les réponses des résidents auprès du pharmacien responsable du patient.

À la lumière de ces résultats, la ligne téléphonique sera élargie à d'autres unités de soins au moyen d'appareils téléphoniques attribués à certaines équipes de pharmaciens, qui serviront également aux appels entre soignants. Les pharmaciens pourront choisir de donner le numéro de téléphone à des parents ciblés.

Formulaire de congé standardisé

Les pharmaciens ayant participé à notre étude ont soulevé le fait que le formulaire n'était pas pertinent pour tous les patients et que son remplissage systématique représentait une charge de travail importante sans retombées favorables, ce qui pourrait expliquer le taux de remplissage de 47,6 % du formulaire de congé standardisé. Ainsi, le formulaire était déposé au dossier, mais n'était pas toujours rempli. En effet, c'était le pharmacien responsable du patient qui remplissait normalement le formulaire de congé standardisé lorsqu'une ou des interventions étaient nécessaires, par exemple avant un congé. Quand il devait ajouter un nouveau médicament sous forme de préparation magistrale ou que le médicament nécessitait une mise au courant spécifique et plus complexe (p. ex : antibiotique intraveineux à domicile) ou encore qu'un médicament nécessitait des démarches supplémentaires auprès des assurances, sa charge de travail s'alourdissait. Étant donné que la majorité de la population pédiatrique a un dossier pharmacologique relativement simple, le formulaire de congé standardisé n'était nécessaire que pour un nombre restreint de patients. Un pharmacien désirant absolument voir un patient avant son congé devait continuer d'utiliser d'autres approches pour le faire, comme un avis verbal à l'infirmière et au médecin traitant.

Plusieurs études mettent en évidence l'utilité d'une liste de contrôle multidisciplinaire à dresser avant le congé d'un patient adulte[13-18]. Voirol et collab. ont évalué l'effet d'un programme de congé standardisé par le pharmacien en pédiatrie et ont noté un impact positif sur le temps nécessaire à l'obtention des médicaments après le congé et une satisfaction accrue des parents[8]. Au Québec, le ministère de la Santé et des Services sociaux considère que le fait d'instaurer une fiche de transfert de soins comme formulaire de congé standardisé est une bonne pratique[19]. De façon générale, ces études montrent qu'un tel formulaire peut contribuer à une optimisation du traitement, à une meilleure communication entre les professionnels de la santé et à un meilleur suivi.

À la lumière de ces résultats, le formulaire de congé standardisé sera revu et amélioré. Les résultats démontrent qu'il est possible d'intégrer le formulaire de congé standardisé à chacun des dossiers, mais le taux de remplissage inférieur à 50 % indique qu'il faut réévaluer la façon de procéder. Des critères de sélection des patients visés par le formulaire seront également déterminés. Avec le déploiement progressif du prescripteur électronique, on pense pouvoir intégrer les éléments clés de ce formulaire à l'outil électronique avec une possibilité de notification automatique envoyée au médecin traitant.

Satisfaction

Les résultats du sondage montrent que les familles sont satisfaites des services et soins pharmaceutiques reçus. Il était difficile de voir une augmentation du taux de satisfaction puisque celle-ci était déjà élevée avec les soins usuels. Il est également difficile d'évaluer l'effet isolé de chacun des volets sur la satisfaction, puisqu'ils ont été implantés de façon simultanée. L'évaluation sera poursuivie afin de s'assurer d'une mise en place optimale. Entre autres, il est prévu d'ajouter une question au sondage général de l'hôpital remis aux parents avant le congé afin de connaître la satisfaction par rapport aux services et soins pharmaceutiques qu'ils ont reçus.

L'intégration des trois volets de l'intervention visant à accroître la visibilité du pharmacien et de son rôle dans l'équipe traitante, afin d'optimiser les soins pharmaceutiques, nous semble réaliste et est peu coûteuse. Intégrée au travail courant des pharmaciens, le coût de l'intervention se limite à l'impression de la brochure d'information (0,65 $ par copie) et à l'achat de quelques téléphones pour l'établissement (2000 $ de frais par année).

Cette étude comporte plusieurs forces. Les résultats reposent sur un échantillon randomisé entre deux groupes comparables. Les répondants et non-répondants au sondage avaient également des caractéristiques similaires en ce qui concerne l'âge, le nombre de médicaments et la durée de l'hospitalisation. Le choix d'un sondage à remplir en ligne de façon anonyme a permis d'obtenir un grand nombre de réponses et de limiter les risques de biais de désirabilité. Le taux de réponses (58 %) est appréciable et supérieur à celui mentionné dans la littérature scientifique[20]. De plus, les participants pouvaient ajouter des commentaires, ce qui a permis de recueillir de l'information supplémentaire et de mettre en contexte les résultats du sondage.

Cette étude comporte également des limites. Les réponses des parents renferment des incohérences, notamment quant au fait d'avoir reçu ou non la brochure et d'avoir fait usage ou non de la ligne téléphonique. Ces incohérences questionnent la validité des réponses, dont celles entourant la satisfaction des parents. Il est possible que des parents aient confondu la brochure d'information avec d'autres informations écrites remises lors de l'hospitalisation ou avec des fiches d'information sur les médicaments parfois remises au congé. De plus, les parents rencontrent de nombreux professionnels de la santé et ils reçoivent beaucoup d'information lors du séjour à l'hôpital, ce qui pourrait causer de la confusion et des incohérences notées dans le sondage des participants. Il est aussi possible que les parents aient rencontré des pharmaciens à d'autres unités de soins avant leur transfert aux unités de pédiatrie générale. Il est aussi possible de contacter un pharmacien de l'établissement pour lui poser des questions sans passer par la ligne téléphonique du projet. Certains répondants semblent également avoir mal compris la différence entre totalement en désaccord et non applicable. Le sondage est rempli en ligne postérieurement à l'hospitalisation et jusqu'à 28 jours après le congé, un biais de mémoire est donc probable. La littérature scientifique rapporte également ce biais. Sidhu et collab. ont évalué la validité d'un sondage demandant à des patients hospitalisés s'ils se souvenaient d'avoir rencontré un pharmacien[6]. Les auteurs notent que la réponse était peu fiable. Ainsi, 36,4 % des répondants disant avoir vu le pharmacien avaient une note au dossier à cet effet et 37,2 % des répondants pour lesquels il y a avait une note du pharmacien au dossier ont répondu ne pas l'avoir vu[6]. Il est également possible que les mots utilisés dans les questions du sondage aient été mal compris (p. ex. confusion possible entre l'expression « résident en pharmacie » et le terme « pharmacien » ou encore entre « brochure sur les services et soins pharmaceutiques » et « feuillet d'information sur les médicaments »). Finalement, certains auteurs de cet article sont des pharmaciens exerçant au sein des unités de pédiatrie évaluées dans le cadre de cette étude et un biais de performance n'est pas exclu.

CONCLUSION

Cette étude a permis d'implanter en établissement de santé une intervention pharmaceutique à trois volets (c.-à-d. brochure d'information, ligne téléphonique, formulaire de congé standardisé) durant une période de cinq mois. Bien que des modifications seront nécessaires pour poursuivre l'implantation de ce type d'intervention, les parents et les soignants concernés ont perçu ce projet comme étant positif. Il semble essentiel que le pharmacien d'établissement

soit davantage visible auprès des patientèles pour optimiser les retombées de sa collaboration. Bien qu'il ne soit pas nécessaire ni réaliste qu'un pharmacien voie tous les patients hospitalisés, compte tenu des ressources disponibles et des besoins pharmaceutiques de ces patients, il est légitime de penser qu'une meilleure visibilité puisse contribuer à de meilleurs soins. Avec l'ajout de nouvelles activités réservées, confiées au pharmacien à l'échelle du Canada au cours des dernières années, les patients peuvent compter sur le rôle croissant des pharmaciens hospitaliers.

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Assessing Use of a Standardized Allergy History Questionnaire for Patients with Reported Allergy to Penicillin

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ABSTRACT

Background: Inappropriate allergy labelling is associated with significant clinical and pharmacoeconomic implications. Detailed antimicrobial allergy assessments represent a key component of antimicrobial stewardship and aid in identifying true type I (immediate hypersensitivity) reactions. The allergy history form currently used at the University Hospital of Northern British Columbia (UHNBC), in Prince George, relies on the assessor's ability to ask appropriate prompting questions to obtain a thorough history, but it may not be sufficient to accurately identify true allergies.

Objective: To compare a standardized allergy history questionnaire and the current allergy history form in terms of the quality and quantity of documentation gathered.

Methods: This prospective observational study involved patients who were admitted to medical and surgical services at UHNBC from November 2018 to January 2019 with a penicillin-class allergy reported on their electronic medical record (EMR). A list of patients with EMR-reported allergies was generated by the hospital's health information software system, and these patients were interviewed using the standardized allergy history questionnaire.

Results: A total of 48 patients were assessed during the study period. Nineteen (40%) of the patients had an inappropriate allergy label on their EMR. Only 36 (75%) had an allergic reaction described on their EMR. Furthermore, only 36 (75%) of the 48 patients had the same allergy recorded on the EMR and on the allergy history form contained in their paper chart, of whom 22 had a documented reaction. The mean time to complete the standardized allergy history questionnaire was 2 minutes.

Conclusions: At the study institution, documentation of allergy histories was often incomplete. Detailed allergy assessments are the first step in identifying true immunoglobulin E–mediated hypersensitivity reactions. Utilization of a standardized allergy history questionnaire is feasible and may serve to improve documentation and overall antimicrobial stewardship.

Keywords: allergy, label, standardized, documentation

RÉSUMÉ

Contexte : L'étiquetage inapproprié de l'allergie est associé à des conséquences cliniques et pharmacoéconomiques importantes. Les évaluations détaillées des allergies antimicrobiennes sont une composante-clé de la gestion antimicrobienne : elles contribuent à déterminer les réactions d'hypersensibilité véritables de type 1 (immédiates). Le formulaire des antécédents d'allergies actuellement utilisé à l'University Hospital of Northern British Columbia (UHNBC), à Prince George, s'appuie sur la capacité de l'évaluateur à poser les questions appropriées pour obtenir un historique détaillé, mais il ne suffit pas de déterminer précisément les véritables allergies.

Objectif : Comparer la qualité et la quantité des informations recueillies au moyen d'un questionnaire normalisé sur les antécédents d'allergies avec celles recueillies au moyen des formulaires.

Méthodes : Cette étude d'observation prospective portait sur des patients admis dans les services médicaux et chirurgicaux à l'UHNBC de novembre 2018 à janvier 2019, dont les dossiers médicaux électroniques (DME) indiquaient une allergie à des médicaments de la classe de la pénicilline. Le logiciel des informations sur la santé a généré une liste des patients présentant les allergies indiquées et ces patients ont été interrogés à l'aide d'un questionnaire normalisé des antécédents d'allergies.

Résultats : Un total de 48 patients a été évalué pendant la période de l'étude. Le DME de dix-neuf (40 %) patients portait une étiquette inappropriée. Seuls 36 DME des patients (75 %) décrivaient une réaction allergique. De plus, seulement 36 (75 %) des 48 patients avaient la même réaction allergique enregistrée à la fois au DME et dans le formulaire des antécédents d'allergies de leur dossier papier, et la réaction de 22 d'entre eux était documentée. Le temps de réponse moyen au questionnaire normalisé sur les antécédents d'allergies était de 2 minutes.

Conclusion : Dans cette étude, la description des antécédents d'allergies était souvent incomplète. Les évaluations détaillées des allergies sont la première étape permettant de déterminer les réactions véritables d'hypersensibilité à l'immunoglobuline E. L'utilisation d'un questionnaire normalisé des antécédents d'allergies est faisable et pourrait servir à améliorer la documentation ainsi que la gestion globale des antimicrobiens.

Mots-clés : allergie, étiquette, normalisé, documentation

INTRODUCTION

Inappropriate antibiotic allergy labelling is a significant issue, contributing to increased antibiotic resistance, longer hospital stays, and increased health care costs.[1-3] Penicillin-class allergies are among the most commonly reported medication allergies, with a prevalence of approximately 10% in the general population and up to 15% in hospitalized patients.[4,5] Numerous factors may contribute to the high prevalence of reported penicillin allergies, including vague allergy histories, inaccurate documentation, and attribution of non-allergic reactions (e.g., amoxicillin rash confounded by viral illness).[6,7] It has been shown that up to 90% of patients with a reported allergy can safely tolerate penicillins, and true penicillin-induced anaphylaxis is rare, with a reported incidence of 0.02% to 0.04%.[5,8,9] Additionally, immunoglobulin E (IgE) antibodies dissipate over time, and approximately 80% of patients with a previous true penicillin allergy no longer react to penicillin after 10 years.[10]

Penicillins and other β-lactam antibiotics are the drugs of choice for many infectious indications and come with a well-established safety profile and relatively low cost.[9] Penicillin allergy labelling has significant clinical and pharmacoeconomic implications. For example, patients with presumed allergy to penicillin may alternatively receive suboptimal antibiotics with broader spectrums of activity and potentially poorer safety profiles (greater chance of toxicity).[1,11] These patients are at higher risk of colonization with resistant pathogens such as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus,* as well as greater risk of morbidity and complications such as *Clostridioides difficile* infection.[11] Additionally, it has been demonstrated that penicillin allergies are associated with increased cost of antibiotic treatment in hospital (by up to 63%) relative to non-allergic patients.[5,12]

Skin testing for penicillin allergy is a well-validated confirmatory method that has been implemented by many antimicrobial stewardship programs.[9] Skin testing is indicated for those with a history of type I (immediate hypersensitivity) reactions and is the gold standard for clinical "delabelling"; this type of testing has been shown to refute more than 80% of allergy labels.[5] The negative predictive value of skin testing is below 100%, so those with a negative response to the initial skin test should proceed to an oral dose challenge[4,6] A true type I reaction manifests as urticaria, angioedema, wheezing, dyspnea, and/or hypotension within 72 hours of administration.[13] Reactions that occur more than 72 hours after drug administration are termed late hypersensitivity reactions and are classified as type II, III, or IV. These are not IgE-mediated reactions, and therefore skin testing does not play a role in their evaluation.[6,13]

The 2016 guideline of the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America recommends that antimicrobial stewardship programs conduct allergy assessments for patients with a history of β-lactam allergy, as well as penicillin skin testing when appropriate.[14] Detailed allergy assessment alone is a key component of antimicrobial stewardship and should be implemented by institutions to accurately identify patients with a true immune-mediated response to penicillins.[15-17] Previous studies have shown that standardized allergy history questionnaires support the acquisition of clinically relevant information[18] and can lead to interventions that are economically feasible.[19] Our organization currently uses a paper allergy history form, which relies on the assessor's ability to ask appropriate prompting questions to obtain a thorough history. The current form is formatted to document the substance to which the patient is allergic and the reaction experienced, but does not collect key information such as when the reaction occurred, the temporal relationship of the reaction to the medication use, details of the reaction itself, and whether the patient has been re-exposed to the medication since the initial reaction. Reliance upon the interviewer to remember to ask these key questions often results in incomplete documentation, as recognized by hospital pharmacists within the organization.

The primary aim of this study was to compare a standardized allergy history questionnaire and the current allergy history form in terms of the quantity and quality of documentation gathered. The secondary aims were to determine the number of potential candidates for clinical delabelling (via penicillin skin test or oral penicillin challenge) and to measure the time required to complete a thorough allergy history using the standardized questionnaire.

METHODS

This prospective observational study involved patients admitted to medical and surgical services at the University Hospital of Northern British Columbia (UHNBC) from November 18, 2018, to January 11, 2019. UHNBC is a teaching hospital with 219 acute care beds located in Prince George, the "hub" of northern British Columbia. Ethics approval was sought from and provided by the University of British Columbia's Clinical Research Ethics Board and the organization's Research Review Committee.

Patients who reported an allergy to a penicillin (penicillin, amoxicillin, amoxicillin-clavulanate, ampicillin, ticarcillin, piperacillin, and cloxacillin) at the time of admission were identified twice weekly by means of reports generated from the organization's health information software system. These allergy reports were obtained as part of the standard admission process, whereby a health care provider completes a basic allergy history form (on paper), which is then scanned and sent to the pharmacy department for entry into the patient's electronic medical record (EMR). The weekly software reports were generated by admission date and included all reported allergies, to capture different penicillins as well

as uncoded (free-texted) medication allergies. The patients identified in this way were invited to participate in the study and were given a minimum of 24 hours to reflect on their participation and provide consent. Patients were excluded if they were under 19 years of age, had been admitted to a service other than those defined in the inclusion criteria, or had been discharged before enrolment.

Consenting patients were interviewed using the standardized allergy history questionnaire (Figure 1), which was adapted from the penicillin allergy questionnaire used by Providence Health Care in British Columbia. One author (J.M.), a postgraduate year 1 pharmacy practice resident, conducted all of the patient interviews and collected all of the data. The time to conduct each questionnaire was documented, as were any current antibiotic orders for the participant at the time of the interview. For all participants, allergy histories (both on paper forms and within the EMR) were updated, and pharmaceutical care was provided on the basis of this information as appropriate. The data were analyzed by descriptive statistics.

Participants with allergies determined to have the potential for clinical delabelling were then classified as having low, medium, or high risk for negative consequences during delabelling; see Table 1 for further details of the risk levels. Risk stratification provides support for clinicians when they are considering whether penicillin skin testing or drug challenges are appropriate. We are not aware of a validated tool available to health care professionals for stratification of patients according to allergy history; therefore, we adopted the allergy classification criteria from an early draft of the delabelling toolkit currently being prepared for British Columbia health authorities by the Provincial Antimicrobial Experts (PACE) group and used these criteria to categorize patients with potential for delabelling. This toolkit determines risk using a risk stratification process similar to that described by Shenoy and others.[20]

RESULTS

A total of 136 patients with reported allergy to penicillins were identified during the data collection period. Of these, 55 were discharged before consenting to participate, and 33 were excluded from data collection for the following reasons: unable to consent (n = 9), consented to participate but was discharged before participation (n = 7), was transferred to a site outside the data collection area (n = 5), readmission of a person who had already participated in this study (n = 5), refused consent (n = 3), was receiving care from the

Patient Interview	
Patient Identified ☐	**Time Started: _____**
1. Confirm - does the patient have a penicillin allergy?	☐ Yes ☐ No ☐ Unknown
2. Penicillin to which patient reacted? (check all that apply)	☐ Penicillin ☐ Amoxicillin ☐ Amoxicillin-clavulanate ☐ Ampicillin ☐ Ticarcillin ☐ Piperacillin ☐ Cloxacillin ☐ Unknown
3. Who told the patient they have an allergy?	☐ Self-reported ☐ Relative ☐ Health Care Professional ☐ Patient cannot recall
4. When did the reaction occur?	☐ <1 yr ago ☐ 1-10 yrs ago ☐ >10 yrs ago ☐ unknown
5. How soon after taking the medication did the reaction occur?	☐ <1 hour ☐ 1-72 hours ☐ >72 hours ☐ unknown
6. What type of reaction did the patient have? (Check all that apply) ☐ Unknown ☐ Hives – red, raised, itchy bumps ☐ Shortness of breath/wheezing ☐ Swelling of the eyes, face, lips, tongue ☐ Hypotension ☐ Nausea, vomiting, diarrhea, cramping ☐ Severe cutaneous reaction (Stevens-Johnson syndrome, toxic epidermal necrolysis) ☐ Other type of rash (describe): Other:	
7. Has the patient received a penicillin since the reaction? ☐ Yes – if yes, which penicillin and when? ☐ No ☐ Don't know	
8. Has the patient ever had a penicillin allergy skin test? ☐ Yes ☐ No	
Time Ended: _____	

FIGURE 1. Allergy history questionnaire, adapted from the Providence Health Care penicillin allergy questionnaire.

interviewer (a potential conflict of interest; $n = 3$), or died before consenting to participate ($n = 1$).

A total of 48 individuals participated in the study and were interviewed using the standardized allergy history questionnaire. The mean age of participants was 60.4 years (standard deviation 19.3 years), and 28 (58%) were female. The drug to which an allergy was listed in the EMR was penicillin for 40 participants, amoxicillin for 10 patients, and piperacillin for 3 patients, with some patients having more than 1 drug listed as an allergen.

For 36 (75%) of the participants, a description of the reaction was documented on the EMR (e.g., "rash"). In addition, 36 (75%) of the participants had the same allergy recorded on both their EMR and the allergy form in their paper chart; for the other participants, reporting in the EMR and the paper chart was inconsistent.

For 19 participants (40%), the allergy label in the EMR was deemed inappropriate, for the following reasons: re-exposure to penicillin without incident ($n = 8$); signs or symptoms of penicillin intolerance, not allergy ($n = 6$); denial of penicillin allergy by the participant during the interview ($n = 3$); and "other" ($n = 2$) (Figure 2).

Twenty-nine (60%) of the participants were identified as candidates for clinical delabelling in accordance with the draft delabelling toolkit. Of those participants, 7 (24%) were classified as having low risk of adverse events during administration of the clinical delabelling protocol, 18 (62%) as having medium risk, and 4 (14%) as having high risk; see Table 1 for more details about the risk levels.

From a feasibility perspective, the mean time to conduct the standardized allergy history questionnaire was 2 minutes (range 1–4 minutes).

TABLE 1. Classification of Allergies for Purpose of Delabelling[a]

Risk Level[b]	Allergy Classification	No. of Patients ($n = 29$)
Low	Unknown reaction or side effect[c]	5
	Poorly described non-anaphylactic symptoms	1
	Delayed (> 72 h) nonspecific rash without IgE features[d]	1
Medium	Urticaria/pruritus, angioedema, laryngeal edema **> 10 years ago** without anaphylaxis	13
	Urticaria/pruritus, angioedema, laryngeal edema **≤ 10 years ago** without anaphylaxis	5
High	Anaphylaxis[e]	3
	Systemic reaction with delayed onset (> 72 h)[f]	1

IgE = immunoglobulin E.
[a]Classification based on an early draft of a delabelling toolkit by the Provincial Antimicrobial Experts (PACE) group, intended for British Columbia health authorities.
[b]Risk of adverse events during administration of a clinical delabelling protocol.
[c]Gastrointestinal intolerance, diarrhea, headache, pruritis without rash, anxiety symptoms.
[d]Urticaria, angioedema, dyspnea, wheezing, stridor, hypoxemia, and hypotension.
[e]Acute onset of skin or mucosal involvement AND respiratory or cardiac instability (dyspnea, wheezing, stridor, hypoxemia, hypotension, hypotonia, syncope).
[f]Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, interstitial nephritis, small-vessel vasculitis.

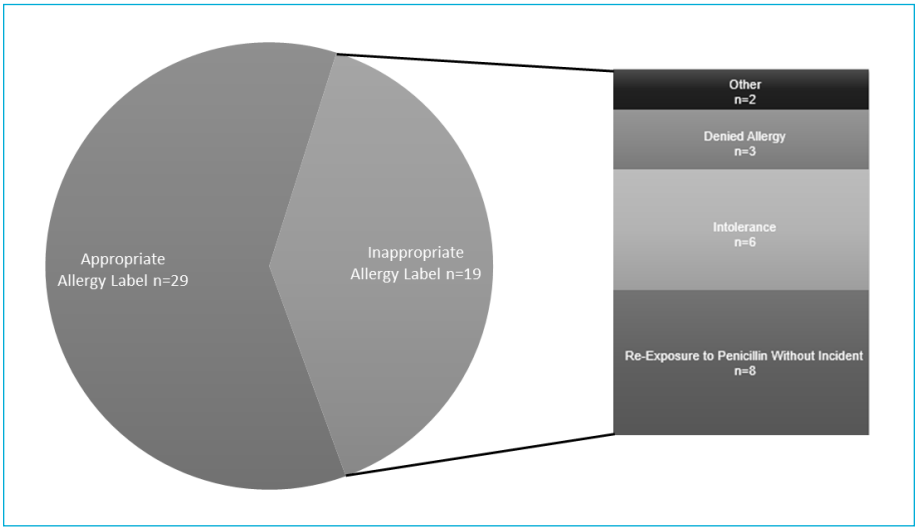

FIGURE 2. Reasons for inappropriate allergy labels on patients' electronic medical records ($n = 48$).

DISCUSSION

The results of this study demonstrate the importance of a comprehensive, standardized allergy assessment and highlight the difference between information recorded in this way and the current standard of practice at the study institution. A substantial proportion of the patients interviewed (40%) had an inappropriate penicillin allergy label on their EMR. Inappropriate labelling is particularly troublesome for allergies to antibiotics, specifically penicillins, because these allergy labels are pervasive and are associated with important clinical and pharmacoeconomic implications.[1,2] These results also showed that patients often reported non-allergic reactions as allergies; as such, formal allergy histories represent an opportunity for patient education about the differences between allergies and intolerances. After administering a standardized allergy history questionnaire, secondary sources of information, such as community pharmacy records, prescription dispensing databases, hospital records, and records of the primary care physician, may be consulted to gather more data about a patient's allergy status; this information may support clinical delabelling without the need for penicillin skin testing or oral challenges. Although skin testing is the gold standard for penicillin delabelling, it is not accessible in all centres, further exemplifying the importance of detailed allergy histories. Only when complete allergy-related information is gathered can informed decision-making occur regarding the use of penicillins.

In addition to serving as a tool for asking appropriate allergy-related questions, a standardized allergy history questionnaire can improve overall documentation. As demonstrated in this study, documentation of allergy histories at UHNBC was often incomplete or incongruent with the various health records being used to provide care. These problems indicate that health care professionals were obtaining suboptimal allergy histories for patients admitted to hospital, which could subsequently affect the quality of care that individuals receive. Anecdotally, allergy history information is sometimes copied from admission forms, ambulance records, medication administration records, or other sources onto the current allergy history form, without verification of the information with a primary source, such as the patient or caregiver. Use of a standardized tool may reduce these practices.

The preferred method of verifying penicillin allergies in patients with features of IgE-mediated reactions is skin testing, which is not currently available within the study organization. Supported by the draft PACE toolkit, graded amoxicillin challenge may be offered to patients with low-risk histories and may be carefully considered for those classified as having medium risk with remote history of a reaction (i.e., more than 10 years before). This method would apply to 25 (86%) of the 29 participants in this study who were identified as candidates for delabelling. Compared with an oral challenge protocol, penicillin skin testing requires more resources, both material and human.[21] If routinely adopted, graded oral amoxicillin challenge provides the potential for delabelling countless penicillin allergies. During data collection by means of the standardized interview, it was common for participants to request further information about oral challenge, as many wished to know their current allergy status; as such, this is a service for which there might be high demand.

Sigona and others[7] found that 25 (75%) of inpatients receiving antimicrobial therapy who were interviewed by pharmacists were candidates for β-lactam therapy, and 65.6% were successfully switched from a non-penicillin antibiotic to a cephalosporin, carbapenem, or penicillin. In our study, 22 (46%) of interviewed patients who were receiving antimicrobial therapy were receiving non-β-lactam antibiotics; however, we did not assess whether these drugs were being administered as alternatives to first-line therapy, and no clinical intervention was undertaken, as doing so would have been outside the scope of this study. Given the high proportion of patients identified as having an inappropriate allergy label, it is likely that many of these patients would have been candidates for β-lactam therapy, depending on the infection.

Our results provide some evidence that the time required to conduct a standardized allergy history questionnaire is minimal, and that it may be feasible for other health care providers to administer the questionnaire. However, this would need to be validated through future research.

The results of this study have informed the revision of an allergy/sensitivity history form that is intended to be deployed across all of the institution's sites in the future.

We acknowledge that this study had a number of limitations. Although obtaining allergy histories is a standard of care performed by pharmacists daily, consent was required from each patient before the interviews, with a minimum 24-hour waiting period before the allergy assessment was conducted. This waiting period, which was requested by the Clinical Research Ethics Board, significantly affected our sample size, because many patients were discharged during the waiting period, before the interview could be conducted. Participants' reports of subsequent exposure (Figure 1, Question 7) were not verified with secondary sources (e.g., primary care clinics, community pharmacies, or dispensing databases), which limits the level of confidence in information about re-exposure. Verification of the history using secondary sources would have been valuable for those who did not recall their allergic reaction; however, this was beyond the scope of the current study. We also acknowledge that the time required for our assessor to complete the standardized allergy history questionnaire may not have been representative of all users, given that the time reported here was based on one person's experience with the tool. However, the team believes that the tool itself is simple and intuitive for health care professionals to use, and should not pose an undue burden on

those using it to obtain an accurate allergy history. We believe that implementation of a standardized allergy history questionnaire by health care professionals in this practice setting would improve appropriate antibiotic use, with benefit for clinical and pharmacoeconomic outcomes; however, further research is required to confirm this hypothesis.

CONCLUSION

In this study, documentation of allergy histories was often incomplete, inconsistent, and unreliable across records in the study institution. A detailed allergy assessment is the first step in identifying true IgE-mediated hypersensitivity reactions and is essential for complete and accurate documentation. Implementation of a standardized allergy history questionnaire may improve documentation of penicillin allergies, antimicrobial stewardship, and ultimately patient care.

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Evaluation of In-Hospital Management of Inhaler Therapy for Chronic Obstructive Pulmonary Disease

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ABSTRACT

Background: In the past decade, the number of inhaled devices approved for management of chronic obstructive pulmonary disease (COPD) has tripled. Management of at-home inhaled COPD therapy can present a problem when patients are admitted to hospital, because only a limited number of these therapies are currently included in hospital formularies and there is a lack of established interchanges.

Objectives: To characterize and evaluate the appropriateness of management of patients' before-admission inhaled therapy upon hospital admission.

Methods: This retrospective chart review involved patients with COPD admitted to a tertiary care centre over a 1-year period (October 2017 to September 2018). Before-admission inhaled therapy was compared with inhalers ordered in hospital and at discharge. Inhaler device type, regimen, therapeutic class, and disease severity were used to assess the appropriateness of inpatient management.

Results: The charts of 200 patients were reviewed. Of these patients, 124 (62%) were kept on the same inhaler, 43 (22%) had one or more of their inhalers discontinued, 35 (18%) had to provide their own medication, and 24 (12%) had their medication changed to a formulary equivalent. An average delay of 2.6 (standard deviation 3.2) days occurred when patients provided their own medication. Formulary substitution resulted in most patients receiving a medication from the same class (75% [18/24]); however, other aspects of therapy, such as device type (17% [4/24]), regimen (29% [7/24]) and drug combination (47% [9/19]), were not maintained. Only 55% (6/11) received an equivalent dose of inhaled corticosteroids when the medication was interchanged to a formulary inhaler.

Conclusions: The majority of patients' inhaled therapies continued unchanged upon admission to hospital, which suggests that despite the proliferation of new inhalers on the market, their use is still limited. For patients who did require interchange to formulary inhalers, maintenance of the same regimen, device, and combination product was rare. Provision of the medication supply by patients themselves often resulted in a delay in therapy.

Keywords: chronic obstructive pulmonary disease, formulary, inhaled therapy

RÉSUMÉ

Contexte : Au cours des dix dernières années, le nombre de dispositifs d'inhalation approuvés pour gérer la maladie pulmonaire obstructive chronique (MPOC) a été multiplié par trois. La gestion de la thérapie à domicile de la MPOC peut présenter un problème lors de l'admission à l'hôpital, car seul un nombre limité de ces thérapies est actuellement inclus dans la pharmacopée des hôpitaux et les tableaux d'équivalence des médicaments font défaut.

Objectifs : Au moment de l'admission à l'hôpital, définir et évaluer l'adéquation dentre l'inhalothérapie des patients avant leur admission et celle offert à l'hôpital.

Méthodes : Cet examen rétrospectif des dossiers concernait des patients atteints d'une MPOC ayant été admis dans un centre de soins tertiaires sur une période d'un an (d'octobre 2017 à septembre 2018). Il portait sur la comparaison entre l'inhalothérapie avant l'admission et les inhalateurs commandés à l'hôpital et au moment du congé. Le type de dispositif d'inhalation, le régime, la classe thérapeutique et la gravité de la maladie ont servi à évaluer la pertinence de la gestion de l'inhalothérapie des patients hospitalisés.

Résultats : L'examen portait sur les dossiers de 200 patients. De ceux-ci, 124 (62 %) ont gardé le même inhalateur; 43 (22 %) ont vu la suppression d'au moins un inhalateur; 35 (18 %) ont dû fournir leurs propres médicaments; et les médicaments de 24 (12 %) d'entre eux ont été remplacés par un équivalent de la pharmacopée. Les investigateurs ont observé un retard moyen de 2,6 jours (écart type 3,2) lorsque les patients fournissaient leurs propres médicaments. La substitution par des médicaments de la pharmacopée a conduit la plupart des patients à en recevoir un de la même classe (75 % [18/24]); cependant, d'autres aspects de la thérapie n'ont pas été maintenus, comme le type de dispositif (17 % [4/24]), le régime (29 % [7/24]) et la combinaison de médicaments (47 % [9/19]). Seuls 55 % (6/11) ont reçu une dose équivalente de corticostéroïdes en inhalation, lors du remplacement du médicament par un inhalateur de la pharmacopée.

Conclusions : La majorité des inhalothérapies des patients sont restées inchangées au moment de l'admission à l'hôpital, ce qui laisse entendre que, malgré la prolifération de nouveaux inhalateurs sur le marché, leur utilisation est encore limitée. Pour les patients qui nécessitaient le remplacement par un inhalateur de la pharmacopée, le maintien du même régime, du même dispositif et du même produit de combinaison était rare. L'approvisionnement en médicaments par les patients eux-mêmes entraînait souvent un retard dans la thérapie.

Mots-clés : maladie pulmonaire obstructive chronique, pharmacopée, inhalothérapie

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive lung disease characterized by fixed airflow obstruction and chronic inflammation.[1] It is the fourth leading cause of death worldwide and a major source of financial and medical burden.[2,3] An estimated 17% of Canadians aged 35 to 79 years meet the criteria of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) for a diagnosis of COPD, based on spirometry, and this proportion is expected to increase.[4]

There is no cure for the irreversible lung damage that occurs in COPD, but pharmacologic therapy is employed to reduce symptoms, prevent exacerbations, and improve patients' quality of life.[2] Three main drug classes—bronchodilators, muscarinic antagonists, and corticosteroids—are used in various combinations and strengths, depending on disease progression and other patient factors. Specific drugs within each class are further classified according to their duration of action, termed "short-acting" or "long-acting". As the prevalence of COPD has increased, so too have the number of inhaler devices and the therapeutic options within each drug class. Since 2010, the number of inhaled devices approved in Canada for the treatment of COPD has almost tripled.[5,6] Inhalers are primarily classified by their mechanism of drug delivery. For COPD, these devices are either pressurized metered dose inhalers, dry powder inhalers, or soft mist inhalers. Although all devices have been shown to be effective and clinical guidelines do not recommend one over another,[2,7] patients' satisfaction with their inhaler is positively correlated with adherence and health status.[8] Consequently, when prescribing these medications, it is clinically important to consider patient preference along with drug coverage and provincial formularies.

Drug classes with a large variety of therapeutic options often present a problem at the time of hospital admission, particularly when no standard equivalence table for the class has been established. Such is the case for the majority of inhaled drugs for COPD. Hospital formularies are commonly utilized to control costs and standardize care by enabling clinicians to become familiar with a smaller subset of medications.[9] Conversely, the risk of medication errors upon admission and discharge may be increased when a patient's home medications are not available on the hospital formulary. In response to this problem, hospitals commonly implement therapeutic interchange, which is defined as the automatic replacement of a prescribed medication with a pre-approved medication from the same drug class that is chemically different, but therapeutically equivalent.[10] An estimated 88% of major Canadian hospitals (> 100 beds) use a therapeutic interchange program,[11] including Vancouver General Hospital (VGH). Relative to the number of devices that are commercially available in Canada, VGH has a limited number of inhaler devices on formulary (complete list available from the corresponding author upon request), in accordance with the provincially mandated hospital formulary for all health authorities in British Columbia.[12] Within VGH, there are no direct therapeutic interchange guidelines for COPD drugs other than inhaled corticosteroids (ICS).[13]

There is a lack of literature characterizing how patients' inhaled medications are dealt with upon admission to hospital and reporting the prevalence of therapeutic interchange for these drug classes. When patients are admitted, the following outcomes are possible for each of their before-admission medications:

- The same medication is provided in hospital (i.e., the medication may be on formulary or the hospital may provide it as a nonformulary item).
- The medication is interchanged with a therapeutic equivalent on the formulary.
- The medication is discontinued until discharge.
- Patients provide their own medication during the hospital stay.

No studies have evaluated inpatient management of medications specifically for COPD, but studies of therapeutic interchange for other indications have elicited concerns about the safety and efficacy of this practice. For example, therapeutic interchange of proton pump inhibitors has been shown to increase the rate of treatment failure (inadequate clinical response, need for dose titration, or discontinuation due to adverse effects)[14] and is associated with more medication discrepancies at discharge than when the same drug is continued in hospital.[15] The overall medication reconciliation error rate for all drug classes has also been shown to be much higher for interchanged medications than for unchanged medications.[9] Even when therapeutic interchange is done correctly, switching devices can lead to decreased patient adherence or improper inhalation technique.[16] Patients may be confused about new treatment regimens or device-specific handling instructions, particularly after a hospital stay during which pharmacotherapy for their other conditions has been adjusted; this situation may lead to duplicate therapy or accidental discontinuation if the errors are not resolved. Furthermore, patients may face financial difficulties and be intentionally nonadherent if their discharge prescriptions include cost-prohibitive drugs.[17] It is therefore important to characterize the prevalence of therapeutic interchange and critically evaluate its consequences in this patient population to ensure safe and effective care.

The purpose of this study was to determine how the inhaled respiratory maintenance medications of patients with COPD were managed when they were admitted to hospital and, in cases where therapeutic interchange occurred, to assess the appropriateness of the medication and regimen prescribed. Appropriateness was evaluated in terms of dose equivalence, similarity of device, maintenance of combination product devices, and drug class, according to COPD severity and clinical guidelines.

METHODS

The study was a retrospective chart review of patients with COPD who were admitted to a tertiary care centre.

International Classification of Diseases (9th Revision) codes were used to identify patients with COPD at discharge who had been admitted to the hospital between October 1, 2017, and September 30, 2018. The inclusion criteria were as follows: patient was taking at least 1 COPD medication by inhalation and was using salbutamol on an as-needed basis. The exclusion criteria were as follows: incomplete records in the patient's chart, admission to the intensive care unit or another critical care area, intubation for respiratory distress, and readmission within less than 30 days. Incomplete records were defined as those missing any portion of data that prevented assessment of the primary outcome. From all admissions that met the initial criteria, a convenience sample was identified by random selection; for this purpose, each of the charts was given a random number, and the charts were selected in ascending numeric order.

Two investigators (B.G. and J.L.) independently abstracted the data. The following baseline demographic and clinical data were collected: age, comorbidities, spirometry results, and the reason and date of admission. In addition, all before-admission inhalers that were being used and all inhalers prescribed upon discharge were recorded.

The primary objective of the study was to determine if patients with COPD who were admitted to hospital had their before-admission inhaler medications continued, discontinued, or therapeutically interchanged, or if the patient supplied their own medication for use in the hospital. For each patient with multiple inhalers that were all managed using the same technique, the inhalers were grouped and counted as one for that method of management. For patients with multiple inhalers that were managed differently, each inhaler was counted individually for the particular technique. After initial determination of how the inhalers were managed, secondary outcomes were also captured. For patients who received at least 1 inhaler from their own supply, the investigators determined whether the inhaler was actually received during the hospital stay and if so, the number of days' delay from the date ordered to the first dose being administered (if any such delay occurred). For patients with at least 1 inhaler interchanged for a formulary inhaler, the secondary outcomes were whether the therapeutic interchange resulted in the same device being ordered, whether the same class of medication was maintained (i.e., short-acting muscarinic antagonist, long-acting muscarinic antagonist, long-acting β-agonist, or ICS), whether the before-admission regimen was maintained, and whether, in the case of ICS therapy, the equivalent dose (as per the VGH therapeutic interchange dosing equivalency chart) was given after the therapeutic interchange. Additionally, if there was an indication for therapeutic optimization (which includes altering the dose of existing medications or adding or removing an inhaled therapy, as outlined in the 2020 GOLD guidelines[2]), the investigators determined whether that was done. If patients had been admitted for a COPD exacerbation and treated per the hospital-based protocol, this was counted as optimization; where applicable, inhalers ordered post-exacerbation were assessed in terms of the primary and secondary outcomes outlined above. At VGH, the administration of all inhaled therapies is either performed or witnessed by nurses and then documented.

For this retrospective study, ethics approval was obtained from the University of British Columbia Clinical Research Ethics Board, and operational approval to conduct the study was obtained from Vancouver Coastal Health.

Descriptive statistics were used to analyze all outcomes. Data were entered into Excel 365 Pro Plus v. 1902 software (Microsoft Corporation), which was used to carry out all statistical analyses.

RESULTS

A total of 623 admissions occurred during the defined time frame; random numbers were assigned to the 623 charts, and a convenience sample of 254 charts was selected for analysis. Of the 254 charts reviewed, 200 met the inclusion criteria. The reasons for exclusion are detailed in Figure 1.

The mean age of patients included in the study was 74.0 (standard deviation [SD] 11.8) years (Table 1). According to

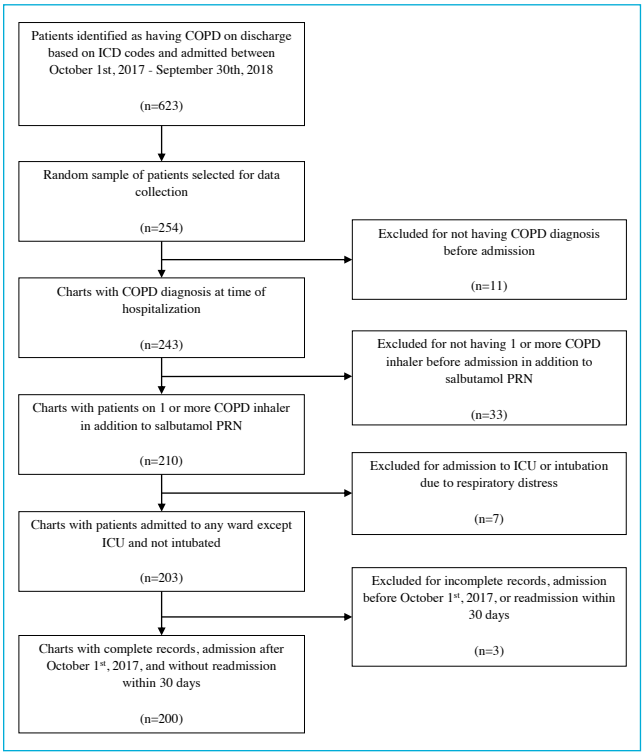

FIGURE 1. Sample selection. COPD = chronic obstructive pulmonary disease, ICD = International Classification of Diseases, ICU = intensive care unit, PRN = as needed.

TABLE 1. Baseline Characteristics

Characteristic	No. (%) of Patients[a] (*n* = 200)	
Patient		
Age (years) (mean ± SD)	74.0 ± 11.8	
Admission for COPD exacerbation	123	(62)
Spirometry		
FEV_1 (%) (mean ± SD) (*n* = 70)	44.7 ± 17.7	
FEV_1/FVC (mean ± SD) (*n* = 50)	0.53 ± 0.11	
Comorbidities		
Respiratory		
Pneumonia	64	(32)
Asthma	26	(13)
Lung cancer	16	(8)
Bronchiectasis	10	(5)
Pulmonary hypertension	9	(5)
Other systems and conditions		
Cardiovascular	151	(76)
Neurological/psychological	97	(49)
Genitourinary/gastrointestinal	83	(42)
Musculoskeletal	25	(13)
Endocrine	63	(32)

FEV_1 = forced expiratory volume in 1 s, FEV_1/FVC = forced expiratory volume in 1 s divided by forced vital capacity, SD = standard deviation.
[a]Except where indicated otherwise.

the most recent spirometry data available, the mean forced expiratory volume in 1 second (FEV_1) was 44.7% (SD 17.7%) of predicted (*n* = 70 patients), whereas the mean ratio of FEV_1 to forced vital capacity (FEV_1/FVC) was 0.53 (SD 0.11) (*n* = 50 patients) (Table 1). For patients with both pre- and post-bronchodilator spirometry values recorded in the chart, the most recent post-bronchodilator values were used for this analysis.

The list of inhalers that patients were using at the time of admission was generated from VGH records; at this hospital, patient interviews are typically used to confirm or update the list as soon as possible after admission. The 200 patients included in the analysis had a total of 326 inhalers for COPD medications for which management was assessed. For the majority of the 200 patients, before-admission inhalers were continued in hospital (62%), followed by discontinuation of the inhaler during hospitalization (22%) and use of the patient's own inhalers (18%) (Table 2). The least common management course was therapeutic interchange (12%) (Table 2).

Among the 35 patients with self-provision of non-formulary inhalers, 27 (77%) received a dose during their hospital stay; among these patients, there was an average delay of 2.6 (SD 3.2) days from the order date to the date of the first dose (Table 2). The other 23% of patients with an order to use their own inhaler did not receive a dose during their hospital stay (Table 2).

