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Do We Give Too Much Significance to Statistical Significance?

Lauren Bresee

If you think back to your introductory statistics course during university, you may recall the topic of hypothesis testing, where the null hypothesis states there is no difference between study groups, and the alternative hypothesis states there is a difference between study groups.[1] Now, as a practising pharmacist, you are conducting a randomized controlled trial (RCT) to evaluate whether an intervention you developed improves patients' adherence to their medication therapy after discharge. Study participants will be randomly assigned to receive your adherence intervention or usual care, and adherence at 90 days after discharge from