TABLE 2. Evaluation of Inpatient Management of Inhalers for Treatment of COPD

Outcome	No. (%) of Patients[a] (*n* = 200)[b]	
Primary[c]		
Continuation of inhaler(s) used before admission	124	(62)
Discontinuation of inhaler(s) used before admission	43	(22)
Patient's own inhaler(s) ordered	35	(18)
Therapeutic interchange of inhaler(s) used before admission	24	(12)
Secondary		
Patient's own inhaler(s) ordered		
Patient's own inhaler ordered and received	27	(77)
Patient's own inhaler ordered and not received	8	(23)
Time without use of inhaler(s) from date ordered (days) (mean ± SD)	2.6 ± 3.2	
Therapeutic interchange of inhaler(s) ordered		
Same device as used before admission (*n* = 24)	4	(17)
Equivalent dose (if inhaled corticosteroid interchanged) (*n* = 11)	6	(55)
Inhaler remained a single-product inhaler (if single product used before admission) (*n* = 5)	5	(100)
Inhaler remained a combination-product inhaler (if combination product used before admission) (*n* = 19)	9	(47)
Same class as medication used before admission (*n* = 24)	18	(75)
Same dosing regimen as used before admission (*n* = 24)	7	(29)
Substitution of inhaler maintained upon discharge (*n* = 23)	12	(52)
Indication for optimization of therapy		
Step-up indication present in chart (i.e., admitted for exacerbation, poor adherence, reports of COPD symptoms, adverse reaction to current inhaler[s])	133	(67)
Received step-up optimization of therapy as per GOLD therapeutic recommendations for those with indication in chart[d]	79	(59)
No alterations/optimizations made to inhalers for those with indication in chart[d]	50	(38)
Received step-down in therapy for those with indication in chart[d]	4	(3)

COPD = chronic obstructive pulmonary disease, GOLD = Global Initiative for Chronic Obstructive Lung Disease, SD = standard deviation.
[a]Except where indicated otherwise.
[b]Total number of inhalers was 326.
[c]For patients with multiple inhalers managed in the same way, the inhalers were grouped and counted as one for that method of management; for patients with multiple inhalers managed differently, each inhaler was counted individually. As a result, the sum of categories for primary outcome is greater than the total number of patients (200) but less than the total number of inhalers (326).
[d]Percentages calculated in relation to the 133 patients with step-up indication present in the chart.

For inhalers with therapeutic interchange, the majority were substituted for a different device, with only 17% (4/24) of the patients remaining on the same device as before admission (Table 2). Similarly, dosing regimens were maintained for only a minority of patients (29% [7/24]) (Table 2). Additionally, for those who were previously taking a combination product with 2 or more inhaled medications, substitution resulted in separation of the combination, with maintenance of the dosing regimen for the components occurring in less than half of cases (47% [9/19]); conversely, all single-product inhalers that were interchanged were maintained as single products (100% [5/5]) (Table 2). Of the patients with combination inhalers that were separated upon admission, 70% (7/10) were returned to their combination inhaler upon discharge. The medication class being administered before admission was preserved upon substitution for most patients (75% [18/24]), as was the dose equivalency for patients who were receiving an ICS (55% [6/11]) (Table 2). Of the 23 patients who had a formulary substitution and had discharge medications documented in the chart, 12 (52%) remained on the substituted inhaler upon discharge (Table 2).

For the majority of patients (67% [133/200]), one or more of the following indications for therapy optimization was present (Table 2): admission for a COPD exacerbation, poor before-admission adherence to their COPD medications, ongoing reports of COPD symptoms, or adverse reaction to 1 or more of their inhaler medications. Of those with indications for optimization, 79 (59%) received a step-up in therapy, whereas 50 (38%) received no alterations to their medications during the hospital stay or upon discharge (Table 2). A small proportion of patients (3% [4]) received step-down therapy, as per the GOLD guideline[2] (Table 2).

DISCUSSION

This study adds to the literature by characterizing the current state of inhaler management when patients were admitted to one tertiary care hospital. Despite the presence of institutional formulary restrictions, the majority of patients with COPD were maintained on their home regimen after admission, which could indicate a lack of prescribing of the newer COPD inhaler medications within the study population. However, elucidating the prescribing practices for COPD medications was beyond the scope of this study and would be an area for future research.

Patients providing their inhalers from home for in-hospital use was the third most common management strategy employed and resulted in a notable delay of, on average, 2.6 days before the first dose of medication was administered. The delay in receipt of a long-term medication could result in worsening of patients' symptoms. In addition, if a patient does not have home medications with them at the time of admission, the onus for procuring the patient's own supply shifts to an external caregiver, which may be impossible for some patients. To decrease potential delays in therapy, a predetermined period during which the patient can bring in their own supply should be defined. Once this period has passed, the pharmacy should re-evaluate the situation and determine if there is a need to obtain a nonformulary supply or if there are possible formulary alternatives that could be used.

Formulary substitution for COPD inhalers was the least common management technique employed at VGH, with only 12% of patients receiving an alternative formulary product. At this hospital, only ICS medications have a defined therapeutic interchange with respect to within-class dosing equivalence, which is likely the reason this approach was less well utilized. Developing therapeutic interchanges for other classes of inhaled therapies may be needed in the future, as the use of newer agents increases.

The appropriateness of any substitutions that did occur was evaluated with respect to maintenance of several factors: device, class of medication, dosing regimen, and single-product or combination-product inhaler. Often it was the delivery device that was not maintained, which resulted in patients being exposed to an unfamiliar inhalation device. If an unfamiliar device is used and proper device technique is not practised, the likelihood of receiving the correct dose decreases, which can alter the control of COPD symptoms.[15] Inhaler technique for patients' regular before-admission medication has been evaluated previously at VGH; in that study, critical errors occurred in 59% of participants.[18] If hospital inpatients are using devices different from what they use at home, an opportunity to reinforce proper technique for home inhalers is lost. For many patients with formulary substitutions, the dosing regimen was also altered, with just under one-third of patients remaining on the same regimen. Also of concern is the possibility that in-hospital substitutions will be maintained upon discharge, which occurred for 52% of our study population. For other medication classes in which therapeutic interchange occurs, such as proton pump inhibitors and angiotensin-converting enzyme inhibitors, previous studies have shown that therapy changes during hospital admission can result in medication errors upon discharge, nonadherence, and associated increased costs to the health care system.[9,19,20]

Another potential barrier to adherence that could be introduced in the inpatient setting is the separation of a combination product into multiple inhalers, which occurred for 47% of the patients in our study who had therapeutic interchange of COPD medications; notably, however, most patients (70%) were returned to their combination product at discharge. The current formulary does not include a combination inhaler for a long-acting muscarinic antagonist and a β-agonist, but it does have single-product inhalers of these drug classes available; as such, unless patients provide their own inhalers, there will likely continue to be separation of combination products for those receiving this specific combination therapy before admission. Seventy-five percent of

the patients received a different medication within the same drug class for long-acting β-agonists, long-acting muscarinic antagonists, and ICS. For substitutions involving long-acting muscarinic antagonist and β-agonist, there are no established equivalent doses between different agents within the same class. In addition, there are variations between specific agents within the same class, such as onset of action, duration, and need for renal adjustment.[21] The clinical impact of such differences is unknown.

With respect to ICS inhalers, for which therapeutic interchange exists, this study showed that just over half of patients (55%) with a therapeutic interchange received an equivalent ICS dose. All but one of the patients who did not receive an equivalent ICS dose had an indication for optimizing therapy. Overall, 67% of the patients had 1 or more indications for alteration of their current therapy, based on GOLD recommendations.[2] The most common indication for therapy adjustment was admission for a COPD exacerbation, which occurred in 62% of the study population. Among the patients with an indication for optimization, therapy was stepped up for the majority (59%), unaltered for a large proportion (38%), and decreased for only a few (3%). The decision to have patients remain on their before-admission therapy may be due to factors such as concerns about adherence, complexity of the regimen, and the prohibitive cost of adding another medication.[22] Future studies could investigate the underlying factors that prevent stepping-up of therapy with respect to COPD inhalers, despite presence of an indication.

The study was a retrospective chart review, and as such was limited by the comprehensiveness and accuracy of the information presented in the charts. Charts without complete information were excluded, as a way of minimizing the impact of incomplete documentation. Of the 4 criteria used to determine indications for optimization, 3 relied on chart notes, and limitations related to the comprehensiveness of chart notes likely prevented us from recognizing some patients who had an indication for optimization. Related to this limitation is the fact that adherence before admission was not always documented. Additionally, the investigators could not guarantee that patients who were to use their own medication supply did not take doses without the knowledge of care providers, despite procedures within VGH requiring the identification of patients' own medications by the pharmacy before administration and documentation on the medication administration record of all medications given. Other factors, such as length of stay, severity of presentation, or the risks versus benefits of a given treatment could affect decisions regarding management of a patient's inhaler therapy during the hospital admission and were beyond the scope of this retrospective chart review. Also beyond the scope of this type of study was any ability to determine whether changes in therapy were intentional, unless such information is clearly stated in the chart. Complete spirometry results were available for only 25% of the patient population; therefore, the diagnosis of COPD could not be confirmed using objective criteria. The secondary outcome of ICS dosing equivalency was based on evidence for asthma-based ICS equivalency, which represents another limitation, given that COPD-specific dosing equivalencies could not be evaluated. Finally, there was no postdischarge follow-up with patients in the community, so the ramifications for those who were discharged with different inhalers could not be investigated.

CONCLUSION

The increasing prevalence of COPD is adding to the burden for patients and health care teams alike. The admission to hospital of rising numbers of patients with COPD highlights the need to develop a safe and efficacious management strategy for COPD inhalers, especially given the limited options currently available on formulary relative to the large number of devices that have entered the market. In this study, most patients were continued on their before-admission inhalers, an approach that for other drug classes has been shown to result in fewer medication errors and fewer patient adherence issues than occur with therapeutic interchange.[9,16] Discontinuation of an inhaler was the second most common management technique, followed by patients supplying their own inhaler. Despite the large number of different devices and medication combinations for COPD currently available, this study showed that it is still possible, with current formulary options, to keep patients on the same inhaler therapy, although this is ultimately dependent on community prescribing practices.

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Hidden Costs of Multiple-Dose Products: Quantifying Ipratropium Inhaler Wastage in the Hospital Setting

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ABSTRACT

Background: Previous studies have quantified wastage involving drugs that are available in multiple-dose formats. Ipratropium bromide by metered dose inhaler (MDI) is commonly used in hospitals, and may be contributing to waste of pharmaceutical and financial resources.

Objectives: The primary objective was to quantify the number of patients in the authors' health authority with waste of at least 1 ipratropium MDI. Secondary outcomes were the total number of wasted inhalers, the total number of wasted doses, the cost of wasted inhalers, the cost of wasted doses, and possible factors or explanations for inhaler wastage.

Methods: A retrospective chart review was conducted for patients with an order for ipratropium by MDI in 2019 at one of the acute care sites within the health authority (predefined sample size 336). The number of inhalers dispensed was compared with doses received to determine the number of inhalers wasted. Each patient's electronic chart was audited for possible factors and explanations for wasting of inhalers.

Results: Of the 336 patients, 79 (24%) had wastage of at least 1 inhaler. In total, 34% (98/290) of all inhalers dispensed and 87% (50 693/58 000) of all doses dispensed were wasted. The total cost of wasted inhalers for the sample population was $2156. The most common reason for inhaler wastage was no doses being administered after an inhaler was dispensed; the second most common reason was dispensing of an extra inhaler associated with a change in directions for use.

Conclusions: The use of multiple-dose MDI products in hospitals can lead to wastage of drugs and financial resources. Procedures need to be implemented to aid pharmacy and nursing staff in ensuring the most efficient use of these products. Evaluations of pilot methods to mitigate this waste are encouraged.

Keywords: drug waste, health expenditures, ipratropium, metered dose inhalers, multidose products

RÉSUMÉ

Contexte : Des études antérieures ont quantifié le gaspillage de médicaments disponibles dans des formats multidoses. Le bromure d'ipratropium administré par inhalateur-doseur (ID) est communément utilisé dans les hôpitaux et pourrait entraîner un gaspillage des ressources pharmaceutiques et financières.

Objectifs : L'objectif principal consistait à quantifier le nombre de patients relevant de l'autorité sanitaire des auteurs, qui étaient source d'un gaspillage d'au moins un ID d'ipratropium. Les résultats secondaires visaient à déterminer le nombre total d'inhalateurs et de doses gaspillés, le coût associé au gaspillage des uns et des autres, ainsi que les facteurs pouvant expliquer cette situation.

Méthodes : Les dossiers des patients ayant reçu une prescription d'ipratropium administrée par ID en 2019 dans l'un des sites de soins intensifs de l'autorité sanitaire ont fait l'objet d'un examen rétrospectif (taille de l'échantillon prédéfinie : 336). Une comparaison entre le nombre d'inhalateurs distribués et les doses reçues a permis de déterminer le nombre d'inhalateurs gaspillés. La vérification de chaque dossier électronique des patients a révélé les facteurs et les explications possibles du gaspillage des inhalateurs.

Résultats : Sur les 336 patients, on a noté un gaspillage d'au moins un inhalateur tous les 79 patients (24 %). Au total, le gaspillage se montait à 34 % (98/290) de tous les inhalateurs distribués et à 87 % (50 693/58 000) de toutes les doses distribuées. Le coût total des inhalateurs distribués à l'échantillon de population se montait à 2156 $. La raison du gaspillage la plus fréquente était l'absence de doses administrées après la distribution d'un inhalateur; la deuxième raison concernait la distribution d'un inhalateur supplémentaire associée à une modification des instructions relatives à son utilisation.

Conclusions : L'utilisation de produits ID multidoses dans les hôpitaux peut entraîner un gaspillage de médicaments et de ressources financières. Des procédures doivent être mises en place pour aider les membres du personnel des pharmacies et le personnel infirmier à utiliser plus efficacement ces produits. Il serait indiqué de procéder à des évaluations de méthodes pilotes pour atténuer ce gaspillage.

Mots-clés : gaspillage des médicaments, dépenses de santé, ipratropium, inhalateur-doseur, produits

INTRODUCTION

Ipratropium bromide is a short-acting muscarinic antagonist indicated for treatment of acute asthma exacerbations and management of chronic obstructive pulmonary disease.[1,2] In our health authority in British Columbia, Canada, ipratropium is available on formulary in the form of metered dose inhalers (MDIs) and nebules.

In the 2018/19 fiscal year (April 2018 to March 2019), ipratropium MDIs represented the second-highest inhaler expenditure for this health authority. MDIs are unique in that they are available only in multiple-dose formats; in Canada, the ipratropium MDI is supplied as a 200-dose canister.[2] The nature of multiple-dose containers contributes to ipratropium wastage, because a full inhaler must be dispensed even if a patient requires only 1 dose during the hospital stay.

During drug shortages, wastage of medication may exacerbate the situation. The conservation of medications is especially important during pandemics, when there may be interruptions in international trading channels and increased demand for supportive and therapeutic agents used to treat the disease underlying the pandemic.[3]

Previously, Berwick and Hackbarth[4] proposed that reducing waste would be an enormous opportunity to reduce health care costs. Ipratropium has the potential for greater wastage than occurs with other inhalers because this drug may be used on an as-needed basis, in addition to regularly scheduled use. Quantifying the amount of ipratropium inhaler waste and possible factors or explanations for the waste may suggest ways to reduce health care costs.[3] Our primary objective was to determine the total number of patients for whom an ipratropium MDI was dispensed and subsequently wasted at acute care sites within our health authority.

METHODS

A retrospective chart review was conducted within 11 acute care sites in Fraser Health Authority. All patients with an order for ipratropium inhaler between January 1, 2019, and December 31, 2019, were eligible for inclusion in the review. Patients were identified through the pharmacy's electronic record, which documents inhalers sent from the dispensary and inhalers removed from automated dispensing cabinets located on the wards. For each patient identified in this way, the account number was then used to pull the corresponding scanned patient chart. The Fraser Health Research Ethics Board deemed this quality improvement review to be exempt from ethics approval, and written informed consent was not required.

To determine the total number of patients with wastage of at least 1 ipratropium inhaler, we considered an inhaler to have been "wasted" if any of the following occurred: the patient did not use an ipratropium inhaler that was dispensed for them at any point during the hospital stay, an extra ipratropium inhaler was dispensed when previously dispensed inhalers contained an adequate supply of the doses that the patient would need during the hospital stay, or an ipratropium inhaler was dispensed for a patient even though the patient did not have an order for this form of therapy. Secondary outcomes were the total number of wasted inhalers, the total number of wasted doses, the cost of wasted inhalers, the cost of wasted doses, and possible factors or explanations for inhaler waste. To determine the number of inhalers and doses that were wasted for each patient, we compared the number of doses (puffs) that the patient received, as documented in the medication administration record (MAR), with the number of inhalers and doses dispensed for that patient. The costs of wasted inhalers and doses were based on the price of an ipratropium inhaler in community pharmacies in British Columbia. We used community pharmacy pricing because our health authority's contract pricing is considered confidential. For each inhaler that was wasted, 1 contributing factor or reason for waste was assigned. The factors or reasons were determined in a systematic, step-wise manner, with explicitly documented reasons (i.e., documented loss, no ipratropium order, no doses administered) taking precedent over factors related to the timing of inhaler removal from an automatic dispensing cabinet or dispensing of an inhaler from pharmacy.

In 2019, a total of 12 810 patients received an ipratropium inhaler at one of the acute sites in our health authority. Our group previously examined wastage of fluticasone propionate/salmeterol combination MDIs and dry powder inhalers and found that 19.6% of patients had an extra inhaler dispensed (i.e., "wasted").[5] Assuming that the effect size would be similar in the context of ipratropium inhaler wastage, a sample size of 333 patient charts was obtained, to yield a 98% confidence level and a 5% margin of error. A random number sequence generator was used to sample charts in a proportional manner with respect to the volume of patients seen at each hospital site. Because of rounding due to the representative chart sample, the final sample size was 336 patients. The primary and secondary outcomes were assessed using descriptive statistics.

Two investigators (K.C.M. and E.M.A.S.) independently extracted data from the patients' charts. For the first 10 charts, duplicate data extraction was performed, and the data were then assessed for appropriate extraction by a third investigator (E.S.Y.A.). Assessment for valid data extraction was also repeated for 5 charts one-third and two-thirds through the data collection process. Any discrepancies or ambiguities in the data were discussed, agreed upon, and resolved.

Data were extracted from the pharmacy electronic record and patient charts. Variables collected included the hospital site, the patient's account number, the number of inhalers dispensed, the number of inhalers removed from an automated dispensing cabinet, the total number of doses the patient received, and any probable reasons for inhaler

wastage if such wastage occurred. Patient characteristics were also recorded, including admission status, number of bed/ward transfers, intubation during visit, and past or current history of chronic respiratory disease, such as asthma or chronic obstructive pulmonary disease. All data containing patient identifiers were stored on a protected drive, and patients were assigned a coded study number. The data were analyzed using descriptive statistics.

RESULTS

A total of 336 patient charts were reviewed. Most patients (284 [85%]) were admitted to hospital (as opposed to having a short emergency department visit), and 263 (78%) had at least 1 bed or ward transfer (Table 1). Past or current history of a chronic respiratory disorder was reported for 247 (74%) of the patients (Table 1).

The number of patients in our health authority for whom at least 1 ipratropium inhaler was dispensed unnecessarily was 79 (24%; range 9% to 80% at individual sites). Of the 290 ipratropium inhalers dispensed, 98 (34%) were wasted. The highest number of inhalers wasted during a patient's hospital stay was 5 inhalers (n = 1 patient). A total of 58 000 doses were dispensed, and 50 693 (87%) of these doses were wasted. For our cohort of 336 patients, the total cost of wasted inhalers was $2156.00, and the total cost of wasted doses was $5576.23.

The most common reason (33%) for inhaler wastage was dispensing of an inhaler from which no doses were administered to the patient (Table 2). In this situation, the inhaler was dispensed for use on an as-needed or regular basis, but there was no record in the MAR of any doses being given. The second most common reason (18%) originated from pharmacy dispensing an extra inhaler in association

TABLE 1. Patient Characteristics

Characteristic	No. (%) of Patients (n = 336)	
Admitted to hospital	284	(85)
Transferred bed or ward during hospital stay	263	(78)
Past or current history of chronic respiratory disease[a]	247	(74)
Chronic obstructive pulmonary disease	169	(50)[a]
Asthma	64	(19)[a]
Other diagnosis	81	(24)[a]
Intubation during hospital stay	71	(21)
At least 1 inhaler removed from automated dispensing cabinet	107	(32)

[a]Percentages do not sum to 74% (the total of those with chronic respiratory disease), because some patients had multiple respiratory comorbidities.

TABLE 2. Factors Contributing to Wastage of Inhalers

Factor	No. (%) of Wasted Inhalers[a] (n = 98)	
Inhaler dispensed, but no doses administered to patient	32	(33)
Pharmacy dispensed extra inhaler when there was an order to change directions for use, even though patient's first inhaler had sufficient number of doses to accommodate the altered directions	18	(18)
Inhaler dispensed even though patient had no order for this form of therapy	15	(15)
Inhaler did not follow patient on transfer	14	(14)
Removal of a second inhaler from automated dispensing cabinet within 24 h of removal of a first inhaler	4	(4)
Loss of inhaler documented in chart note or medication administration record	1	(1)
Nursing provided extra inhaler from automated dispensing cabinet when there was an order to change directions for use, even though patient's first inhaler should have had sufficient number of doses to accommodate the altered directions	1	(1)
Unable to determine	13	(13)

[a]Percentages do not sum to 100% because of rounding.

with a change in directions for use, even though the patient's current inhaler still contained a sufficient number of doses to accommodate the modified administration. Similarly, in 1 instance, an inhaler was wasted because nursing staff provided the extra inhaler from an automated dispensing cabinet after an order was written to change the directions for use. There was only 1 instance in which the wastage or loss of an inhaler was explicitly documented on the MAR as "not available" and "pharmacy [was] called."

DISCUSSION

This retrospective chart review quantified the magnitude of waste of ipratropium MDIs within our health authority, showing that for 24% of patients who received ipratropium inhalers, at least 1 inhaler was wasted. This is similar to the findings in a previous study of wastage of fluticasone/salmeterol inhalers, in which 19.6% of patients had a wasted inhaler.[5]

When the total cost of wasted inhalers in the sample population was extrapolated to all 12 810 patients with an ipratropium order in 2019, we calculated more than $82 000 in excess drug spending. Additionally, when the cost of wasted doses was extrapolated to all patients who received ipratropium in this health authority in 2019, we estimated that wastage could represent over $212 000. Retail pricing is typically higher than contract pricing for the health authority, so these calculations may overestimate the true budget implications for the hospital setting. Nonetheless, the actual implications are likely to be substantial enough to warrant the same level of concern, especially given that health authorities are publicly funded.

The dispensing of an inhaler without the patient receiving any doses was the most common reason for wastage, accounting for 33% of all inhalers wasted. In these instances, no doses were recorded on the MAR, which suggests that the patient either did not require any doses or was discharged before doses were required. In this situation, we assumed that dispensed inhalers were not returned to stock or used by another patient. To help mitigate waste secondary to this reason, dispensing of as-needed ipratropium orders could be delayed for patients who do not present with an acute respiratory condition. Alternatively, inhalers in ward stock could be dispensed in sealed bags, to ensure drug integrity and allow subsequent re-dispensing if the seal is not broken.

The second most common reason for wastage of inhalers in our chart review was dispensing of a new inhaler when there was a change in the ipratropium order, even though the patient's first inhaler had doses remaining, according to the doses recorded on the MAR. In this situation, instead of checking whether an inhaler had already been dispensed, the pharmacy automatically dispensed a new inhaler. Staff education is required to address this factor. One suggestion for improvement is to increase awareness among pharmacy and nursing staff of the potential for this form of waste and to encourage staff to use the patient's previously dispensed inhalers with doses remaining.

Waste assessment is particularly important for drugs dispensed in multiple-dose formats, which have a greater potential for waste than their single-dose counterparts. For example, a patient who has a prescription for the manufacturer's recommended dose of ipratropium (2 puffs given 4 times daily[1,2]) and the average length of hospital stay (7 days[6]) would use about 60 puffs of ipratropium. In our health authority, after the patient is discharged, the remaining 140 puffs in the canister would not be shared with another patient, and the canister would be discarded. In contrast, single-dose formulations, such as tablets, are prepared in unit-dose packaging and are typically dispensed daily or with, at most, a few days' supply.

Minimizing the cost of wasted doses is a complex issue. The ideal solution would be for manufacturers to produce inhalers with fewer doses or for hospitals to adjust their policies to allow certain patients to take their inhalers home after discharge. Another possibility would be to use the patient's own supply of multidose inhalers, which has previously been shown to result in cost savings.[7] In times of tremendous drug shortage, exploring the possibility of cleaning and recycling partially used inhalers might be another option.[8] Should a common canister program be implemented, protocols would be needed to minimize the risk of infection.[8]

Our evaluation had several limitations related to the nature of retrospective chart reviews. Four of the hospitals included in the analysis did not have automated dispensing cabinets, which meant that removals of inhalers from ward stock could not be tracked electronically. This might have resulted in an underestimation of inhaler waste, given that any inhalers removed from ward stock at those hospitals could not have been quantified unless their removal was explicitly documented (hand-written) in the chart. In addition, ipratropium MDIs require priming before the first use, which involves the purposeful wasting of the first 2 actuations.[2] We did not account for these priming puffs, because priming of inhalers is not normally documented in the patient chart and thus we could not be sure how often each inhaler was primed. Not accounting for priming doses may have led to overestimation of waste; however, the number of priming puffs is minimal relative to the total number of puffs in a canister, and is unlikely to have affected our primary outcome. In some cases, no inhaler was billed (i.e., there was no electronic record of dispensing) even though a patient was documented to have received doses. This situation could have led to underestimation of inhaler waste. Finally, in some cases it was challenging to determine the reason for inhaler wastage, and ultimately we were unable to determine the reason in 13 cases. Additionally, we did not evaluate clinical need (or lack thereof) as a potential reason for inhaler wastage. Patients who received ipratropium without a valid clinical indication may have further contributed to inhaler waste.

Notably, our study did not take into consideration the potential costs associated with time spent by pharmacy and nursing staff in finding lost inhalers or increasing communication among staff. It is possible that procedural changes to address the problems outlined here could increase staff workload, resulting in additional costs that might outweigh the savings achieved by reducing inhaler waste. We would encourage the testing and evaluation of a variety of methods and policies to decrease pharmaceutical waste and the spending associated with multiple-dose inhaler products.

CONCLUSION

This retrospective chart review highlighted significant waste of pharmaceutical and financial resources related to ipratropium MDI inhalers. These results represent compelling support for more organized and consolidated drug distribution in hospitals. To help mitigate waste, health care institutions should consider stricter protocols related to inhaler dispensing, and all hospital staff should be made aware of the waste occurring with multiple-dose format drugs, such as MDIs. In addition, effective communication between pharmacy and nursing staff should be promoted to help ensure that medications are not dispensed unnecessarily.

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Effect on Patients' Outcomes of a Change to Biosimilar Filgrastim Product in Autologous Stem Cell Mobilization

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ABSTRACT

Background: Following addition of a biosimilar filgrastim product to the formulary, sites in the authors' provincial health authority transitioned from using the originator filgrastim to the biosimilar for autologous stem cell mobilization.

Objective: To assess the effect on patient outcomes of a universal change to use of the biosimilar filgrastim in stem cell mobilization.

Methods: This retrospective pre–post study included patients undergoing autologous stem cell mobilization at 2 cancer hospitals in Alberta, Canada, between July 1, 2018, and November 30, 2019. Clinical outcomes were investigated for patients treated with a granulocyte colony-stimulating factor (biosimilar or originator product) for mobilization before stem cell transplant, approximately 6 months before and after the defined date of product change.

Results: In total, 102 patients were treated with the originator product and 101 patients with the biosimilar. Effectiveness was similar between the originator and biosimilar products, with 98% successful harvest of stem cells in all patients treated. Independent *t* tests showed no statistically significant differences between patients receiving the originator and those receiving the biosimilar in terms of time from mobilization to collection (difference of means –0.9 days, 95% confidence interval [CI] –2.12 to 0.32), time for neutrophil engraftment (difference of means 0 days, 95% CI –0.36 to 0.36), time for platelet engraftment (difference of means 1 day, 95% CI –0.55 to 2.55), average length of stay (difference of means –0.7 day, 95% CI –2.71 to 1.31), and CD34+ value (difference of means -1×10^6/kg body weight, 95% CI –2.11 to 0.11). A 98% rate of conversion to use of the biosimilar filgrastim was achieved, with an estimated annual drug-cost saving of $67 500.

Conclusions: In this pre–post study, changing to the biosimilar product from the originator maintained clinical effectiveness outcomes while decreasing overall drug expenditures. A well-planned change to the biosimilar product, executed in conjunction with clinician consultation and monitoring of effectiveness outcomes, can ensure appropriate patient therapy while significantly improving the uptake of biosimilars and decreasing expenditures for biologic drugs.

Keywords: biosimilar, filgrastim, autologous stem cell transplant

RÉSUMÉ

Contexte : À la suite de l'ajout d'un produit filgrastim biosimilaire à la liste des médicaments, les sites relevant de l'autorité sanitaire provinciale des auteurs sont passés de l'utilisation du filgrastim princeps à la version générique pour la mobilisation des cellules souches autologues.

Objectif : Évaluer l'effet sur les résultats des patients d'un changement généralisé visant à utiliser le filgrastim générique pour la mobilisation des cellules souches.

Méthodes : Cette étude rétrospective pré-post comprenait des patients soumis à une mobilisation des cellules souches autologues dans deux hôpitaux de cancérologie en Alberta (Canada) entre le 1er juillet 2018 et le 30 novembre 2019. L'examen des résultats cliniques des patients traités à l'aide d'un facteur stimulant les colonies de granulocytes (G-CSF) (générique ou princeps) pour une mobilisation avant la greffe de cellules souches a eu lieu environ six mois avant et après la date du changement de produit.

Résultats : Au total, 102 patients ont été traités à l'aide du produit princeps et 101 patients à l'aide du générique. Les deux produits présentaient une efficacité similaire, et 98 % de réussite dans la récolte de cellules souches chez tous les patients traités. Des tests *t* indépendants n'ont montré aucune différence statistique significative entre les patients recevant le princeps et ceux recevant le biosimilaire en termes de temps allant de la mobilisation à la collecte (différence des moyennes –0,9 jour, intervalle de confiance [IC] 95 % –2,12 à 0,32); temps de la prise de la greffe neutrophile (différence des moyennes 0 jour, IC 95 % –0,36 à 0,36); temps de la prise de la greffe des plaquettes (différence des moyennes 1 jour, IC 95 % –0,55 à 2,55); durée moyenne du séjour (différence des moyennes –0,7 jour, IC 95 % –2,71 à 1,31) et valeur CD34+ (différence des moyennes -1×10^6/kg masse corporelle, IC 95 % –2,11 à 0,11). Un taux de conversion de 98 % visant à utiliser le filgrastim générique a été atteint, avec une estimation des économies annuelles sur le coût des médicaments de 67 500 $.

Conclusions : Dans cette étude pré-post, le passage du produit princeps au générique a préservé l'efficacité des résultats cliniques, tout en diminuant les dépenses générales liées au médicament. Un changement bien programmé pour passer au produit générique, mené conjointement avec la consultation d'un clinicien et un contrôle des résultats d'efficacité, peut assurer une thérapie du patient appropriée tout en améliorant grandement la prise de produits génériques et en diminuant les dépenses associées aux médicaments biologiques.

Mots-clés : biosimilaire, générique, filgrastim, greffe de cellule souche autologue

INTRODUCTION

Filgrastim is a granulocyte colony-stimulating factor (GCSF) hematopoietic agent[1] used in stem cell mobilization protocols before autologous stem cell transplant (ASCT) in patients with hematologic malignancies. A biosimilar product for the originator filgrastim product has been available in Canada since 2016.[1] In the period of 2018 to 2019, following a formulary addition by the Drugs and Therapeutics Committee of the provincial health authority (Alberta Health Services [AHS]), all sites transitioned from using the originator filgrastim to the biosimilar product for most indications, including autologous stem cell mobilization. The aim of the current study was to compare the effectiveness of the 2 products for mobilization, given that comparative data have not been well investigated for this indication in Canada.

Biosimilar drugs demonstrate a high degree of similarity to an already authorized biologic drug, with no expectation of clinically meaningful differences in effectiveness or safety between the biosimilar and the originator product.[2,3] However, in Canada and other parts of the world, the uptake of biosimilars has not reached its full potential.[4,5] Previous publications have described barriers to biosimilar uptake.[6,7] Despite there being no expected difference in effectiveness between a biosimilar and its originator product, prescribers have limited comfort and confidence when biosimilars enter the market.[6,8] This lack of uptake may be more discernible when products are being prescribed for "at-risk" patient populations, for which there is a lack of data in the studies submitted for approval of the biosimilars.[6,8] At-risk patient populations are people with the highest potential for serious consequences from a failure of therapy, as well as low tolerance for treatment failure because of the acuity of their condition or previous treatment failures. Our study applied this definition to patients undergoing preparation for stem cell mobilization and ASCT. We aimed to address the data gap and clinical comfort issue related to this indication for a Canadian biosimilar filgrastim product.

At the time of planning for the project, literature was beginning to emerge regarding the use of biosimilar filgrastim products in ASCT. Searches for published studies of autologous stem cell mobilization with biosimilar filgrastim were conducted in the PubMed and ClinicalTrials.gov databases and using the Google search engine. A 2016 meta-analysis by Schmitt and others[9] included 30 studies (involving a total of 1541 patients who underwent autologous transplant) that used biosimilar filgrastim products (Zarzio™ or Ratiograstim™/Tevagrastim™). The meta-analysis showed no significant differences between the biosimilars and originator product in terms of number of apheresis sessions, CD34+ cell count, and time to recovery of neutrophil count or platelet count after engraftment.[9] Another review article[10] included 7 retrospective and prospective studies comparing biosimilar filgrastim with originator filgrastim; the findings of these trials supported effectiveness of the biosimilar in terms of both mobilization and transplant-related outcomes. Several recent studies have investigated the use of biosimilar filgrastim in ASCT, concluding that biosimilar filgrastim is safe to use for stem cell mobilization, with no disparity in clinical effect.[7,8,11,12]

In the literature, Canadian data are notably lacking, except for 1 poster abstract describing the experience at a Saskatchewan cancer centre after a switch to the biosimilar Grastofil® for ASCT.[13] Marketing surveillance and pharmacovigilance data on adverse effects are monitored and reviewed by the Canadian regulatory body, Health Canada, and have not revealed any unexpected post-authorization signals for biosimilars at this time.[14] Because biosimilar products are not exact copies of one another, and because there are some important differences in national policies for approval of biosimilars and drug formulary coverage elsewhere in the world, Canadian findings are of value to support jurisdictional decisions. The results of the current health care improvement project will add to the available literature, helping to support clinical practice. Increasing the uptake of biosimilars within organizations can reduce health system drug expenditures and increase patients' access to high-cost medications.[7]

The goal of this study was to confirm the similarity between the biosimilar and originator filgrastim products by comparing clinical outcomes for patients in Alberta who were treated with GCSF for stem cell mobilization before ASCT at the Cross Cancer Institute (CCI) in Edmonton and the Tom Baker Cancer Centre (TBCC) in Calgary, approximately 6 months before and after a defined date of product change (January 1, 2019, for CCI; July 1, 2019, for TBCC). Clinical outcomes and parameters for mobilization and engraftment were assessed. Although not predefined as formal outcomes of the study, percent uptake (an indicator of the extent of change in product used from the originator to the biosimilar) and drug expenditure savings were also calculated.

METHODS

This study was a retrospective pre–post data review for patients who underwent autologous stem cell mobilization and transplant at the CCI and the TBCC, which provide a range of health care services for Albertans with cancer.[15] At these 2 facilities combined, more than 200 patients undergo ASCT annually. Patient care is managed by the Northern Alberta Blood and Marrow Transplant Program (in Edmonton) and the Alberta Blood and Marrow Transplant Program (in Calgary), involving treatment management provided by hematology physicians, nurses, pharmacists, and various support staff. Data for all patients are prospectively collected within the transplant programs as part of quality assurance programs, with patient consent provided for research and regulatory body review.

The study used data from consecutive patients treated at each centre with originator filgrastim in the 6 months before the defined date of product change or the biosimilar product in the 6 months afterward. The time frame of 12 months total was determined as being suitable to collect data for 100 patients at each centre, based on historical average annual numbers of ASCT patients at each site. Quality management consultants at each site collect and manage the data for their respective sites, and the separate data sets were combined for the purpose of this study. All data were anonymized, such that patient identity could not be discerned during the statistical analysis.

Participants

Consecutive patients with all categories of diagnosis who underwent stem cell mobilization were included in the data set. The overall study period was from July 1, 2018, to November 30, 2019.

The dosage of filgrastim prescribed for patients was based on standardized provincial dose banding according to patient weight categories; for each patient, the optimal dose of filgrastim was selected (5–10 μg/kg daily) according to the patient's weight and risk factors. Advanced age, diagnosis of non-Hodgkin lymphoma, previous radiation therapy or extensive chemotherapy, previous treatment with lenalidomide, previous mobilization failure, low pre-apheresis circulating CD34+ cell counts, diabetes, and smoking are risk factors for poor mobilization or failure.[16] Filgrastim was administered either alone or in combination with mobilizing chemotherapy agents.[16] Patients received GCSF beginning on the day indicated in the protocol and continuing until completion of apheresis, typically for between 3 and 7 days of GCSF therapy. For mobilization by combined chemotherapy and GCSF, usual regimens had patients starting GCSF on about day 7 to 9, with apheresis scheduled for days 12 to 14, whereas mobilization involving salvage chemotherapy regimens had patients starting GCSF on day 14, with apheresis on days 19 to 21. In cases with predicted poor mobilization based on risk factors, if optimal mobilization was not achieved with filgrastim with or without chemotherapy (total CD34+ cell counts $< 20 \times 10^6$ cells/L after 4 days of GCSF) or there had been a prior failed attempt at mobilization with GCSF with or without chemotherapy, plerixafor was administered. Apheresis, directed by the CD34+ count, was performed with the Spectra Optia apheresis system (Terumo BCT). The minimum apheresis volume was 8 L. All patients received the same level of care and follow-up from the respective transplant programs.

Interventions

The formulary product to be used for stem cell mobilization and collection was changed from originator filgrastim to the biosimilar in January 2019 (at the CCI) and July 2019 (at the TBCC), which defined the time point of comparison. After treatment with GCSF, the clinical effectiveness of stem cell mobilization was determined using data routinely collected by the blood and marrow programs. The primary effectiveness parameters were time from mobilization to collection, CD34+ cells collected, time to neutrophil engraftment, time to platelet engraftment, average length of stay, and success of mobilization. A harvest of CD34+ cells equal to or greater than 2×10^6 cells/kg body weight per transplant was defined as successful collection. Neutrophil engraftment was defined as an absolute neutrophil count of 0.5×10^9/L, and platelet engraftment was defined as a platelet count of 20×10^9/L. Time to neutrophil and platelet engraftment was defined by the first date of 3 and 7 consecutive values, respectively, over the threshold value. Secondary outcomes were use of plerixafor, GCSF dose, duration of GCSF therapy, processing volume, number of collections, and survival status. Baseline characteristics were included for comparison of patient age at time of transplant, sex, cancer diagnosis, and chemotherapy protocol (mobilization with GCSF and chemotherapy combined or with GCSF alone).

Statistical Analysis

Descriptive statistics were used to report the study variables. Means and standard deviations were calculated for normally distributed continuous variables, medians and ranges for non-normally distributed continuous variables, and frequencies and proportions for categorical variables. The correlation between 2 categorical variables was determined using χ^2 tests, and means were compared between the 2 study arms using independent *t* tests. A *p* value less than 0.05 and 95% confidence intervals (CIs) for the difference between means were used for determining statistical significance. Two-sided tests were used for the analysis, which was performed with SPSS software, version 25 (IBM Corporation). Patients with incomplete data for any of the variables were excluded from the final statistical analysis for that parameter. The impact on drug expenditures was estimated on the basis of a 17% per unit savings of the biosimilar compared with the originator (according to product pricing on the Alberta Drug Benefit List: $173.19 for 300 μg of the originator product and $144.31 for 300 μg of the biosimilar product), an estimated 200 patients undergoing ASCT annually, and an average dosage of 650 μg daily for 5.4 days (according to values calculated in this study).

Ethical Considerations

The ethical aspects of implementing and studying the interventions in this study were guided by *A Project Ethics Community Consensus Initiative (ARECCI) Ethics Guideline Tool*.[17] The ARECCI screening tool[18] was used to assess the ethical risk of this quality improvement project, which was assessed as "somewhat more than minimal risk". Thus, the "second opinion review" process was completed, which classified the project as a health care improvement project

and therefore determined that the protocol did not require review through the Health Research Ethics Board (HREB) Cancer Committee.[19]

RESULTS

Overall, the study included data from 102 consecutive patients treated with originator filgrastim and 101 patients treated with the biosimilar product, all of whom underwent stem cell mobilization according to institutional guidelines. Of the 203 patients, 105 were treated at the CCI and 98 at the TBCC.

Baseline patient characteristics (Tables 1 and 2) were similar, with almost equal numbers of patients treated with originator filgrastim (n = 102) and the biosimilar (n = 101). The median age of patients at the time of transplant was 59 years, and 63.1% (128/203) were male. The proportions of male and female patients using each product were similar. The most common diagnosis was multiple myeloma (106/203 [52.2%]) and the least common was germ cell disease (5/203 [2.5%]). A greater proportion of patients with multiple myeloma were treated with the biosimilar product than with the originator (55/101 [54.5%] versus 51/102 [50.0%]), whereas more of the patients with lymphoma were treated with the originator product than with the biosimilar (44/102 [43.1%] versus 38/101 [37.6%]). Survival was similar between groups: 94.1% (96/102) in the originator group versus 96% (97/101) in the biosimilar group.

The results indicated similar effectiveness for the originator filgrastim and biosimilar products when used for stem cell mobilization before ASCT. Combined results are reported in Table 1 and Table 2. In addition, site-specific results for all parameters were analyzed for the CCI and the TBCC individually; no significant differences in results were observed between the 2 centres (data not shown). The primary effectiveness parameters are reported in Figure 1, Table 1, and Table 2. There were no statistically significant differences between the originator and the biosimilar in the time from mobilization to collection (difference of means –0.9 days, 95% CI –2.12 to 0.32, p = 0.13), time for neutrophil engraftment (difference of means 0 days, 95% CI –0.36 to 0.36, p = 0.82), time for platelet engraftment (difference of means 1 day, 95% CI –0.55 to 2.55, p = 0.22), or average length of stay (difference of means –0.7 day, 95% CI –2.71 to 1.31, p = 0.46). The average CD34+ collection was 7.2×10^6 cells/kg body weight for originator filgrastim and 8.2×10^6 cells/kg body weight for the biosimilar (difference of means -1×10^6 cells/kg body weight, 95% CI –2.11 to 0.11, p = 0.06). Both values surpassed what is considered a successful harvest. The mean number of collections was 1.4 in both groups (p = 0.65). Successful harvest of stem cells was achieved in 98% of the patients, with mobilization failure for 2 patients in each group.

Overall, 26.0% of the patients required use of plerixafor, 23.5% in the biosimilar group and 28.4% in the originator group (p = 0.42). Data on plerixafor use were missing for 3 patients (about 2%). The average daily GCSF dose was 634.7 µg in the originator group and 662.8 µg for the biosimilar (difference of means –28.1 µg, 95% CI –86.21 to 30.01, p = 0.34). The dosage of GCSF has been standardized within the organization according to the number of transplants and other previously defined risk factors for failed

TABLE 1. Baseline Characteristics of Patients and Induction Therapy

Characteristic	No. (%) of Patients[a] Overall (n = 203)	Originator (n = 102)	Biosimilar (n = 101)
Age at transplant (years)			
Mean ± SD	55.8 ± 12.4	55.6 ± 12.4	55.9 ± 12.5
Median (range)	59 (18–78)	59 (24–78)	59 (18–72)
Sex			
Male	128 (63.1)	69 (67.6)	59 (58.4)
Female	75 (36.9)	33 (32.4)	42 (41.6)
Diagnosis			
Autoimmune condition (Fabry disease, scleroderma, multiple sclerosis)	10 (4.9)	5 (4.9)	5 (5.0)
Lymphoma (Hodgkin and non-Hodgkin disease)	82 (40.4)	44 (43.1)	38 (37.6)
Multiple myeloma	106 (52.2)	51 (50.0)	55 (54.5)
Germ cell disease	5 (2.5)	2 (2.0)	3 (3.0)
Mobilization with GCSF alone			
Yes	14 (6.9)	8 (7.8)	6 (5.9)
No	189 (93.1)	94 (92.2)	95 (94.1)

GCSF = granulocyte colony-stimulating factor, SD = standard deviation.
[a]Except where indicated otherwise.

TABLE 2. Comparison of Originator Filgrastim and Biosimilar Product

Variable	Group; Mean ± SD[a] Originator (*n* = 102)	Biosimilar (*n* = 101)	*p* Value[b]	Difference of Means[c] (95% CI)
Age at transplant (years)	55.6 ± 12.4	55.9 ± 12.4	0.84	−0.3 (−3.73 to 3.13)
Time from mobilization to collection (days)	11.2 ± 4.4	12.1 ± 4.4	0.13	−0.9 (−2.12 to 0.32)
CD34+ cells collected (× 10^6/kg body weight)	7.2 ± 3.4	8.2 ± 4.5	0.06	−1 (−2.11 to 0.11)
Time to neutrophil engraftment (days)	11.7 ± 1.3	11.7 ± 1.3	0.82	0 (−0.36 to 0.36)
Time to platelet engraftment (days)	17.8 ± 6.7	16.8 ± 4.2	0.22	1 (−0.55 to 2.55)
GCSF				
Dose (µg/day)	634.7 ± 204.1	662.8 ± 215.1	0.34	−28.1 (−86.21 to 30.01)
Duration of delivery (days)	5.4 ± 2.4	5.4 ± 2.7	0.89	0 (−0.71 to 0.71)
Processing volume (L)	26.9 ± 15.8	23.8 ± 15.3	0.16	3.1 (−1.21 to 7.41)
Length of stay (days)	20.4 ± 5.9	21.1 ± 8.4	0.46	−0.7 (−2.71 to 1.31)
No. of collections	1.4 ± 0.6	1.4 ± 0.5	0.65	0 (−0.15 to 0.15)
Failed mobilization, no. (%)				
Yes	2 (2.0)	2 (2.0)	0.86	NA
No	100 (98.0)	99 (98.0)		
Plerixafor administered, no. (%)[d]				
Yes	29 (28.4)	23 (23.5)	0.42	NA
No	73 (71.6)	75 (76.5)		NA
Survival status, no. (%)				
Alive	96 (94.1)	97 (96.0)	0.53	NA
Deceased	6 (5.9)	4 (4.0)		NA

CI = confidence interval, GCSF = granulocyte colony-stimulating factor, NA = not applicable, SD = standard deviation.
[a]Except where indicated otherwise.
[b]Independent *t* test.
[c]Originator minus biosimilar.
[d]For the biosimilar group, data were missing for 3 patients, so percentages were calculated with a denominator of 98.

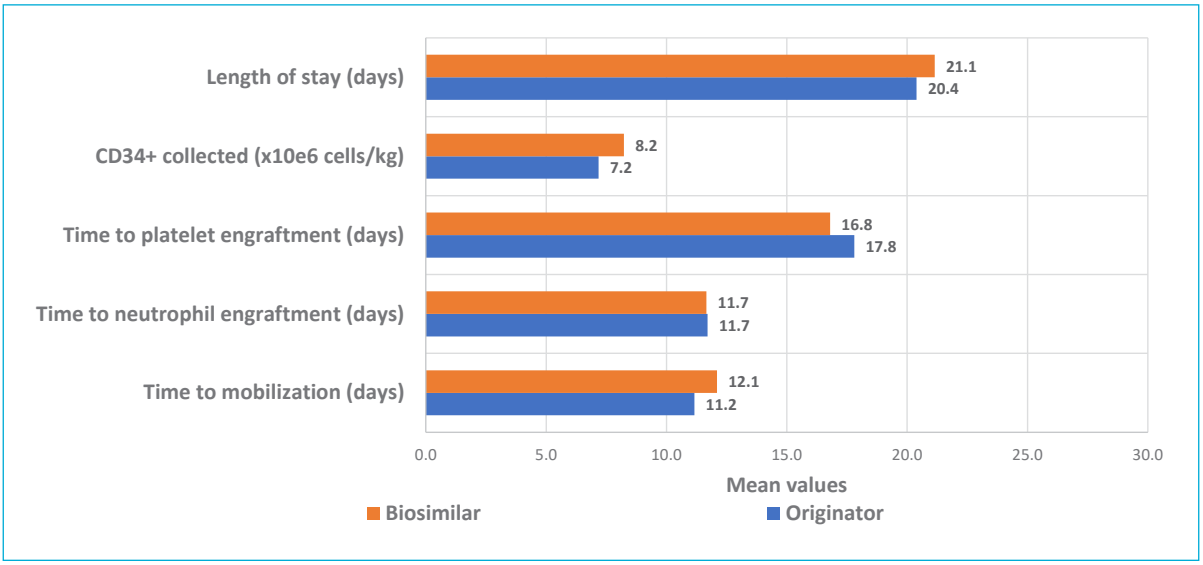

FIGURE 1. Comparison of originator and biosimilar filgrastim for primary effectiveness parameters. CD34+ counts are reported as number of cells × 10^6/kg body weight.

mobilization,[16] starting with weight-based banding (< 60 kg, 300 μg daily; 60 to 90 kg, 480 μg daily; and > 90 kg, 600 μg daily), with adjustment for risks. The mean duration of GCSF therapy was 5.4 days for both groups, and processing volume was also similar between originator and biosimilar (difference of means 3.1 L, 95% CI −1.21 to 7.41, $p = 0.16$).

At each of the 2 study sites, the rate of conversion to use of the biosimilar after the defined date for switching products was 98%, with an estimated 17% saving on the cost of the drug alone, amounting to $67 500 in annual drug costs for this indication. There were 3 patients who continued to receive the originator product after the defined date of switching to a biosimilar. These patients were either treated during the product transition period at the site or were given the originator product for reasons that were not clearly specified but likely attributable to order error. These patients were not included in our analysis.

DISCUSSION

Overall, this study demonstrated similarity of effectiveness between the originator filgrastim and biosimilar product for stem cell mobilization, providing real-world data to address prescribers' concerns about using the biosimilar. In particular, CD34+ cell collection was higher, although not significantly so, with biosimilar filgrastim than with originator filgrastim. This result is similar to that of a prospective non-inferiority study,[12] which found a nonsignificant trend toward increased mobilization in the biosimilar arm. These results should be confirmed in future studies. The clinical importance of this difference may depend on individual patient acuity, since both values in our study exceeded the minimum of 2×10^6 cells/kg body weight that is considered to represent a successful harvest. Other descriptive measures showed similarity between the groups of patients treated with the originator product and the biosimilar, confirming no differences in baseline characteristics. There was also no difference in the use of plerixafor, an agent used in circumstances of suboptimal collection or mobilization failure with filgrastim.

Prescribers' hesitancy in using biosimilars, due to a lack of confidence in biosimilars in general[6,8] and specifically in the context of stem cell mobilization,[7] is a barrier that has been discussed in the literature. Such hesitancy has been observed in the study organization to date, with poor uptake of 2 other biosimilar products, for nonhematological conditions, that have been added to the organization's acute care formulary.[20] However, there are some important differences between these other biosimilars and filgrastim, such as their indications for use in chronic conditions and differences in program support offered by manufacturers, which have negatively affected uptake. As such, it may be difficult to directly compare all biosimilars available on the organization's formulary. Factors that may have improved uptake of the biosimilar filgrastim include 2 provincially coordinated bone marrow transplant programs and consensus of prescribers in their use of filgrastim for patients undergoing ASCT.

The filgrastim biosimilar is the first biosimilar to be evaluated in this organization using patient-specific parameters of effectiveness. Assessing these parameters in patients treated with originator versus biosimilar filgrastim products provides additional data to confirm the equivalency of the biosimilar in terms of effectiveness. Such data are missing from the Health Canada approval process for biosimilars; instead, that process allows extrapolation of results.[2] Confirming equivalency of the biosimilar helps to support prescribing decisions, as well as guiding future decisions about the formulary status of each product. Information gained in this type of study may also be applied to future biosimilar products being considered for addition to the AHS provincial drug formulary.

Improved uptake of biosimilars is consequential to the sustainability of the health care system, given the substantial potential of these agents to reduce the costs associated with the biologics class of drugs.[3, 21-23] The list price of biosimilar filgrastim is approximately 17% lower than that of the originator product, which represents an opportunity for savings if it were to be used for all formulary indications. Filgrastim was 1 of the top 10 drugs by expenditure in the AHS in the 2017/18 and 2018/19 fiscal years (internal data), which could translate into significant savings with robust uptake. However, although biosimilar filgrastim was listed on the AHS provincial drug formulary for a different indication (neutropenia) in December 2017, a follow-up utilization audit found less than 30% uptake of the biosimilar after 12 months, a value that increased to approximately 63% by 18 months. The achievement of 98% uptake for the indication of autologous stem cell mobilization stands in stark contrast, and perhaps speaks to the value of health care improvement initiatives and coordinated program efforts within AHS to capitalize on organizational drug budget savings. Given that prescriber resistance was one of the barriers to use of biosimilars raised in a previous publication,[7] the results of this study could help support clinical practice, improve use of biosimilars within the organization, reduce drug expenditures, and increase patients' access to high-cost medications. Additionally, using the biosimilar product is in line with government-funded outpatient drug plans and criteria for reimbursing biosimilar products as the first choice before the originator product.[24] Alignment between acute care and ambulatory drug formularies is important to support continuity of care for patients and to promote system-wide health care savings.

Limitations

The main limitations of this study pertain to its observational design and small patient numbers. A retrospective study design cannot remove sources of bias or establish causality between exposure and outcome.[25] Our data were limited to what was

available through the electronic databases of the Northern Alberta Blood and Marrow Transplant Program and the Alberta Blood and Marrow Transplant Program. Additionally, the assessment of safety parameters was limited because the chart review did not include extraction of information about the adverse effects of each filgrastim product used; however, data on adverse effects are now being collected by both transplant programs and may be reported in a future publication. Because the study was focused on 2 oncology acute care facilities within the same organization, the findings may not be generalizable to other hospitals in the same province or to other health care organizations in Canada or internationally. Despite these limitations, use of an observational study design in this circumstance allowed for expedient and cost-effective use of existing staff resources to investigate real-world data to answer a clinical question. The limited number of patients and the short time frame for the study prevented use of a non-inferiority or prospective randomized study design, but may be considered for future research.

CONCLUSION

A coordinated change to using the biosimilar filgrastim product on our drug formulary was supported by a follow-up health care improvement study, confirming similarity of effectiveness between the originator product and the biosimilar in patients who underwent ASCT at 2 sites. This study provides valuable information to support prescribing decisions, as well as future decisions regarding the formulary status of both products. What was learned in this study can also be applied to future consideration of other biosimilar products for addition to the acute care formulary to increase cost savings, improve the sustainability of the health care system, and improve prescriber confidence in biosimilar drug products.

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The Clinician Scientist

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INTRODUCTION

Clinical research is an essential component of health sciences that focuses on improving knowledge about the diagnosis, prevention, and treatment of diseases, through a variety of methodologies, with the ultimate intent of enhancing the health and quality of life of individual patients or populations.[1-3] Because health problems are multidimensional, an interdisciplinary approach to research is necessary to establish innovative and adaptive solutions.[4-6] Clinician scientists lead clinical research, are essential components of the research infrastructure of academic health care centres, and have traditionally had a background in medicine.[3] However, clinicians from other health care sciences, such as nutrition, nursing, physiotherapy, and pharmacy, have become increasingly common in the past 20 years.[7] The unique competencies and perspectives of pharmacists make them suitable to lead multidisciplinary research teams to address unanswered therapy-related questions and to close important gaps between drug-related knowledge and the bedside.[3] Although we are not aware of official data, it is our observation that clinician-scientist pharmacists are increasingly securing funding from federal funding agencies (e.g., Canadian Institutes of Health Research [CIHR] or the US National Institutes of Health) in recent years, either as members of interdisciplinary research teams or as principal investigators.[5,8] In addition, pharmacists are increasingly publishing in high-impact medical journals (including the *New England Journal of Medicine*, *The Lancet*, *BMJ*, *JAMA*, *Chest*, *Cochrane Database of Systematic Reviews*, and *CMAJ*).[9-20] In 2010, an American College of Clinical Pharmacy (ACCP) committee on the pharmacist as clinician scientist searched the ClinicalTrials.gov trial registration website using the term "PharmD" and found a total of 523 active studies with pharmacists as principal investigators.[8] On November 16, 2020, we repeated the ACCP's search and found 2094 studies, an important increase in the registration of studies by pharmacists in just 10 years. Pharmacists have also been recognized as principal investigators by granting agencies. In fact, it was nearly 40 years ago, in 1983, that the ACCP obtained clarification that pharmacists were allowed by the US Food and Drug Administration to be principal investigators.[8]

Clinician-scientist pharmacists are typically specialists in a specific clinical area who divide their time between practice and research. Relevant research ideas are drawn from their pharmacy practice experiences and generate new knowledge that can be directly applied in the clinical setting to improve patient outcomes.[7] Traditionally, pharmacy-based researchers have had an academic background, focusing on specific disciplines such as pharmacokinetics, pharmacology, therapeutics, pharmacogenomics, drug safety, pharmacoepidemiology, and pharmacoeconomics. Our own observations indicate that an increasing number of pharmacy clinicians have become involved in clinical research in various areas, including cardiology, critical care, geriatrics, infectious diseases, mental health, nephrology, and oncology. Despite the growing body of new knowledge that results directly from pharmacist-initiated research, we believe that pharmacists remain underrepresented among clinician scientists. A Canadian survey published in 2012 indicated that pharmacists were interested in becoming more involved in clinical research; however, respondents noted key barriers that needed to be addressed, such as lack of time, lack of institutional support, and lack of expertise or training.[21]

The objective of the current review is threefold: to describe the suggested training and role of the clinician-scientist pharmacist, to highlight barriers and facilitators to the training and employment of pharmacists to assume this role, and to identify keys for a successful career as a clinician scientist.

TRAINING

There is no single specific pathway for pharmacists to pursue a career as clinician scientists.[2] Following an entry-level baccalaureate or doctoral degree in pharmacy, many clinician scientists will pursue training with a year 1 residency program or a master's degree in advanced pharmacotherapy and possibly a year 2 residency. Although these programs generally seek to develop some research competencies, the curriculums are structured to ensure that individuals can become clinical experts, with only a limited introduction to research. As such, advanced training in research methodology and statistics is necessary if a pharmacist is to become an independent, competitive researcher and be successful in obtaining extramural funding.[22]

A variety of program options are available to pharmacists for advanced research training, which can be classified into 2 main pathways: fellowships and graduate studies. Mostly available in the United States, fellowships are 1- or 2-year hospital- or industry-based programs. Fellowship programs are typically affiliated with a university and focus on various methods of research in a wide variety of clinical domains. At the time of writing (late 2020), the ACCP listed more than 60 fellowship programs that were available in the United States. Fellowship programs vary considerably with respect to clinical subspecialties (e.g., infectious diseases, transplant medicine, critical care), research methodologies (e.g., clinical research, pharmacokinetics, health services research, laboratory-based research), and settings (e.g., university laboratory, hospital and community settings, pharmaceutical industry).[23] Most fellowship programs involve some aspect of patient care and academia; however, 50% to 75% of a fellow's time is dedicated to research activities. The objectives, expectations, and end goals of these programs vary widely, to provide a highly individualized experience to the trainee. Fellowship programs seeking endorsement by the ACCP must meet specific minimum criteria, including at least 3000 hours dedicated to research activities over 2 years.[23] Eligible applicants typically are required to have a master's or doctoral degree (PharmD) and residency training or equivalent clinical experience. Trainees in research fellowships can expect to gain experience in all aspects of clinical research, including protocol development, grantsmanship, study design, study coordination and conduct, statistical analysis, and manuscript preparation.[24]

Graduate studies, including master's (MSc) and doctoral (PhD) programs, are offered by various health science faculties, including faculties of pharmacy, nursing, and medicine. Pharmacy faculties across Canada and the United States offer MSc and PhD programs in pharmaceutical sciences, with various options such as clinical sciences and translational research. MSc degrees generally take 2 years to complete, whereas PhD programs require 4 to 6 years. MSc programs involve coursework in research methods and statistics, a research project leading to the publication of 1 or 2 scientific articles, and preparation of a thesis. PhD programs generally include additional research methods and advanced statistics courses, the development of a research program including protocol writing and grantsmanship, the publication of 3 or more scientific articles, a qualifying examination, and the writing of a thesis. Dual-degree PharmD/MSc or PharmD/PhD programs, which are becoming more prevalent in the United States, have the advantage of streamlining research training and providing students with a clear path toward graduate studies. Although similar programs for physicians (MD/MSc and MD/PhD programs) are increasingly popular among faculties of medicine and medical students in Canada, Canadian faculties of pharmacy have yet to offer such programs. Postdoctoral studies, which follow graduate studies, are highly encouraged for pharmacists who intend to pursue research and academia as their primary career, but may also enable clinician scientists to acquire additional experience and competencies, thereby increasing their competitiveness in obtaining research funding. In Canada, many clinician-scientist pharmacists have pursued MSc or PhD programs in clinical epidemiology, experimental medicine, and clinical sciences offered in faculties of medicine.

Both training paths offer advantages, but they also have drawbacks, which have become a source of long-standing debate in the United States.[22,23,25] Fellowship programs offer less academic classwork than graduate studies, along with a salary, a more hands-on approach to research, and the potential to conduct and participate in multiple research projects rather than just thesis work; however, no such programs are offered in Canada. In contrast, graduate studies offer an opportunity to acquire a strong theoretical foundation in research methods, a structured academic program, and a recognized degree that can open the door to academia, but they are long and arduous endeavours that may depend on grants for financial support, although certain faculties offer some forms of funding (e.g., internal grants or teaching assistant positions). Most importantly, both fellowships and graduate studies enable the development of essential skills, such as critical reasoning, problem-solving, and hypothesis generation. In addition, these programs facilitate the development of a research network.

In both fellowship programs and graduate studies, the most important elements to consider are the choice of the preceptor/professor and the institution. Finding the right fit with a supervisor and institution will not only provide the best opportunity to ensure development of targeted research competencies through the proposed research program, but will also provide opportunities to develop research networks and mentoring relationships.

CURRENT STATE

Historically, physicians have made up the majority of clinician scientists, and this concept is well established in the medical field in Canada, with a number of structured programs and career paths available once medical training is complete.[26,27] For other health care professionals, the development of a career path for clinician scientists is less well established.[7] Although the exact number of clinician-scientist pharmacists in Canada is not known, it is likely small relative to the pharmacy workforce as a whole and relative to the clinician scientists from other health care professions (e.g., nursing and medicine). In Canada, most clinician-scientist pharmacists practise in academic health centres that have an affiliation with a hospital research centre, and they have university cross-appointments as either clinical professors or clinician scientists. Some faculties, such as the Leslie Dan Faculty of Pharmacy at the University of Toronto, have developed

specific career paths for clinician scientists. These relationships and affiliations are necessary for all clinician scientists to enable and support research endeavours by making available research infrastructure, research networks, and resources such as methodological, contract, and financial support. In some cases, the clinician scientist will obtain career grants from granting agencies (federal or provincial) or local health science centres. For example, in the province of Quebec, the Fonds de recherche Santé–Québec offers clinician scientist grants for health care professionals. These 4-year grants are competitive, cover about half of a person's salary, and are renewable to a maximum of 3 terms (Junior 1, Junior 2, and Senior Clinician Scientist). Applicants must have a faculty appointment and must guarantee that at least 50% of their time is devoted to their research program. The CIHR offers a similar program. To our knowledge, however, few clinician-scientist pharmacists have followed this path, leaving these opportunities to other health care professionals.

The profession of pharmacy needs to engage and build a workforce of clinician-scientist pharmacists in Canada. At the present time, we believe that clinician-scientist pharmacists are rare in hospital research centres and pharmacy faculties, with most pharmacists having to choose between full-time pharmacy practice and full-time research. Ideally, we should strive as a profession to have at least one trained clinician-scientist pharmacist within the ranks of every university-affiliated hospital pharmacy department, to develop and support programs of research and to mentor or supervise research trainees. For this to happen, there is a need to develop university cross-appointed and funded clinician-scientist positions within hospital pharmacy departments, with 50% or more protected research time. From the perspective of the pharmacy department there are benefits to this investment. Many hospitals and their pharmacy departments identify research as a priority within their vision and mission statements. Investing in clinician scientists, including clinician-scientist pharmacists, is one way to support these objectives. Research productivity can provide regional, national, and international recognition, which can be used in the recruitment of staff and learners. The designated clinician-scientist pharmacist could provide methodological support and mentorship to residents conducting research projects, as well as to other clinical staff with less experience, with the overall goal of promoting an integrative culture between clinical work and research. Furthermore, in large institutions, the pharmacy department is often involved in the conduct of many trials and research projects initiated by other researchers, clinicians, and industry partners. Having a pharmacy research leader within the department, someone who plays a supportive role in the conduct of research involving the pharmacy, could ensure that the department's needs and role are always considered and that pharmacy is represented within affiliated research organizations and research ethics boards.

BARRIERS AND FACILITATORS

Over recent years, there has been a reduction in the number of clinical research trainees across all health professions.[27,28] One qualitative study identified 3 main barriers perceived by clinical scientists in Canada: research training, research salaries, and research grants.[29] To these, we must add the challenges of having an active clinical practice and maintaining up-to-date clinical competencies, while balancing the workload associated with staying competitive in multidisciplinary research funding opportunities (e.g., through CIHR), managing active research projects, and disseminating their results. Lack of support early in a person's career, particularly among those in their first academic position, has also been identified as a key barrier to maintaining a clinician-scientist workforce.[27]

Maintaining an active clinical practice represents an additional challenge for clinician scientists who are trying to secure research funds. An applicant's research experience is an important criterion in these efforts, and clinician scientists have the added difficulty of competing with full-time researchers.[7,29] Lack of dedicated time for research is not unique to pharmacists or clinician scientists. Protected research time is more likely in academic positions, but in both academic and clinical settings it is usually dependent on grant funding. Some grants and funding awards will even allow for salary support, which typically is used to fund the protected research time, but this model depends on the duration of funding and means that sustainability is necessarily competitive.

For pharmacists who are willing to develop a clinical research career, specific research training opportunities are scarce. There is a need to develop dedicated programs within Canadian faculties of pharmacy and thus a critical need for clinician-scientist pharmacists to act as mentors and to seek positions as professors and research directors. Pharmacy faculties should aim to develop flexible programs for practising clinical pharmacists who wish develop research competencies, as well as combined PharmD/MSc or PharmD/PhD programs in clinical research to recruit young students early in their studies and new clinician-scientist positions to enable the training of graduate student pharmacists. Strategies for more recruitment of pharmacy students to graduate programs also need to be introduced. These strategies may already exist in the basic science departments within pharmacy faculties and could be adopted by pharmacy practice departments.

To advance clinical pharmacy research, pharmacy students need to be more aware of research career paths early in their programs of study. Enabling undergraduate pharmacy students to participate in research opportunities early on is one of the keys to success.[30] During first-year residency programs, research projects should be supported by experienced research teams to ensure that research experiences

are positive and to ensure that residents have opportunities to publish their work.[31] Given that most residency projects in Canadian and US programs remain unpublished,[32] there is clear room for improvement. In addition, pharmacy education needs to engender an attitude of inquisitiveness and scholarly thinking among pharmacists.[33] This attitude should be nurtured early in the pharmacy curriculum (or even before) and groomed throughout entry-level studies to ensure the training of candidates who will engage in advanced research training and provide a pipeline of clinician scientists. Students should be encouraged to move beyond studying with the basic goal of passing exams and to focus more on developing skills in critical thinking, problem-solving, and scientific reasoning. Suggestions to improve critical thinking have included enabling a thoughtful learning environment, enabling students to understand the processes needed to execute cognitive operations, and guiding and supporting their efforts until they can perform on their own.[33]

FUTURE DIRECTIONS

The funding of dedicated research positions for clinician-scientist pharmacists by health care institutions, pharmacy faculties, granting agencies, or a combination of these is essential for the career development of clinician-scientist pharmacists. Canada has a highly competitive research environment, with more good research projects being proposed than funding opportunities can support, which leads to low success rates in the major grant competitions (e.g., those of the CIHR).[34] Clinician-scientist pharmacists should also explore alternative granting sources such as foundations and other local granting agencies.

A recent consensus panel for the training and early-career support of physician scientists issued recommendations that could inspire the pharmacy profession.[27] The panel recommended the establishment of a national council to provide oversight of clinician-scientist programs, capacity development for funding and mentorship support, and development of interdisciplinary networks of clinician-scientists, and to ensure that faculties cover the scientific basis of health care and include research methods in their curriculums.[27] In particular, the development of mentorship programs within the pharmacy profession seems essential to support clinician scientists and to enable them to lead successful research and clinical careers.[3] Identifying and training mentors should thus be a priority within our profession.

Finally, given that initiating a research program is not an easy undertaking and necessitates plenty of hard work and passion, aspiring clinician-scientist pharmacists need to be dedicated and should expect to work extremely hard, often on their own time, to obtain grants, design studies, and be successful in research. Establishing a record of success in a research program is one potential way of negotiating and obtaining protected research time for future projects.

CONCLUSION

Clinician scientists represent an essential component of the research infrastructure of academic health care centres, but few pharmacists have followed this career path. Although the pharmacy profession has made important strides over the past decades, Canada needs to engage and build a workforce of pharmacists that includes clinician scientists. In the past 3 to 4 decades, pharmacists have established themselves as essential members of the bedside clinical team. They should now use their drug-related knowledge to inform clinical research and patient care.

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Advanced Pharmacist Practitioner Series

The article about pharmacists as clinician scientists that appears in this issue concludes the Advanced Pharmacist Practitioner Series, which has been focused on enabling hospital pharmacists and pharmacy departments to advance and broaden the scope of pharmacy practice across Canada. The following is a complete list of the articles that have appeared in this series.

The advanced pharmacist practitioner: a new series in the *Canadian Journal of Hospital Pharmacy* (Stephen Shalansky). *Can J Hosp Pharm*. 2019;72(1):42-8.

Advanced strategies in pharmacy experiential education (Michael Legal). *Can J Hosp Pharm*. 2019;72(3):239-44.

Pharmacy informatics: where medication use and technology meet (Daniel Cortes, Jodie Leung, Andrea Ryl, and Jenny Lieu). *Can J Hosp Pharm*. 2019;72(4):320-6.

Role of the US Veterans Health Administration clinical pharmacy specialist provider: shaping the future of comprehensive medication management (M Shawn McFarland, Julie Groppi, Terri Jorgenson, Tera Moore, Heather Ourth, Andrea Searle, and Anthony Morreale). *Can J Hosp Pharm*. 2020;73(2):152-8.

Recognition of advanced practice pharmacists in Australia and beyond: considerations for Canadian practitioners (Rochelle M Gellatly and Kirsten Galbraith). *Can J Hosp Pharm*. 2020;73(3):225-31.

The clinician scientist (David R Williamson, Salmaan Kanji, and Lisa Burry). *Can J Hosp Pharm*. 2021;74(2):130-4.

Utilisation de l'intelligence artificielle en pharmacie : une revue narrative

par Laura Gosselin, Maxime Thibault, Denis Lebel et Jean-François Bussières

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RÉSUMÉ

Contexte : L'intelligence artificielle (IA) est une avancée technologique qui consiste à amener une machine à imiter une forme d'intelligence.

Objectifs : L'objectif principal est d'effectuer une revue narrative des études évaluant la faisabilité et l'impact de l'IA en pharmacie. L'objectif secondaire est de développer une carte heuristique entourant l'IA en santé.

Sources des données : Nous avons consulté quatre bases de données, soit PubMed, Medline, Embase et CINAHL.

Sélection des études et extraction des données : Quatre stratégies de recherche ont été élaborées. Sélection des articles sur la base du titre, de l'abrégé puis du texte par une assistante de recherche, suivie d'une révision par un pharmacien de l'équipe. Les articles pris en compte doivent décrire ou évaluer la faisabilité ou l'impact de l'IA en pharmacie.

Synthèse des données : À partir de la revue documentaire, 362 articles ont été sélectionnés au départ, 18 d'entre eux ont été retenus selon les critères d'inclusion. De façon générale, on note que les études ont été surtout menées aux États-Unis (72 %, 13/18). Les études portent, par ordre d'importance décroissant, sur la prédiction de la réponse aux traitements et la prédiction d'effets indésirables (33 %, 6/18), la priorisation des patients (28 %, 5/18), l'adhésion thérapeutique (22 %, 4/18), la validation d'ordonnances et la prescription électronique (17 %, 3/18) et d'autres thèmes (p. ex. diagnostic, coûts, assurance, vérification de volumes de seringue).

Conclusions : Cette revue narrative met en évidence 18 études évaluant la faisabilité et l'impact de l'IA en pharmacie. Ces études ont utilisé différentes approches méthodologiques dans divers domaines d'application, en officine comme en établissement de santé. Il est encore trop tôt pour prédire les retombées de l'IA en pharmacie, mais ces études soulignent l'importance de s'y intéresser.

Mots-clés : pharmacie, intelligence artificielle, revue narrative

ABSTRACT

Background: Artificial intelligence (AI) can be described as an advanced technology in which machines display a certain form of intelligence.

Objectives: The primary objective was to perform a narrative review of studies evaluating the feasibility and impact of AI in pharmacy. The secondary objective was to create a mind map of AI in health care.

Data Sources: Four databases were consulted: PubMed, Medline, Embase, and CINAHL.

Study Selection and Data Extraction: Four search strategies were developed. Initial selection of articles was based on their titles and abstracts; the full texts were then evaluated by a research assistant, with review by a pharmacist. Articles were included if they described or evaluated the feasibility or impact of AI in pharmacy.

Data Synthesis: A total of 362 articles were identified by the literature review, of which 18 met the inclusion criteria. The studies were mainly conducted in the United States (72%, 13/18). The article topics were, in decreasing order, prediction of response to treatments and adverse effects (33%, 6/18), patient prioritization (28%, 5/18), treatment adherence (22%, 4/18), validation of prescriptions and electronic prescription (17%, 3/18), and other themes (e.g., diagnosis, costs, insurance, and verification of syringe volume).

Conclusions: This narrative review highlighted 18 studies evaluating the feasibility and impact of AI in pharmacy. The studies used various methodologies in different settings, both retail pharmacies and hospital pharmacies. It is still too soon to predict the implications of AI for pharmacy, but these studies emphasize the importance of attention in this area.

Keywords: pharmacy, artificial intelligence, literature review

INTRODUCTION

L'intelligence artificielle (IA) est une avancée technologique qui consiste à amener une machine à imiter une forme d'intelligence. Le Grand Dictionnaire terminologique précise qu'il s'agit d'un « domaine d'étude ayant pour objet la reproduction artificielle des facultés cognitives de l'intelligence humaine dans le but de créer des systèmes ou des machines capables d'exécuter des fonctions relevant normalement de celle-ci. L'IA touche à de nombreux domaines, comme les sciences cognitives et les mathématiques, et à diverses applications, notamment en reconnaissance des formes, en résolution de problèmes, en robotique, dans les jeux vidéo ainsi que dans les systèmes experts »[1]. L'Office québécois de la langue française propose un lexique de 85 termes associés à l'IA[2].

Dans le domaine de la santé, l'IA a été utilisée en imagerie médicale afin d'assister la reconnaissance visuelle d'images recueillies lors d'examens radiologiques[3]; elle a également été utilisée pour l'optimisation de choix de traitement en oncologie[4].

Compte tenu de l'informatisation de toutes les ordonnances des patients dans les dossiers pharmacologiques depuis quelques décennies, tant en officine qu'en établissement de santé, ces bases de données représentent une réelle occasion de développer des modèles d'apprentissage automatique afin de prédire des éléments utiles à la pratique pharmaceutique. Les données provenant des dossiers médicaux électroniques sont évidemment à l'avant-plan des sources utiles au développement de l'IA et peuvent être combinées aux données tirées de la pratique de la pharmacie.

Flynn souligne qu'il existe différentes possibilités mais également de la confusion entourant les concepts et les termes utilisés ainsi que plusieurs craintes liées à l'utilisation de l'IA dans la pratique pharmaceutique[5].

Puisqu'il s'agit d'un sujet d'actualité en émergence et que l'IA représente une opportunité en pharmacie, nous nous sommes intéressés à l'utilisation de l'IA dans la pratique pharmaceutique.

L'objectif principal était d'effectuer une revue narrative des études évaluant l'utilisation de l'IA en pratique pharmaceutique.

MÉTHODES

Sources des données et sélection des études

Dans un premier temps, nous avons recensé les concepts, les termes et les applications de l'IA en pharmacie à partir d'articles d'intérêt général, d'une séance de remue-méninges et de travaux préliminaires. Sur la base des termes obtenus, nous avons développé par itération une carte heuristique des termes applicables à l'IA en pharmacie. Ces travaux préliminaires et cette carte heuristique ont contribué à clarifier le vocabulaire pertinent pour notre stratégie de recherche.

Dans un deuxième temps, nous avons mené une recherche sur les études évaluant l'utilisation de l'IA en pratique pharmaceutique. Nous avons consulté quatre bases de données, soit PubMed, Medline, Embase et CINAHL.

Dans PubMed, nous avons utilisé la stratégie de recherche suivante : ((((Pharmacy Service, Hospital) OR « Pharmacy »[MeSH]) OR « Community Pharmacy Services »[MeSH]) AND « Artificial Intelligence »[MeSH]).

Dans Embase, nous avons utilisé la stratégie de recherche suivante : (artificial intelligence/ or artificial neural network/ or network learning/ or learning algorithm/ or supervised machine learning/ or unsupervised machine learning/ or support vector machine/ or exp Machine learning/ or (AI or IA or neural network * or ((deep or machine) and learning)).ti,ab,kw. AND pharmacy/ or hospital pharmacy/ or clinical pharmacy/).

Dans CINAHL, nous avons utilisé la stratégie de recherche suivante : (MH(artificial intelligence OR deep learning OR machine learning) OR TI(AI OR IA or neural network* or ((deep or machine) and learning)) OR SO(AI or IA or neural network* or ((deep machine) and learning)) AND TI(pharmacy OR hospital pharmacy service* OR clinical pharmacy OR community pharmacy service*) OR SO(pharmacy OR hospital pharmacy service* OR clinical pharmacy OR community pharmacy service*)).

Chaque stratégie de recherche a nécessité que nous sélectionnions les articles sur la base du titre, puis de l'abrégé puis du texte complet. Les abrégés de conférences pertinents ont aussi été retenus. La sélection a été effectuée par une assistante de recherche et par un pharmacien de l'équipe. Les divergences ont été résolues par consensus. Les articles retenus devaient décrire ou évaluer l'utilisation de l'IA dans un domaine applicable à la pratique de la pharmacie. Compte tenu de l'émergence de cette discipline, nous nous sommes intéressés à deux dimensions plus spécifiques, soit la faisabilité de recourir à l'IA en pharmacie et les mesures d'impact de son utilisation. Ont été exclus les articles sans rapport avec l'IA, qui n'avaient pas de données originales, qui ne parlaient pas d'utilisation applicable en pratique pharmaceutique en milieu communautaire ou hospitalier.

Extraction des données

À partir des articles retenus, nous avons constitué un tableau synthèse de lecture comportant le premier auteur, l'année de publication, le pays, le type d'étude, les objectifs, la description de l'utilisation de l'IA en pharmacie, la taille de l'échantillon (*n*), les principaux résultats, les limites et la pertinence de leur utilisation dans la pratique pharmaceutique. Le tableau synthèse nous a permis de déterminer les réussites et les difficultés liées à l'utilisation de l'IA en pharmacie.

Aucune analyse statistique n'a été menée.

SYNTHÈSE DES DONNÉES

La figure 1 illustre la carte heuristique des termes applicables à l'IA en santé. Ainsi, l'IA repose sur l'utilisation d'un ensemble de données qu'on peut exploiter à partir de différentes méthodes, dont l'apprentissage automatique dans une variété de champs d'application. L'utilisation de ces données comporte des enjeux éthiques. Cette carte heuristique aide à la mise en contexte des études retenues dans notre revue narrative.

À partir de la revue documentaire, nous avons sélectionné 362 articles au départ et retenu 18 selon les critères d'inclusion. Après l'exclusion des articles sur la base du titre et du résumé, il en restait 33, dont 15 ont été exclus. Trois étaient des doublons et 12 ont été exclus sur la base du texte complet, car ils ne comportaient pas de données originales, n'avaient pas de rapport avec l'IA, ne parlaient pas de pharmacie ou ne s'appliquaient pas à la pharmacie communautaire ou hospitalière. Enfin, l'un des articles compris dans cette revue narrative est une version améliorée d'un article exclu de notre sélection et publié par le même auteur[6].

La figure 2 présente la cartographie de sélection des articles inclus et exclus.

De façon générale, on note que les études ont été surtout menées aux États-Unis (72 %, 13/18).

Elles portent, par ordre d'importance décroissant, sur la prédiction de la réponse aux traitements et la prédiction d'effets indésirables (33 %, 6/18), la priorisation des patients (28 %, 5/18), l'adhésion thérapeutique (22 %, 4/18), la validation d'ordonnances (17 %, 3/18) et d'autres thèmes (p. ex. diagnostic, coûts, assurance, vérification de volumes de seringue).

En ce qui concerne la réponse aux traitements et la prédiction d'effets indésirables, les études ont en général pour but d'aider à prédire la capacité du patient à répondre ou non à un traitement, le risque de développer un effet indésirable ou les paramètres pharmacocinétiques.

En ce qui a trait à la priorisation des patients, les études se concentrent sur la sélection de patients dans le but d'offrir une intervention à ceux qui ont le plus de chances d'en bénéficier. Ces études sont nombreuses à offrir des interventions ciblant l'adhésion thérapeutique, mais d'autres

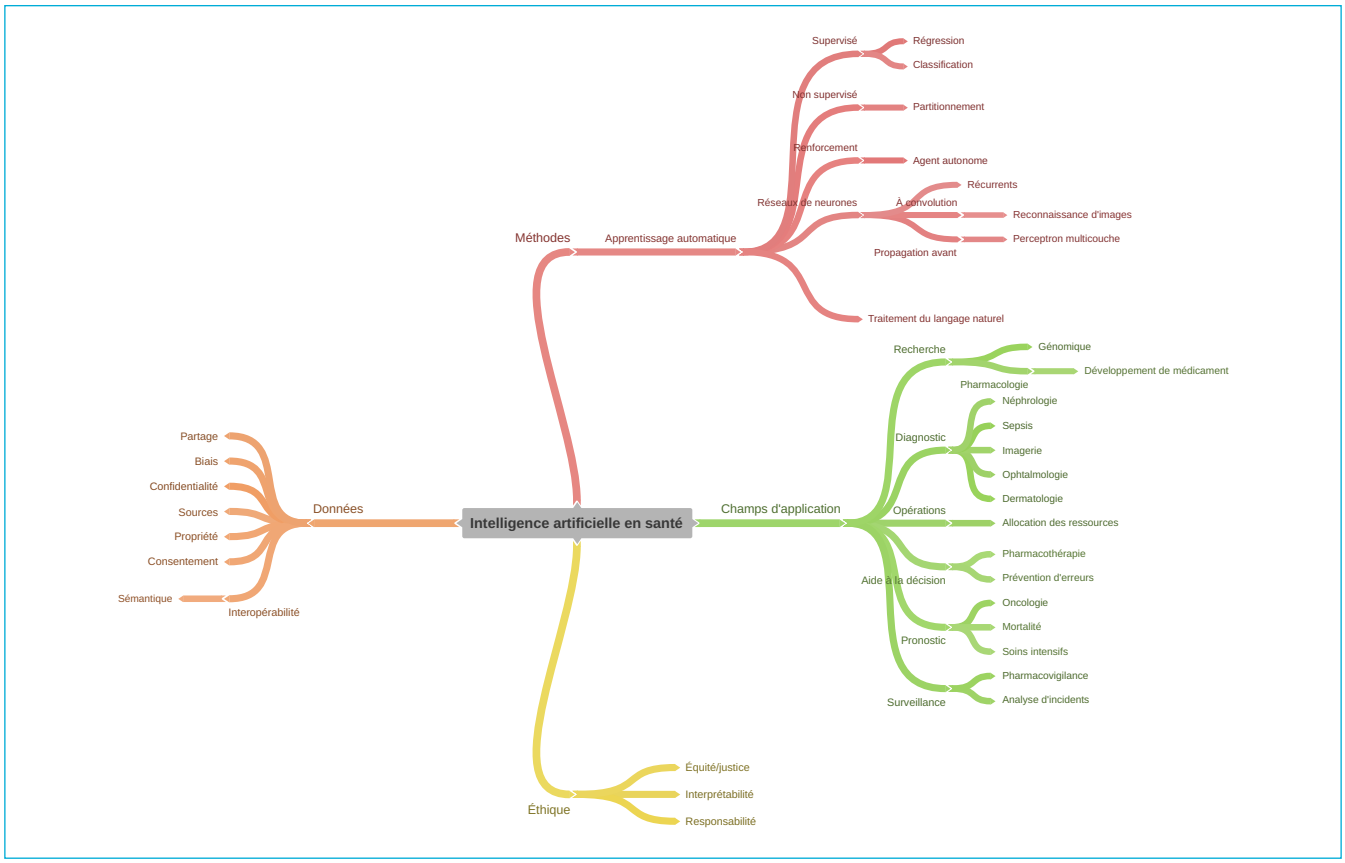

FIGURE 1. Carte heuristique des termes applicables à l'intelligence artificielle en santé.

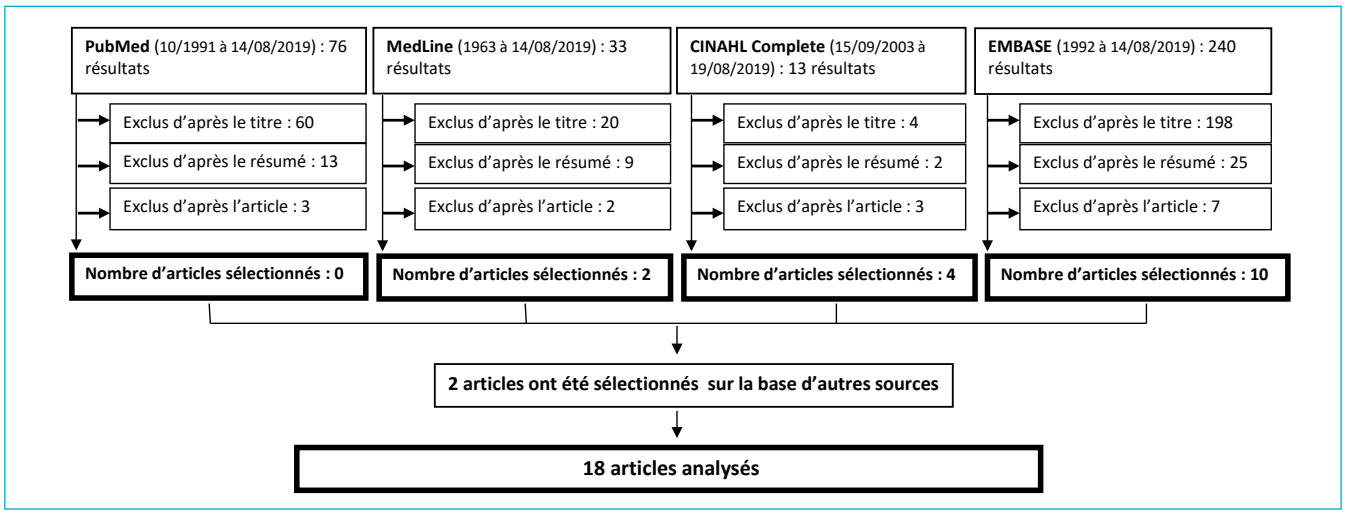

FIGURE 2. Cartographie de sélection des articles sélectionnés et exclus.

ciblent la prévention d'événements dont le coût est élevé ou qui alourdissent trop le système de santé.

Dans le contexte de la validation d'ordonnances et de la prescription électronique, l'objectif principal des études est d'optimiser l'aide à la décision offerte au moment de l'entrée d'une ordonnance ou de sa validation, pour éviter les alertes inutiles et réduire la désensibilisation aux alertes. On remarque aussi des tentatives de signaler au prescripteur ou au pharmacien les ordonnances statistiquement aberrantes, c'est-à-dire sortant des modèles de prescription habituels. Ceci est un élément nouveau par rapport à l'aide à la décision classique basée sur des règles préprogrammées.

Les autres études discutent d'analyse de rapports d'incidents, d'analyse d'images pour déterminer le volume de liquide dans des seringues ainsi que de pharmacoéconomie.

Le tableau 1 présente un profil synthèse des études[6-23] évaluant la faisabilité et l'impact de l'IA en pharmacie.

DISCUSSION

Cette revue narrative présente une revue originale des études évaluant la faisabilité et l'impact de l'IA en pharmacie. Des 362 articles recensés au préalable, seulement 18 d'entre eux publiés de 2003 à 2019 ont été retenus. Ceci représente une proportion très limitée de ce qui se publie actuellement sur l'IA. À titre d'exemple, l'utilisation du terme MeSH « *Artificial intelligence* » dans la base de données PubMed met en évidence 1248 articles publiés en 2000 contre 8091 en 2018.

Le recours à l'IA, peu importe les méthodes utilisées, nécessite un historique de données en quantités suffisantes pour créer des modèles qui pourront être utilisées en temps réel ou de façon asynchrone. En pharmacie, on détient un historique de données important, compte tenu que l'informatisation des ordonnances remonte à plusieurs décennies et que les données recueillies ne sont généralement pas détruites au fil du temps. Normalement, une pharmacie d'officine ou d'hôpital peut traiter de 500 à 1500 ordonnances par jour. Cinq études sur 18 ont été menées sur des données issues de la pratique en pharmacie communautaire.

La revue narrative met en évidence différentes approches méthodologiques de prédiction, par exemple l'utilisation de réseaux de neurones (n = 4), des arbres boostés (n = 2) ou de régression logistique (n = 2). Certaines études comparent ou combinent plus d'une approche. Dans huit études, l'approche utilisée n'est pas décrite. Ceci n'est pas étonnant étant donné que certains auteurs ne veulent pas décrire leur approche en détail, parce qu'elle pourrait être intégrée dans des produits commerciaux vendus par la suite aux cliniciens et aux établissements de santé. Par contre, certains groupes appellent maintenant à la transparence des techniques utilisées, afin que les cliniciens soient en mesure de comprendre comment sont générées les prédictions de ces outils et qu'ils voient clairement les limites de ces techniques[24]. En outre, les données recueillies ne permettent pas de déterminer les approches à privilégier. L'approche optimale doit être déterminée au cas par cas selon le problème clinique en question.

La revue narrative met en évidence différents domaines d'utilisation (p. ex. pharmacovigilance, priorisation des patients, adhésion thérapeutique, validation des ordonnances). Le recours à l'IA est émergent et il est encore trop tôt pour déterminer les domaines où les retombées seront plus intéressantes pour la pratique pharmaceutique. De façon générale, on peut dire qu'il est pertinent d'explorer des modèles de prédiction si l'on détient un bon ensemble de données et si l'on a déterminé un besoin de prédiction pour soutenir le travail du pharmacien ou de soignants en santé.

Parmi les études recueillies, au moins huit s'intéressent aux maladies chroniques. Une part importante de la population est atteinte de maladies chroniques, qui accaparent une proportion importante des ressources humaines, matérielles et financières dans le domaine de la santé. Les chercheurs font le pari que l'utilisation de l'IA dans le cadre des maladies chroniques pourrait, si les modèles développés ont une bonne capacité prédictive, avoir un jour un impact favorable sur les ressources nécessaires, compte tenu du grand nombre de patients atteints dans le monde. De façon générale, le suivi des maladies chroniques repose sur un nombre circonscrit de paramètres cliniques et de médicaments par affection et il pourrait être intéressant de prédire les médicaments, les tests de laboratoires et les suivis pertinents à effectuer afin de réduire les risques de morbidité, de réhospitalisation et de mortalité. Plusieurs études recensées dans la revue s'intéressent à l'adhésion au traitement dans le contexte des maladies chroniques, afin de prioriser les interventions de pharmaciens pour les patients davantage exposés à un risque de non-adhésion. Compte tenu des conséquences importantes en termes de complications médicales et des coûts de santé liés à la non-adhésion, ce type d'utilisation de l'IA par les pharmaciens a certainement du potentiel[25].

L'utilisation du terme IA n'est pas forcément toujours appropriée. Il est peut-être tentant de mentionner l'expression « intelligence artificielle » dans le titre ou le résumé d'un article afin d'attirer l'attention, même si le sujet ne repose pas sur l'utilisation réelle de l'IA. Notre revue documentaire nous a permis de voir que certains articles présentés sous cette expression portaient plutôt sur des outils d'aide à la décision, l'utilisation d'algorithmes ou de règles permettant de prioriser des patients, sur des conditions cliniques, des médicaments ou d'autres paramètres dans le travail du pharmacien. Plusieurs logiciels intègrent des outils d'aide à la décision (p. ex. afficher une alerte au pharmacien qui valide une ordonnance si la clairance à la créatinine est inférieure à un seuil d'alerte prédéterminé pour ce médicament, afficher une alerte en présence d'une duplication, d'une interaction médicament-médicament ou d'une allergie) sans que ceci soit du domaine de l'IA. À notre avis, l'utilisation de l'IA représente une véritable avancée dans la pratique

TABLEAU 1 (partie 1 de 4). Profil synthèse des études évaluant la faisabilité et l'impact de l'intelligence artificielle en pharmacie

Référence	Pays	Objectifs	Type d'IA	*n*	Résultats	Limites	Domaines et lieu	Thème d'utilisation de l'IA
Daheb et al. (2013)[7]	Canada	Développer un modèle de réseau de neurones artificiels (RN) pour prédire l'élimination du médicament pendant la dialyse en fonction des propriétés du médicament et des conditions de dialyse	RN	NA	Il est possible de prédire l'élimination par dialyse des médicaments selon les RN	Analyse *in vitro* seulement	Dialyse; hôpital	Réponse au traitement et prédiction des EI
Dilley et al. (2015)[8]	États-Unis	À partir d'une vaste base de données de réclamations, construire un algorithme facilitant le choix du médicament antiépileptique pour un patient donné en fonction de sa similarité avec les patients analysés dans le modèle	Non précisé	Non précisé	Le fait de recevoir le traitement prédit par le modèle était associé à un plus grand délai avant un prochain changement de traitement	Abrégé seulement, peu de détails; seulement 17 % des patients ont reçu le traitement prédit par le modèle	Épilepsie; hôpital	Réponse au traitement et prédiction des EI
Dockery et Mueller (2013)[9]	États-Unis	Identifier les patients qui risquent de ne pas suivre leur traitement au cours des six prochains mois en pharmacie communautaire	RL	Non précisé	Le modèle a permis de prédire la non-adhésion avec une exactitude de 70,4 %; ceci variait en fonction du médicament et de l'adhésion antérieure	Abrégé seulement, peu de détails	Maladies chroniques; pharmacie communautaire	Priorisation des patients, adhésion thérapeutique
Fong et al. (2017)[10]	États-Unis	Classer les rapports d'événements de sécurité des patients en fonction de la modélisation du texte libre des rapports d'événements afin de réduire le temps de révision par le comité des pharmaciens	Traitement du langage, arbres de décision, MVS	774 rapports d'événement	L'aire sous la courbe ROC des prédictions de catégories de rapports variait entre 0,81 et 0,96	Modèle basé uniquement sur le texte libre plutôt que sur une terminologie de référence	Qualité et risques; hôpital	Réponse au traitement et prédiction des EI
Glennon et Errabelli (2018)[6]	États-Unis	Analyser l'impact d'un programme de sensibilisation à l'adhésion au traitement personnalisé, utilisant une approche analytique pour la priorisation des patients à cibler	Non précisé	Non précisé	Dans le groupe bénéficiant de l'intervention ciblée, 20 % de plus de patients ont atteint une proportion de jours couverts de 80 % (mesure d'adhésion standardisée)	Abrégé seulement, peu de détails; intervention confuse, il n'est pas clair si l'avantage est dû au ciblage des patients par l'IA ou à l'intervention en observance offerte	Maladies chroniques; hôpital puis suivi en communauté	Priorisation des patients, adhésion thérapeutique
Gracey et al. (2018)[11]	États-Unis	Évaluer l'efficacité de l'utilisation de l'IA pour cibler les patients devant bénéficier d'interventions par rapport aux approches de ciblage traditionnelles visant à améliorer l'observance du traitement	Non précisé	Groupe contrôle, *n* = 14 377 Groupe traditionnel, *n* = 5423 Groupe IA, *n* = 24 527	L'adhésion du groupe IA était de 6,11 % supérieure à celle du groupe témoin et de 7,8 % à celle du groupe traditionnel	Abrégé seulement, peu de détails; observance calculée à partir de données d'assurance	Maladies chroniques; pharmacie communautaire	Priorisation des patients, adhésion thérapeutique

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TABLEAU 1 (partie 2 de 4). Profil synthèse des études évaluant la faisabilité et l'impact de l'intelligence artificielle en pharmacie

Référence	Pays	Objectifs	Type d'IA	*n*	Résultats	Limites	Domaines et lieu	Thème d'utilisation de l'IA
Hill et al. (2017)[12]	États-Unis	Déterminer les caractéristiques des patients associées à un risque élevé de non-adhésion aux médicaments pour les traitements hypolipidémiants	RL, forêts aléatoires, arbres boostés	69 227 patients	Il a été possible de prédire la non-adhésion avec une aire sous la courbe ROC de 88,5 % à l'aide des arbres boostés; Les meilleurs facteurs prédicteurs étaient un taux de LDL de départ faible et le non-renouvellement d'antihypertenseurs	Abrégé seulement, peu de détails; étude rétrospective seulement, il n'est pas clair qu'un ensemble de tests appropriés a été utilisé l'étude se focalise sur les hypolipidémiants et utilise le renouvellement d'autres médicaments pour prédire l'adhésion, alors que dans la réalité, on voudrait prédire l'adhésion à tous les traitements de manière simultanée	Maladies chroniques; pharmacie communautaire	Priorisation des patients, adhésion thérapeutique
Holloway et al. (2018)[13]	États-Unis	Décrire une technique de modélisation prédictive et conçue pour identifier les participants qui risquent d'être confrontés à un événement dont le coût est élevé (de 25 000 $ ou plus)	Non précisé	863 323 membres	Il a été possible de prédire la survenue d'événements coûteux à l'aide de modèles prédictifs, et des interventions préalables pourraient prévenir ces événements	Abrégé seulement, peu de détails; aucune donnée précise sur la performance du modèle; affirmations sur la prévention d'événements coûteux qui ne sont pas appuyés par la méthode décrite	Gestion des coûts; hôpital	Coûts d'assurance
Hu et al. (2017)[14]	États-Unis	Utiliser l'apprentissage automatique pour la sélection efficace des patients à inscrire à un programme de gestion des cas à l'urgence pour diminuer les visites récurrentes	*Gradient boosting*, arbres boostés, analyse discriminante linéaire, RL	190 009 membres	Il est possible de prédire les visites récurrentes à l'urgence à la fois des patients qui utilisent souvent ce service et de ceux pouvant devenir des utilisateurs récurrents	Données limitées, absence de certains facteurs de risque connus de visites fréquentes à l'urgence; analyse basée exclusivement sur des données d'assurances	Urgence; hôpital	Priorisation des patients
Jovanović et al. (2015)[15]	Serbie	Explorer l'applicabilité de réseaux de neurones à contre-propagation, associés à un algorithme génétique pour la prédiction de taux sériques de topiramate en fonction de la détermination de facteurs importants pour sa prédiction	RN à contre-propagation, algorithme génétique	88 concentrations mesurées	Il est possible d'utiliser un tel modèle pour prédire les concentrations sériques de topiramate; le facteur prédictif le plus important était la dose, puis la fonction rénale, lesquels expliquaient ensemble la grande majorité de la variabilité	Données extrêmement limitées; utilité pratique incertaine par rapport aux techniques plus simples	Épilepsie, pharmacocinétique; hôpital	Réponse au traitement et prédiction des EI
Kvancz et al. (2016)[16]	États-Unis	Déterminer la capacité d'un système d'apprentissage automatique à découvrir les patients atteints d'une maladie rare non diagnostiquée dans une base de données de réclamations	Non précisé	170 millions de patients, 1002 diagnostics potentiels définis	Les auteurs affirment que leur méthode permet d'identifier des patients qui risquent d'avoir une maladie rare encore non diagnostiquée	Résultats flous, aucune donnée sur l'efficacité réelle	Maladies rares; lieu non précisé	Diagnostic

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TABLEAU 1 (partie 3 de 4). Profil synthèse des études évaluant la faisabilité et l'impact de l'intelligence artificielle en pharmacie

Référence	Pays	Objectifs	Type d'IA	*n*	Résultats	Limites	Domaines et lieu	Thème d'utilisation de l'IA
Matanza et al. (2011)[17]	France	Évaluer la validité du lien entre l'utilisation d'hypnotiques, la survenue de chutes et l'intérêt potentiel de réduire l'utilisation d'hypnotiques	RN bayésiens	1020 mois d'observation, 1565 chutes signalées	L'analyse de corrélation classique n'a pas démontré de lien entre l'utilisation d'hypnotiques et les chutes alors que le réseau de neurones a trouvé un lien	Analyse réalisée à l'unité de soins et non du patient, utilité prédictive en vie réelle incertaine	Gériatrie; hôpital	Réponse au traitement et prédiction des EI
Regmi et al. (2019)[18]	États-Unis	Développer un système capable de lire et de rapporter le volume de médicament liquide présent dans les seringues	RN	500 échantillons	Le réseau de neurones a démontré une efficacité de 95 à 99 % pour la détermination du volume de liquides dans les seringues	Besoin d'une base mousse de polystyrène dans laquelle on place la seringue pour standardiser l'image capturée par le système	Préparations non stériles; hôpital	Vérification de volumes de seringues
Schiff et al. (2017)[19]	États-Unis	Évaluer l'exactitude, la validité et l'utilité clinique des alertes d'erreur de médication générées par un système d'aide à la décision utilisant un dépistage probabiliste des anomalies	Non précisé	747 985 patients, 300 dossiers révisés en détail	75 % des alertes générées par le système ont été jugées cliniquement utiles pour prévenir des problèmes liés à la médication	Étude soutenue financièrement par le développeur privé du logiciel à l'étude; analyse réalisée rétrospectivement, hors du contexte clinique	Hôpital	Validation d'ordonnances, prescription électronique
Segal et al. (2019)[20]	Israël	Évaluer la précision, la validité et l'utilité clinique des alertes d'erreur de médication générées par un système utilisant un dépistage probabiliste des anomalies, comparativement à un système classique dans un environnement hospitalier	Non précisé	3160 patients	L'alerte n'a visé que 0,4 % des ordonnances; 80 % des alertes ont été jugées cliniquement utiles; 43% des alertes ont mené à une action subséquente	Une seule personne a réalisé l'évaluation des alertes; l'étude a été réalisée dans une seule unité de soins d'un seul hôpital; analyse réalisée rétrospectivement, hors du contexte clinique	Médecine interne; hôpital	Validation d'ordonnances, prescription électronique
Thai et al. (2016)[21]	États-Unis	Déterminer les facteurs de risque d'hypoglycémie chez les adultes atteints de diabète de type 2 traités avec des antidiabétiques et quantifier le risque d'hypoglycémie sur la base de la totalité des facteurs de risque déterminés	Non précisé	558 963 patients	Les auteurs ont pu développer un algorithme prédictif du risque d'hypoglycémie; les facteurs de risque déterminés sont les antécédents d'hypoglycémie, l'âge, l'utilisation de sulfonylurées ou d'insuline, le sexe et d'autres facteurs	Abrégé seulement, peu de détails; analyse basée uniquement sur des réclamations d'assurance	Diabète type 2; hôpital puis suivi en communauté	Réponse au traitement et prédiction des EI
Woods et al. (2014)[22]	États-Unis	Rapport de la première mise en œuvre d'une alerte d'ordonnance atypique lors de la prescription de cinq médicaments couramment associés à un risque élevé	Distribution des probabilité	5201 phrases uniques d'ordonnances	68 alertes ont été générées durant une période de 92 jours; 50 alertes n'ont pas été prises en compte, et 28 ordonnances ont été modifiées par la suite	Analyse limitée à seulement 5 médicaments; analyse basée uniquement sur la fréquence statistique des combinaisons de médicaments, de dose et de fréquence sans égard aux caractéristiques du patient	Hôpital	Validation d'ordonnances, prescription électronique

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TABLEAU 1 (partie 4 de 4). Profil synthèse des études évaluant la faisabilité et l'impact de l'intelligence artificielle en pharmacie

Référence	Pays	Objectifs	Type d'IA	*n*	Résultats	Limites	Domaines et lieu	Thème d'utilisation de l'IA
Yamamura et al. (2003)[23]	Japon	Identifier des patients des soins intensifs, dont les concentrations sanguines d'aminoglycosides risquent d'être sous-thérapeutiques à l'aide de la modélisation par réseau de neurones artificiels	RN	89 patients	La sensibilité et la spécificité du réseau des neurones se sont révélées supérieures à une régression logistique multivariée	Analyse basée sur très peu de données et sur 2 molécules uniquement	Soins intensifs; hôpital	Pharmacocinétique

EI = effets indésirables, IA = intelligence artificielle, LDL = lipoprotéine de basse densité (« *low density lipoprotein* »), MVS = machine à vecteurs de support, RL = régression logistique, RN = réseau de neurones.

pharmaceutique et il est essentiel que les pharmaciens s'y intéressent. Par exemple, l'American Society of Health-System Pharmacists a publié en 2006 (mise à jour en 2016) un énoncé afin que chaque département de pharmacie d'un établissement de santé se dote d'un pharmacien qui se consacre à l'informatique clinique[26].

Cette revue narrative confirme l'émergence de l'IA en pharmacie. Ces articles constituent la pointe de l'iceberg et de nombreuses initiatives émergent un peu partout dans le monde. Il semble nécessaire que les pharmaciens s'y intéressent et que des collaborations s'établissent entre chercheurs en IA et cliniciens. Ce type de collaboration existe au quotidien, mais il génère encore peu d'applications cliniques utilisées en pratique. Les centres de recherche, les facultés de pharmacie, les ministères de la Santé, les établissements de santé, les chaînes et bannières devraient s'intéresser à l'IA. Bien que ce fait soit peu évoqué dans les articles de la présente étude, l'IA ne peut progresser sans le partage de données à des experts en modélisation et prédiction. Le partage de ces données, même anonymisées, n'est pas forcément permis ou sécuritaire compte tenu des enjeux de protection des renseignements personnels. Une réflexion sur les exigences juridiques entourant la confidentialité s'impose pour que les données disponibles en pharmacie soient exploitées de façon éthique, sécuritaire et adéquate.

Cette revue narrative comporte des limites. La consultation n'a porté que sur quatre bases de données; il serait intéressant de consulter d'autres bases de données, ciblant davantage le domaine de l'IA, dont la recherche fondamentale (p. ex. arXiv) et les publications découlant de conférences et de regroupements de chercheurs du domaine (p. ex. NeurIPS, ICML, ICLR, MLHC). Les stratégies de recherche utilisées ciblaient spécifiquement le critère de « pharmacie » ou de « pratique pharmaceutique ». Notre recherche a mis en évidence des articles pertinents qui ne comportaient pas le terme « *pharmacy* » mais dont le contenu aurait pu s'appliquer à la pratique pharmaceutique. Par exemple, Tomašev et collab. se sont intéressés à la prédiction de la survenue de l'insuffisance rénale aigüe[27]. Les médicaments sont évidemment un facteur de risque majeur de cette complication, de même qu'une réduction importante de la fonction rénale affecte l'élimination d'un grand nombre de médicaments. Ce type de modèle pourrait être grandement utile à la pratique pharmaceutique. Chen et collab. se sont intéressés à la prédiction des ordonnances futures en fonction des ordonnances passées du patient[28]. Zhao et collab. se sont intéressés à la détection d'effets indésirables médicamenteux à partir de dossiers électroniques[29]. Il pourrait être utile de faire une sélection de concepts et de termes pertinents à l'exercice de la pharmacie afin de recenser davantage d'articles intégrant l'IA en santé, qui sont importants pour la pratique pharmaceutique. Il pourrait être intéressant en outre d'utiliser d'autres termes, tels que : apprentissage automatique et *machine learning*, pour accroître le nombre d'articles potentiellement pertinents.

CONCLUSION

Cette revue narrative met en évidence 18 études évaluant la faisabilité et l'impact de l'IA en pharmacie. Ces études mettent en relief différentes approches méthodologiques et divers domaines d'application, en officine comme en établissement de santé. Il est encore trop tôt pour prédire les retombées de l'IA en pharmacie, mais ces études soulignent l'importance de s'y intéresser.

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Hospital Pharmacists' Documentation of Vancomycin and Aminoglycoside Prescriptive Authority

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INTRODUCTION

As pharmacists advance in direct patient care roles, it is important that their clinical decisions be recorded in the medical record to ensure continuity of care. Multiple pharmacy professional organizations have emphasized documentation as a critical component of the provision of collaborative patient care by health care professionals.[1-3] The expanding scope of practice for pharmacists in Saskatchewan includes collaborative prescriptive authority, which requires an explicit prescribing agreement between physicians and pharmacists, based on shared responsibilities and liabilities.[4-6] The Saskatchewan College of Pharmacy Professionals (SCPP) defines documentation as a critical component of the collaborative practice agreement.[4-6]

In the Saskatchewan Health Authority (SHA) – Regina area, the Regina Pharmacy and Therapeutics Committee has authorized a practice agreement enabling pharmacists to serve as collaborative prescribers of vancomycin and aminoglycosides for adult patients receiving acute care. The agreement stipulates that the pharmacist will initiate and maintain documentation as per current Pharmacy Department procedures for *all* patients who are receiving vancomycin and aminoglycosides. Furthermore, the agreement specifies that the pharmacist will document all interventions and recommendations regarding dose determination, serum drug levels, phone calls with prescribers, nephrotoxicity risk factors, need for increased monitoring, and other pertinent information in the chart, whether or not the regimen is changed.

A Steering Committee consisting of pharmacists and infectious disease physicians developed a procedure for pharmacists to use in operationalizing the agreement, which outlines in detail dose determination, monitoring, and documentation expectations. All pharmacists in our organization undergo a certification process before participating in the agreement. Certification includes a review of protocols and procedures, case-based application, and a written examination incorporating a documentation component.

Previous local research identified gaps in the frequency of documentation and omission of specific components of the progress note.[7,8] Tangedal and others[8] assessed prescriptive authority competency related to application of the vancomycin protocol. They identified deficiencies in documentation relating to aspects such as nephrotoxic risk factors, requirements for future trough levels, and validity of trough samples drawn (i.e., relative to start time and at steady state).

A pharmacists' working group (the Documentation Working Group or DWG) was established in November 2016 to facilitate increased documentation of all pharmacists' interventions in the progress notes of the patient chart.[9] As one part of their targeted activities, the group sought to determine the extent of adherence with documentation expectations as outlined by the collaborative practice agreement.

METHODS

The DWG conducted a retrospective audit of chart documentation by pharmacists in the fourth quarter of 2017. Our institution did not require approval from the ethics review board for this quality improvement initiative. A drug use evaluation report was generated to identify patients who received at least 1 dose of vancomycin, gentamicin, or tobramycin in the month before and including the audit date. A convenience sample of the patients on this list who remained as inpatients at either the Pasqua Hospital or the Regina General Hospital on the date of the audit was selected, based on ease of evaluator access to patient charts.

The audit consisted of 2 distinct components. In the first component, 3 members of the DWG reviewed the charts to determine the presence or absence of any progress notes, as outlined in the documentation requirements of the pharmacist procedures supporting the collaborative agreement. Notes were stratified by type, either as notes for empiric therapy or as follow-up notes after measurement of serum levels. For the second component, a random subset of these

notes was selected for further analysis. Seven DWG members (including L.R. and C.G.) reviewed the notes to determine the presence of each specific element outlined in the procedure. The results of both components of the audit were reviewed by the DWG and next steps established.

An educational session was conducted to present results of the first audit, reinforce procedural requirements, and engage pharmacy staff in evaluation of various sample notes, applying the same assessments as were used by DWG members.

A second audit was completed in the fourth quarter of 2018, using the same methods as the first, to assess adherence to documentation requirements. A data collection tool was utilized for the second audit to build greater consistency among assessors, although the factors assessed remained the same.

RESULTS

In the first audit, a total of 51 charts were evaluated, with identification of 162 instances requiring documentation, as per the procedure. A note was present in 137 of these instances (84.6% adherence rate). In the second audit, 88 charts were evaluated. Notes were present in 253 of the 295 instances where notes were expected (85.8% adherence rate). Table 1 depicts adherence rates stratified by note type. In both audits, the vast majority of patients whose charts were reviewed (98%) had received vancomycin.

Table 2 and Table 3 depict the breakdown of adherence to documentation requirements for specific elements in the empiric therapy notes and the notes prepared after measurement of serum levels, respectively. The elements most commonly omitted from empiric therapy notes included specification of a monitoring plan for evaluation of serum levels and serum creatinine. Notes documented after measurement of serum level frequently lacked assessment of the appropriateness of the measured serum level, interpretation of serum level results, and specification of duration of therapy.

DISCUSSION

Documentation is an integral component of the collaborative practice agreement model, intended to increase the clarity of the decision-making rationale among health care team members, as specified by legal and professional requirements.[1-4] According to the SHA – Regina area collaborative practice agreements for management of vancomycin and aminoglycoside therapy, it is expected that all interventions by pharmacists will be documented within the medical record. In this study, the DWG found that documentation was present in 84.6% and 85.8% of expected instances in the first and second audits, respectively. Although the documentation of empiric therapy notes tended to be higher than for follow-up notes, the absence of any documentation on initiation of therapy in 5%–10% of evaluated patient charts is concerning. In addition, 9 of the audited charts had no notes indicating a pharmacist's involvement in collaborative prescribing. These omissions may have resulted from a lack of easy access to the paper-based patient chart, initiation of therapy during hours of limited pharmacist availability, or pharmacists' perceptions that notes are not reviewed extensively by other health care providers, making the inclusion of a note a lesser priority. Further study of the factors leading to these omissions, with identification of supportive actions to achieve complete documentation in all cases, is required.

All note components were weighted equally within the audits. Omissions of date, time, pharmacist identification outside of signature, and contact information all contributed to non-adherence. Although all components are important, the DWG members felt there was greatest potential impact on patient care when documentation related to assessment of serum levels, interpretation of results, action plan, and rationale for clinical decision-making was absent. These omissions remain consistent with those previously reported by Tangedal and others,[8] although documentation was not the primary focus of their study. The most common omissions after measurement of serum levels occurred when dose adjustments made daily in the critical care population were documented solely in the physician's orders section of the chart, with no corresponding progress note documentation to provide the rationale or details of level assessment. The Steering Committee confirmed that this practice did not meet the intent of the collaborative practice agreement. This was re-emphasized during the educational session. In the second audit, documentation of serum level assessments increased from 39% to 66%, interpretation of results from 55% to 82%, and action plan and dose adjustments from 68% to 97% (Table 3).

TABLE 1. Frequency of Note Presence in Patient Chart Progress Notes

	Audit Number; No. of Notes Present/Expected (%)	
Note Type	**First Audit**	**Second Audit**
Empiric therapy	65/69 (94.2)	86/96 (89.6)
After measurement of serum level	72/93 (77.4)	167/199 (83.9)
Total	137/162 (84.6)	253/295 (85.8)

TABLE 2. Inclusion of Required Elements of Empiric Therapy Notes, as Specified in Vancomycin-Aminoglycoside Collaborative Prescribing Procedures[a]

Note Element	Audit Number; No. (%) of Notes	
	First Audit (*n* = 26)	Second Audit (*n* = 80)
Date and time of note	18 (69)	54 (67)
Indication	19 (73)	74 (92)
Desired target trough	19 (73)	68 (85)
Nephrotoxic risk factors	24 (92)	62 (77)
Frequency of serum creatinine monitoring	13 (50)	52 (65)
Serum creatinine (date of result and creatinine clearance calculation)	17 (65)[b]	43 (54)
Interval based on estimated creatinine clearance		62 (77)
Loading dose, if required	22 (85)	70 (87)
Dose, including weight	22 (85)	59 (74)
When serum levels expected, if at all	17 (65)	70 (87)
Name of note writer (printed *and* signed)	12 (46)[c]	56 (70)
Writer's contact information		51 (64)

[a]Note elements do not sum to note totals because each note contains more than 1 required element.
[b]In the first audit, data for date of serum creatinine result and clearance calculation were combined with dosing interval based on the estimate creatinine clearance.
[c]In the first audit, data for name and signature of note writer were combined with data for contact information.

TABLE 3. Inclusion of Required Note Elements after Assessment of Serum Level, as Specified in Vancomycin-Aminoglycoside Collaborative Prescribing Procedures[a]

Note Element	Audit Number; No. (%) of Notes	
	First Audit (*n* = 38)	Second Audit (*n* = 119)
Date and time of note	31 (82)	99 (83)
Date and time of serum level	22 (58)	63 (53)
Results reported in mg/L	26 (68)	116 (97)
Any discussion with prescriber	NA	NA
Assessment of serum level (e.g., "sample drawn appropriately at steady state")	15 (39)	79 (66)
Interpretation of result	21 (55)	97 (82)
Action plan, including dose adjustment if required	26 (68)	115 (97)
When next level due	21 (55)	94 (79)
Duration of treatment	4 (11)	43 (36)
Name of note writer (printed *and* signed)	19 (50)[b]	36 (30)
Writer's contact information		40 (34)

NA = not available (expectation that discussions with prescribers would be documented, as per procedure, but unable to confirm by means of methodology used in this study).
[a]Note elements do not sum to note totals, because each note contains more than 1 required element.
[b]In the first audit, data for name and signature of note writer were combined with data for contact information.

Professional guidelines (from the Canadian Society of Hospital Pharmacists[2] and the American Society of Health-System Pharmacists[1]) have not established defined criteria for adequate documentation, although a requirement for complete documentation can be inferred. A relative paucity of data exists examining pharmacists' prescribing within a collaborative practice framework. A study in Calgary that was designed to evaluate independent pharmacist prescribing practices in a population of acute care inpatients found, as a secondary outcome, that documentation occurred in 58% of a random sample of 50 patient charts audited.[10] Adam and others[11] assessed the rates of documentation by clinical pharmacists throughout a patient's hospital stay, utilizing chart assessment processes similar to our audits. In their study, most patients received "minimal documentation" (72.3%) defined as at least 1 intervention described in writing, rather than "extensive documentation" (10.4%), defined as 2 or 3 notes, primarily at points of transitions in care.[11] These studies do not directly relate to the expectations required within collaborative agreements, but they reinforce recognition of the importance of complete documentation by pharmacists, as well as recognition of gaps between expectations and performance.

Numerous factors may have affected our results. The assessors differed between the 2 audits, potentially increasing the risk for observational bias. In an attempt to build greater consistency, a more rigorous data collection tool was used for the second audit, which might have affected the assessments. Notes were selected for assessment at random and did not encompass all pharmacists included within the collaborative agreement. The complement of pharmacists changed during the auditing timeframe, with 26% (14/54) of our pharmacist team having less than 2 years of experience at the time of the second audit. The impact of staff change is not known, as the audit was not set up to compare results between pharmacists with more and less experience. Recent training may have been beneficial in ensuring awareness of requirements, although the opportunity for application of learning after receipt of training may have varied. Educational initiatives to improve documentation have been supported in the literature, with emphasis on the need for ongoing and repetitive reinforcement.[12] Although our collaborative prescribing agreement procedures were guided by a multidisciplinary steering committee, collaborative stakeholders were not surveyed directly to determine their perceptions about the adequacy of documentation to meet communication needs. Finally, given that pharmacists' documentation is strictly paper-based in the SHA – Regina area, these results may not be directly applicable to practices with access to electronic documentation.

Transitioning to electronic documentation by pharmacists in a patient's electronic chart, with templated requirements built into the software framework, may help to address the barriers to documentation that we identified, including lack of time, poor access to paper-based charts in a timely manner, and uncertainty as to what to document.[9,11] Our organization is moving toward this technology in the future. As future collaborative prescribing roles are developed, agreements should clearly specify expectations and requirements for documentation. Engaging with stakeholders proactively during creation of these agreements may assist in ensuring that documentation meets requirements for all parties. Continuous quality improvement initiatives are integral to ensure that documentation expectations are met.

CONCLUSION

Although adherence to documentation requirements was high (> 84%), further investigation is needed to elucidate mechanisms for enhancing documented communication within collaborative prescribing situations. An educational intervention presented to staff after the first audit, to highlight documentation requirements, resulted in improved adherence in the second audit, with inclusion of components essential to patient care.

Utilization of electronic mechanisms for documentation and software supports to force documentation functions may be beneficial. Within the certification process, expectations for clear and complete documentation must be emphasized. Regular audits and education with all pharmacists should continue.

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Best Possible Medication Histories by Registered Pharmacy Technicians in Ambulatory Care

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INTRODUCTION

Medication reconciliation is a formal process involving collaboration among health care professionals, patients, and their families or caregivers to communicate patients' accurate and comprehensive medication information across transitions of care.[1] It is a strategy for reducing unintentional medication discrepancies, which occur when there is a change — not intended by the original prescriber — in medications taken by patients between one setting (e.g., home) and another (e.g., hospital).[2-6] Unintentional medication discrepancies lead to inaccurate medication information, which could potentially lead to adverse drug events and outcomes (e.g., hospital readmissions).

Medication reconciliation requires that an accurate list of a patient's medications (i.e., a best possible medication history [BPMH]) be obtained and compared with medications ordered in the health care institution to allow identification and resolution of any discrepancies. Obtaining a BPMH involves gathering information from multiple sources (e.g., community pharmacy, government claims, interviews) and using it to develop a comprehensive medication list.[7] Preparing the BPMH is the first step in the medication reconciliation process; without it, medication reconciliation cannot take place.[1,8]

To optimize use of limited health system resources, several studies have described the use of registered pharmacy technicians (RPhTs) to obtain BPMHs in tertiary and acute care institutions[9-11]; however, the model has not yet been explored in the ambulatory care context. In ambulatory care, implementing patient safety initiatives, including medication reconciliation, presents unique challenges. Unlike patients admitted to hospital for an overnight stay, patients in ambulatory settings often visit their health care providers and return home the same day. When follow-up is scheduled, it may be weeks or months after the original visit.

The RPhT-conducted BPMH program described here was developed at Women's College Hospital, Canada's only academic ambulatory hospital. Until May 2017, Women's College Hospital lacked a formal BPMH and systematic medication reconciliation program in many of its clinical areas. Having an established, institution-wide, interprofessional medication reconciliation program (including a formal BPMH process) was an institutional goal linked to Accreditation Canada's required organizational practices, which at the time required a documented and coordinated medication reconciliation program in at least 1 ambulatory patient care area.[12] This paper describes our experience developing and implementing a program that features RPhT-conducted BPMHs in an ambulatory care institution.

METHODS

The Template for Intervention Description and Replication (TIDieR) checklist[13] was used as a guide to describing the RPhT-conducted BPMH program.

Setting

The RPhT-conducted BPMH program was implemented in the preadmission clinic (PAC) of the institution's surgical services department, which operates only on weekdays. PAC staff members schedule patients for an in-person or telephone assessment, which occurs before their surgery date. The BPMH program was implemented only for in-person appointments. Before piloting the program, a process map of the existing workflow (Figure 1) was created to determine the stage at which BPMHs would be conducted. After testing different flows, a process was finalized that worked well for both patients and staff (Figure 2).

Development of Written Training Materials

Written training materials were developed through discussions with the pharmacy and surgery team and using resources from the Institute for Safe Medication Practices Canada (ISMP Canada).[14] The content included a description of the medication reconciliation process, the rationale

for medication reconciliation in ambulatory care, comprehensive steps to obtaining an accurate BPMH, a description of the patient interview approach, and tips.

Training

Four RPhTs were trained by one pharmacist (I.M.F.) to obtain BPMHs. First, the RPhTs completed a BPMH workshop for pharmacy technicians, an external program offered by ISMP Canada.[14] In addition to this off-site certification program, the RPhTs underwent a 2- to 7-week training program developed by the institution. The training program was modelled after a program at another institution,[15] adapted for the ambulatory care setting. The RPhTs were trained one at a time, and the training consisted of 5 main stages.

Stage 1, RPhT reviews written training materials: The RPhT reviewed the written training materials about medication reconciliation and the RPhT's role in the process.

Stage 2, pharmacist conducts BPMH while RPhT observes: To model patient interviewing, the pharmacist (I.M.F.) conducted at least 15 BPMH interviews (over 1–3 days), with direct observation by the RPhT. The same pharmacist conducted each set of interviews and obtained patient consent before observation by the RPhT. After each interview, the pharmacist and the RPhT discussed the encounter and

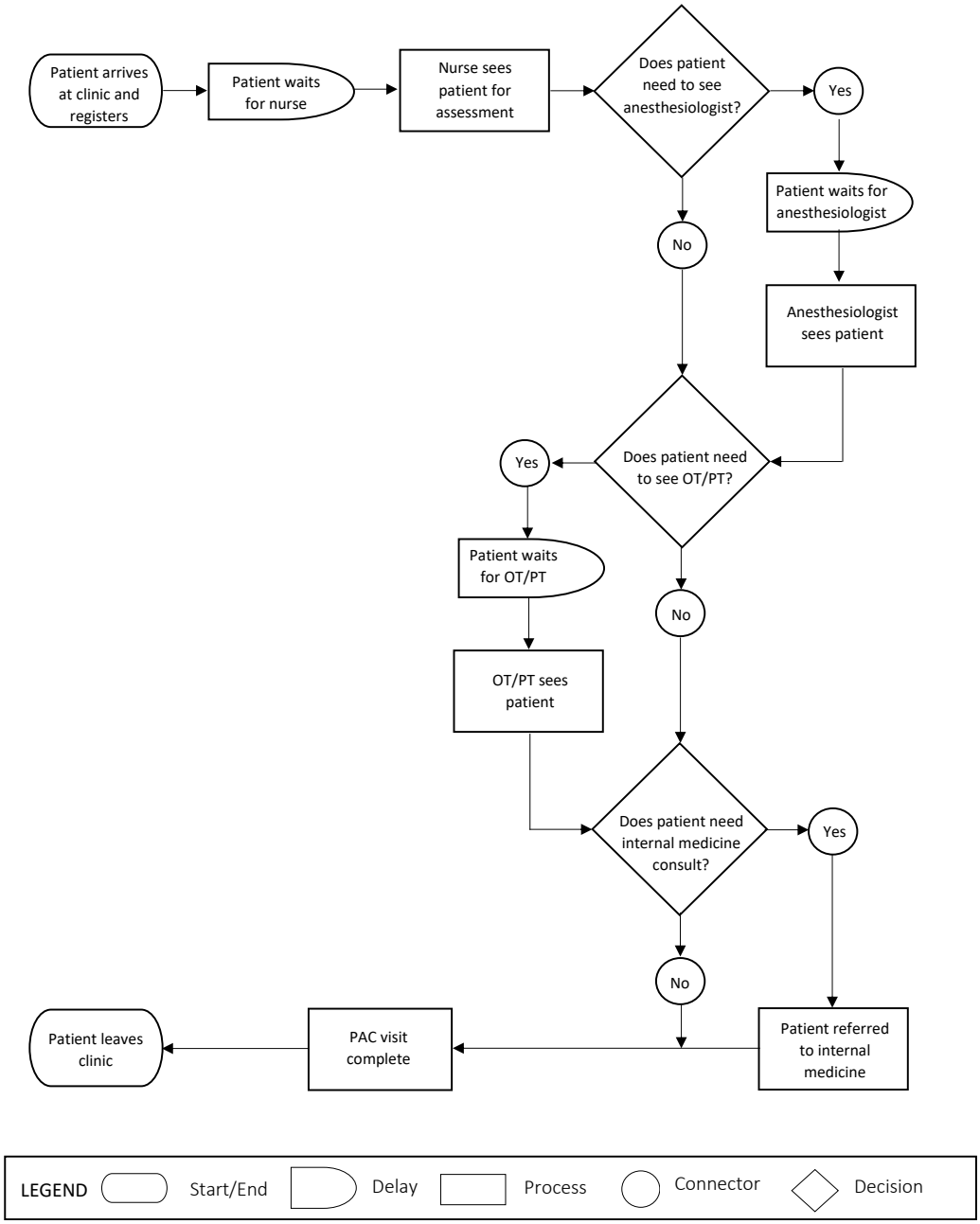

FIGURE 1. Preadmission clinic (PAC) flow before implementation of the best possible medication history (BPMH) program conducted by registered pharmacy technicians (RPhTs). OT = occupational therapist, PT = physiotherapist.

addressed any questions that the RPhT had. The minimum number of interviews to be observed was chosen arbitrarily; after observation of 15 interviews, the RPhT was given the choice to either observe more interviews or proceed to the next stage of training.

Stage 3, RPhT conducts BPMH while pharmacist observes: Each RPhT was required to conduct at least 25 patient interviews under direct supervision of the pharmacist. The pharmacist made notes during the interview and provided verbal feedback to the RPhT after each one. After the minimum 25 interviews, the RPhT and pharmacist discussed proceeding to independent patient interviews (i.e., without direct observation by the pharmacist). Factors that played a role in this decision included demonstration of verbal and nonverbal communication skills, adherence to the BPMH interview guide (Appendix 1, available at https://cjhp.journals.publicknowledgeproject.org/index.php/cjhp/issue/view/204), and the RPhT's self-assessed readiness to proceed.

Stage 4, RPhT independently conducts BPMHs (without pharmacist observation), and pharmacist audits all BPMHs for accuracy: After each independently conducted interview, the pharmacist audited the BPMH documentation form (Appendix 2, available at https://cjhp.journals.publicknowledgeproject.org/index.php/cjhp/issue/view/204)

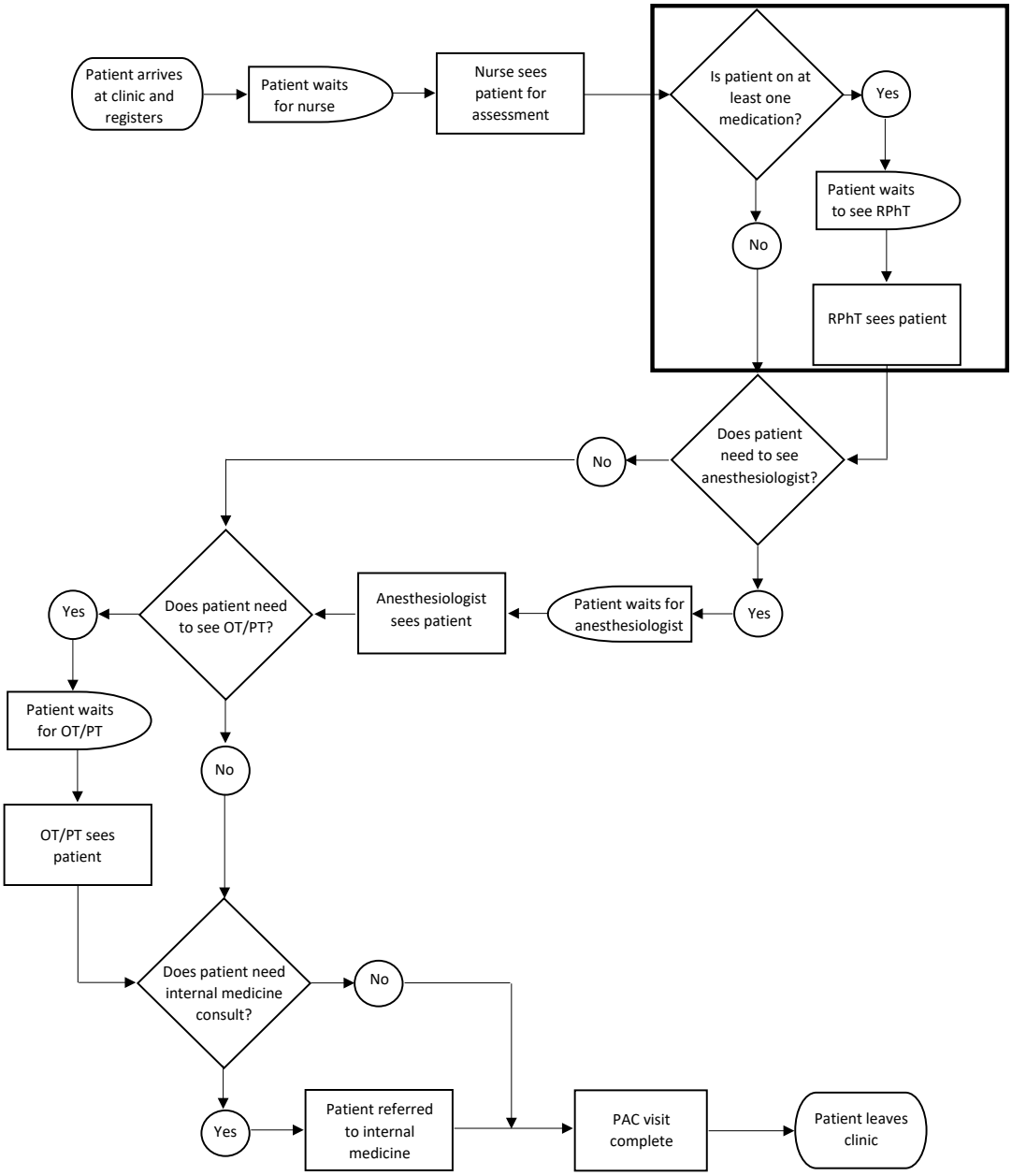

FIGURE 2. Preadmission clinic (PAC) flow after implementation of the best possible medication history (BPMH) program conducted by registered pharmacy technicians (RPhTs). Section enclosed in a thick-line box reflects process change relative to Figure 1. See legend in Figure 1 for explanations of box shapes. OT = occupational therapist, PT = physiotherapist.

to ensure that the RPhT had completed all relevant sections. Specifically, the pharmacist checked for the following elements:

- medication name, specifically including the generic name (accurately spelled) and strength
- dose, dosage form, route, frequency, patient-reported indication (if known)
- allergies
- antibiotic use in previous 3 months
- comments on adherence
- history of analgesic medications (e.g., nonsteroidal anti-inflammatories, opioids)
- community pharmacy information
- medication information sources (at least 2)
- RPhT name, designation, signature, date

To be certified as BPMH-trained, the RPhT had to complete 75 consecutive BPMHs without the pharmacist finding any inaccuracies.

Stage 5, RPhT independently conducts BPMHs, with random audits by pharmacist when needed: Once certified as BPMH-trained, the RPhT conducted BPMHs independently, with random audits by the pharmacist for quality assurance. Inaccuracies identified during these random audits were brought to the attention of the RPhT, with discussions on strategies to minimize errors.

Documentation Tool

An essential component of the BPMH is accurate documentation of a patient's medication list, as verified against secondary information sources; this is what makes a BPMH more reliable than a traditional medication history. A BPMH documentation form specific to surgical services (Appendix 2) was created with guidance from Safer Healthcare Now,[1] as well as discussion among the pharmacy and surgery teams. After every BPMH, the RPhT signed the completed documentation form (Appendix 2) and stored it in the patient's paper chart (at the time of program implementation, the PAC did not have electronic medical records).

Outcome Measures

The main outcome measure was BPMH compliance, which was defined as the proportion of eligible patients whose BPMHs were completed by an RPhT:

$$\frac{\text{Total number of patients with completed BPMH}}{\text{Total number of patients eligible for BPMH}}$$

Before implementing the program, the proportion of eligible patients who received a complete BPMH was 0%, and the aim was to increase the proportion to 80%.

The BPMH Process

The RPhT-conducted BPMH program consisted of 3 key phases and involved trained RPhTs, pharmacists, and nurses, as follows.

Phase 1, nurse refers eligible patients to RPhT: Individual patients who were booked for an in-person assessment at the PAC first had a consultation with a nurse. During this consultation, the nurse assessed patients' eligibility for a BPMH before referring them to the RPhT. Patients were eligible for a BPMH if they were taking more than 1 medication (i.e., prescription medications, over-the-counter products, vitamins, herbals, supplements).

Phase 2, RPhT conducts a BPMH in the PAC: The RPhT performed BPMH interviews from Monday to Friday for eligible patients referred by the nursing staff. For patients with medication coverage through the provincial insurance program, the RPhT accessed an online portal before interviewing the patient and printed a preliminary list of prescribed medications covered through this program. For patients without medication coverage through the provincial insurance program, the RPhT did not contact any community pharmacies before conducting the BPMH interview, because a patient's preferred community pharmacy (or pharmacies) was not known until the time of the assessment visit. After each interview, the RPhT contacted the patient's medication information sources (gathered during the encounter) to verify the information obtained.

Phase 3, pharmacist tracks BPMH compliance: The pharmacist conducted monthly tracking of BPMHs and calculated adherence.

Integrating RPhT-Conducted BPMH within Medication Reconciliation Process

After obtaining the BPMH and completing the documentation, the RPhT used the information to identify patients who would benefit from medication reconciliation upon discharge, according to prespecified criteria (Appendix 3, available https://cjhp.journals.publicknowledgeproject.org/index.php/cjhp/issue/view/204). During the first 2 months, the RPhT practised identifying these eligible patients but did not track them, because the information was not required until the medication reconciliation component of the program was implemented. Once the medication reconciliation component was in effect, the RPhT tracked eligible patients, which allowed the pharmacist to conduct medication reconciliation.

For each patient, the surgical procedure was performed approximately 7 days after the PAC consult. On the day of surgery, before the procedure, nursing staff used the documented BPMH to capture any changes to the patient's medications.

RESULTS

During the evaluation period (May 2017 to April 2018), a total of 2185 patients were identified as being eligible for a BPMH. Of these, 2001 patients (92%) had a BPMH completed by one of the trained RPhTs (Table 1), which exceeded the target 80%. A mean of 9 BPMH interviews

were conducted per day (standard deviation [SD] 3.7; minimum 1, maximum 19). A total of 184 interviews (8%), could not be completed for various reasons: patient not referred by nursing staff (51% [93/184]), limited staffing (22% [41/184]), missed appointment (10% [18/184]), and other reasons (17% [32/184]). The mean time spent (including review of the chart and consultation with other sources to obtain additional information) was 10 minutes (SD 4.8; minimum 4, maximum 30). Approximately 33% of patients (536/1646) were identified by RPhTs as potentially benefiting from medication reconciliation by a pharmacist upon discharge.

The RPhTs all had more than 10 years of practice experience but varied in their experience conducting BPMHs (minimum none, maximum 4 years). Variations in other aspects of the training process are detailed in Table 2.

DISCUSSION

Prior studies have explored RPhT-conducted BPMHs as part of the medication reconciliation process[16-18]; however, to our knowledge, this project is the first to describe the application of RPhT-conducted BPMHs in an academic ambulatory setting. The surgical services department of the ambulatory care hospital was chosen because it is an area with frequent transitions in care (i.e., preadmission consults on one day, followed by surgery and discharge on a different day). Each transition point represents an opportunity for unintentional medication discrepancies to occur. Before implementation of the RPhT-conducted BPMH program, traditional medication histories were gathered by nurses during PAC appointments, but secondary sources of information were not used for verification. The institution's priority was to implement

TABLE 1. Eligible Patients with BPMH Completed per Month

Month	No. of Patients Eligible for BPMH	No. (%) of BPMHs Completed by RPhT		No. (%) of Patients Identified for Medication Reconciliation	
2017					
May	222	180	(81)	Data not available	
June	194	175	(90)	Data not available	
July	194	179	(92)	18	(10)
August	169	158	(93)	24	(15)
September	147	140	(95)	48	(34)
October	152	142	(93)	32	(22)
November	202	182	(90)	43	(24)
December	96	93	(97)	38	(41)
2018					
January	207	177	(85)	62	(35)
February	205	187	(91)	89	(48)
March	204	198	(97)	90	(45)
April	193	190	(98)	92	(48)
Total	2185	2001	(92)	536	(32*)

BPMH = best possible medication history, RPhT = registered pharmacy technician.
*The RPhT assessment of patients for medication reconciliation eligibility began in July 2017. Between July 2017 and April 2018, there were 1646 patients for whom a BPMH was completed by the RPhT, which served as the denominator for calculating the proportion of patients identified as potentially benefiting from medication reconciliation.

TABLE 2. Characteristics and Training Cycles of Registered Pharmacy Technicians

RPhT	Experience (yrs)		Length of BPMH Training (wks)	No. of Pharmacist Interviews Obs. by RPhT	No. of RPhT Interviews Obs. by Pharmacist	Attempts Conducting 75 Consec. BPMHs[a]	No. of Interviews Audited
	Total in Practice	With BPMH					
1	> 25	0	5	25	38	3	110
2	17	0	7	19	43	4	125
3	10	2	3	15	27	1	92
4	18	4	2	15	28	0	75

BPMH = best possible medication history, Consec. = consecutive, Obs. = observed, RPhT = registered pharmacy technician.
[a]Without error.

an RPhT-conducted BPMH program that would be easily integrated into existing workflow, with minimal disruptions. RPhTs are in a unique position to perform BPMHs because they are knowledgeable about medication names, formulations, strengths, and dosing schedules.[19] The use of RPhTs to conduct BPMHs therefore complements pharmacists' roles in reconciling and providing medication management.

A key learning from this initiative was an appreciation of the time and resources required to effectively and efficiently implement patient safety programs within health care institutions. Successful implementation of the RPhT-conducted BPMH program required training of the RPhTs, development of new tools, ongoing communication with our interprofessional team, data collection, and iterative changes to workflow. As such, time constraints were a significant barrier to BPMH compliance. In addition, having one pharmacist oversee both the PAC (i.e., training RPhTs, auditing BPMHs, addressing BPMH-related issues) and postoperative unit (i.e., performing medication reconciliation before discharge) posed logistical challenges, as there were occasions when the pharmacist was needed simultaneously in both units.

Another lesson from this project was that consistent communication with members of the health care team is fundamental to ensuring optimal uptake of new programs. In the early stages of the RPhT-conducted BPMH program, one of the barriers to BPMH compliance was low referral of eligible patients to the RPhT. This was attributable to multiple factors: inadequate understanding of the BPMH process, lack of clarity about BPMH eligibility criteria, and slow adaptation to the new workflow. These issues were, however, addressed through constant communication (emails, meetings, reminders) with the staff and leaders of the interprofessional teams.

A third important lesson involved patients whose medications were not covered through the provincial insurance program, for whom the RPhTs were unable to obtain a preliminary list of medications before the BPMH interviews. In addition, a number of these patients did not bring their medication vials to the PAC. As such, the RPhTs were only able to verify medication information with their community sources (e.g., pharmacies, nursing home) after the interview was completed (i.e., after source contact information was obtained). This led to inefficiencies, such as having to phone the patient back at the end of the day to clarify any discrepancies identified. Since it was not possible to reach patients at all times, this retrospective approach to addressing discrepancies impeded completion of the BPMH. It might have been helpful in this situation to have hospital volunteers call patients ahead of their PAC visits to gather community pharmacy information and remind the patient to bring their medication vials. This would have allowed the RPhT to contact the pharmacy before the BPMH interview so that any discrepancies could be addressed during the interview.

One limitation of this project was that the BPMHs were not audited for medication discrepancies. The pharmacist audited the BPMHs to ensure that all required information had been gathered and documented. The pharmacist also checked for accurate spelling of medication names, use of appropriate units, and use of dangerous abbreviations. However, the pharmacist did not access the secondary sources (e.g., community pharmacy–generated lists) to verify the information that the RPhT had documented. Doing so would have enabled the pharmacist to assess the comprehensiveness (e.g., identifying errors of omission) and accuracy (e.g., correct doses) of RPhT-conducted BPMHs.

Another limitation was lack of validation of the criteria used to select patients who might be suitable for medication reconciliation by a pharmacist at the time of discharge. These criteria were developed using literature information about high-risk medications[20-22] and consensus among the interprofessional team regarding patients who would most benefit from medication reconciliation upon discharge.

Future projects could expand on this work by identifying discrepancies in RPhT-conducted BPMHs to further assess their training and competency in fulfilling this role. Identifying such discrepancies would also assist with the development of strategies to address them according to the level of severity (e.g., omission of a prescription medication versus omission of a vitamin or supplement). In addition, future work could explore patients' views and experiences of RPhT-conducted BPMH, to gain insight into the perceived acceptability and impact of this model on their care.

CONCLUSION

Overall, this project demonstrated that RPhT-conducted BPMHs can improve compliance with BPMH practices within ambulatory care. Future evaluation efforts could focus on exploring patients' experiences with this model and determining how RPhT-conducted BPMH can help to improve the overall medication reconciliation process.

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Small and Transient Effect of Cannabis Oil for Osteoarthritis-Related Joint Pain: A Case Report

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INTRODUCTION

The Arthritis Society, a Canadian health charity, describes osteoarthritis (OA) as "a progressive disease of the whole joint that leads to breakdown of joint cartilage and underlying bone."[1] OA can affect any joint in the body, with symptoms that differ from one individual to the next, the most common being joint pain, joint stiffness, and swelling. OA is the most common form of arthritis and currently affects more than 10% of the adult population in Canada.[2] The prevalence of OA increases with age; as such, with aging of the Canadian population, the general prevalence of arthritis is expected to increase to 20% (or 7 million) by 2031.[3] Consequently, there is a powerful impetus to find effective solutions to manage this condition.

Current pharmacological approaches to the treatment of chronic pain associated with OA rely primarily on long-term use of acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, and injectable corticosteroids, and may include other drugs such as gabapentin. Over-the-counter supplements, such as glucosamine and chondroitin, may be considered, given that they may provide symptomatic relief for some patients.[4] The use of these medications has been the mainstay of therapy for quite some time; however, some patients continue to experience uncontrolled pain while taking the usual therapies. As such, cannabis and cannabinoids are now being investigated as adjuncts for the treatment of OA-related pain.[5] The shift in therapeutic cannabis research is based on the realization that, among the diverse array of biological activities exhibited by cannabinoids, the endocannabinoid system has been shown to play a role in pain perception, as well as modulating inflammation.[6,7] This report describes an elderly patient with severe OA of the hips, knees, and shoulders who used cannabis products, including cannabidiol (CBD) and tetrahydrocannabinol (THC), in an attempt to manage pain.

CASE REPORT

An 85-year-old woman with severe OA was admitted to a long-term care home on August 15, 2018.* Her OA was noted to be particularly severe in the left hip and knee, an assessment that was confirmed by radiography. She had difficulty with transfers secondary to her OA and was non-ambulatory; therefore, she used a wheelchair for mobilization. Her medical history included atrial fibrillation, type 2 diabetes mellitus, and open-angle glaucoma. She reported an allergy to penicillin. Medications before admission included apixaban 5 mg twice daily, metoprolol 50 mg twice daily, ramipril 5 mg twice daily, atorvastatin 20 mg daily, insulin glargine 22 units in the morning and 15 units at bedtime, and 1 drop of latanoprost 0.005% in each eye once daily at bedtime. Her pain control medications were acetaminophen 650 mg daily, diclofenac gel 10% (compounded) twice daily, gabapentin 300 mg 3 times daily, hydromorphone 2 mg 4 times daily and 2 mg hourly as needed (PRN), and fentanyl patch 75 µg/h every 3 days. The resident denied the use of any over-the-counter medications or natural health products.

Until December 2018, the resident was using hydromorphone 1 mg PRN, 5 to 7 times monthly; at that time, however, her pain worsened, and PRN use of hydromorphone also increased substantially, up to 5 to 7 times daily. After evaluation at a cannabis clinic and subsequent assessment by the general practitioner, the resident was started on CBD Oil Drops (CannTrust Inc) at a concentration of 25 mg/mL. The initial dosage was 0.2 mL (5 mg) orally twice daily; the dose was titrated up by 0.2 mL every week to reach 3.0 mL (75 mg) orally twice daily in February 2019. Immediately upon the introduction of CBD oil, her use of PRN hydromorphone declined to 3 to 5 times daily. The patient noted that the CBD made her "sleepy sometimes", but no other adverse effects were reported. We were encouraged by the resident's reduced analgesic requirements, which were not accompanied by any self-reported change in perceived pain. However, the reduction in PRN use was transient, lasting only 1 week, and use of hydromorphone subsequently returned to the levels that were in use immediately before initiation of CBD oil (i.e., 5–7 times daily), even as the resident continued taking CBD oil at a dosage of 3.0 mL orally twice daily.

*The patient provided informed consent for publication of this report.

After her admission to the long-term care facility, the resident was assessed several times according to the Pain Assessment Tool used in the facility, which was adapted from a tool used by the Fraser Health Authority. The scale ranges from 0 (no pain) to 5 (extreme pain). No pain rating was available for December 2018, when CBD oil was started. However, in August 2018, the occupational therapist reported that the resident had a lot of joint pain (as documented in the Recreation Record), and in September 2018, the resident rated her pain and discomfort level as 5 out of 5. Subsequent ratings in February and March 2019, after initiation of the CBD oil, were 4.25 and 3.5 out of 5, respectively. Before starting CBD oil, the resident's participation in recreation activities was severely limited. However, in February and March 2019, she was able to join in most of the activities. In addition, there was improvement on the pain flowsheet, which is used to track pain intensity (on a scale of 0 to 5) before and after an intervention. For example, on 3 separate occasions in January 2019, the resident's pain was reduced from 3 to 1 an hour after administration of CBD oil. The reduced pain scores and increased activity level documented during these later assessments may have been attributable to a co-analgesic effect between the CBD oil and all of the resident's other pain medications.

Once the CBD oil was titrated to the desired dose in March 2019, THC oil 25 mg/mL was also trialled, at the urging of the family, at a dosage of 0.1 mL 3 times daily. The THC oil was discontinued 1 week later because of self-reported adverse events, such as dizziness, unclear speech, and cognitive impairment. The resident stated "[she did] not want to feel that way again."

DISCUSSION

Pharmacological approaches to the treatment of OA pain have typically focused on NSAIDs and opioids. Treatment of OA pain usually follows a stepwise approach, beginning with topical and oral analgesics, then shifting to NSAIDs, injectable corticosteroids, and eventually opioids.[4] Patients whose pain remains uncontrolled with conventional pain management therapies may turn to alternative interventions for pain management, such as cannabinoids.

OA can be quite debilitating, and patients must often use their prescribed medications for long periods, despite certain repercussions of long-term usage and potential drug interactions. For example, acetaminophen can cause drug-induced hepatotoxicity when administered at high doses or with concomitant alcohol consumption.[8] Similarly, adverse cardiovascular, renal, gastrointestinal, and cerebrovascular risks have been observed with long-term NSAID use.[9] Additionally, in elderly patients with multiple comorbidities and polypharmacy, there is a concern about increased risk of drug interactions between pain medications and other medications, such as warfarin and corticosteroids.[10] Finally, opioids have a plethora of potential adverse effects, including significant risks of dependence, overdose, and drug interactions.[11,12] The use of co-analgesics, such as CBD oil, may be opioid-sparing.

It is imperative that research be directed toward alternative interventions for chronic pain, such as cannabinoids and other cannabis products. In the case reported here, the patient's PRN use of hydromorphone declined substantially for a brief period after she started CBD oil, but subjective pain measures (i.e., changes in pain scale and activity level) showed a mild but more sustained improvement over time. Hence, clinicians should be open to the possibility of adding cannabinoids to current therapies for the management of chronic OA pain.

OA pain can manifest as a combination of nociceptive, neuropathic, and inflammatory pain, which explains why multitargeted pharmaceutical approaches are required in many cases. The body's endocannabinoid system has been shown to ameliorate all these modalities of pain subtypes.[13] Studies with animal models have demonstrated that under the inflammatory physiological conditions seen in arthritic joints, certain receptors of the endocannabinoid system (i.e., cannabinoid receptors 1 and 2 [CB1 and CB2] and fatty acid amide hydrolase [FAAH] receptors) are expressed to a greater extent in the synovium of OA joints, including localized and upregulated expression of CB1 and CB2 receptors relative to control joints.[14] Moreover, a significant component of OA pain and disease progression is related to increased local inflammatory states. Further investigations are required to elucidate these underlying mechanisms and perhaps provide more evidence for the clinical utility of cannabinoids; however, several barriers to such research remain. There have been few large-scale controlled clinical studies investigating the pain-alleviating effects of cannabinoids. Pharmacologically plausible reasons for the benefit of cannabinoids in the management of chronic pain, in combination with exploratory research on self-administration of cannabis by those with OA and chronic pain conditions, suggest avenues for more research.[15] The Canadian Rheumatology Association[16] has stated that medical cannabis is not an alternative to standard care but may provide symptomatic relief for some individuals (for example, in the case reported here, as an adjunct to fentanyl and hydromorphone).

Future investigations should take into consideration the low, yet highly variable oral bioavailability of CBD. Perhaps inhalation, mucosal administration, or administration in the form of lipid nanoparticles will lead to more accurate and reliable dosing.[17] Excessively high doses of CBD can yield unpleasant adverse effects, such as major fatigue and dizziness; therefore, subsequent studies should be conducted to decipher what dose and titration method are appropriate, especially for elderly patients, and these studies should include careful monitoring for adverse events. Additionally, future studies should evaluate the clinical utility of CBD use for different populations, to determine who is most likely to benefit.

CONCLUSION

This case report suggests the potential for adjunctive use of cannabinoids in managing OA pain. Positive outcomes from the use of CBD oil in this case included a small reduction in PRN hydromorphone use, a consistent post-dose reduction in pain, and slight improvement in terms of functionality and participation relative to the situation in the months before the patient started CBD treatment. The changes observed in this case might have resulted from a placebo effect; as such, it will be important for high-quality clinical trials to be conducted to evaluate the efficacy of cannabinoids in treating OA pain.

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Granulicatella Infection of the Central Nervous System in a 3-Year-Old Girl

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INTRODUCTION

Granulicatella spp., previously known as nutritionally variant *Streptococcus* spp., belong to the normal flora of the oral cavity, genitourinary tract, and intestinal tract. *Granulicatella* spp. have been reported to cause endocarditis, pancreatic abscess, wound infection, vertebral osteomyelitis, conjunctivitis, cirrhosis, endophthalmitis, keratopathy, and otitis media, but the true incidence rates are unknown.[1] The literature on management of central nervous system (CNS) infection with *Granulicatella* spp. is limited. The infectious diseases team at the Children's Hospital of Eastern Ontario (CHEO) encountered a 3-year-old child with *Granulicatella adiacens* and elevated total nucleated cells in the cerebrospinal fluid (CSF) following suboccipital craniotomy. This report describes the challenge of antimicrobial management in this case.

CASE REPORT

A previously healthy 3-year-old girl presented to the hospital with a 4-week history of headache and vomiting.* Magnetic resonance imaging (MRI) of the head showed a solid and cystic posterior fossa mass centred in the cerebellar parenchyma, accompanied by hydrocephalus. The patient subsequently underwent suboccipital craniotomy for resection of the tumour and insertion of an external ventricular drain.

On postoperative day 5, MRI showed mild interval increase in the suboccipital fluid collection in CSF spaces. On postoperative day 7, the ventricular drain was removed, and CSF was collected from the device; analysis of the CSF showed an elevated total nucleated cell count (Table 1). On the same day, the patient's body temperature spiked to 38°C. Within 24 h, culture plates of the CSF sample showed growth of *G. adiacens* (nutritionally variant *Streptococcus*), identified by matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry. The pathology report indicated that the brain tumour was a grade 1 pilocytic astrocytoma.

*The patient's mother provided written consent for publication of this case report.

On postoperative day 8, the patient's body temperature rose to 38.9°C. She underwent debridement of the craniotomy wound, lumbar puncture, and collection of CSF; the CSF contained many white blood cells and showed growth of *G. adiacens* (Figure 1; Table 1). This 30-kg patient was started on IV therapy with penicillin G 2 million units every 4 h (400 000 units/kg daily) and gentamicin 30 mg q8h (3 mg/kg daily) for synergistic coverage. On this day, the patient was very irritable and reported headache and difficulty moving her head and neck.

On postoperative day 15, the patient's body temperature spiked to 38.5°C, despite 8 days of treatment with penicillin and gentamicin. MRI on the same day showed interval increase in the size of the suboccipital fluid collection. Around the same time, the public health laboratory reported the following minimum inhibitory concentrations (MICs) for the *G. adiacens* isolate (from the sample collected on postoperative day 7): penicillin 4 μg/mL (resistant), ceftriaxone 2 μg/mL (intermediate), meropenem 0.5 μg/mL (sensitive), and vancomycin 1 μg/mL (sensitive). The patient's antibiotic therapy was changed to meropenem 1200 mg IV q8h (120 mg/kg daily).

On postoperative day 19, repeat CSF analysis showed a decrease in the total nucleated cell count and no bacterial growth (Table 1). Repeat MRI of the head showed interval decrease in the size of the suboccipital fluid collection and no evidence of hydrocephalus. Nevertheless, on postoperative day 33, nasal congestion and discharge occurred, and the patient's body temperature was 38.4°C. The blood neutrophil count had decreased from 1.7×10^9/L to 0 over the 9-day period from postoperative day 24 to 33. With a Naranjo score[2] of 6, the neutropenia was attributed to the administration of meropenem over the previous 18 days (based on the following criteria: established reports of neutropenia due to meropenem[3]; adverse event appearing after the suspected drug was administered; no alternative causes; and objective evidence with low neutrophil count). Nasopharyngeal swab showed rhinovirus RNA, which indicated a viral infection. The meropenem was subsequently changed to vancomycin 450 mg IV q6h (60 mg/kg daily) on postoperative day 34,

later adjusted to 390 mg q6h (52 mg/kg daily) because of the high vancomycin trough level on day 36.

On postoperative day 41, repeat lumber puncture showed continued elevation of total nucleated cell count (Table 1); however, the CSF showed no bacterial growth, and the patient was afebrile and asymptomatic, with normal neutrophil and white blood cell counts (4.6×10^9/L and 8.5×10^9/L, respectively). On postoperative day 44, the patient was determined to be clinically stable for discharge home, and therefore the vancomycin was discontinued 10 days after initiation. Overall, the patient had received 30 days of effective antimicrobial therapy, as per susceptibility results of the *G. adiacens* isolate (Table 2).

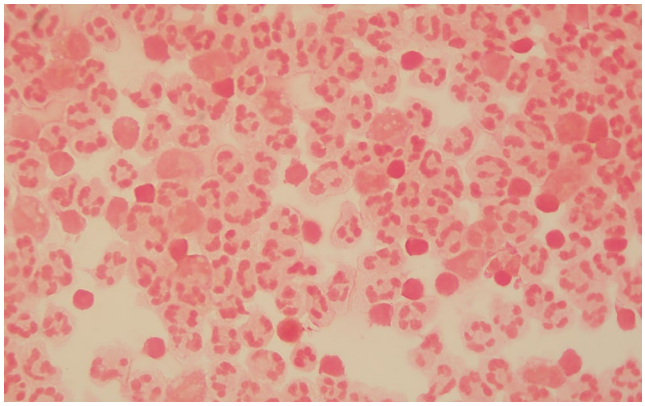

FIGURE 1. On postoperative day 8, Gram staining of the cerebrospinal fluid revealed many white blood cells but no organisms.

At the follow-up outpatient appointment, 116 days after discharge, the patient had been clinically stable and required no additional antimicrobials.

DISCUSSION

CNS infection with *Granulicatella* is rare. A search of our regional microbiology laboratory database for the period October 2, 2018, to October 2, 2019, revealed no other case of *Granulicatella* spp. in CSF samples collected from the 16 affiliated hospitals. In the same study period, there were 16 cases of *Granulicatella* bacteremia.

A previous case series of 5 patients (age 2.5–53 years) illustrated CNS infection with *Abiotrophia*/*Granulicatella* (previously collectively known as nutritionally variant *Streptococcus*) in detail, but it included only 1 pediatric patient.[1] Unlike the 4 adult patients in that case series, who had neurosurgery, the 30-month-old girl experienced oral mucosal ulceration with concomitant dental caries, which allowed invasion of commensal flora.[4] This patient received ampicillin for 32 days, rifampin for 32 days, and gentamicin for 7 days. Despite the antimicrobial therapy, she had recurrent seizures, as well as persistent left hemiplegia and hypotonia 8 weeks after diagnosis. It is uncertain whether her long-term sequelae were due to the CNS infection or underlying Down syndrome. To the author's knowledge, the current case is the first report of *G. adiacens* infection of the CNS in a pediatric patient who had neurosurgery. Unlike

TABLE 1. Trends in Analysis of Cerebrospinal Fluid

Characteristic of CSF	Reference Range	Postoperative Day 7	8	19	41
Colour	NA	Colourless	Xanthochromic	Xanthochromic	Colourless
Appearance	NA	Clear	Turbidity 2+	Clear	Turbidity 1+
Red blood cells ($\times 10^6$/L)	0–1	329	72	6	127
Total nucleated cell count ($\times 10^6$/L)	0–5	261	2787	288	319
Neutrophils*	<0.001	0.99	0.76	0.32	0.49
Lymphocytes*	<0.8	0.01	0.04	0.53	0.35
Mononuclear leukocytes*	<0.15	Not done	0.20	0.15	0.16
No. of cells counted in differential counts	NA	100	100	100	100
Glucose (mmol/L)	2.0–4.4	Not done	1.2	2.1	1.7
Protein (g/L)	0.15–0.60	Not done	1.05	2.14	Not done
Gram stain	NA	A few white blood cells; no organism seen	Many white blood cells; no organism seen	Many white blood cells; no organism seen	Many white blood cells; no organism seen
Culture growth	NA	*Granulicatella adiacens*	*Granulicatella adiacens*	No growth	No growth

NA = not applicable.
*Results for neutrophils, lymphocytes, and mononuclear leukocytes are reported as the respective proportions of the total nucleated cell count.

TABLE 2. Antimicrobials Administered, in Chronological Order

Postoperative Period	Drug and Dosage
Days 8–15	Penicillin G 2 million units IV q4h (400 000 units/kg daily) Gentamicin 30 mg IV q8h (3 mg/kg daily)
Days 15–33	Meropenem 1200 mg IV q8h (120 mg/kg daily)[a]
Days 34–36	Vancomycin 450 mg IV q6h (60 mg/kg daily)[a]
Days 36–44	Vancomycin 390 mg IV q6h (52 mg/kg daily)[a]

[a]Effective antimicrobial therapy, as per the result for *Granulicatella adiacens* susceptibility.

the previously described pediatric patient,[1] the patient in the current case had clinical recovery after 30 days of effective antimicrobial therapy.

Of note, the adult patients in the aforementioned case series underwent various neurosurgical procedures before the CNS infection developed: excision of recurrent astrocytoma; computed tomography–guided myelography with injection of contrast medium; clipping of an aneurysm of the middle cerebral artery, followed by placement of a ventriculoperitoneal shunt; and craniotomy with resection of ethmoid sinus carcinoma.[1] These patients also had prolonged intubation (4–60 days) before the CNS infection. It is unknown whether the neurosurgery or the intubation led to the CNS infection. It is also unknown why the cases of *Abiotrophia*/*Granulicatella* infection of the CNS published to date have all involved female patients; the current evidence is insufficient to support gender predilection for *Abiotrophia*/*Granulicatella* infections of the CNS. The 4 adult patients in the case series[1] received various antimicrobial regimens: ceftriaxone (10 d) and gentamicin (10 d) concurrently; vancomycin (10 d) and fosfomycin (10 d) concurrently, followed by cefixime (10 d) and rifampin (10 d) concurrently; penicillin (28 d) and gentamicin (28 d) concurrently; and penicillin (28 d) and gentamicin (14 d). Although all 4 adult patients were stable at the end of their therapy, it is uncertain which of these antimicrobials was mainly responsible for the patients' improvement.

Empiric Antimicrobials

There is no established guidance as to which antimicrobials should be started empirically for *Granulicatella* infection of the CNS. The guidance for treatment of infective endocarditis due to *Abiotrophia*/*Granulicatella* typically recommends penicillin or another cell-wall agent (ampicillin, ceftriaxone, or vancomycin) combined with an aminoglycoside.[5,6] The American Heart Association states that *Abiotrophia*/*Granulicatella* endocarditis in children should be treated like enterococcus endocarditis, if the penicillin MIC is greater than 0.5 µg/mL.[7] Like adults, children should be treated with a cell-wall agent combined with an aminoglycoside.[7]

As illustrated in previous case reports, empiric antimicrobial therapy for *Abiotrophia*/*Granulicatella* infection of the CNS has tended to follow this recommendation for a cell-wall agent combined with an aminoglycoside.[1] However, clinicians should be aware that *Granulicatella* spp. could have variable susceptibility to penicillin.[8] For example, among 162 isolates of *Granulicatella* spp. submitted to the Public Health Ontario Laboratory, the rate of susceptibility to penicillin was only 65.4%, compared with 87.6% susceptibility to ceftriaxone and 97.5% susceptibility to meropenem.[9] Gentamicin has poor CNS penetration relative to penicillin.[10] As demonstrated in the current case and previous reports, long-term use (≥ 17 days) of meropenem can induce neutropenia, which warrants routine monitoring of patients' complete blood count; usual management is removal of the offending drug.[3] Although clinical evidence is lacking, clinicians may consider using ceftriaxone as the empiric therapy for *Abiotrophia*/*Granulicatella* infection of the CNS, because of its good sensitivity and CNS penetration.[9,11]

Synergy and Susceptibility Testing

Official synergy testing, including time–kill curve and microdilution checkerboard methods, is time-consuming and has high inter-laboratory variability; therefore, such testing is not always available in clinical laboratories.[12] These laboratories may instead perform synergy "screening" with high-dose aminoglycosides on *Enterococcus* spp., but not on *Abiotrophia*/*Granulicatella* spp.; the Clinical and Laboratory Standards Institute (CLSI) has no interpretive criteria for the susceptibility of *Abiotrophia*/*Granulicatella* spp. to aminoglycosides.[13] Clinicians and laboratorians should know that susceptibility testing of *Abiotrophia*/*Granulicatella* must be done by broth dilution, not disk diffusion, as per the CLSI recommendation; this testing may have a long turnaround time in reference laboratories.

When a microorganism is resistant to penicillin, no effective cell-wall agent is present to facilitate penetration of the aminoglycoside to the target site. Nevertheless, it has been suggested that susceptibility testing of *Granulicatella* spp. does not correlate with clinical outcomes and thus should not be routinely performed.[14] One case report described a 32-year-old patient with CNS infection secondary to *G. adiacens* resistant to penicillin who recovered well with 28 days of penicillin therapy and 14 days of gentamicin treatment.[1]

However, if a patient's condition deteriorates with the empiric combination of penicillin and aminoglycoside, clinicians should consider requesting susceptibility testing with penicillins and cell-wall agents, even though CLSI guidance states that such testing is optional.[13] This CLSI guidance is not specific to *Abiotrophia*/*Granulicatella* infection of the CNS, which can lead to long-term sequelae.[4] In the current case, the patient had recurrent fever despite 8 days of penicillin and gentamicin therapy. It could be argued that the patient's suboccipital fluid collection contributed to her

fever. Nevertheless, the increase in the size of fluid collection, as shown by MRI, suggested that the patient's antimicrobial therapy had failed at that time. Without susceptibility testing, the patient would have been at risk of receiving ineffective antimicrobial therapy for weeks.

Duration of Therapy

According to guidance from the Infectious Diseases Society of America,[15] the duration of antimicrobial therapy for meningitis depends on the isolated pathogen, although that approach is based on tradition rather than evidence-based data. Repeat CSF analysis is recommended for patients with no clinical response after 48 h of antimicrobial therapy.[15] In pediatrics, infection due to certain organisms may require repeat lumbar punctures to document CSF sterilization; antimicrobial therapy should be continued for 2 weeks after the first sterile CSF sample.[15]

There is currently no established guidance on duration of antimicrobial therapy for *Granulicatella* infection of the CNS. Endocarditis secondary to *Granulicatella* spp. generally requires treatment with penicillin or a cell-wall agent for 4 to 6 weeks, in addition to aminoglycosides for at least 2 weeks.[7,8] In the case series of 5 patients with *Abiotrophia*/*Granulicatella* infection of the CNS, patients recovered after 10 to 32 days of antimicrobial therapy.[1] A study of 118 infants showed a higher mortality rate among those with repeat positive CSF culture results than among those with repeat negative culture results (26% versus 7%); however, *Abiotrophia*/*Granulicatella* was not isolated from any of these infants.[16] The patient described here had negative results on CSF culture on postoperative days 19 and 41, which suggests that the CNS infection was under control.

CONCLUSION

If clinical deterioration occurs in a patient with *Granulicatella* infection of the CNS, despite empiric treatment with a combination of penicillin and aminoglycoside, clinicians should not assume that this antibiotic regimen will provide a synergistic effect; instead, they should request susceptibility testing of the organism found in the CSF. Clinicians may consider ceftriaxone as empiric therapy for *Abiotrophia*/*Granulicatella* infection of the CNS because of its good CNS penetration and in vitro sensitivity. Administration of vancomycin may not be ideal for a pediatric patient because it entails frequent therapeutic drug monitoring. There is currently no recommended duration of antimicrobial therapy for *Granulicatella* infection of the CNS; repeat CSF culture may be considered to determine sterility. If a patient requires weeks of meropenem therapy, the clinician should monitor complete blood count to avoid meropenem-associated neutropenia.

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Should Antipsychotic Polypharmacy Be Used for Patients with Schizophrenia and Related Psychoses?

THE "PRO" SIDE

Schizophrenia is a serious psychiatric condition characterized by psychotic symptoms (e.g., hallucinations, delusions, and disorganization), negative symptoms (e.g., anhedonia, avolition), cognitive symptoms, and deficits of executive function.[1] Worldwide, schizophrenia is one of the top 20 causes of disability, partly owing to its early onset and persistent symptoms.[2]

Antipsychotics form the cornerstone of therapy for schizophrenia. Medications in this class are considered to have comparable effectiveness, with the exception of clozapine,[2] which is the only antipsychotic agent indicated for treatment-refractory schizophrenia.[3] However, the use of clozapine is complicated by significant, multifaceted barriers, including the need for frequent blood monitoring, inadequate clinician knowledge or experience, inadequate staff resources to support the use of clozapine therapy, and service fragmentation.[4] Such barriers limit the feasibility of clozapine therapy for many patients. As a result, clinicians may administer other antipsychotics in combination to relieve patients' distressing symptoms.

Antipsychotic polypharmacy (APP) is defined as the concurrent use of 2 or more antipsychotics. The prevalence of APP is estimated to range from 12.9% to 35%.[5] In a 2010 Canadian study, prevalence was estimated at 25.7% in a single metropolitan area.[6] Despite APP being common practice, international guidelines have provided little guidance. The 2017 Canadian schizophrenia guidelines[7] and the 2021 American Psychiatric Association guideline[2] provide no firm recommendations on APP; in contrast, the 2019 guidelines of the British Association for Psychopharmacology stated that APP can be used but requires careful monitoring.[8] As pharmacists, we may view the prescribing of two agents within a therapeutic class as duplicate therapy. However, we should thoroughly examine the evidence for APP to better appreciate its role in the care of patients with schizophrenia.

Recent studies have attempted to evaluate the efficacy and safety of APP. Notably, the Cochrane Collaboration recently reviewed antipsychotic combinations for schizophrenia.[9] Comparing antipsychotic combination therapy with monotherapy, the authors found a 27% relative reduction in the risk of having no clinical response, with a number needed to treat of 9. The benefit was more pronounced when an antipsychotic was added to clozapine, and combinations involving clozapine had a number needed to treat of 7. Concerns were raised about the high risk of bias in the studies included in the review and inconsistencies in terms of observed benefits related to various outcomes. Consequently, firm conclusions could not be drawn to inform clinicians, despite the clinically relevant benefit. This uncertainty adds to the confusion surrounding APP, despite some evidence of benefit.

In situations where meta-analysis of randomized studies is inconclusive, well-designed observational research can fill the knowledge gap. In the usual evidence-based medicine paradigm, meta-analyses of randomized controlled trials are considered to be the top of the evidence hierarchy. However, owing to the stringent inclusion and exclusion criteria used in randomized studies, trial participants are not always representative of the patients in clinical practice. One exploratory study found that only 13.5% of all patients in a psychiatric clinic were recruited into a study performed in that clinic, which suggests significant selection bias.[10] In fact, studies often exclude patients with history of nonadherence, comorbid substance use, and unstable living situations, all of which frequently co-occur for patients with schizophrenia. Such exclusions call into question whether efficacy studies reflect true effectiveness in schizophrenia research. Observational studies may better reflect clinical practice because they involve real-world patients. This is perhaps best highlighted by the evidence for long-acting depot antipsychotics: randomized data have found no evidence of benefit, but multiple observational studies have shown benefits.[11] The reason for discrepant findings is likely that nonadherent patients, who may benefit from long-acting depot antipsychotics, are not enrolled in randomized studies.

APP may be another example where observational studies provide better estimates of effect. In 2019, Tiihonen and others[12] published a nationwide study from Finland exploring the effectiveness of APP. This large study, involving 62 250 people with schizophrenia, systematically assessed the risk of hospitalization associated with individual antipsychotics and combinations of these drugs. The study employed within-individual analyses and other rigorous methods to address confounders and selection bias. Relative to monotherapy, combination therapy was found to reduce the risk of psychiatric rehospitalization by 7% and all-cause hospitalization by 9%.[12] These results reaffirmed

the findings of the aforementioned meta-analysis by the Cochrane Collaboration.[9] Intriguingly, combining clozapine with aripiprazole was found to reduce the risk of psychiatric hospitalization more than any monotherapy.[12] This nationwide observational study highlighted the real-world benefits of APP, and clinicians can thus be reassured that APP can indeed improve patient outcomes.

The evidence supporting the benefits of APP has been mounting, although valid concerns have been raised about its safety.[13] Reassuringly, recent meta-analyses have found no evidence of increased serious adverse events or discontinuation of therapy due to adverse events.[9,14] There was also no evidence of increased somatic hospitalization with antipsychotic combinations, relative to no antipsychotic therapy, in the Finnish study.[12] Interestingly, addition of a dopamine-2 (D2) partial agonist (e.g., aripiprazole) has been found to improve prolactin levels in antipsychotic-induced hyperprolactinemia.[14] Overall, the current evidence suggests that the tolerability of APP is similar to that of monotherapy.

From a psychopharmacological perspective, clinicians tend to combine antipsychotics that have different receptor affinity profiles (D2 receptors, serotonin receptors) and different side effect profiles (e.g., movement, metabolic). As a class, the antipsychotics consist of individual agents with different receptor affinities.[2] The dopamine hypothesis of psychosis highlights D2 receptors as important therapeutic targets, and antipsychotic agents have variable activity on these receptors.[1,2] Additionally, antipsychotics differ in their affinities for other dopamine receptor subtypes, as well as for serotonin receptor subtypes.[2] While it may seem counterintuitive to combine two medications from the same therapeutic class, APP takes advantage of the different pharmacological profiles of each agent, such as combining clozapine (low D2 affinity) with risperidone (high D2 affinity). Given their expertise in pharmacology, pharmacists can play an important role in choosing antipsychotic combinations.

Although APP ought not to be the default treatment for patients with schizophrenia, it can be helpful in certain patients who experience no response to monotherapy. Growing evidence supports combining clozapine with another antipsychotic for additional benefits.[9,12] Given the suffering and unmet needs that can result from uncontrolled schizophrenia symptoms, APP can have a significant positive impact on a patient's life. It is therefore time to consider APP as a viable therapeutic option to improve patient outcomes.

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THE "CON" SIDE

Antipsychotic polypharmacy (APP) is a common practice in treating schizophrenia. In particular, treatment-resistant schizophrenia accounts for about 30% of all patients with schizophrenia, and these patients often receive antipsychotic combination therapy, even though clozapine (the first-line therapy) is the only medication approved for this indication. However, before starting clozapine, about 60% of patients receive treatment with combinations of antipsychotics, an approach that is not based on guideline recommendations.[1] Clozapine is widely underutilized, with many clinicians opting to increase current antipsychotic doses, add a second antipsychotic, change to a long-acting injection formulation,

or add a mood stabilizer before starting a clozapine trial.[2] Up to 4 non-clozapine antipsychotics may be trialled before clozapine initiation, which can lead to delays in appropriate treatment of 2 to 5 years after diagnosis of treatment-resistant schizophrenia.[3] Delays in initiating clozapine are associated with poor response, and patients gain less benefit from clozapine if there is a delay.[1] Yoshimura and others[4] found an 81.6% response rate when clozapine was started within a window of 2.8 years, compared with response rates of only 30.8% among those with clozapine initiation delayed beyond 2.8 years. Barriers to clozapine initiation include prescribers' fears, local practices, geographic location, and lack of resources supporting the services required by patients receiving clozapine.[5] Given that clozapine is the only therapy with proven benefit in this population, it is imperative that these barriers be addressed to improve clinical outcomes and minimize the delay in effective therapy.

Current antipsychotic therapies primarily improve the positive symptoms of schizophrenia (e.g., hallucinations, delusions). A 2017 Cochrane meta-analysis on the use of APP showed benefits in terms of symptom improvement, but the evidence came from low-quality, open-label studies that included heterogeneous patient populations with various phases of illness.[6] Additionally, clozapine and non-clozapine combinations were used, thus making it difficult to apply the findings to treatment-resistant or treatment-responsive patients.[6] There were also few data related to functional outcomes. Functional status is a critical domain of schizophrenia that is not well characterized and is seldom included as a study outcome. In the few reviews of APP that have assessed functional outcomes (e.g., Global Assessment of Functioning scale), there was no difference between APP and monotherapy, likely because the studies included in the reviews were small and short in duration.[6] Even well-designed observational data should be interpreted with caution. Tiihonen and others[7] found that APP significantly reduced the risk of psychiatric hospitalizations, with clozapine and aripiprazole being the best combination for this result. However, a closer look at the data shows that there may be no difference between clozapine monotherapy and clozapine combinations, given the overlap of confidence intervals (CIs). Furthermore, the minimal benefit of combining clozapine and aripiprazole (hazard ratio [HR] 0.42, 95% CI 0.39–0.46) relative to clozapine monotherapy (HR 0.49, 95% CI 0.47–0.51) may have been due to residual confounding.[7]

APP is a major contributor to high-dose prescribing, which often exceeds the maximum licensed daily dose and defined daily dose.[8] The defined daily dose is the "assumed average maintenance dose per day for a drug used for its main indication in adults"[9] and is used to compare the cumulative dose of antipsychotic therapy, either as a single agent or as part of a polypharmacy regimen.[10] Antipsychotic dosing is considered excessive when the ratio of prescribed daily dose to defined daily dose (PDD/DDD) is greater than 1.5.[10] Procyshyn and others[10] found that patients with APP received persistently high doses of antipsychotics, with a PDD/DDD ratio of 1.94, whereas PDD/DDD was 0.94 for those receiving antipsychotic monotherapy. Specifically, higher proportions of patients with schizophrenia would receive excessive daily dosing compared with other indications for antipsychotics (e.g., bipolar disorder).[10] A dose-response meta-analysis of antipsychotic drugs showed that doses identified to be 95% effective were often lower than the recommended maximum doses, whereas doses higher than an equivalent of 3–5 mg of risperidone provide limited additional benefit[11] and led to significant concerns for increased adverse effects.

APP is associated with increased movement, metabolic, cardiac, and neurocognitive adverse effects,[12] which can lead to additional medication therapy. In particular, anticholinergic medications are often prescribed to alleviate extrapyramidal symptoms caused by antipsychotics. With higher rates of extrapyramidal symptoms, the use of anticholinergic agents increases, often also at high doses.[12] Antipsychotics themselves have anticholinergic activity at the muscarinic receptors, which adds to the burden of anticholinergic-related adverse effects such as cognitive impairment, constipation, dry mouth, urinary retention, and blurred vision. The burden of adverse effects is one of the most commonly reported reasons for medication non-adherence, with dry mouth and sexual dysfunction being significantly more common in patients receiving polypharmacy.[13]

Reducing high doses of antipsychotics and switching to monotherapy can be accomplished safely. Essock and others[14] showed that patients who were switched from polypharmacy to monotherapy had shorter time to all-cause discontinuation, with about 20% in the "switch to monotherapy" group reverting to their original polytherapy regimen. However, this was an open-label study in which patients and assessors were biased in terms of associating changes in symptoms with changes in medications. In fact, of patients assigned to the "switch to monotherapy" group, 69% were able to successfully switch to monotherapy with no change in symptoms or psychiatric hospitalizations relative to the "stay on polypharmacy" group.[14] Additionally, Yamanouchi and others[15] demonstrated that alternative methods, such as gradual dose reduction over 12 weeks, can also be successful in reducing high doses related to polypharmacy, with no worsening of psychotic symptoms.

Overall, there is currently limited evidence to support the use of APP in most patients with schizophrenia. Although there is considerable evidence related to the use of APP, it is flawed and difficult to apply, and it does not include many clinically important outcomes (e.g., functional outcomes). In addition to significant safety concerns, APP delays initiation of effective monotherapies (e.g., clozapine), and efforts should be made to optimize trials of monotherapy before adding more antipsychotics to a patient's regimen.

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The winner of the **Distinguished Service Award** (sponsored by Pharmascience Inc.) is **Margaret Gray** (Edmonton, AB).

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Excellence in Pharmacy Practice — Interprofessional Collaboration Award
Sponsored by **Teva Canada Limited**
Addressing Medication Appropriateness and Polypharmacy in Frail Older Adults in Primary Care (completed at Misericordia Hospital Geriatric Outpatient Clinic and Edmonton Oliver Primary Care Network, Edmonton, AB)
Cheryl A Sadowski

Excellence in Pharmacy Practice — Leadership Award
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Leadership During a Crisis (completed at Horizon Health Network, New Brunswick)
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Excellence in Pharmacy Practice — Patient Care Award
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Improving Decision-Making in Empiric Antibiotic Selection (IDEAS) (completed at Sunnybrook Health Sciences Centre, Toronto, ON)
Marion Elligsen

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Addressing Medication Appropriateness and Polypharmacy in Frail Older Adults in Primary Care

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

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Background: Older adults have the greatest complexity for care and are at risk for polypharmacy and medication safety concerns. Most medications for seniors are started in primary care, yet there are few pharmacists providing care in this setting.

Objectives: The purpose of our research was to develop an interprofessional seniors-focused clinical service within a Primary Care Network (PCN) in Edmonton, Alberta. The objectives were to determine if a pharmacist-led team assessment could result in reduced medication burden, reduced potentially inappropriate medications (PIM), and improved medication safety.

Methods: The Geriatric Outpatient Clinic (GOC) team from the Misericordia Community Hospital worked with the Edmonton Oliver PCN to develop process of care pathways for referral, assessment, and documentation. Pharmacists with interest in geriatrics through the PCN completed training at the GOC. Patients in the PCN were identified based on the Edmonton Frail Scale for referral to the Seniors Hub and underwent a geriatric assessment.

Results: The initial analysis included 54 patients (61% female, mean age 82 years), with a mean of 5 chronic conditions, enrolled over a 1 year period. Hyperpolypharmacy (10 or more medications) was identified in 67% of patients. The reasons for assessment were falls/mobility (33%), cognition (30%), and polypharmacy/medication review (15%). The pharmacists identified that 61% of patients had untreated conditions, 57% had PIM, and 41% had unnecessary medications. The total number of medications showed a non-significant decline, from 12.1 to 11.7, but the number of PIMs decreased from 1.15 to 0.9 (p=0.006).

Conclusions: The PCN staff rarely found medications as a reason for referral, yet the majority of frail seniors have medication related problems. The implementation of a pharmacist-led assessment for frail community dwelling seniors reduced the number of PIMs and addressed medication undertreatment.

Keywords: geriatrics, primary care, potentially inappropriate medications, interprofessional team, frailty, medication review

Leadership During a Crisis

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

Doucette D[1]
[1]Pharmacy Services, Horizon Health Network, New Brunswick

Background: Leadership during a crisis requires looking out for the needs of others. Leaders need to act decisively while considering input from followers, stakeholders and clients/patients. A disaster or pandemic plan can help guide the preparation, initial response and recovery phases however leaders also need flexibility to adjust to rapidly changing conditions and to be open to opportunities when others will see barriers.

Objective(s): To describe strategies and tactics used to manage a regional multi-site pharmacy service in the early months of the COVID-19 pandemic.

Methods: Various approaches were used during the pandemic of which several will be described as successes and lessons learned in leading teams with communication, visioning, setting expectations for staff, attending to relationships and maintaining positive staff morale.

Results: Examples to be shared of leveraging communications to build trust and inspire staff, pivoting staff to ensure redundancy in priority roles, managing inventory of essential medications and COVID vaccines, and building new bridges with other internal departments and external partners.

Conclusions: Effective leadership in a crisis demands the leader communicate clearly, concisely and with purpose. Varied methods are often needed to keep staff informed and inspired, to maintain trust and focus on delivering essential services even when conditions may be changing and beyond one's control.

Keywords: leadership, COVID-19, pandemic, communication

Improving Decision-Making in Empiric Antibiotic Selection (IDEAS)

Excellence in Pharmacy Practice — Patient Care Award
*Sponsored by Steri*Max *Inc.*

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**Co-Principal Investigators*

Background: Timely initiation of adequate antibiotics has been associated improved patient outcomes. However, selecting adequate empiric antibiotics is difficult due to rising resistance rates and the competing desire to apply antimicrobial stewardship principles.

Objectives: The objective of this project was to develop, implement and evaluated two interventions to optimize empiric antibiotics using prospective audit and feedback.

Methods: The interventions included providing suggestions to prescribers at two points in the empiric period: (1) prior to availability of any culture results, empiric therapy was altered to ensure concordance with prior cultures that have predictive relevance for future infection; and (2) when Gram-negative bacteremia was identified, previously derived and validated multivariable models were used to recommend the most narrow-spectrum adequate antibiotic. The interventions were evaluated simultaneously using a quasi-experimental design comparing two 9-month periods (pre and post-intervention) at Sunnybrook Health Sciences Centre, Toronto, Ontario.

Results: The first intervention increased the proportion of patients that received concordant therapy from 73% (72/99) in the control group to 88% (76/86) in the intervention group (p=0.01). The median time to concordant therapy was significantly shorter in the intervention group (25 vs 55 hrs; p<0.001). The median duration of unnecessary vancomycin therapy was reduced by 1.1 days (95% CI 0.5 – 1.6 days, p<0.001). The second intervention increased the proportion of patients who were on the most narrow-spectrum adequate therapy at the time of culture finalization from 44% (88/201) in the control group to 55% (100/182) in the intervention group (p=0.04). Time to adequate therapy was similar in the intervention and control groups (5 vs 4 hours; p=0.95).

Conclusions: Together, these interventions demonstrated that systematic decision support interventions can simultaneously improve the adequacy of empiric antibiotic coverage while decreasing overall use of broad-spectrum empiric agents.

Keywords: antimicrobial stewardship, clinical decision-making, antibiotic resistance, anti-bacterial agent

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4. Cutaneous Mucormycosis Infection: Isavuconazole as an Oral Stepdown Option in Patients with Contraindicated Drug Interactions to Posaconazole
5. Lamotrigine Dosing with Competing Drug Interactions: A Case Report

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ORIGINAL RESEARCH / RECHERCHE ORIGINALE

Atrial Fibrillation Patients' Experiences with Combination Antithrombotic Therapy Post-Percutaneous Coronary Intervention

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Background: Up to 30% of patients with atrial fibrillation (AF) have coronary artery disease (CAD). Many of these patients undergo percutaneous coronary intervention (PCI), requiring combination antithrombotic therapy (ATT) with antiplatelet (AP) agent(s) of variable durations and an oral anticoagulant (OAC) which may require dose adjustment. The complexity of these regimens may contribute to non-adherence, increasing the risk of thrombosis and/or bleeding.

Objective: To describe patient experiences with combination ATT, including unplanned modifications, after discharge from acute care.

Methods: This was an observational study. Eligible patients had documented AF requiring OAC, underwent a PCI and were discharged on combination ATT. Follow-up contact was planned at 1-, 3-, 6-, and 12-months post-PCI.

Results: Thirty-two patients were enrolled from January-September 2020. Follow-up data was collected for 26 patients (81.3%) at 1-month, 17 patients (53.1%) at 3-months, and 10 patients (31.3%) at 6-months post-PCI. Of the 26 patients with any follow-up data, 12 (46.2%) had at least one unplanned modification, and 6 (23.1%) had additional modifications at other follow-up time points for a total of 23 unplanned modifications. Four patients had unplanned modifications related to invasive procedures. Nine patients experienced modifications to APs and 9 patients experienced modifications to OACs. The most common modifications with AP therapy was a change in duration. The most common OAC modifications included dose reduction and discontinuation. Two patients did not stop acetylsalicylic acid when intended and both experienced bleeding. Two patients experienced a stroke; one after, and one resulting in, an unplanned modification to OAC.

Conclusion: Almost 1 in 2 patients with AF who underwent PCI experienced an unplanned modification to their ATT. Most patient-reported modifications appeared to be prescriber-driven. This underscores the challenges of managing combination ATT for patients and clinicians alike. Close monitoring and effective interdisciplinary communication are needed to optimize patient outcomes.

Assessment of a Standardized Discharge Prescription Implemented to Reduce Opioid Use Post-Surgery

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Background: Excessive prescribing of post-operative opioids is a recognized contributor to opioid misuse and related harms. As part of a provincial initiative to address the issue, a standardized discharge prescription was implemented for patients receiving day surgery, consisting of 20 hydromorphone tablets with part-fills of 10 tablets allowed every 3 days.

Objective(s): Primary: To evaluate the impact of reducing opioid quantities prescribed and part-fill use on patient's pain control. Secondary: To assess the feasibility of implementing follow-up calls on clinical pharmacy technician's (CT) workflow.

Methods: Prior to the implementation of this quality improvement initiative, as standard of care, nurses called patients 24-hours post-surgery. In the new process, CTs called patients who received the prescription on day 7 using a standardized questionnaire. Outcomes included number of standardized prescriptions dispensed, hydromorphone tablets consumed, patients who filled the second part-fill, pain score on day 7 assessed with a 5-point scale [0-no pain, 5-difficult to manage pain], and mean time taken to conduct the calls per day.

Results: Between November 2019-March 2020, 47 patients received a CT-led follow-up call. Of these 47 patients, 38 received the standardized discharge prescription without alterations by prescribers. At 7 days post-surgery, of 970 hydromorphone tablets prescribed, 29% were consumed with a mean of 6 tablets per patient (SD 7). Eighteen-percent of patients filled the second part-fill, 9% consumed all hydromorphone prescribed and 34% did not consume any hydromorphone. Patients reported a mean pain score of 1.6 on a 5-point scale (SD 1.6). The mean time for the calls was 29 minutes per day (0.01 Full-Time Equivalent of CT per day).

Conclusion(s): Reducing opioid quantities prescribed and using part-fills in the post-surgery discharge prescription helped reduce the availability of opioids in the community without compromising patients' pain relief. Follow-up calls were also feasible to incorporate into the CTs' workflow.

A Retrospective Analysis of Pharmacy Turnaround Times for Clinical Trial-Associated vs Non-Clinical Trial Intravenous Anticancer Regimens

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Background: Pharmacy turnaround time, which is the time required to process an intravenous admixture, is a metric of interest to outpatient pharmacies preparing sterile anticancer drugs. As anticancer drug research expands and evolves, there is a need to understand pharmacy service requirements for preparation of intravenous compounds within clinical trials.

Objective: To determine whether the pharmacy turnaround time for sterile intravenous admixtures of clinical trial regimens prepared at Odette Cancer Centre differs significantly from that for non-clinical trial regimens.

Methods: We estimated a multivariate linear regression model of pharmacy turnaround time for all intravenous anticancer regimens. Regimens administered in a separate hematology clinic were excluded. Timestamp data was retrospectively obtained from the CHARM patient management system over the 6-month period from July to December 2019. Pharmacy turnaround time was posited to depend on regimen type (clinical trial, non-trial) and time of day (lunch period, standard shift). Statistical analysis was conducted at a significance level of 0.05.

Results: A total of 9685 regimens were analyzed; 1054 clinical trial regimens and 8631 non-trial regimens. The multivariable model found that clinical trial regimens took 9.25 minutes longer to prepare than non-trial regimens (95% C.I. 7.00-11.49, $p<0.0001$). Any regimens prepared during the lunch period (1130h-1330h) took, on average, 20.39 minutes longer than those prepared during standard shifts (95% C.I. 18.91-21.87, $p<0.0001$).

Conclusion: Clinical trial regimens and regimens prepared during the lunch period were associated with longer processing times for pharmacy. These relationships should be confirmed prospectively using a precise measure of turnaround time and further investigated to explore the root cause factors. Findings may be of interest to pharmacy administrators and may be used to inform resource management for sterile compounding processes in the pharmacy department.

Evaluating the Impact of a Standardized Order Form on Appropriate Ordering and Use of Dexmedetomidine for Sedation in an Adult Intensive Care Unit

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Background: Dexmedetomidine is a novel intravenous sedative that does not produce respiratory depression or deep sedation. Its cost and inconsistent evidence demonstrating benefit compared to other sedatives have been prohibitive to its use as a first-line sedative in the intensive care unit (ICU). In November 2017, a standardized order form was implemented at a tertiary academic hospital to promote appropriate prescribing and use of dexmedetomidine.

Objective: To evaluate whether implementation of a standardized order form increased appropriate ordering and use of dexmedetomidine for sedation in an adult ICU.

Methods: A retrospective before-and-after study was conducted to assess adherence of dexmedetomidine ordering and use against institution-specific criteria for appropriateness. One hundred courses of dexmedetomidine (50 before and 50 after implementation) were adjudicated against criteria outlined in the standardized order form. Each course was adjudicated for appropriateness of both initial ordering and ongoing use. Data on adequacy of sedation and hemodynamic adverse effects were also collected. Descriptive statistics were used for data analysis.

Results: Standardized order forms from February 2015 to May 2020 were reviewed for 99 patients prescribed dexmedetomidine. Patients were primarily young men (85% male, mean age 43 +/- 19 years) admitted to an ICU due to trauma (68% trauma, 27% medicine, 5% surgery). The implementation of the standardized order form did not significantly improve ordering or use of dexmedetomidine (appropriate ordering: 86% before vs. 90% after, p=0.54; appropriate use: 84% before vs. 80% after, p=0.60). A non-significant reduction in duration of infusion was noted (mean 57.9 hours before vs. 48.6 hours after, p=0.08).

Conclusion: Implementation of a standardized order form did not increase appropriate ordering or use of dexmedetomidine, although a reduction in infusion duration was observed. Results will inform future iterations of the standardized order form to improve dexmedetomidine use.

Susceptibility Patterns for *Enterococcus spp.* Clinical Isolates Collected over a 14-Year Period at Sunnybrook Health Sciences Centre

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Background: *Enterococci* are commensal gram-positive cocci that are a common cause of urinary tract infections, endocarditis, intra-abdominal, skin, soft tissue and wound infections. While *E. faecalis* remains the most common pathogenic *Enterococci*, the frequency of *E. faecium* infections have increased globally.

Objective: To investigate the antimicrobial resistance patterns of *Enterococci spp.* clinical isolates collected at Sunnybrook Health Sciences Centre (SHSC) over a 14-year study period.

Methods: A retrospective review of susceptibility data for *Enterococcus spp.* clinical isolates collected from patients admitted to SHSC between October 2002 and September 2016 was completed with data extraction from the SHSC microbiology database. Trends in susceptibility to ampicillin, ciprofloxacin, gentamicin, nitrofurantoin, tetracycline and vancomycin were analyzed using linear regression models with a significance level of <0.05.

Results: Among the 2617 *Enterococcus* isolates, 57% (n=1486) were *E. faecalis*, 30% (n=775) *E. faecium* and the remaining 14% (n=356) were classified as other *Enterococcus* species. The majority of isolates came from blood cultures (n=1176, 45%). Susceptibility trends were assessed from 2008 forward. Of the *E. faecalis* and *E. faecium*, <1% and 10% were vancomycin resistant, respectively. For the aggregate of all *Enterococcus* isolates, the sensitivity to ampicillin and nitrofurantoin decreased each year by 3.2% (p=0.0055) and 3.4% (p=0.006), respectively. For *E. faecalis*, susceptibilities for ciprofloxacin (+3.9% susceptible/year, p=0.0117), gentamicin (+3.9% susceptible/year, p=0.0144) and tetracyclines (+7% susceptible/year, p=0.42) increased over time. Conversely, nitrofurantoin susceptibility increased by 24% each year (p=0.0013) for *E. faecium*. Although *E. faecium* susceptibility to tetracyclines (-4.5% susceptible/year) demonstrated a noteworthy decline, it was not statistically significant (p=0.562).

Conclusion: Enterococcal antibiotic susceptibility improved at SHSC during the study period. However, *E. faecium* infections constituted a substantial proportion (30%) of Enterococcal clinical isolates during the study period. *E. faecalis* and *E. faecium* demonstrated heterogenous susceptibility patterns supporting species targeted antimicrobial stewardship interventions for *Enterococcus*.

Managing Opioids and Mitigating Opioid Risks in Patients with Cancer: An Environmental Scan of the Attitudes, Confidence, and Practices of Pharmacists Practicing in Canada

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Background: The use of prescription opioids in Canada has increased steadily over the past 2 decades, with increases in overdose and death. Opioids are the mainstay of treatment for cancer-related pain (CP). Patients with cancer are not immune to the risks associated with opioid use but are underrepresented in available literature outlining risk mitigation strategies. Pharmacists would be ideally placed to employ risk mitigation practices to support safe and effective opioid use for patients with CP.

Objectives: Describe the attitudes, confidence, and practices among pharmacists in Canada when providing care for patients using opioids for CP management.

Methods: An environmental scan of pharmacists who provide direct patient care in Canada. An electronic questionnaire was distributed via email by pharmacy organizations, and online platforms. The questionnaire consisted of Likert-scale and open-ended questions and was open for 6 weeks. Analysis was conducted using descriptive statistics and qualitative content analysis.

Results: Eighty-one responses from 9 provinces were included in analysis. Respondents endorsed limited and varied practices when caring for patients with CP managed by opioids. Pharmacists were more confident in their ability to assess and provide education compared to managing these patients. Less than 50% of pharmacists were aware of resources available for their patients with aberrant medication taking behaviors, opioid use disorder, and/or patients at high risk of opioid overdose and 25% participated in education surrounding those topics. Education and resources were the most commonly reported facilitators and barriers to resource use.

Conclusions: Pharmacists in Canada report employing opioid risk mitigation practices with low but varied frequency when caring for patients receiving opioids for CP. They endorsed varied confidence and limited awareness of available provider and patient education. These findings can help inform development of education models and guidelines which will serve to support pharmacists in their care of this patient population.

Quality Improvement Assessment of Discharge Medication Reconciliation for Surgery Patients

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Background: Pharmacist-led medication reconciliation and patient education at discharge have been shown to decrease hospital readmissions when part of a medication management care bundle. Currently at our institution, these discharge services for surgical patients are prescriber-led with minimal pharmacy involvement. An opportunity exists to increase pharmacist involvement when providing discharge services for surgical patients.

Objectives: Our primary objective was to identify the proportion of surgical patients with at least one unintentional medication discrepancy at discharge. Our secondary objectives were to identify the proportion of surgical patients with at least one potential adverse drug event (PADE) at discharge and to identify the barriers and facilitators to providing interprofessional medication reconciliation and patient medication education at discharge.

Methods: This was a retrospective, quality improvement study that enrolled 160 general, thoracic, gynecologic oncology, and urology surgical patients discharged between August 1 and October 2, 2018. Focus groups with healthcare professionals were used to identify any barriers and facilitators to providing interprofessional discharge services. Descriptive statistics were used to identify trends in the data.

Results: Overall, 61.3% (98/160) of patients were discharged with at least one unintentional medication discrepancy and 39.4% (63/160) were discharged with at least one PADE. In total, there were 343 discrepancies with the most common being drug omission (62.7%). The most common barriers identified were resource limitations and a lack of time to complete discharge services. The most common facilitators included getting buy-in from prescribers and ensuring advanced notice of discharge to all team members.

Conclusion: The majority of surgical patients included in our study were discharged with at least one unintentional medication discrepancy. Various barriers and facilitators were identified from focus groups with healthcare providers. Common discrepancy awareness and implementation of pragmatic facilitators may enhance the delivery of an interprofessional collaborative practice model at discharge for surgical patients.

Second Dose Antimicrobial Delays in Sepsis and Septic Shock

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Background: Early recognition and timely initiation of antimicrobials are the cornerstone of treatment for sepsis and septic shock. Current evidence suggests that optimizing the time to first doses of antimicrobials can improve clinical outcomes. Little evidence exists describing the timing of subsequent doses of antimicrobials in this population.

Objectives:

Primary Objective: to determine the frequency and extent of delays greater than or equal to 25% of the recommended dosing interval in first-to-second dose parenteral antimicrobial administration for patients admitted through the emergency department (ED) with sepsis or septic shock.

Secondary Objective: to compare the frequency and extent of delays according to (1) the prescribing service (ED physician compared to an admitting/consulting physician); (2) how the order was written (one-time dose orders compared to ongoing orders); (3) when the institution's sepsis order sets are used.

Methods: This retrospective chart review occurred at a single, tertiary care teaching hospital for adult patients with sepsis or septic shock receiving the initial 2 doses of antimicrobials within the institution between January 2016 and December 2019. Descriptive statistics were used to examine patient demographics and characterize delays in antimicrobial therapy. Inferential statistics were used to assess secondary objectives.

Results: Of 158 included patients, 52 (33%) patients experienced at least 1 delay in therapy. A total of 313 second doses were administered, with 60 (19%) doses delayed. Of these delayed doses, the median extent of delay was 48% (median: 1.48, IQR: 1.28 – 1.76). These delays occurred independently of the prescribing service (p-value: 0.19) and how the order was written (p-value: 0.41). The institution's sepsis order sets were not used for any patients included in this study.

Conclusion: Delays in first-to-second dose antimicrobial administration occurred in one third of patients, suggesting an opportunity for quality improvement initiatives to further explore this issue.

Potentially Inappropriate Drug Duplication in a Cohort of Older Adults with Dementia

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Background: Drug duplication in non-steroidal anti-inflammatory drugs (NSAIDs), selective serotonin reuptake inhibitors (SSRIs), loop diuretics, ACE-inhibitors, and anticoagulants is considered potentially inappropriate by the STOPP criteria.

Objective(s): To complete a drug utilization review of drug duplication for NSAIDs, SSRIs, loop diuretics, ACE-inhibitors, and anticoagulants in a cohort of older adults with dementia to assess concordance with prescribing guidelines.

Methods: A retrospective cohort study using administrative claims of Nova Scotia Seniors Pharmacare beneficiaries. The cohort was defined by ICD 9/10 codes for dementia between March 1, 2005 and March 31, 2015. Prescription drug dispensation data and sociodemographic characteristics were collected over the same period. Duplication was two drugs from the same class were dispensed at times allowing them to be in the patient's possession at the same time. We reported duplication in overlapping prescriptions, duration of overlap, and age at dementia diagnosis. All reporting was stratified by sex.

Results: We reported concurrent NSAID, SSRI, loop diuretic, ACE-inhibitor, and anticoagulant use in Nova Scotia Seniors Pharmacare beneficiaries with dementia (NSSPBD) (table 1). NSAID duplication was most commonly seen for celecoxib with naproxen or diclofenac. The most common SSRI pair was sertraline with citalopram. ACE-inhibitor duplication was largely combination products of ACE-inhibitor with a diuretic duplicated with the parent ACE-inhibitor; presumably to increase ACE-inhibitor dose without increasing diuretic exposure (115/183 cases (62.8%)). Duplicate anticoagulants combined oral with parenteral administration, likely for bridging. Neither NSAIDs, SSRIs loop diuretics, ACE-inhibitors, nor anticoagulants showed a sex difference in risk for drug duplication.

Conclusion(s): There was drug duplication for NSAIDs and SSRIs in NSSPBD. Loop diuretic duplication was rare but of long duration. Drug duplication in NSSPBD indicates an area requiring intervention.

For the table that goes with this abstract, please see Abstract Appendix, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/204

Multidisciplinary Lung Cancer Care Pathway for EGFR Positive Advanced Non-Small Cell Lung Cancer Patients at the Sunnybrook Odette Cancer Centre: A Process Map

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Background: Cancer care is a complex and often fragmented process involving a variety of specialized healthcare providers. Increased use of oral anticancer medications (OAMs) has introduced additional complexity. Cancer Care Ontario has published pathways outlining best practices for the management of patients across the continuum of various stages of lung cancer. Real-world descriptions of the complex pathway are absent from scholarly literature.

Objective: To create a multidisciplinary process map describing the sequence of tasks clinical and non-clinical staff at Sunnybrook Odette Cancer Centre (SOCC) contribute to the diagnosis and management of EGFR positive advanced non-small cell lung cancer (EGFR+aNSCLC).

Methods: Four medical oncologists, two nurses, four pharmacists, two registered pharmacy technicians, one drug reimbursement specialist, and five administrative support staff were interviewed and observed over a 3-month period (January 2019 – March 2019). Interview responses, field notes, and internal documents were used to construct a process map, which was iteratively revised based on participant feedback. Opportunities to optimize the patient care pathway were identified.

Results: The process map is composed of 38 steps and illustrates the coordination of care across SOCC administrative staff and four teams (Lung Diagnostic Assessment Program, Lung Clinic, Oral Anticancer Medication Program, Outpatient Pharmacy). Delayed access to molecular pathology results created redundancy and delayed treatment decisions. Opportunities to improve communication between pathology and medical oncology, clinicians and patients, and Odette staff and community-based practitioners were identified. Creating combined OAM-supportive care electronic order sets and facilitating documentation by pharmacy technicians and drug reimbursement specialists would improve communication and efficiency.

Conclusions: This is the first real-world depiction of the complex EGFR+aNSCLC patient journey. Process mapping was an effective way to illustrate the multidisciplinary EGFR+aNSCLC care pathway at the SOCC and assisted with the identification of opportunities to improve service quality and efficiency.

Management of Febrile Neutropenia and Application of the Clinical Index for Stable Febrile Neutropenia Tool in a Retrospective Cohort of Breast Cancer Patients

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Background: Febrile neutropenia (FN) is a well-known and potentially life-threatening complication of cytotoxic chemotherapy; however, FN patients at low-risk for complication can be safely managed in outpatient settings. The Clinical Index for Stable Febrile Neutropenia (CISNE) is a validated tool used to identify candidates for ambulatory care.

Objectives: To describe FN management patterns in a retrospective cohort of breast cancer patients presenting to the Sunnybrook Health Sciences Centre Emergency Department (ED) and evaluate the accuracy of the CISNE tool for predicting risk of complication.

Methods: Breast cancer patients who received curative anthracycline- and/or taxane-based chemotherapy between August 2013 and July 2019 and visited the Sunnybrook Health Sciences Centre ED during the active treatment phase were identified from institutional databases. Demographic, treatment, and clinical information was extracted from electronic medical records for each FN ED encounter. CISNE scores were calculated for each FN ED encounter. Sample characteristics and CISNE performance were descriptively summarized.

Results: Sixty-six (5%) of the 1259 patients identified had an FN event during the active treatment phase. Seventy-two FN events were identified. Primary prophylaxis with granulocyte colony stimulating factors was provided in 64 (89%) cases. Most FN cases occurred during cycle 1 of the anthracycline phase (72%, 52/72), with presentation most often between cycle day 6-10 (79%, 57/72). Seventy-eight percent (56/72) of FN cases were admitted for inpatient care, with a 4-day median length of stay (range 1-12 days). Twenty-one percent (12/56) of inpatient encounters were classified as "low-risk" by the CISNE. However, 42% (5/12) of "low-risk" inpatients required an acute change in clinical management during the course of admission.

Conclusions: FN was an infrequent occurrence in breast cancer patients receiving curative cytotoxic chemotherapy. The subjective nature of CISNE parameters and retrospective reporting bias may limit tool accuracy when applied to early breast cancer patients.

Improving Patient Medication Management Capacity through a Self-Medication Program in a Rehabilitation Inpatient Setting

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Background: A self-medication program (SMP) is designed to help hospital patients better manage their medications by increasing medication knowledge, promoting independence, and preparing them for discharge. Studies that have assessed SMP have shown benefits in medication knowledge and patient satisfaction, but effectiveness has not been demonstrated.

Objective: To determine factors associated with better medication management and adherence in patients participating in an inpatient SMP.

Methods: This was a prospective cohort pre and post study of patients participating in an SMP in a rehabilitation hospital in Canada. Patients consented and were enrolled in the study from November 17, 2016 to January 15, 2018. The Drug Regimen Unassisted Grading Scale (DRUGS) was used to assess patient's medication management capacity pre- and post-SMP while in hospital. The proportion of days covered (PDC) evaluated medication adherence six months after hospital discharge using community pharmacy records and patient telephone interviews. Chi-square and multivariate analyses to determine significant factors associated with medication management and adherence were performed.

Results: Ninety patients (mean age 56.9 years, 51.1% male) were enrolled in the study. Patients participated in the SMP on average 42.9 days (± 32.6 SD) and were discharged home on 11.3 (±5.2 SD) medications. Mean DRUGS scores significantly increased from 86.3% (±16.9 SD) pre-SMP to 92.3% (±13.9 SD) post-SMP (p=0.0002). Medication regimen complexity and cognitive impairment were associated with DRUGS score changes on univariate analysis. Mean PDC was 1.0 (±0.2 SD) in 78 patients with evaluable data. Multivariate analysis did not reveal any factors significantly associated with DRUGS score or PDC.

Conclusions: Patients demonstrated significantly better medication management capacity after participating in a SMP in a rehabilitation setting. Medication adherence after discharge was very high and was not associated with medication management abilities while in hospital.

Antimicrobial Resistance Trends of *Staphylococcus aureus* Isolates Collected from Patients at Sunnybrook Health Sciences Centre over 14 Years

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Background: *Staphylococcus aureus* are designated as methicillin-susceptible (MSSA) or methicillin-resistant (MRSA), based on beta-lactam antibiotic resistance mediated by the *mecA* gene. Published Canadian data is heavily focused on MRSA resistance trends. The present analysis discusses both MRSA and MSSA, offering a more complete picture of *S. aureus* resistance patterns.

Objective: To identify antimicrobial resistance trends in *S. aureus* clinical isolates at Sunnybrook Health Sciences Centre (SHSC) from 2002 until 2016.

Methods: Susceptibility data was extracted from the SHSC Microbiology Database for *S. aureus* isolates collected from patients starting October 2002 until September 2016. Using univariate linear regressions with a significance level of <0.05, resistance trends for cefazolin, ciprofloxacin, clindamycin, cloxacillin, erythromycin, gentamicin, moxifloxacin, nitrofurantoin, penicillin, rifampin, tetracycline, sulfamethoxazole-trimethoprim, and vancomycin were generated for MSSA and MRSA isolates.

Results: The prevalence of antimicrobial-resistant and multidrug-resistant MSSA increased over time (+1.0%/year and +0.5%/year, respectively). MSSA resistance increased to ciprofloxacin (+0.5%/year), penicillin (+1.7%/year), and sulfamethoxazole-trimethoprim (+0.1%/year). Conversely, a significant decrease in resistance was found for MRSA isolates to ciprofloxacin (-1.7%/year), clindamycin (-4.0%/year), erythromycin (-1.4%/year), moxifloxacin (-4.0%/year), and rifampin (-0.5%/year). For all other antimicrobials analyzed, there were no significant trends in MSSA or MRSA resistance. One hundred percent (7398/7398) of MSSA isolates were susceptible to cloxacillin and over 99% (3556/3559) were susceptible to cefazolin. In addition, 100% (1819/1819) MRSA isolates identified across the 14-year study period were susceptible to vancomycin.

Conclusion: MSSA resistance rates to individual antibiotics increased or remained stable, whereas MRSA resistance rates decreased or remained stable. The modest reduction in MRSA resistance at SHSC may be a commentary on the reversibility of institution-level antimicrobial resistance due to more prudent antimicrobial use and infection control policies. However, multivariate models would be required to confirm this optimism.

Real World Comparison of Gefitinib, Afatinib, Erlotinib, and Osimertinib in Advanced Non-Small Cell Lung Cancer Patients: A Multicenter Retrospective Cohort Study

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Background: Our single-centre study at Sunnybrook Health Sciences' Odette Cancer Centre (OCC) found exposure to oral anticancer medication (OAM) clinical pharmacy services (CPS) increased the likelihood of early treatment interruption in non-small cell lung cancer (NSCLC) patients, but the effect was confounded by OAM prescribed.

Objective: To evaluate OAM agent, treatment centre, and OAM-dedicated CPS exposure as predictors of early OAM modification, disease progression, and survival in a multicenter retrospective cohort of advanced NSCLC patients.

Methods: Electronic medical records were reviewed for OAM-naïve NSCLC patients from OCC and Princess Margaret Cancer Centre (PMCC) prescribed gefitinib, afatinib, erlotinib and osimertinib between January 2012 and December 2018. Likelihood of early OAM modification (temporary hold, dose reduction, or discontinuation within two months of starting therapy), disease progression at 36 months, and mortality at 36 months were assessed using multivariable logistic regression and cox-proportional hazards models. Predictors included OAM agent (gefitinib as referent), treatment centre, and CPS exposure.

Results: Two-hundred and sixty-nine patients from OCC (53%) and 236 patients from PMCC (47%) were identified. The majority were prescribed gefitinib (336 gefitinib, 64 afatinib, 66 erlotinib, 39 osimertinib) and were unexposed to OAM-CPS (358 unexposed, 147 exposed). Afatinib (OR 4.92, 95% CI 2.63-9.20, p<0.001) and erlotinib (OR 2.06, 95% CI 1.10-3.88, p=0.025) use was associated with increased likelihood of OAM modification. Erlotinib use was associated with increased likelihood of disease progression (OR 1.68, 95% CI 1.24-2.27, p=0.001) and death (OR 2.46, 95% CI 1.72-3.53, p<0.001). Afatinib use reduced likelihood of mortality at 36 months (OR 0.55, 95% CI 0.32-0.96, p=0.036).

Conclusion: Afatinib increased the likelihood of early OAM modification but was associated with a survival advantage at 36-months. Erlotinib was inferior to gefitinib for all outcomes, consistent with its use in the second line setting. Treatment centre and OAM-CPS exposure did not predict early OAM modification, disease progression, or mortality.

A Retrospective Review of Opioids Prescribed for Post-Surgical Acute Pain in Children upon Hospital Discharge

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Background: Nearly 60% of opioids prescribed for pediatric post-surgical patients remain unconsumed after therapy to treat pain. Opioid stewardship has emerged to address concerns surrounding opioid prescription (mis)use. Opioid stewardship practices identified by Drug Free Kids Canada are defined as coordinated interventions to improve, monitor, and evaluate opioid use.

Objectives: The objective of this retrospective review was to assess prescribing patterns of pediatric post-discharge surgical opioid prescriptions and identify the amount of opioids prescribed in opioid-naïve patients from January 1st to June 30th 2019. This multi-phase project will help define modern opioid stewardship programs.

Methods: All children under the age of 19 with opioid discharge prescriptions following a surgical procedure were included. Electronic medical charts (EPIC) were used to determine medication prescribed, length of therapy, number of total doses, dose and frequency. Types of surgeries (day and inpatient) were general, orthopedic, cardiac, urologic, plastic, ear/throat, dental, and oro-maxillofacial.

Results: A total of 3594 surgical procedures were performed, 1095 (30%) prescribed opioids. Morphine represented ~91% (n=985) and hydromorphone represented ~9% (n=102) of opioids prescribed; mean length was 3.4 (±2.3) days, where ~42% (n=454) were under 3 days, and ~82 percent (n=886) were under 4 days. When dichotomizing by body weight across all surgery types the mean doses (mg/kg) were as follows:

Conclusions: Our findings indicate that pediatric post-discharge surgical opioid prescriptions were within or below recommended Lexicomp guidelines for dose (mg/kg), most were for less than 4 days. Future research will be focused on assessing un-used opioids that remain post treatment, safe disposal and adequate use of non-opioid medications in an effort to describe the success of stewardship programs.

Trends in Opioid Adverse Event Reporting Rates in Canada since 1965

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Background: Opioids are frequently used to treat acute and chronic pain. However, opioid-related adverse reactions (AR) are common and have been associated with worse outcomes. Only 5% of drug-related AR (including opioids) would be reported to health authorities. Even though the government has issued clinical recommendations and policies, the opioid crisis is raging in Canada and little is known about declaration opioid-related AR at the population level.

Objective: To investigate how rates of opioid-related AR declarations occurring in and out of hospitals have evolved since 1965 in Canada.

Methods: We conducted a retrospective study examining the trends of opioid-related AR declared to Canada Vigilance from January 1st, 1965 to October 31, 2019 using Canada Vigilance and Statistic Canada databases. Yearly rates of AR declarations were computed and descriptive analyzes were performed along with a Joinpoint regression and a post-hoc sensitivity analysis.

Results: Among 14,135 AR, oxycodone was the most and normethadone was the least involved causing agent. The highest and lowest rates of AR declaration were 3.2 and 0.1 per 100,000 person-years, respectively in 2015 and 1965. Since 1965, with physicians, pharmacists are among those reporting the least (respectively n=2,062 and n=2,379) compared to health care professionals (n=2,838) and non health care professionals (n=3,366). Overall, from 1965 to 2019, trends of AR declarations increased. Precisely, a non-significant decrease was measured from 1965-2003 (0.31%, standard error ± 0.59, p=0.6045), then an increase of 25.59% ± 6.18% until 2012 (p=0.0002) and finally a decrease of 23.90% ± 7.53% until 2019 (p=0.0026). The post-hoc sensitivity analysis revealed similar findings.

Conclusion: Opioid-related AR declarations seem to increase in Canada, even though huge fluctuations were observed in the last 20 years. Knowing that the absolute number of AR might be seriously underestimated, upcoming studies should investigate how to overcome this gap, along with clinician-pharmacists.

Risk of Burnout in Hospital Pharmacists Transitioning to an Electronic Health Record

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Background: High levels of burnout have been correlated with increased medical errors, higher patient mortality ratios and increased clinician depression. Electronic health records (EHR) have been identified as contributing to higher burnout rates in physicians.

Objective: Assess and compare the risk of burnout before, during and after implementation of an EHR in Alberta and identify stressors related to burnout.

Methods: An anonymous longitudinal survey containing the Maslach Burnout Inventory (MBI), demographics, pharmacy stressors and career satisfaction was distributed to Alberta Health Services pharmacists in September 2019 (Y1) and 2020 (Y2). The EHR was implemented at some sites in November 2019 and October 2020. Individual MBI scores were calculated and a binary logistic regression was used to analyze high risk scores against demographic information, stressors and career satisfaction. The survey will be redistributed yearly for 3 more years as the EHR is implemented at other sites.

Results: Response rates were 14.7% (Y1) and 14.1% (Y2). Pharmacists with high burnout risk comprised 40% and 46% of respondents in Y1 and Y2, respectively, and was driven by emotional exhaustion. In pharmacists using the EHR the risk of burnout was 43%. Several factors were identified as significant predictors of burnout in Y1: years of practice, a hostile work environment, inadequate support for administrative duties, feeling contributions are underappreciated and overall career satisfaction. In Y2 only lack of time available for professional growth significantly predicted a high risk of burnout.

Conclusion: Similar to other clinicians, hospital pharmacists are at an increased risk of burnout. These preliminary results does not show an increased risk with the implementation of EHR.

Potential Drug-Drug Interactions in Hospitalized COVID-19 Patients (CATCO-DDI)

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Background: Therapies for managing COVID-19 disease may interact with other drugs, particularly in hospitalized patients with comorbidities.

Objectives: Characterize the prevalence of drug-drug interactions (DDIs) between investigational/approved medications for managing COVID-19 (COVID-meds) and co-medications (co-meds) in hospitalized COVID-19 patients.

Methods: Multicentre retrospective observational study of hospitalized COVID-19 patients screened for the CATCO trial between 1-Apr-20 and 15-Sep-20. Patients' co-meds were assessed for potential DDIs with the following COVID-meds: hydroxychloroquine (HQ), lopinavir/ritonavir (LPV), remdesivir (REM), dexamethasone (DEX), azithromycin (AZ), interferon beta-1B (IFN) and tocilizumab (TOC). The Liverpool-COVID DDI website and Lexicomp were used to identify and characterize DDI severity (red: do not co-administer, amber: potential interaction) and potential clinical impact. QT prolongation risk was assessed with the Tisdale risk score. The primary outcome was the prevalence of subjects with ≥1 potential clinically significant (red/amber) DDI between each COVID-med and co-med. Secondary outcomes included DDI severity and potential clinical impact. Descriptive statistics are presented as medians (range) or proportions.

Results: Data from 51 patients are available: 61% male, age 74 (44-95) years, 6 (1-15) comorbidities, Tisdale risk score 6 (31.4% moderate risk, 11.8% high risk) and 10 (0-19) co-meds. LPV had the highest rate of potential DDIs (92.2%, 45% red, 3 DDIs per patient) with risk of increased co-med toxicity (most commonly psychotropics, anticoagulants/antiplatelets), while REM and IFN had the least (2% and 9.6%, respectively). Most patients (75%) had ≥1 DEX DDI (mostly amber, 1per patient) with risk of increased co-med toxicity. The most common DDIs with HQ and AZ involved increased risk of QTc prolongation. Over one-third (35%) of patients were deemed ineligible for CATCO at screening due to DDIs with LPV.

Conclusions: Hospitalized COVID-19 patients are at high risk of DDIs with many investigational/ approved COVID medications. Routine DDI screening is recommended, ideally using both general and COVID-specific DDI resources.

Population Pharmacokinetics of Vancomycin in Paediatrics – A Systematic Review

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Background: Vancomycin is commonly used to treat gram-positive bacterial infections in the paediatric population, but dosing can be challenging. Population-based PK (PopPK) modelling can improve individualization of dosing regimens.

Objective: The primary objective was to describe popPK of vancomycin and factors that influence PK variability in paediatric patients.

Methods: Systematic searches were conducted in Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, International Pharmaceutical Abstracts and the grey literature without language or publication status restrictions from inception to August 17, 2020. Any observational study that described popPK analyses of vancomycin in paediatric populations were included. Risk of bias was assessed using National Heart, Lung and Blood Institute Study Quality Assessment Tool for Observational Cohort.

Results: Seventy-two observational studies (n=10,457 patients with at least 27,257 serum vancomycin concentrations) were included. The mean age was 2.5 years (range: 1 day to 18 years), serum creatinine was 47.1 ± 33.6 µmol/L, creatinine clearance was 97.4 ± 74.4 mL/min/1.73m^2. Most studies found that vancomycin pharmacokinetics was best described by one-compartment model (70.8%). There was wide range of clearance and central volume of distribution (Vd) values (range: 0.014 to 0.27 L/kg/h, 0.18 to 1.5 L/kg, respectively) with inter-individual variability as high as 50.4% for clearance, 232% for Vd and proportional residual variability up to 40.8%. Most significant covariates for clearance were weight, age, and serum creatinine or creatinine clearance; for Vd was weight. Variable dosing recommendations were suggested.

Conclusions: Numerous popPK models of vancomycin were derived, however, external validation of suggested dosing regimens and analyses in subgroup paediatric populations such as dialysis patients are still needed before a popPK model with best predictive performance could be applied for dosing recommendations. Significant intra- and inter-individual PK variability were present, which demonstrated need for ongoing therapeutic drug monitoring and site-specific derivation of pharmacokinetic models for vancomycin.

Pathways to Developing Independent Clinical Pharmacist Practitioners: Is There a Better Way Forward?

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Background: The scope of practice of Canadian pharmacists varies widely, ranging from traditional dispensing roles to independent direct patient care practice with prescribing authority. Given the substantial body of literature that supports the beneficial impact of pharmacists in direct patient care, it would be desirable to address barriers and enhance enablers to pharmacists attaining clinical pharmacist practitioner (CPP) level of practice. Access to a greater number of CPPs could benefit the Canadian healthcare system.

Objectives: To propose a pathway that facilitates the attainment and/or recognition of CPP level practice in Canada. This pathway will be informed by the perspectives of current Canadian CPPs and other key healthcare system stakeholders.

Methods: Qualitative descriptive study which employs thematic analysis and grounded theory methodology. Semi-structured interviews were conducted with two main populations nominated by their peers: I) Canadian CPPs (N=13) and II) Canadian healthcare system stakeholders (key individuals identified from academia, regulatory and practice domains; N=6). Thematic analysis of the interviews yielded emergent themes, concepts and representative quotes. Grounded theory methodology utilized these themes and concepts in developing CPP pathways.

Results: Key theme categories that were identified amongst Canadian CPP and healthcare system stakeholder interviews included: I) A sense of dissatisfaction with the status quo for pharmacy practice II) A need for pharmacists to reframe their role and better advocate for themselves within the healthcare system. Pathways forward may include development of a unified national credential which signifies high level practice or increased advocacy for provincial government implementation of expanded pharmacist scope, as has been done in certain provinces.

Conclusions: Pathways for increasing CPP level practice are attainable; however, pharmacists first need to clearly define their role within the Canadian healthcare system.

Opioid Prescribing and Usage Patterns among Orthopaedic Fracture Patients in an Alternate Level of Care Unit at a Community Teaching Hospital

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Background: In response to the opioid crisis, limiting opioid use in acute pain management is recommended. At North York General Hospital, patients with fractures, whether managed surgically or conservatively, are often prescribed opioids. The extent to which they remain on opioids is unknown. The literature reports prolonged opioid use, 6 months and longer, among fracture patients.

Objective: To assess whether opioid usage is minimized without compromising pain control in fracture patients who are deemed medically stable and transferred to an alternate level of care (ALC) unit.

Methods: A retrospective observational study was conducted to examine opioid prescribing patterns, usage and pain scores in fracture patients who were transferred to the ALC unit from June 1, 2018 to May 31, 2019. Patients were followed until discharge. Medical records of these patients during the study period were reviewed. Fracture patients on at least one opioid at time of transfer were included. Duration of opioid use post-fracture, daily dose of opioids (converted to morphine milligram equivalents (MME)) prescribed and used, as well as pain scores on transfer and discharge were collected. Descriptive statistics were calculated.

Results: Thirty-six of 52 fracture patients met the inclusion criteria. Patients were prescribed opioids for an average of 30 days post-fracture. Opioids were discontinued at discharge in 17 of 36 patients (47%). There was a 49.1% reduction in the mean MME prescribed at transfer versus discharge (24.7 mg vs. 12.6 mg). There was a 74.8% reduction in the mean MME used on transfer compared to discharge (14.9 mg vs 3.8 mg). Seventeen of 36 patients (47%) had complete resolution of pain scores at discharge.

Conclusion: This study demonstrates that in medically stable fracture patients in an ALC unit, there is de-prescribing of opioids, reduced opioid usage and reduction in pain at discharge compared to time of transfer.

Medication Management Education for Chronic Kidney Disease: Development of a Conceptual Digital Media Framework

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Background: Patients with chronic kidney disease (CKD) have complex treatment regimens requiring extensive medication management support and education. Patients increasingly rely on digital resources for health information, necessitating the need to tailor requirements in digital education tools for this population.

Objective: To objective of this study was to develop a conceptual framework for digital media supporting medication management in patients with CKD.

Methods: A prospective qualitative study design was followed to derive a conceptual framework. First, patients with advanced CKD participated in semi-structured interviews to discuss their experiences in medication management, including needs and preferences for education delivery. A scoping review followed, using OVID Medline, CINAHL, PubMed and EMBASE databases from 1946 to 2020. Studies describing CKD medication education tools were analyzed to identify common features. Finally, a conceptual framework for digital medication management education was developed, integrating thematic findings from patient interviews and the scoping review.

Results: Eleven patients were interviewed, reporting strong adherence and understanding of their medication regimens. Knowledge gaps included side-effects, sick-day management, and over-the-counter (OTC) medication safety. For digital medium, participants reported a preference towards websites and electronic documents over video or audio-based formats. Ten eligible papers described 13 CKD medication education tools. Themes in the review included medication adherence, safety, and CKD medications. The framework for digital media education includes content focused on practical daily medication management written in lay language, delivered through an accessible and familiar platform. Suggested medication topics include an overview of CKD-specific drug classes, adherence, sick-day management, and OTC safety. Targeting sick-day management, a digital infographic incorporating principles from the framework was developed and implemented.

Conclusion: Digital media represents a potential channel for medication management education. The proposed framework can inform the development of future tools tailored to the specific needs and preferences of the CKD patient population.

Improving Communication during External Hospital Transfer: Development and Pilot of a Transfer Medication Reconciliation Form

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Background: Transitions in patient care are vulnerable to preventable medication errors. Medication reconciliation (MR) at care transitions has been declared a Required Organizational Practice by Accreditation Canada and an effective method for reducing medication errors and improving communication. The Saskatoon area of the Saskatchewan Health Authority does not have a formalized process for transfer medication reconciliation (TMR).

Objective: To develop and pilot a standardized form and process for MR when a patient is transferred from one acute care facility to another.

Methods: The study involved 5 phases: development of a paper-based TMR form; Plan-Do-Study-Act cycles to refine content, comprehension, and flow; transition to an electronic form; development of work standards and education for intended users of the form; and pilot of the form and process on the wards. Completed TMR forms were assessed through quality audits and survey feedback from end users.

Results: The TMR form underwent 12 revisions. Work standards, educational posters and presentations were provided to end users. Thirty-one TMR forms were completed at sending sites. Quality audits showed 19 (61.3%) TMR forms were completed with all medications reconciled correctly. However, almost 10% of best possible medication history (BPMH) medications were not reconciled on the TMR form. Twenty-seven (87.1%) forms arrived at receiving sites and 20 (74.1%) were used as admission orders. Survey data showed the TMR form was user-friendly and improved the transfer of medication information, but barriers to use included time constraints, lack of education/awareness, and lack of physician on site to complete form.

Conclusions: The results show a structured, collaborative, electronic TMR form and standardized process that promotes review of key documents can reduce medication discrepancies at transfer, enhance efficiencies, and improve communication of medication information. Engagement and education of all users of the form is essential for future implementation.

Geographic Variation in Antithrombotic Therapy for Patients with Atrial Fibrillation Undergoing PCI across 5 Zones in Alberta, Canada

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Background: Combination antithrombotic therapy is recommended for atrial fibrillation (AF) patients undergoing percutaneous coronary intervention (PCI). Two of the five zones of Alberta have PCI facilities and patients may be followed outside these zones, so antithrombotic therapy may differ.

Objectives: To describe geographic variation and associated factors in use of direct oral anticoagulants (DOAC), warfarin, no anticoagulant, and P2Y12 inhibitors, and thrombotic and bleeding events in Alberta, Canada.

Methods: Using linked administrative data, this retrospective review included patients with AF undergoing PCI with stenting from September 2014 to December 2019 who filled prescriptions for anticoagulants and P2Y12 inhibitors. Valvular AF, non-AF indication for anticoagulation, and non-Alberta residency were exclusions.

Results: Of 1305 patients included: 23% female, median age 72 years and 63% acute coronary syndromes. Proportion of patients on anticoagulants (53%) was consistent across zones (p=0.47) with increasing age associated with increased anticoagulant use. Calgary and South used significantly more warfarin (42.6% vs 27-32%, $p < 0.05$ for comparisons of Calgary to North, Central, Edmonton; 51.0% vs 27-32%, $p < 0.05$ for comparisons of South to all others), with the remainder filling DOACs. Greater patient weight, previous myocardial infarction, and PCI after publication of the PIONEER-AF PCI trial were associated with greater DOAC use. In those on anticoagulants, clopidogrel was the predominant P2Y12 inhibitor in all zones though use was significantly greater in Calgary (95% vs 81-88%, $p < 0.05$ for comparisons to Edmonton, Central, North). Associations were found between older age and warfarin use with increased bleeding events, and female sex and previous MI with increased thrombotic events.

Conclusions: Almost half of patients were not on anticoagulants after PCI. South and Calgary had greater proportions of warfarin than other zones. Anticoagulant choice was not associated with recurrent thrombotic events; however, warfarin was associated with an increase in bleeding events.

Factors Associated with the Prescription of Fluoroquinolones as an Initial Treatment Option for Community-Acquired Pneumonia in Adult Patients in a University Hospital

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Background: Fluoroquinolones (FQ) are antibiotics often targeted by antimicrobial stewardship strategies because of their overuse and the established link between their use and *Clostridioides difficile*-associated diarrhea.

Objective: To identify factors associated with prescribing a FQ as first-line antibiotic treatment for community-acquired pneumonia (CAP) in adult hospitalized patients before and after the publication of local treatment guidelines.

Methods: Cross-sectional etiological study with retrospective data collection from between 2014 to and 2018. Medical records of patients 18 years or older admitted for CAP treatment were reviewed. Several variables related to the patient and their hospitalization episode at the time of prescription of the antibiotics (e.g., COPD, penicillin allergy) were considered. These factors were analyzed using Pearson's chi-squared and T-Student tests based on the presence or absence of a fluoroquinolone in the initial treatment.

Results: A total of 98 out of 451 patients (22%) received a FQ as first-line therapy. There were significantly fewer FQ prescribed after publication of the local guidelines (31 % before vs. 13 % after, $p < 0.0001$). Age greater than or equal to 75 years was significantly associated with a higher rate of prescribing FQ compared to other treatments (78% vs. 61%, $p = 0.0027$). Smoking is a factor that appears to be a deterrent to the use of FQ compared to other treatments (7% vs. 15%, $p = 0.0313$). There was no significant difference in other co-morbidities, allergies, or recent antibiotic use.

Conclusion: An age of 75 years or older is the main objective factor significantly associated with the prescription of a fluoroquinolone as initial treatment for CAP in hospitalized patients. The other objective factors studied did not show an association, which may indicate the potential for subjective factors to influence prescribers.

Exploratory Study to Assess the Efficacy of a 4-Step Cleaning Protocol and Its Lasting Effect after 30 Days

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Background: Guidelines recommend deactivating, decontaminating, cleaning and disinfecting surfaces exposed to antineoplastic drugs, but products used and cleaning frequencies vary per center. Some surfaces in pharmacy Departments remain systematically contaminated over the years.

Objectives: Explore the efficacy of a 4-step cleaning protocol and its lasting effect on surface cyclophosphamide contamination after 30 days, in Canadian hospital pharmacies.

Methods: Nine Directors of pharmacy departments were contacted in 2020. Sites that were systematically contaminated were identified. Surface cyclophosphamide contamination was quantified at T0 (at the end of a working day), T1 (after a 4-step decontamination consisting of a detergent, 2% sodium hypochlorite, alcohol 70% and water) and T2 (at the end of a working day, 30 days later). Cyclophosphamide was quantified by ultra-performance liquid chromatography-tandem mass spectrometry.

Results: Nine hospitals were recruited and 17 sampling sites were identified. One front grille of the hood sample was excluded (unexplained outlier value). 88% (14/16) of T0 samples were contaminated. After the 4-step cleaning protocol, 44% (7/16) of T1 samples were not contaminated and 94% (15/16) of concentration was lower than T0 concentration. After 30 days, 75% (12/16) of T2 samples were contaminated again, but 100% (16/16) of T2 cyclophosphamide concentration was lower than T0 concentration. The 4-step cleaning had a lasting effect on the storage areas (n=2); they were not contaminated at T1 nor at T2. Seven samples had an increased concentration in T2 (>0.001 ng/cm^2), six were similar and three decreased.

Conclusions: The 4-step cleaning protocol proved insufficient to remove all cyclophosphamide traces, but it reduced the contamination. The effect lasted after 30 days, especially on the storage shelves which were entirely free of contamination both at T1 and at T2. A future study will explore the effect of an improved cleaning protocol (i.e., using a microfiber wipe and less liquid).

Evaluating the Influence of Intravenous Ketamine on Post-Operative Opioid Use in Surgical Patients at a Tertiary Care Centre

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Background: Intravenous (IV) ketamine is one strategy for reducing opioid use postoperatively. Subanesthetic doses of IV ketamine have been shown to improve the efficacy of opioids, increase pain control, and exemplify opioid-sparing effects when used in adults as postoperative analgesia.

Objectives: To determine the impact of IV ketamine on opioid usage in hospital, opioids prescribed within 24 hours of discharge, and pain scores in surgical patients.

Methods: A retrospective trial was conducted in surgical patients exposed to IV ketamine compared to those not exposed to IV ketamine. Patients were matched for age, surgical service, and sex. Primary outcomes include mean opioid use postoperatively on day 0 through day 3, mean opioid use 24 hours prior to discharge, and patient-reported pain scores. Secondary outcomes include the use of naloxone and the presence of hallucinations or delirium during admission. All opioid doses were converted to oral morphine equivalents. The mean and standard deviation were used to capture opioid usage and pain scores, and the student's t-test was used to compare outcomes between groups.

Results: A total of 104 patients were included in the trial. Overall, there was no significant difference in mean total opioid use in hospital in patients exposed to ketamine compared to those that were not (171.7 mg versus 115.5 mg, p=0.09), nor was there any difference in opioid use 24 hours prior to discharge (28.2 mg versus 12.2 mg, p=0.14). Patient-reported pain scores did not differ between groups. More patients in the ketamine group experienced hallucinations compared to those not exposed to ketamine (5 versus 0, p=0.02).

Conclusions: Overall, subanesthetic doses of IV ketamine used post-operatively in surgical patients did not decrease opioid use or patient-reported pain. Though the incidence was small, IV ketamine did increase hallucinations. Results will help guide post-operative analgesia and strategies to reduce opioid use.

Drug Prescriptions Requiring Compounding at a Canadian University Affiliated Pediatric Hospital: A Cross-Sectional Study

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Background: Many drugs administered to Canadian children remain unavailable in commercial formulations that suit their needs. This leads to compounding which can increase the risk of dosing error, exposure to unsafe excipients, and therapeutic failure. Though compounding is common in pediatrics, the importance of this practice in recent years is not well described.

Objectives: To determine the proportion of 1) active prescriptions (aRx) of compounded drugs for enteral administration (CDEA) in hospitalized children, among all aRx; 2) hospitalized children prescribed at least 1 CDEA, among all children with aRx.

Methods: In this retrospective study conducted at a Canadian academic pediatric hospital, all aRx for hospitalized patients under 18 years of age were identified using the hospital pharmacy database on 2 randomly selected summer and winter days. Demographic data was collected from medical records for patients with at least 1 aRx. CDEA was defined as any drug requiring manipulation including solids, such as tablet splitting, and liquids, such as solutions prepared with an active ingredient.

Results: A total of 606 hospitalized children with 5465 aRx were included in this study. Overall, CDEA represented 13.1% (n=714) of all aRx, and 23.2 % of aRx for enteral administration. Nearly half of patients (N=298 [49.2%]) were prescribed at least 1 CDEA. CDEA were mostly liquids (n=478 [66.9%]), and included mainly drugs of central nervous and cardiovascular systems (Table 1).

Conclusion: Availability of suitable pediatric formulations in Canada remains challenging, with compounding still required to treat almost half of the hospitalized pediatric population. International collaboration is mandatory to facilitate access to child-friendly formulations as they become available in trusted foreign jurisdictions.

For the table that goes with this abstract, please see Abstract Appendix, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/204

Description of Pharmacists' Interventions during the Prescription Validation Process Using a Pharmaceutical Care Model Based on Patient Prioritization in a Specialized Hospital

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Background: The validation of prescriptions in a hospital setting is an integral part of the pharmacists' tasks to ensure an adequate and safe medication dispensing process. A new patient prioritization-based pharmaceutical care model was recently implemented in our hospital. Considering the lack of data and multiple recent changes in pharmaceutical care, it is essential to redefine the role of pharmacists during the prescription validation process.

Objective(s): The main objective was to describe the interventions performed by pharmacists during the prescription validation process in a center using a new pharmaceutical care model based on patient prioritization.

Methods: A prospective study identifying oral and written interventions made by pharmacists during the prescription validation process using a pharmaceutical care model, during a 21-day period. Data collection was carried out from computerized pharmacological files and a standardized collection tool. The pharmacists' written consent and the project approval by the local ethics committee were obtained.

Results: A total of 1651 interventions during the prescription validation process were carried out, of which 1076 were verbal and 575 written. The most frequent interventions were related to pharmaceutical opinions (26.3%), prescriptions at admission (12.0%), drug doses (11.3%) and administration schedules (10.7%). Amongst the interventions, 53.2% (n = 878) were documented in the patient's pharmacological or medical file and 339 (20.5%) stemmed from the pharmaceutical care model. The activities reserved to pharmacists according to Bill 41 represented 206 interventions (12.5%).

Conclusion(s): Many types of interventions are performed by pharmacists during the prescription validation process in our hospital. This study provides a portrait of the pharmacists' interventions using a pharmaceutical care model based on patient prioritization.

Delivery of Clinical Pharmacy Services at Odette Cancer Centre during the COVID-19 Pandemic

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Background: Virtual methods have been innovatively utilized by healthcare professionals to provide a variety of clinical services during the COVID-19 pandemic. In March 2020, the Odette Cancer Centre pharmacy modified the delivery of clinical pharmacy services (CPS) to minimize patient contact and decrease the risk of viral transmission. As part of the modified delivery model, CPS such as best possible medication histories (BPMH), baseline assessments, and medication therapy counsels were conducted via telephone.

Objective: To describe the Odette Cancer Centre Pharmacy's modified CPS delivery model for ambulatory patients treated with intravenous anticancer therapy during the first wave of the COVID-19 pandemic.

Methods: The modified CPS delivery model was implemented on 25 March 2020. A process map illustrating differences in workflow between the standard and modified CPS delivery models was created, and challenges to remote CPS delivery were identified. The number of BPMH/baseline assessments and medication therapy counsels completed virtually and in-person were tracked over a six-week follow up period and summarized as process metrics.

Results: The high-level process map illustrates the stepwise differences in workflow for a single patient across a four-day period. During the six-week follow up period, 202 BPMH/baseline assessments and 199 medication therapy counsels were completed. Seventy-four percent (149/202) of BPMH/baseline assessments and 36% (74/199) of medication therapy counsels were provided remotely. Challenges to remote CPS delivery included patient acceptance and lack of technology to support system-level processes.

Conclusion: By incorporating remote delivery approaches, clinical pharmacy service levels at the Odette Cancer Centre were maintained during the first wave of the pandemic without significant investment in resources. Further research to develop, refine, and individualize virtual clinical pharmacy care models will help to consolidate the role of these approaches in the post COVID-19 pandemic era.

Characterizing the Role of Home Care Pharmacists in the Edmonton Zone

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Background: With the gradual shift towards outpatient health care delivery in Canada, the need for home care services is increasing. Home care patients often have multiple comorbidities and correspondingly complex medication regimens; however, there is limited literature exploring the role of home care pharmacists and the clinical activities that they perform.

Objectives: To describe the type and frequency of clinical activities performed by home care pharmacists upon initial consultation. To determine which patient characteristics resulted in the highest number of clinical activities, and the frequency of pharmacist initiated clinical interventions and recommendations.

Methods: Retrospective chart review of patients who had an initial consultation with home care pharmacists within the Edmonton Zone from June 2018 to May 2019.

Results: Amongst 318 patients (89.6%), 60.1% were female and the median age was 79 (IQR 68-86). The median number of medical conditions and medications was 6 and 10, respectively. Of a total of 1172 clinical activities, there was a median of 3 (IQR 2-5) per patient and this did not change for those with the top 5 most common medical conditions namely, hypertension, type 2 diabetes, osteoarthritis, depression and dyslipidemia. The most common activities were patient counselling (13.7%), collaboration with another health provider (13.4%), and deprescribing (11.9%). Among all activities, pharmacists made 562 interventions and 610 recommendations. Older age, and having more medications was associated with an increased number of clinical activities (increase of 0.01, p= 0.003, and 0.03, p <0.001, for each additional year of age and each additional medication, respectively).

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

Cannabis Use, Experiences, and Perspectives in a Hemodialysis Population: A Descriptive Patient Survey

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Background: Patients with end-stage kidney disease (ESKD) suffer an average of 13 symptoms per day. Pharmacologic treatment options are limited by adverse effects, high pill burden, and poor efficacy. Interest in cannabis as a therapeutic alternative to manage refractory symptoms has been described in the literature. Currently, limited data exists about cannabis use or patient perspectives in the ESKD population.

Objectives: The objectives of this study were to characterize the use of cannabis among hemodialysis (HD) patients, describe patient perspectives related to cannabis, and explore patient experiences related to cannabis and the healthcare team.

Methods: We developed a 33-item questionnaire about cannabis with input from nephrology expert groups (pharmacists, nephrologists, nurse practitioners, and current HD patients). Patients of a tertiary hospital ambulatory HD unit were invited to complete the anonymous questionnaire. Descriptive analyses were performed.

Results: Three hundred HD patients were invited to participate, and 52 patients (17%) completed a questionnaire. Eleven patients (21%) reported cannabis use within the last 3 months. Most reported using cannabis recreationally (73%) and/or for symptom management without medical authorization (45%). Apart from recreation, the most reported reasons for use were insomnia, anxiety, and non-neuropathic pain. Smoked dried flower was the predominant method of consumption (73%). Among patients who used cannabis, 82% believed it has beneficial health effects and 18% believed it has harmful effects. Only 8% reported ever being asked about cannabis by a member of the HD team.

Conclusion: This is the first characterization of cannabis use among HD patients. Key findings were that a significant proportion of patients who use cannabis do so with minimal healthcare involvement, use via the smoked route is common, and a majority of patients surveyed believe cannabis has beneficial effects. These findings represent opportunities for patient education initiatives and harm reduction strategies.

Canadian Hospital Pharmacists' Perceptions of Preparedness and Wellbeing during the Coronavirus Disease 2019 Pandemic

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Background: The perceptions of some healthcare workers have been evaluated during the coronavirus disease 2019 (COVID-19) pandemic, but little is known about the perceptions of hospital pharmacists.

Objectives: To evaluate pharmacists' perceptions of their preparedness for the COVID-19 pandemic and to report their mean Warwick-Edinburgh Mental Wellbeing Score (WEMWBS).

Methods: Pharmacists working in a Canadian hospital inpatient setting during the COVID-19 pandemic were invited to participate in an online survey. Part A was a 46-item survey instrument including statements related to directions and support from leadership, personal protective equipment practices, professional role, and work environment. Part B assessed the mental wellbeing of respondents using the validated 14-item WEMWBS. The survey was open from July 21 to September 11, 2020. Descriptive analyses were used.

Results: A total of 457 hospital pharmacists from across Canada consented to participate in the study. Seventy-four percent of respondents were female with 64% aged 25-44 years old. Sixty-seven percent of respondents agreed they felt confident that their pharmacy department had been managing the pandemic effectively. The majority of respondents (81%) agreed their workplace had been able to manage the patient demand and had confidence they would continue to. The majority of respondents agreed their teams were working well together despite the stress they perceived they were under. Twenty-two percent of respondents did not agree they received training for COVID-19 infection prevention and control practices. The mean WEMWBS score was 48.9 +/- 8.6, indicating average mental wellbeing.

Conclusions: After the first wave of the COVID-19 pandemic, pharmacists perceived their hospitals, departments and teams were able to manage the pandemic. Ensuring all hospital pharmacists receive training for effective COVID-19 infection prevention and control practices is crucial. How their perceptions and wellbeing have changed since the second wave of the pandemic is unknown.

Implementation of an Antimicrobial Suggests Order in a CPOE System

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Background: Antimicrobial stewardship teams provide recommendations for antimicrobial optimization without consistent documentation of the interventions. Recent implementation of computerized prescriber order entry (CPOE) has supported electronic documentation of recommendations and tracking of acceptance rates.

Objectives: The objective of this study was to describe the implementation of Antimicrobial Stewardship Suggests orders as a tool for audit-and-feedback interventions in a large tertiary care academic hospital.

Methods: The Antimicrobial Stewardship Program (ASP) implemented an information technology developed CPOE-based "Antimicrobial Stewardship Suggests" order. The ASP Team routinely used this tool for documenting recommendations on prospective audit-and-feedback and hospital wide antimicrobial surveillance for patients during a 1-year period from January 1, 2020 to December 31, 2020. The orders generated an alert for the primary team to acknowledge by accepting or rejecting the suggestions. Rates of acknowledgement and full adoption of recommendations were assessed.

Results: During the study period, a total of 1153 electronic conversational interventions were made using the Antimicrobial Stewardship Suggests tool. Of these, 1024 (89%) were acknowledged by the admitting clinical service. The most common interventions included no drug indication (32%), de-escalation (25%) and bug-drug mismatch (15%). Stewardship recommendations were fully adopted in 93% of cases.

Conclusions: Our CPOE-based alert tool for communicating antimicrobial stewardship interventions proved to be effective in supporting judicious antimicrobial use and documentation of antimicrobial stewardship interventions.

Acetylsalicylic Acid Desensitization in Patients with Coronary Artery Disease

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Background: Allergy to acetylsalicylic acid (ASA) can be problematic for patients with imperative cardiologic indications for dual antiplatelet therapy with ASA and clopidogrel. In 2007, the first ASA desensitization protocol was used in our center. In 2019, following a literature review, two ASA desensitization protocols were adopted; a short and a long one depending on the severity of the previous allergic reaction. The most suitable ASA desensitization protocol for patients with ASA hypersensitivity remains to be determined.

Objective(s): The main objective was to describe our experience with desensitization in patients with ASA hypersensitivity who completed a desensitization protocol. The success rate of ASA desensitization was determined. The cases requiring a modification to the protocol to achieve successful desensitization or those where the desensitization was unsuccessful were described. Finally, the management of allergic reactions when the desensitization failed was also reported.

Methods: A longitudinal descriptive study with retrospective data collection including patients who completed an ASA desensitization protocol between January 2007 and June 2020 was performed.

Results: The study included 105 episodes of administered ASA desensitization protocols. The overall success rate of the desensitization protocol is 92.4%. There is no statistically significant difference between the success rate for the ASA desensitization protocols, whichever the one used. Of the 105 protocols administered, 19 patients experienced a hypersensitivity reaction. Of these, 12 patients had their desensitization protocol modified. A total of six patients failed to complete the ASA desensitization protocol. The study could not determine whether adherence to the pre-protocol desensitization recommendations had an impact on the outcome.

Conclusion(s): The desensitization protocols used have a high success rate. A study including a larger number of patients will be necessary to determine if there is a statistically significant difference between the old and the new protocol.

System-Level Interventions to Decrease Opioid Prescribing at Discharge in General Surgery: A Systematic Review

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Background: Previous studies have shown that general surgery patients are often prescribed opioids in greater quantities than are used. Overprescribing has been shown to be a contributor to chronic opioid use and the development of opioid use disorder.

Objective(s): The purpose of this systematic review is to evaluate system-level interventions aimed at reducing opioid discharge prescription quantities.

Methods: A systematic review of general surgery opioid stewardship literature was conducted using the databases PubMed, EMBASE and MEDLINE from database inception to June 22, 2020. The search terms used included: "opioid", "general surgery", "quality improvement" and "prescribing". Included studies were assessed for quality of study design and risk of bias using three validated critical appraisal tools. The primary outcome was the change in opioid quantities prescribed on discharge. Studied interventions were assessed for feasibility of implementation at our institution.

Results: The search strategy yielded nine primary studies; seven pre-post studies and two interrupted time series analyses, including a total of 17,551 general surgery patients. Six studies reported that the implementation of general surgery-specific opioid prescribing guidelines was associated with a 25-70% reduction in the quantity of opioids prescribed. Two studies reported that opioid prescribing legislation did not result in a reduction in opioid quantities prescribed at discharge. One study evaluated the addition of stand-alone oxycodone to the hospital formulary, which was not associated with a statistically significant reduction in the quantities of opioids prescribed on discharge. In the studies that reported safety outcomes, hospital visits for uncontrolled pain and opioid refill requests are uncommon.

Conclusion(s): The implementation of general surgery-specific opioid prescribing guidelines is a safe and effective method of reducing opioid prescribing quantities at discharge. We recommend that St. Michael's hospital implement and disseminate general surgery-specific, opioid prescribing guidelines.

Coordination and Delivery of Remote Clinical Pharmacy Services during the COVID-19 Pandemic: A Survey of Pharmacy Professionals at Cancer Centres across Canada

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Background: Clinical pharmacy services such as medication reconciliation, medication counselling, and toxicity follow up are integral elements of cancer patient care. Pharmacy professionals responded to the challenge of maintaining oncology clinical pharmacy services (CPS) while minimizing patient contact during COVID-19 pandemic restrictions.

Objective: To survey pharmacy professionals from across Canada and describe how cancer centre pharmacies adapted to deliver oncology CPS at the onset of the COVID-19 pandemic.

Methods: Pharmacy professionals at Canadian cancer facilities were invited to complete an online questionnaire. Recruitment occurred via the Canadian Association of Pharmacy in Oncology and Oncology Pharmacists of Toronto Regional Association networks. Survey items addressed practice site characteristics, changes to oncology CPS delivery models to accommodate COVID-19 pandemic restrictions, and barriers and facilitators to maintaining oncology CPS during the pandemic. Responses were summarized using descriptive statistics.

Results: Twenty-one (45%) of the 47 respondents were from Ontario, with the remainder distributed across the provinces and one territory. Of the 43 participants who completed the survey, 63% (27/43) reported a decrease in face-to-face CPS interactions, and 63% (27/43) reported an increase in telephone CPS encounters during the first pandemic peak. Video communications were seldom used before or during the pandemic. Most respondents (34/43, 79%) were confident that CPS levels were maintained during the pandemic. Flexibility in the method and timing of service provision was a commonly reported facilitator to CPS delivery during the pandemic. Common factors which impeded successful CPS delivery included lack of resources (technology, equipment) and inadequate time to plan.

Conclusion: Most pharmacists were satisfied with the level of oncology CPS maintained during the first wave of the COVID-19 pandemic. The majority of sites adapted by increasing telephone consultations and decreasing in-person encounters. Opportunities to improve remote CPS delivery include improved access to video technology and development of virtual patient-education aids.

Patient Satisfaction and Experience with Oral Anticancer Medication Pharmacy Services at the Odette Cancer Centre: A Cross-Sectional Survey Study

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Background: In 2015 the Odette Cancer Centre introduced clinical pharmacy services (CPS) to optimize the care of patients prescribed oral anticancer medications (OAMs). As part of this program, pharmacists employ information and communication technology to provide OAM education and remote toxicity management support.

Objective: To evaluate patient satisfaction and experience with the OAM CPS of the Odette Cancer Centre.

Methods: Breast cancer, lung cancer, and leukemia patients who completed 1-3 months of OAM therapy (palbociclib, afatinib, erlotinib, gefitinib, osimertinib, ibrutinib) between January-March 2020 were recruited to participate. Participants completed an investigator developed questionnaire about counselling experiences and ability to self-manage OAM toxicities, as well as three validated surveys: (1) Health literacy, (2) modified Satisfaction with Medication Information Scale (mSIMS), and (3) Part B of Satisfaction with Medication Information Scale (SCIP-B). Associations between health literacy, satisfaction, and reported medication self-management behaviors were assessed with chi-squared tests.

Results: Thirty-four patients completed the study. Among the 24 patients reporting OAM toxicity, 19 (79%) indicated they were the first person to identify the side effect, and 11 (46%) reported independent self-management. High rates of satisfaction were reported for OAM CPS and the OAM information provided (median aggregate mSIMS score 19/22, median aggregate SCIP-B score 24/30). One participant (3%, 1/34) was identified as having inadequate health literacy. OAM drug interactions (58% endorsement), toxicities (58% endorsement), indication (55% endorsement), and onset time (39% endorsement) were identified as the most important things to know about OAMs. No statistically significant relationship between health literacy, patient satisfaction, and reported ability to self-manage OAM toxicity was found.

Conclusion: Patients reported high levels of satisfaction with OAM CPS and OAM information provided by the Odette Cancer Centre pharmacists, and identified drug interactions, drug toxicity, indication, and onset time as the top four things to know about OAMs.

Risk of Prosthetic Joint Infection Treatment Failure in an Outpatient Intravenous Program

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Background: Prosthetic joint infections (PJIs) are a major complication of total joint replacement surgeries. Treatment includes surgical intervention with prolonged courses of intravenous (IV) antibiotics in outpatient IV programs. The risk of PJI relapse or reinfection is high and may be associated with risk factors.

Objectives: To identify PJI treatment failure rate and risk factors in patients admitted to an outpatient IV program.

Methods: A retrospective chart review was conducted in adult patients with PJI admitted to an outpatient IV program between July 1, 2013 and July 1, 2019. Chi-square tests were used to examine demographic data, comorbidities, surgical intervention, pathogens and antimicrobial regimens. Treatment failure included infection relapse and reinfection and was further defined by pre-determined criteria.

Results: One hundred patients associated with 137 admissions to the outpatient IV program for PJI were included. Twenty-eight patients had multiple admissions and accounted for 65 of the total admissions. Most common location of PJI was knee (52%) and hip (41%) and methicillin-susceptible *Staphylococcus aureus* was the most frequent pathogen (22.6%). Patient comorbidities included obesity (58%), diabetes (41%), smoking (25%) and depression (24%). The overall rate of treatment failure was 56.2%. Risk factors associated with treatment failure vs. success were diabetes (50.9% vs. 29.8%; p = 0.03), depression (32.1% vs. 14.9%; p = 0.04), chronic liver disease (9.4% vs. 0%; p = 0.03), previous history of methicillin-resistant *S. aureus* infection (13.2% vs. 2.1%, p = 0.04) and Gram positive infections (63.6% vs. 43.3%; p = 0.02).

Conclusion: The overall PJI treatment failure rate in the study population was high. Patients with diabetes, depression and chronic liver disease experienced higher incidences of failure. Primary prevention of modifiable comorbidities and increased monitoring of high-risk patients is required to ensure successful eradication of PJI in outpatient IV programs.

Clinical Utility of Switching to Insulin Degludec from Other Basal Insulins in Patients with Type 1 or 2 Diabetes

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Background: Insulin degludec has demonstrated superiority in clinical trials compared to some basal insulins, but the effects of switching Canadian adults with type 1 or 2 diabetes mellitus (T1DM, T2DM) to degludec in clinical practice are unknown.

Objectives: To evaluate the clinical effectiveness and safety of switching insulin-treated adults with either T1DM or T2DM to degludec under conditions of routine clinical practice.

Methods: This was a retrospective observational cohort study of patients in Alberta (using administrative databases and electronic medical records (EMR)) who were switched to degludec between December 1, 2018 and December 1, 2019 and were followed till March 1, 2020. We used interrupted time series for the primary outcome analysis.

Results: A provincial cohort of 5294 patients, 287 of which were also included in the clinic cohort, were analyzed. After switching to degludec, the adjusted HbA1c decreased by -0.28 [95% CI, -0.37; -0.19] % (p <0.001) and is predicted to be sustained post-switch (p<0.001). Rates of all-cause hospitalizations/emergency department (ED) visits (p = 0.5/p = 0.3) and diabetes-related ED visits (p = 0.3 (T1DM), p = 0.1 (T2DM)) remained consistent post-switch vs pre-switch. The proportion of clinic patients with EMR-documented hypoglycemia post-switch vs pre-switch was not statistically significant (p = 0.8 (T1DM), p = 0.6 (T2DM)). In the clinic cohort, at switch, there was an average basal insulin dose reduction of 11.2% (T1DM), 12.3% (T2DM), and 16.3% (patients with insulin resistance) (p<0.001 vs pre-switch), which was sustained at follow-up.

Conclusions: Patients with T1DM or T2DM who have inadequate glycemic control or find their current basal insulin dosing inconvenient (especially those with insulin resistance) may benefit from switching to degludec with a potential for a small improvement in HbA1c at lower basal insulin doses.

Vancomycin Loading Doses in Critical Care Practice: A Retrospective Audit

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Background: Vancomycin is a critical agent against MRSA infections in ICU. Patients often have wide fluctuations in volume of distribution, impeding success of conventional maintenance dosing. Vancomycin loading can help rapidly achieve therapeutic drug concentrations. New guidelines debate the use of Bayesian derived AUC-guided dosing versus monitoring trough levels.

Objectives: Primary outcome characterizes the practice of vancomycin loading in an urban ICU. Secondary outcome reported concordance rates to guidelines, generating practice recommendations.

Methods: This study is a retrospective audit for quality improvement. A chart review on ICU patients receiving vancomycin from January to March 2018 was completed by recording information with customized extraction sheets. Data was analyzed with pivot tables using a spreadsheet program.

Results: 94 cases were identified. Prominent indications for vancomycin included pneumonia and abdominal infections. One fifth had positive blood cultures for staphylococcus aureus. 67% were vancomycin loaded, usually with 1-2g. 29% were dosed at 25-30 mg/kg and guideline concordant. Two-thirds of these doses achieved a trough of 10-20 mg/L. One third were dosed within 20-24.9 mg/kg and half achieved levels over 15 mg/L. 9% developed an acute worsening in renal function. 70% of dialysis patients were loaded with less than 25 mg/kg. 29% achieved a trough of 10-20 mg/L and 71% achieved troughs over 15 mg/L. Two-thirds of patients in this audit survived ICU.

Conclusion: Starting vancomycin early for critically ill patients suspected of MRSA infections is vital for survival. Guidelines suggest a vancomycin loading dose range of 25-30 mg/kg. Most patients in this study were underdosed yet achieved therapeutic levels. This audit suggests expanding the loading dose range to 20-30 mg/kg and a lower 20-25 mg/kg range for dialysis patients with recoverable kidney function to avoid further nephrotoxicity. The audit refrains from making trough level suggestions, but raises hypothesis seeking questions for future clinical studies.

Feasibility of a Pharmacy Student-Led Screening Program to Prioritize Hospital Patients for Clinical Pharmacy Activities: A Pilot Project

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Background: Prioritizing patients for clinical pharmacy activities is challenging and requires further study. Entry-level Pharm D programs have

increased demand for Canadian pharmacy practice placements. Programs which integrate pharmacy learners into patient care could support learning, and potentially increase access to clinical pharmacy services.

Objectives: Determine feasibility of a pharmacy student-led patient screening program which provides pharmacy students with opportunities to practice information gathering and communication skills and helps unit-based pharmacists prioritize patient care activities.

Methods: This was a prospective, single-site, observational study. Patients admitted to a 35-bed family practice unit at The Dr. Everett Chalmers Regional Hospital, a 314-bed regional hospital in Fredericton, NB during the study timeframe were eligible. A Pharmacy Patient Screening Tool (PPST), workload and audit forms were developed, and a pharmacy student was trained to complete study forms. The student and two pharmacists were interviewed at study completion and responses underwent thematic analysis.

Results: The student screened 95 patients. Ten screenings were randomly audited, with a student to pharmacist discrepancy rate of 1.0%. Average screening time was 15 minutes per patient, with an average of 2 minutes per patient to review with the pharmacist. Thematic analysis revealed that the program increased the student's therapeutic knowledge, communication and data collection skills. Hands-on learning was identified as very valuable. Pharmacists felt that the student utilizing the PPST helped their workflow and patient prioritization, and that the student contributed to patient care via the screening program.

Conclusions: Results suggest it is feasible for a pharmacy student to screen patients using the PPST. The tool has the potential to integrate students into clinical pharmacy activities and aid in patient prioritization. Future directions involve PPST validation and exploring additional student-led processes to optimize patient outcomes, workflow efficiency, and student learning.

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Opioids Co-Prescribed with Sedatives: Prescribing Patterns Following an Intensive Care Unit Admission

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Background: Opioid misuse is a health care crisis in Canada. Opioids and sedatives are utilized in the intensive care unit (ICU), and the use of opioids is promoted by the recommended analgesia-first approach. Opioids co-prescribed with sedatives have been associated with adverse events, including death. The impact of the analgesic-first approach on continuation of opioid-sedative combinations after an ICU admission at our institution is unknown.

Objectives: To determine the rates of opioid co-prescriptions following an ICU admission, and to identify risk factors associated with continuation of hospital-initiated opioid co-prescriptions.

Methods: This was a retrospective chart review of patients admitted to two ICUs at a tertiary care centre between April 1, 2018 and March 31, 2019. Baseline characteristics were obtained from an ICU clinical database and medication information was collected from medication reconciliation forms. An opioid co-prescription was defined as an opioid prescribed in combination with a sedative (benzodiazepine, z-drug, gabapentinoid, tricyclic antidepressant, or antipsychotic). Opioid co-prescriptions were categorized as "hospital-initiated" or "any". "Any" included home opioid co-prescriptions continued in hospital and hospital-initiated. Factors independently associated with hospital-initiated opioid co-prescription were analyzed by multivariable logistic regression.

Results: At ICU transfer 23.0% (169/735) were prescribed any opioid co-prescription of which 20.1% (147/733) were hospital-initiated. At hospital discharge 8.6% (44/514) were prescribed any opioid co-prescription of which 4.9% (25/513) were hospital-initiated. Male gender, home opioid co-prescription, surgical patient, prolonged hospital stay, and in-hospital mortality were risk factors for hospital-initiated opioid co-prescription at ICU transfer. Younger age, home opioid co-prescription, surgical patient, and prolonged hospital stay were risk factors at hospital discharge.

Conclusions: Hospital-initiated opioid co-prescriptions were common at ICU transfer but occurred less frequently at hospital discharge. Pharmacists can monitor for important risk factors such as younger age, male gender, home opioid co-prescription, surgical patient, and prolonged hospital stay.

Measuring Dispensing Capacity in a Chemotherapeutic Compounding Pharmacy

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Background: Due to an increase in the aging population, the number of new cancer cases have been steadily increasing in Canada within the last 10 years. We expect the demand for sterile compounded chemotherapeutic drugs to continue to increase for the next 10 years. For this reason, understanding the current workflow and capacity of Hospital Oncology Sterile Compounding unit is important. Two technicians (Chemo 1 and Chemo 2) begin their work day at 7:30 A.M. 90% of chemotherapeutic preparations are mixed before 12 A.M. The technicians utilize protective clothing and a biological safety cabinet. The technicians usually rotate stations so it is a different pair of technicians working in the clean room every day. A time motion study is crucial to provide deeper understanding of current workload as well as safe sterile compounding capacity.

Objective: Determine the total daily capacity by measuring the time for fixed tasks and variable tasks. Comparing the sterile compounding procedure against Sterile Compounding Guidelines.

Methods: This study will capture the workflow details daily from Monday to Friday. Data collection will be done using a pre-completed data collection form. Data is divided into variable and fixed tasks. Additionally, the final delivery form (IV bag, syringe or infuser) is also recorded. Fixed time is measured using a timer. Variable time will be measured using a clock located in the clean room. Secondary objective is measured against a predetermined checklist. Data analysis is performed on Excel.

Results: The average time to prepare one compound is 5 minutes and 43 seconds. The total morning maximum capacity is 47 compounds. Certain drugs require longer reconstitution time.

Conclusion: Current maximum capacity may be increased should there be any future increases in demand for sterile compounded chemotherapeutic drugs.

Stability of Dr. Reddy's Cabazitaxel in the Manufacturer's Original Vials, and Non-PVC Bags at -20°C, 4°C, and 25°C

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Background: Generic versions of cabazitaxel raises the question about the reliability of extending stability data between brands.

Objective: To evaluate the stability of Dr. Reddy's cabazitaxel reconstituted with the manufacturer's diluent then diluted to concentrations of 0.1 and 0.26mg/mL with 0.9% sodium chloride (NS) or 5% dextrose (D5W) stored in non-PVC bags at 25°C and 4°C for 21 days and -20°C for 49 days. Three additional vials of cabazitaxel reconstituted with the manufacturer's diluent to a concentration of 10mg/mL in the original glass vial were evaluated at -20°C for 49 days.

Methods: On day 0, Dr. Reddy's cabazitaxel was reconstituted in the original glass vial with the provided diluent to a concentration of 10mg/mL and three vials were stored at -20°C. The remaining vials were further diluted to concentrations of 0.1 and 0.26mg/mL with NS and D5W in non-PVC bags. Three units of each were stored at 25°C, 4°C, and -20°C. Physical inspection and concentrations were evaluated on days 0,1,2,3,4,5,7,9,11,14,18,21 for samples stored at 25°C and 4°C; and on days 0,7,14,21,28,35,42,49 for samples stored at -20°C.

Results: The analytical method separated degradation products from cabazitaxel such that the concentration was measured specifically, accurately (deviations from known averaged 0.93%) and reproducibly (replicate error averaged≤1.04%). Multiple linear regression revealed significant differences in percent remaining due to study day ($p<0.01$), diluent ($p<0.01$), temperature ($p<0.01$), and concentration ($p<0.01$). During the study period, solutions retained ≥98% of the initial concentration for all diluents, concentrations, and storage temperatures.

Conclusions: Dr. Reddy's cabazitaxel reconstituted and diluted with NS and D5W to concentrations of 0.1 and 0.26mg/mL are physically and chemically stable ≥21 days when stored in non-PVC bags at 25°C and 4°C. When stored at -20°C, all concentrations and diluents, including 10mg/mL reconstituted with the manufacturer's diluent stored in original glass vials, are stable for ≥49 days.

Hospital Pharmacists' Readiness to Independently Prescribe or Deprescribe Controlled Substances and Narcotic Medications

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Background: Pharmacists practicing in Alberta, Canada have had an expanded scope of practice since 2007. Any pharmacist can legally continue and prescribe narcotic and controlled substances during states of emergency like the Fort McMurray wildfire or the pandemic. We sought to measure and compare Alberta pharmacists' attitudes towards prescribing or deprescribing of controlled substances and narcotics in non-emergency situations.

Objective: The primary objective was to compare the attitudes between community and hospital pharmacists in Alberta towards independently prescribing or deprescribing narcotics and controlled substances. The secondary objectives were to assess their level of readiness, identify barriers and determine ways that pharmacists would use this authority to improve patient care.

Methods: The study was an anonymous self-administered electronic survey of pharmacists registered with the Alberta College of Pharmacy who agreed to receive emails about research. The survey was composed of multiple choice, ranking, and open-ended questions to gather demographic data, practice setting information and attitudes towards both independently prescribing and deprescribing narcotics and controlled substances. Data was quantified and reported from responses received.

Results: Of the 1135 surveys returned, hospital pharmacists made up 15.4% of respondents. Compared to community pharmacists hospital pharmacists were more motivated (28.6% vs.17.4%) and felt it was more important (28.6% vs. 18.2%) to have the authority to prescribe or deprescribe narcotics and controlled drugs. Advantages were better crisis management, improved patient care and increased autonomy. Patient expectations, liability, lack of follow up and need for training were identified as barriers.

Conclusion: Hospital pharmacists are more willing to incorporate prescribing and deprescribing of narcotics and controlled drugs into their practice than community pharmacists.

Exploration of Patients' Perspectives on Enablers and Barriers to Medication Adherence in the Treatment of Depression

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Background: Non-adherence to antidepressants is well-described, with up to 60% of patients discontinuing antidepressants within the first three months. To our knowledge, few studies have explored patients' perspectives regarding their needs and expectations around antidepressants. A better understanding of these factors will benefit the development of educational strategies that improve medication adherence and treatment outcomes in patients with depression.

Objectives: To identify and describe patients' enablers and barriers to adherence to antidepressants, and to explore the educational needs of patients around initiating or continuing antidepressants.

Methods: A qualitative descriptive study using individual, semi-structured interviews was conducted. Eligible participants were outpatients at an academic family health team diagnosed with depression and who had a new antidepressant prescription within three months of recruitment. Interviews were performed by phone or video, audio-recorded, and transcribed verbatim. Transcripts were coded using inductive thematic content analysis by two independent coders.

Results: This was a pilot study based on the transcripts of 4 patient interviews. Four key themes were identified: perceived effects of antidepressants, patient-provider relationship, access and ease of administration, and social relationships. In terms of enablers, participants alluded to visual reminders, feeling informed by their healthcare provider, and observing noticeable improvement in their mood. In terms of barriers, participants reflected on social stigma, perceived subtle benefits of the medication, and adverse effects from taking antidepressants. Patients expressed that education should be evidence-based, tailored to their symptoms, and presented in both written, verbal, and digital formats.

Conclusion: In order to address key barriers and identify benefits to treatment, a combination of strategies targeting both patients and prescribers should be implemented. Examples include shared-decision making, regular patient-provider follow-up, and identifying personalized treatment goals.

PHARMACY PRACTICE / PRATIQUE PHARMACEUTIQUE

"Good job!" Feedback Training for Pharmacists Teaching in a PharmD Program Simulation Lab

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Background: Feedback is an essential element for pharmacy students on their path to professionalization and widely used in professional practice labs. However, students report that they receive poor quality feedback. This is also reflected in the literature. Our professional practice labs are facilitated by pharmacist clinical instructors (CIs) who are generally selected based on clinical proficiency as opposed to teaching skills. Nevertheless, if CIs are not able to communicate their clinical knowledge and observations in a useful and meaningful way, it will hinder student growth and achievement of required practice competencies.

Description: We describe an intervention rooted in a cognitive constructivist paradigm to improve the quality of CI's written feedback in a required 3rd year patient care simulation lab in a PharmD. Program.

Action: An orientation workshop was developed and included experiential training on providing effective feedback. All CIs (n=45) observed a role play involving a student-patient interaction and provided written feedback using the course rubric. CIs then conferred with each other in small groups to discuss their ratings and comments, and to reconcile or justify any differences. This activity was followed by a didactic session on best practices in feedback and writing comments.

Evaluation: A post-session survey indicated 100% of participants either strongly agreed or agreed that the session helped them prepare for their role. CIs felt the feedback activity was helpful to benchmark their assessments with each other and gave them a better understanding of the expectations of each component of the rubric. Respondents also reported an improved understanding of the types of comments that were useful to foster student development. Suggestions for improvement included increasing opportunities to practice. Anecdotally, students have reported increased satisfaction regarding the practicality of CI's feedback.

Implications: A simple intervention can improve feedback quality and could be used in future experiential practice settings.

Baseline Inventory of SHA-Regina Pharmacy Department's Wellness and Environmental Priorities

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Background: Workplace wellness programs led by frontline committee members have demonstrated improved health behaviours, reduced elevated health risks, improved productivity, and improved satisfaction. Wellness also includes the health of the environment, which healthcare has a significant impact on through single use plastics, pharmaceuticals, and other personal and professional practices.

Description: A Pharmacy Department wellness committee (Living Well Committee) was established with the mission to promote and implement initiatives for 1) environmental sustainability applicable to the workplace and at home, and 2) enhanced pharmacy employee's wellness in all domains. The first goal of this committee was to complete a staff wellness and environmental inventory to serve as a baseline for prioritizing and measuring committee activities.

Action: A presentation to staff was completed to introduce the Living Well Committee and provide context for departmental wellness and environmental issues. The environmental inventory consisted of observing and documenting current practices within the department in main categories (e.g., paper use, plastic use, recycling, power use). The wellness inventory involved pharmacists and pharmacy technicians independently completing a validated wellness assessment. Staff were then asked to complete a survey to identify the top three wellness domains and environmental priorities for the Living Well Committee.

Evaluation: The environmental and wellness survey was completed by 22 staff members (22/80, 28%). The top three wellness domains identified were occupational (32%), environmental (23%), and emotional wellness (18%). The top environmental areas were paper use (73%), recycling (64%), pharmaceutical use and wastage (55%), and single-use plastics (50%). These responses were corroborated by the environmental inventory.

Implications: The Living Well Committee will use the survey results to tailor initiatives based on identified priorities. This will ensure initiatives align with departmental needs to support a healthy and sustainable workplace, which will enable staff to provide optimal and environmentally sustainable patient care.

Reducing Pharmacists' Alert Fatigue: A Data-Informed Approach

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

Description: In 2019, North York General Hospital (NYGH) began to utilize a data analytics tool to quantify and guide efforts to improve pharmacists' alert fatigue. Additional information including type, severity and frequency of medication CDS alerts were also reviewed. At baseline, pharmacists dealt with over 80% of all medication CDS alerts at NYGH amounting to approximately 373 alerts per day per pharmacist. Pharmacists' override rate was over 90% indicating a high likelihood of alert fatigue. Data analysis showed that alerts were mainly for non-significant duplicate orders or drug interactions.

Action: Three targeted interventions were designed to reduce pharmacists' alert fatigue. First, a filter to suppress unnecessary duplicate checking with home medications was implemented. Second, the drug-drug interaction alerts firing threshold was increased from "moderate" to "major". Finally, shifting of "moderate" drug interaction alerts from an interruptive to a non-interruptive, on-demand function.

Evaluation: Alerts decreased by 74.3% when comparing the data 1 month prior to 1 month post- implementation. For NYGH pharmacists, this reduced alerts to 97 per day per pharmacist. However, override rate was minimally reduced from a pre-intervention rate of 97.3% to a post-intervention rate of 96.0%. Further analysis on override rates and improvements are being planned for next phase.

Implications: Data analytic tools help to quantify medication CDS alerts, guide system improvements and identify areas for further analysis. It is imperative that hospital pharmacies review and re-assess alert settings periodically to manage excess alerts and to decrease alert fatigue.

Systèmes d'aide à la préparation magistrale de médicaments : une revue de littérature

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Introduction : Une bonne compréhension du flux de travail des préparations magistrales stériles et non stériles est nécessaire à la prestation sécuritaire de soins. De plus, le cadre normatif applicable aux préparations magistrales est de plus en plus exigeant.

Objectif : Décrire la littérature entourant les systèmes d'aide à la préparation magistrale de médicaments (SAPMM).

Méthode : Revue de littérature à partir de Pubmed, Embase, Google Scholar. Ont été inclus les études comportant une évaluation de l'impact des SAPMM publiés en anglais ou en français du 1er janvier 2015 au 31 décembre 2020.

Résultats : Des 31 études identifiées par le titre, 16 ont été retenues après analyse du résumé et du texte. Une majorité des études proviennent des États-Unis (75%, 12/16); plusieurs études évaluent l'impact pré-post d'un SAPMM (63%, 10/16). Les études évaluent des produits commerciaux (14/16) ou maison (2/15). Les SAPMM incluent, selon la solution proposée, un logiciel d'aide à la préparation (16/16 études), l'utilisation de lecteurs code-barres (15/16), la prise de photos ou de vidéos (16/16) et la gravimétrie (6/16). Les études ont évalué l'impact des SAPMM sur les erreurs (13/16), le temps de préparation (7/16) et de validation (4/16), sur les coûts (6/16) et la satisfaction du personnel de la pharmacie (3/16). Plusieurs études suggèrent que les SAPMM sont associés à une détection accrue des erreurs de préparation et une perception de sécurisation du circuit de préparations magistrales. Toutefois, il est difficile de conclure à l'impact des SAPMM sur la charge de travail et les coûts.

Conclusion : L'utilisation de SAPMM est associée à une capacité accrue de détection d'erreurs de préparation. D'autres travaux sont nécessaires afin d'évaluer le rapport avantage-coût de ces systèmes.

Mots clés : Préparations magistrales, systèmes d'aide à la préparation magistrales, erreurs

Implementing a Pharmacist Scope of Practice Policy in a Large Community Teaching Hospital

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Background: As pharmacist scope of practice evolves, opportunities arise for hospital pharmacists to practice more independently. Traditional models can lead to delays in addressing drug therapy problems and optimizing medication management.

Description: The Pharmacists' Clinical Scope of Practice Policy grants hospital pharmacists the ability to independently adapt and modify prescriptions, reorder home medications, and order lab tests, if in the patient's best interest and the pharmacist possesses the necessary knowledge, skills and judgement.

Action: A stepwise roll-out process was conducted to ensure smooth and sustainable implementation of the policy. Existing policies and surveys were utilized to assess current practice and hospital pharmacists' perceptions on full clinical scope. Meetings with stakeholders were conducted to obtain feedback on policy development and education strategies. The policy received final approval by the Medical Advisory Committee. Before implementation, policy awareness was created through pharmacist training sessions, and hospital-wide communication. Post-implementation, weekly touch-points and quality assurance activities were organized.

Evaluation: We sought to characterize and assess the impact of the policy by conducting a post-implementation Plan-Do-Study-Act (PDSA) cycle. In total, 479 orders were written over the first 30 days by pharmacists under the scope of practice policy. Preliminary analysis of the data has suggested 97.7% of pharmacist orders complied with the policy. The leading intervention was adaptations (49.7%), and 57.4% of interventions have enhanced patient safety. A sustainability PDSA cycle is planned for 1 year post-implementation.

Implications: Pharmacists adhered to the Pharmacists' Clinical Scope of Practice policy and their interventions led to improved efficacy, safety and optimization of medical management. Further understanding its impact and pharmacists' experience, may empower pharmacists to practice at their fullest scope and could inspire change within the current model of hospital pharmacy practice.

Seamless Care between Clinical Pharmacists Caring for Patients with COVID-19 through the Implementation of an Electronic Handover Tool

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Background: At the beginning of the COVID-19 pandemic, it was predicted that hospitals would accommodate both a high volume of COVID-19-related patient admissions as well as frequent patient transitions of care, including discharge. Effective communication between healthcare providers during transitions of care is crucial for promoting patient safety and continuity of care.

Description: A mnemonic-based electronic handover tool was created to facilitate streamlined communication between clinical pharmacists caring for patients hospitalized with COVID-19.

Action: The *COVID Handover Tool* was developed, refined, and implemented by clinical pharmacists working in COVID-19 care areas in early 2020. The tool provided a standardized template to communicate basic patient information and pharmaceutical care issues. The patient-specific handover tools were stored centrally using OneNote™, and shared for updating amongst pharmacists as patients transitioned between COVID-19 care areas (e.g., intensive to acute care).

Evaluation: Pharmacists were surveyed to assess the tool's ease of use, perceived usefulness, and other subthemes. All eight clinical pharmacists working in COVID-19 care areas responded to the survey (100% response rate). The majority of respondents agreed or strongly agreed it was easy to learn to use the tool, and that the content was relevant and organized. Half agreed or strongly agreed that the tool made handover easier, quicker, and more effective. Responses trended towards neutrality regarding the tool being useful in respondents' jobs. Most pharmacists continued using previous handover methods in addition to or instead of the tool.

Implications: Survey responses suggest the *COVID Handover Tool* is intuitive, and facilitated organized and efficient patient handover between clinical pharmacists. Pharmacist perceived usefulness during the study period was mixed, and the tool has been updated further based on feedback. The tool is adaptable to any patient care area or population, and may be useful to other institutions for patient handover between clinical pharmacists.

Quality Audit of Best Possible Medication Histories by Pharmacy Technicians in Ambulatory Care Clinics

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Background: In 2019, the organization implemented electronic Medication Reconciliation (eMedRec) in Ambulatory Care clinics where medication management was a major component of care, and where medication

reconciliation must be provided, according to Accreditation Canada. Four clinics requested pharmacy technicians' support to document the Best Possible Medication Histories (BPMHs).

Description: Pharmacy trained and deployed pharmacy technicians to document BPMHs for patients at their initial visits with a prescriber. In 2020, the organization sought to measure the quality of the BPMHs obtained by pharmacy technicians by comparing them to BPMHs obtained by pharmacy students who had been trained and certified by pharmacists.

Action: In July 2020, two pharmacy students were trained by a pharmacist to obtain BPMHs. Checklists were developed to provide the pharmacy students with criteria to compare documentation. The students met with the technicians prior to the audit to explain the reason for the audit, and show them the measurement criteria. The pharmacy students called and obtained BPMHs for patients previously contacted by technicians. The students then compared the BPMHs they obtained with the BPMHs obtained by the technicians. They then identified and recorded the differences between the two BPMHs. The pharmacy students conducted the audit from July 30 to August 11, 2020.

Evaluation: The pharmacy students contacted 102 patients and reviewed 679 order sentences/prescriptions. Four discrete items were compared on each order sentence. The total number of discrete items compared equals 2,716. This number is the denominator. There were 111 differences between the BPMHs documented by technicians and the BPMHs obtained by students. This represents a 96% concurrence rate between the BPMHs completed by the technicians and the BPMHs recorded by the students. This accuracy is consistent with that stated in the literature.

Implications: Utilizing pharmacy technicians to document BPMHs is an effective and efficient option for ambulatory clinics.

Gestion des approvisionnements de médicaments en pandémie à la COVID-19 : expérience québécoise en établissement de santé

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Contexte : Un état d'urgence sanitaire a été déclaré le 13-3-2020 au Québec et des pénuries de médicaments étaient anticipées.

Description : Décrire la gestion de l'approvisionnement en médicaments hospitaliers durant la pandémie à COVID-19.

Action : Une cellule de crise composée de six chefs de départements de pharmacie est formée, arrimée à deux pharmaciennes conseil, le personnel des groupes d'approvisionnement en commun et le Ministère de la santé. Une liste de 120 médicaments critiques et une simulation des besoins par jour-patient COVID-19 est établie avec mise à jour périodique en tenant compte de sondages terrain auprès de pharmaciens de soins intensifs et des projections ministérielles en nombre de cas anticipés. Des rencontres sont organisées avec les fabricants afin d'évaluer les enjeux. En vertu d'un arrêté ministériel, deux réserves de médicaments sont établies (#1-mai-août 2020 et #2-septembre 2020-juin 2021) avec la collaboration des grossistes. Différentes rencontres statutaires sont établies afin de discuter et de relayer l'information à tous les chefs de départements. De nombreuses actions sont menées (p.ex. demande de changement de priorisation de fabrication de médicaments auprès de certains fournisseurs, changements de pratiques cliniques, partage de médicaments inter-hôpitaux pour limiter les pertes par péremption, partage urgent pour pallier des pénuries). Les seuils d'inventaire de médicaments par hôpital sont rehaussés: médicaments critiques (>90 jours), autres médicaments (>60 jours), médicaments d'oncologie (>30 jours).

Évaluation : En dépit du nombre d'hospitalisations liées aux deux vagues d'infections, il n'y a pas eu de pénuries de médicaments dans les hôpitaux du Québec et nous sommes en mesure de faire face à la prochaine année.

Implications : La cellule de crise de pharmaciens hospitaliers est pérennisée avec la création du Centre d'acquisitions gouvernementales du Québec. La prestation sécuritaire de soins repose notamment sur un approvisionnement adéquat de médicaments et des actions concertées avec les chefs de département de pharmacie hospitaliers.

Mots clés : COVID19, Approvisionnement en médicaments, hôpital, pénurie

Evaluation of Expanded Pharmacist Coverage in Critical Care Areas during COVID-19

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Background: During the first wave of the COVID-19 pandemic, an increased need for critical care pharmacist (CCP) coverage in the two medical/surgical intensive care units (ICUs) at the Queen Elizabeth II Health Sciences Centre (QEII HSC) in Halifax, Nova Scotia was identified.

Description: CCP coverage was expanded in two medical/surgical ICUs from 8 hours per day, 5 days per week excluding holidays to 8 hours per day, 7 days per week including holidays.

Action: Workflow within the pharmacy department was rearranged so that two CCPs, on a rotating schedule, provided dedicated clinical coverage to each ICU seven days a week. CCPs were not responsible for dispensary coverage during this time period.

Evaluation: A 22 question survey was developed by the research team and distributed to all health care providers (HCP) who work in the medical/surgical ICUs. Survey questions solicited HCP perceptions and opinions on the impact of expanded CCP coverage; importance of 25 evidence-informed CCP activities was assessed via 5-point Likert scale. Clinical pharmacist output, reported as the number of drug-therapy problems (DTPs) addressed over a 6-week period, was retrospectively evaluated. The majority of respondents agreed/strongly agreed with the following: CCP are integral members of the multidisciplinary healthcare team, CCP play an important role in improving patient outcomes, CCP presence in the unit and on patient care rounds allows HCP to concentrate on their own professional responsibilities, and that the expanded CCP coverage improved patient care. The majority of respondents categorized 23 of the 25 CCP activities as very important. During the 6-week time period, four CCPs addressed 798 DTPs for 140 discreet patients: an average of 5.7 DTPs per patient.

Implications: HCPs felt that expanded CCP coverage improved patient care and that evidence-informed CCP activities were very important. Given the perceived impact of CCP in the ICU, novel staffing models are being explored to optimize CCP coverage.

Development and Implementation of a Novel Model for Pharmacist Practice Expectations on Medicine Wards in Hospital: The Pharmacists' Circle of Care

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Background: Our pharmacy program previously set task-list style practice expectations based on staffing levels for mixed acuity wards. Regional restructuring based on acuity created a need to redefine pharmacist practice expectations in medicine.

Description: The *Pharmacists' Circle of Care* (PCC) is a novel approach to practice expectations. The PCC transforms the task-list style approach into a fluid decision making tool allowing pharmacists to use their professional judgement to prioritize work while still providing guidance regarding the standardized activities expected of decentralized clinical pharmacists. The PCC maintains a minimal number of mandatory activities, then describes other functions paired with a 4-level prioritization scheme.

Action: A group of clinical resource pharmacists developed a practice model for medicine wards. Small group, problem-based training sessions with facilitated discussions were provided to front line pharmacists at 3 hospitals.

Evaluation: An online survey was conducted at the 3 hospitals to gather feedback on the PCC. The primary objective was to determine pharmacists' perceptions of the utility of the PCC. Secondary objectives were to better understand where pharmacists perceive their time is spent and to determine how frequently pharmacists utilize this practice model. The survey was circulated to 29 pharmacists; 19 responded (66%). Respondents indicated they used the PCC for training new staff as well as teaching pharmacy learners (15, 79%), followed by prioritizing their own work (7, 37%). Respondents indicated that the PCC confirmed what they already do when prioritizing daily work tasks (14, 74%); this indicates this tool is reflective of the realities of hospital practice. Most respondents indicated their activities were ones which prevented imminent harm (7, 37%) promoted patient flow (4, 21%) or were mandatory (4, 21%).

Implications: The PCC empowers pharmacists to prioritize their activities to have the greatest impact on patient care while balancing the demands of a fluid practice environment.

The Pharmacy Services Employee Engagement Team Journey

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Background: Alberta Health Services (AHS) Pharmacy Services employee engagement team formed in 2018 as a change network of leaders and employees nicknamed the Rebel Alliance (RA). The purpose was to develop, implement, monitor and sustain the AHS Pharmacy Services Pharmacy Services strategic objective of ensuring that pharmacy employees are actively engaged in transformative changes.

Description: The RA supports pharmacy leaders in improving skills and knowledge in active listening of frontline employees, showing respect and appreciation for their opinions and actively involving employees in decision making opportunities.

Actions: The RA launched a communication strategy involving storytelling through the Star Wars theme, paralleling characters and universal concepts of rebellion with healthcare language and ideas of patient safety, just culture, and employee engagement. The formation of mini-networks amongst members of the Pharmacy Leadership Team (PLT) helped build capacity for engagement work throughout Alberta.

Evaluation: The RA grew from five individuals in July 2018 up to16 members from across the province. Additionally, 30% of PLT signed a pledge of commitment to enhance employee engagement as well as participated in sessions about the importance of opinions, as outline in Table 1. Lastly, the strategic objective will be further evaluated through the results of the 2019 AHS Gallup survey, with a goal to increase the engagement score of employees to feel that their opinion counts to 4.0 (out of a 5 point Likert scale) by 2021. In 2016, AHS Pharmacy Services employees answered this question with a mean of 3.29.

Implications: The implications of enhancing employee engagement is greater employee retention, positive patient experiences as well as improved safety and quality care outcomes.

For the table that goes with this abstract, please see Abstract Appendix, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/204

Using Gap Analysis Tools to Determine Compliance with Hazardous Sterile Preparation Standards in Chemotherapy Outreach Program of Saskatchewan Sites

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Background: Compliance with National Association of Pharmacy Regulatory Authorities (NAPRA) model standards is required by the Saskatchewan College of Pharmacy Professionals.

Description: To assess current state compared to the NAPRA model standards a gap analysis can be completed. Conducting the gap analysis survey at all Chemotherapy Outreach Programs of Saskatchewan (COPS) sites provides an opportunity to determine local and provincially commons deficiencies. For completeness, Saskatchewan Cancer Agency (SCA) sites in Regina and Saskatoon were also included in the gap analysis.

Action: The CSHP Assessment Tool for Aseptic Compounding (ATAC) was purchased for each site to provide gap analysis based on CSHP Compounding: Guidelines for Pharmacies (2014). An in-house survey we named the Hazardous Sterile Preparation Assessment Tool (HSPAT) was developed to survey specific statements for hazardous sterile compounding also based on the CSHP Compounding: Guidelines for Pharmacies (2014). Both tools cross referenced for statements similar to the NAPRA standard.

Evaluation: Across the 11 Key Parameters for sterile preparation identified by ATAC, the average score was 58.5% for non-urban sites while large urban sites scored better at 71.6 %. The parameters directly associated with the compounding process (5, 6, and 7) the scores improved to 79.1% for COPS and 76.3% for SCA sites.

Implications: Within Saskatchewan, pharmacies are quite good at preparing to compound, compounding, and labelling of sterile hazardous preparations. Improvements are generally needed to controlled work areas, staff training, and quality assurance processes. A standardized, province-wide program should be developed to address gaps followed by repeating the gap analysis survey to gauge success.

For the figure that goes with this abstract, please see Abstract Appendix, available at https://www.cjhp-online.ca/index.php/cjhp/issue/view/204

The Impact of Pharmacist-Initiated Screening on Influenza Vaccination Status of Hospitalized Patients at a Community Academic Hospital

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Background: Approximately 12,200 Canadian hospitalizations are attributable to influenza each year, straining valuable resources. Routine influenza immunization is a key preventative measure that can significantly reduce hospitalizations, yet immunization remains below the national goal for high-risk patients. Many discharged patients remain unvaccinated representing a missed opportunity for hospitals.

Description: Standing orders have shown to improve in-patient immunization, however, assessment is a required step despite vaccine eligibility. Pharmacists can serve an important role by assessing vaccination history and eligibility. To increase immunization rates of patients at a community academic hospital, pharmacist-initiated influenza vaccination screening was implemented in the 2013-14 influenza season.

Action: A standardized workflow was developed for pharmacists to proactively assess and identify opportunities for influenza immunization in hospitalized patients which included: initial screening during the Best Possible Medication History interview, confirmation of vaccine eligibility and patient consent, and discussion of vaccination with the most responsible provider. Electronic documentation templates and yearly pharmacist education sessions were developed to facilitate the process.

Evaluation: A statistical process control chart was retrospectively constructed for 9 influenza seasons (2010-11 to 2018-19) using influenza vaccine orders (IVO) and pneumococcal vaccine orders (PVO) as a non-dependent control. Pharmacist-initiated screening resulted in special-cause variation starting in 2013-14, with 1 standard deviation (8.7 orders/1000 admissions), 2 standard deviations (11.3 orders/1000 admissions) and exceeding the upper control limit (13.8 orders/1000 admissions) by the last 2 years of analysis. PVO rates did not show special-cause variation. Mean IVO per season increased by 126% after implementation of pharmacist-initiated screening (6.2±1.5 vs. 14±1.9 orders/1000 admissions, $p<0.05$) and was consistent in the adult subgroup ≥60 years. No change was observed in PVOs.

Implications: Pharmacist-initiated vaccination screening led to increased influenza immunization rates. Expansion of in-patient pharmacist-initiated vaccine screening for other important vaccines (e.g. pneumococcal) should be considered for improved uptake.

Audit of Clinical Pharmacists' 3-Day Antimicrobial Reviews Using EPIC®

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Background: Research has shown that pharmacists play an integral role in improving the appropriateness of patient's antimicrobial therapy, dose with therapeutic drug monitoring and reducing antimicrobial costs. At our institution, the unit pharmacists and the dedicated antimicrobial stewardship pharmacist play an important role in evaluating antimicrobial therapy for their respected teams.

Description(s): Through the use of the electronic health information system (EPIC®) an antimicrobial tool was developed which prompts pharmacists to reassess and document their assessments of their patients' antimicrobials after three days of therapy. It is an expectation of the clinical pharmacists to review and document their assessments of their patient's antimicrobial therapy for interventions such as intravenous to oral step down, spectrum narrowing, and therapeutic drug monitoring.

Action: An audit was done throughout July 2020 to assess how often pharmacists on inpatient units were completing the antimicrobial review on the third day of therapy and on the quality of documentation of the assessment.

Evaluation: It was found 65% of all reviews were being completed on the 3rd day of therapy. When analyzed by different units; the intensive care unit (ICU) had the highest rate, 91%, followed by general internal medicine (GIM), 81%. Quality assessments of documentation were completed for the ICU and GIM units. In review of the documentation; ICU and GIM pharmacists documented the antibiotic 100 versus 96%, indication 100 versus 96%, duration 83 versus 93%, dose 93 versus 1% and pharmacists' next steps 90 versus 49% of the time respectively.

Implications(s): To improve best practices to better patient care two practice changes were recommended from these results; 1) Standardized documentation using a smart phrase manager for thorough assessment and 2) Documenting assessments in patients' charts to further foster implementation of interventions and to advocate for the pharmacist's role in antimicrobial stewardship.

Redesigning a Pharmacy Resident Antimicrobial Stewardship Rotation

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Background: Antimicrobial Stewardship (AS) is a mandatory one-week pharmacy resident program rotation. Prior to 2020, five residents would complete this rotation individually. The model consisted of daily clinical AS rounds, twelve hours of AS teaching sessions and a 3-hour resident lecture series. A 3-week Infectious Diseases (ID) rotation follows later in the year.

Description: A formal redesign of the resident rotation structure was trialed to improve the quality and efficiency of AS content delivery for five residents.

Action: The AS rotation was restructured to have all 5 residents complete their one week of AS training concurrently. Residents participated in prospective audit-and-feedback (PAF) AS rounds and targeted antimicrobial reviews then tracked their own metrics. They also participated in 15 hours of case-based education sessions on clinical microbiology, antimicrobial stewardship metrics, pharmacokinetics, pneumonia, urinary tract infections, skin/soft tissue infections, perioperative antibiotics, and antibiotic allergies. A pre-post rotation survey was administered.

Evaluation: Preceptors indicated that the new model created consistency and efficiency in curriculum delivery. It set a foundation to increase residents' comfort working up more complex patients on subsequent rotations. Pre and post-rotation surveys indicated that residents felt more confident being able to identify and intervene on antimicrobial drug therapy problems. They also reported a better understanding of antimicrobial stewardship and how to apply metric analysis to quality improvement initiatives. Over 1 week, residents reviewed 439 antibiotic orders and identified 129 interventions. Seventy percent of the interventions occurred during PAF rounds versus targeted antibiotic reviews.

Implications: Overlap of pharmacy residents in a rotation can be an effective method of mentoring pharmacy residents in AS and ID related topics. This model offers the benefit of collaborative education, consistency in foundation of antimicrobial knowledge, offers a forum for knowledge application and increases efficiency for preceptors.

Patient Pay Iron Infusion in an Ambulatory Care Setting

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Background: Choosing Wisely Canada recommends to limit the use of blood transfusions in hemodynamically stable anemic patients, which led to an increased use of iron infusions in the ambulatory care setting. Iron isomaltoside, a new intravenous iron approved by Health Canada in 2018, is offered to outpatients in addition to iron sucrose starting April 1, 2020.

Description: Drug access facilitator pharmacy technicians helped patients navigate the switch to iron isomaltoside from iron sucrose depending on patient coverage and preferences. Iron sucrose is covered under the Exceptional Access Program (EAP) through the Ontario provincial government while iron isomaltoside is only covered by private insurance.

Action: A hospital iron task group created order sets and a patient information pamphlet to facilitate the change to patient pay iron infusions. Iron sucrose has appeared to require a lengthier infusion time requiring longer chair time compared to iron isomaltoside. To evaluate this observation, an audit was conducted on patient usage of iron sucrose and iron isomaltoside.

Evaluation: Iron sucrose patient data was collected and compared from April 1, 2019 to March 31, 2020, and from April 1, 2020 to Dec 31, 2020. A total of 243 patients used iron sucrose in 2019 while 77 and 92 patients, respectively, used iron sucrose and iron isomaltoside in 2020. Iron sucrose required a 2-14 days lag time for EAP approval while iron isomaltoside did not. Iron sucrose also required lengthier infusion time ranging from 5.5 to 6 hours while iron isomaltoside required an average of 2 hours infusion time. Revenue from prescriptions was $2068.10 for iron sucrose and $5069.93 for iron isomaltoside.

Implication: Using iron isomaltoside in the ambulatory care setting decreases chair time and has no approval lag time, while providing a greater source of revenue to the outpatient pharmacy in comparison to iron sucrose.

CASE REPORTS / OBSERVATIONS CLINIQUES

Adrenal Insufficiency Secondary to Inhaled Corticosteroids in Paediatric Twins

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Background: Inhaled corticosteroids (ICS) are the first-line treatment for asthma in paediatrics. Through suppression of the hypothalamic-pituitary-adrenal axis, ICS therapy has been associated with adrenal insufficiency; however, the incidence and risk factors are not well described.

Case Description: Four-year-old identical twin girls were found to have adrenal insufficiency following long-term, high-dose ICS therapy. Both patients were diagnosed with asthma before age one and subsequently treated with mometasone, titrated to 800 mcg/day. After multiple admissions for acute otitis media and other respiratory infections, endocrinology investigations resulted in a diagnosis of adrenal insufficiency for both girls. Chronic oral hydrocortisone was initiated as physiologic replacement with planned stress dosing to prevent hospital admissions, and the dose of maintenance ICS was decreased.

Assessment of Causality: Based on the Naranjo Scale, this case is considered a probable adverse drug reaction (score = 8). The same reaction occurring in identical twins both on high-dose ICS therapy is another compelling argument for causality.

Literature Review: A Cochrane review investigating adrenal insufficiency manifesting as growth suppression found that children receiving high-dose ICS exhibited slower growth velocity compared to low-dose ICS. A nested case-control study showed greater risk of hospital-diagnosed adrenal insufficiency with higher doses of ICS (odds ratio 1.84; 95% confidence interval 1.16-2.90). There are few studies comparing the frequency of adrenal insufficiency with different ICS, but some data suggests ciclesonide carries less risk of adrenal suppression.

Importance to Practitioners: Adrenal insufficiency can be a serious consequence of ICS treatment, and no guidance on the choice of ICS in this context exists. Patients on long-term, high-dose ICS therapy should be monitored for signs and symptoms of adrenal insufficiency. As accessible front-line healthcare practitioners, pharmacists are well-suited to participate in the safety monitoring of ICS therapy.

Acetazolamide Induced Hypersensitivity Reaction in a Pediatric Low-Grade Glioma Patient: A Case Report

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Background: Acetazolamide is a reversible inhibitor of the enzyme carbonic anhydrase. It can be used off-label for treatment of hydrocephalus, and intracranial hypertension. This case report describes a hypersensitivity reaction to acetazolamide of a young boy for which acetazolamide was being used for increased intracranial pressure post- neurosurgery.

Case Description: We present a 2-year-old male patient with a low-grade glioma who underwent a debulking neurosurgery procedure. Post-surgical procedure he was started on a chemotherapy protocol consisted of vincristine and carboplatin. The following day, he was started on acetazolamide for elevated intracranial pressure and two days after this developed the first of a series of cyclic fevers with chills and a blanchable diffuse red rash that did not appear to be pruritic. He was started on multiple antibiotics and antipyretics that did not aid in the resolution of the fever, and no infectious source could be identified with blood cultures or imaging. It was determined that acetazolamide was the potential cause of a drug-fever and rash and was therefore discontinued 17 days after initiation. The patient's fevers and rash subsequently improved over the course of the next week, and no other cause was identified.

Assessment of Causality: This case of hypersensitivity to acetazolamide would receive a score of 4 on the Naranjo Scale, indicating a possible adverse reaction.

Literature Review: Case reports have described other severe cutaneous adverse reactions such as Stevens-Johnson Syndrome to acetazolamide. A case-series of acetazolamide post-cataract surgery also describes cutaneous adverse reactions.

Importance to Practitioners: Acetazolamide is a medication that is used in hospital to treat patients for different indications. Recognizing that a hypersensitivity reaction could develop secondary to acetazolamide and differentiating this from an infection or other causes is important in discontinuing the causative medication as well as avoiding unnecessary use of antipyretics and antibiotics.

Visual Hallucinations Associated with Levodopa-Carbidopa Formulation Change

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Background: Levodopa-carbidopa is the mainstay therapy for Parkinson's disease (PD). Approximately 5% of patients with PD on levodopa-carbidopa develop visual hallucinations correlated with dose and duration of therapy, as well as PD severity and progression. Levodopa-induced hallucinations often respond to dose reduction. Among the main pharmacokinetic differences between controlled release (CR) and immediate release (IR) formulations are a longer half-life and time-to-peak with the CR formulation, thus producing more stable plasma concentrations and lower likelihood of adverse effects.

Case Description: An 85-year-old woman with PD was well-maintained on IR levodopa-carbidopa for several years. She was inadvertently ordered the CR formulation in hospital and developed visual hallucinations. In response, a dose reduction was made which slightly improved but did not resolve the hallucinations entirely. The pharmacist noticed the discrepancy and switched the patient back to the IR formulation at home dose. The patient's hallucination resolved within 24 hours.

Assessment of Causality: This case of visual hallucination received a score of 4 on the Naranjo Scale indicating a possible association with the use of CR levodopa-carbidopa. The CR formulation was designed to provide release over 1.6 hours, thereby requiring less frequent dosing. As patient received CR formulation at the same frequency, this may have potentially led to drug accumulation and visual hallucinations. Unfortunately, no drug levels were taken to confirm this hypothesis.

Literature Review: A 5-year randomized multicenter study demonstrated that both the IR and CR levodopa-carbidopa formulations maintained similar level of PD control after 5 years, despite its progressive nature. There are no studies comparing the difference between IR and CR formulations in visual hallucination incidences.

Importance to Practitioners: Adverse drug reactions such as visual hallucinations should be considered when switching between levodopa-carbidopa formulations. This case also illustrates the importance of medication reconciliation as this adverse reaction may have been preventable.

Cutaneous Mucormycosis Infection: Isavuconazole as an Oral Stepdown Option in Patients with Contraindicated Drug Interactions to Posaconazole

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Background: Mucormycosis is a fungal infection with high morbidity and mortality and few therapeutic options. Patients most often affected include those with poorly controlled diabetes, hematological malignancies and transplant recipients. The most common pathogens are *Rhizopus* spp, *Mucor* spp, and *Lichtheimia* spp. The hallmark of disease is tissue necrosis and black, necrotic eschars. Successful treatment is dependent on timely diagnosis and involves a combination of surgical debridement and systemic antifungal therapy. Intravenous (IV) liposomal amphotericin B is considered the drug of choice but is limited by the administration route and nephrotoxicity in long-term therapy.

Case Description: Fifty-nine-year-old female with multiple comorbidities including schizophrenia (stable on quetiapine) and poorly controlled type II diabetes mellitus was admitted with right forearm cellulitis that developed a black eschar. The wound was debrided and tissue cultures grew *Rhizopus oryzae*. Intravenous liposomal amphotericin B was initiated. After 2 weeks of IV therapy and good clinical response, the patient was transitioned to oral treatment and discharged. Posaconazole is specifically covered by the Ontario Drug Benefit Exceptional Access Program (EAP) for this indication. A drug interaction between posaconazole and quetiapine excluded its use. Oral isavuconazole was initiated as an alternative and outpatient coverage obtained through the EAP.

Assessment of Causality: Posaconazole is a strong inhibitor of CYP3A4 and can prolong the QT interval. Co-administration with CYP3A4 substrates that also prolong the QT interval (i.e., quetiapine) is contraindicated due to increased risk of proarrhythmic effects. Isavuconazole is a moderate inhibitor of CYP3A4 and in clinical trials resulted in dose-related shortening of QTc intervals.

Literature Review: A 2019 guideline by the European Confederation of Medical Mycology and other publications support the use of isavuconazole as an oral step-down option for stable mucormycosis infections.

Importance to Practitioners: Isavuconazole is an oral-stepdown option for patients with mucormycosis and drug interactions with posaconazole.

Lamotrigine Dosing with Competing Drug Interactions: A Case Report

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Background: In refractory epilepsy, seizure control necessitates multiple anti-epileptic drugs (AEDs), for which drug interactions must be considered. Little is known regarding lamotrigine dosing in the presence of competing interactions. In general, enzyme inhibition occurs faster than induction making dosing of lamotrigine with AED polytherapy challenging.

Case Description: Seven-year-old admitted for refractory status epilepticus. After failing loading doses of levetiracetam, valproic acid, and continuous midazolam infusion, the patient was loaded with phenobarbital and maintenance valproic acid was started. Home medications included lamotrigine, which was held for 2 days and re-started at a 50% dose reduction given the risk of increased levels with valproic acid. Lamotrigine levels ranged from 13.7 to 20.8 µmol/L (reference range of 9 to 60 µmol/L) for the 5-day period after resumption of therapy and no adverse drug effects were reported.

Assessment of Causality: Lamotrigine clearance can be largely influenced by drug interactions. Valproic acid is an enzyme inhibitor that can increase levels by approximately twofold, whereas phenobarbital can decrease levels through enzyme induction. In this case, even with a dose reduction and holding lamotrigine, levels were within therapeutic range.

Literature Review: One study concluded that lamotrigine clearance decreased with the addition of valproic acid, however phenobarbital did not result in a statistically significant increase in clearance. The combination of lamotrigine plus an inhibitor and inducer resulted in decreased clearance, but to a lesser extent than an inhibitor alone. Another study noted combination of lamotrigine with valproic acid and phenobarbital resulted in decreased clearance, however only 4.9% of patients had elevated levels outside of the therapeutic range.

Importance to Practitioners: Drug interactions between lamotrigine and other AEDs can significantly impact the efficacy and safety profile of lamotrigine. Risk of lamotrigine toxicity increases above 60 µmol/L as well as being dependent on the rate of titration.

Entamer des conversations d'une importance capitale sans rompre les ponts

par Shirin Abadi

Au fil des ans, j'ai rencontré plusieurs situations au cours desquelles j'ai observé que des gens, moi y compris, hésitaient à faire part de points de vue importants, car ils s'inquiétaient de la réception de ceux-ci. Il est plus facile d'être d'accord avec les personnes qui nous entourent que d'offrir un point de vue différent, en particulier si nous nous entretenons avec des cadres supérieurs ou des personnes ayant plus d'expérience que nous. Alors, comment doit-on aborder ces situations? Comment entamer des conversations qui revêtent une importance capitale sans rompre les ponts?

Dans certains environnements d'affaires, si vous ne proposez pas de point de vue différent pendant une réunion, vos collègues vous dévalorisent. Les gens s'attendent à obtenir des points de vue différents, qui ne sont pas traités comme des exceptions, et ils n'apprécient guère des raisons comme « On a toujours fait comme ça. » Ils ne préconisent pas la réflexion de groupe, mais ils accueillent favorablement les séances de remue-méninges. En fait, souvent, c'est ainsi que naît l'innovation : en réfléchissant aux idées impensables. Vous savez? Celles qu'on accueille en levant les yeux au plafond?

Mais on pourrait dire que l'environnement des soins de santé est un milieu différent, peu enclin à prendre des risques, qui met une insistance particulière sur la sécurité du patient. Nos options de travail avec les partenaires stratégiques sont limitées, aussi ne voulons-nous pas risquer de rompre nos liens avec eux. Le monde de la pharmacie clinique est relativement restreint, c'est pourquoi, nous ne souhaitons pas que nos paroles ou nos actes se retournent contre nous. Qu'est-ce que je dis face à ces arguments? Le « comment » est aussi important que le « quoi »! Le contenu est important, mais la manière de s'exprimer ou d'aborder une situation est tout aussi importante, sinon plus.

Permettez-moi d'expliquer cela plus en détail en vous indiquant une approche toute simple pour exprimer votre point de vue « radical » :

1. Déterminer l'objectif commun de la discussion. Quel fil conducteur rassemble les intervenants? Quelle est la mission du projet ou la vision sous-jacente, quel est le travail de la commission ou celui du comité, etc.?
2. Cerner le problème que chacun essaie de résoudre. Tout le monde peut-il s'accorder sur ce point?
3. Explorer les options qui peuvent être retenues. Il s'agit d'un aspect crucial du processus, où les gens doivent écouter sans tirer de conclusions hâtives. C'est la phase du remue-méninges. Inviter chacun à creuser et à noter des idées. Créer un espace sécurisant, où l'on accueille une diversité de points de vue.
4. Examiner les avantages et inconvénients de chaque option. Cela peut inclure une analyse des coûts et des recettes, une étude de la sensibilité aux risques ainsi que des considérations budgétaires. Plus votre analyse est approfondie, plus les fondements de votre décision finale seront solides.
5. Prenez votre décision définitive en vous basant sur les étapes 1 à 4.

Ce processus vous dit-il quelque chose? Eh bien, il ressemble à celui que nous utilisons pour déterminer et résoudre les problèmes liés à la pharmacothérapie, où chaque étape d'une communication efficace est empreinte de transparence et de respect. En adoptant une approche systématique pour faciliter les conversations d'une importance capitale, nous pouvons détourner l'attention de la personne qui offre un point de vue différent et nous focaliser sur l'aspect le plus nécessaire de la proposition à faire valoir, soit résoudre un problème important.

[Traduction par l'éditeur]

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Engaging in Crucial Conversations without Burning Bridges

Shirin Abadi

Over the years, I've come across multiple situations in which individuals (myself included) have hesitated to share important perspectives, because of concerns about how the information might be received. It's a lot easier to agree with those around us than to offer a different perspective, particularly if we're talking to individuals in senior roles or those with more extensive experience. So, how should one approach these situations? How does one engage in crucial conversations without burning bridges?

In certain business settings, if you don't offer a different perspective during a meeting, your contribution may be considered less valuable. Offering a diverse opinion is an expectation, not an exception, and using rationales like "this is how we've always done it" are not appreciated. Group-thinking is highly discouraged, and brainstorming is very much embraced. In fact, a lot of times, this is how innovation is born, by considering the unthinkable ideas, you know, the ones that are usually met with rolling eyes!

But, you might say, the health care setting is a different environment, one that is risk averse, where patient safety is highly emphasized. We have limited options for working with strategic partners, so we don't want to burn any bridges. The clinical pharmacy world is relatively small, so we don't want anything we say or do to backfire—and what do I say to all that? It's about the "how" as much as it's about the "what"! Content matters, but how you say something or approach a situation matters just as much, if not more.

Let me elaborate by providing you with a simple approach for expressing your "radical" point of view:

1. Identify the common goal of the discussion. What is the thread that brings everyone together? What is the mission/vision for the project/committee work/departmental task, etc.?
2. Determine the problem that everyone is trying to solve. Can everyone agree on that?
3. Explore the options that can be pursued. This is a crucial component of the process, where people need to be encouraged to listen and to not jump to conclusions. This is the brainstorming phase. Encourage everyone to dig deep and to jot down ideas. Create a safe space where diverse opinions are welcomed.
4. Examine the pros and cons of each option. This may include a cost-benefit analysis, exploration of risk tolerance, and budgetary considerations. The more in depth your analysis, the more solid the rationale behind your ultimate decision.
5. Make your final decision based on steps 1–4.

Does this process ring a bell? Well, it's similar to the process we use for drug therapy identification and resolution, and effective, transparent, and respectful communication is engrained at every step of the way. By using a systematic approach to enable crucial conversations, we can take attention away from the individual offering a diverse perspective and focus on the value proposition where it's needed most: to solve an important problem.

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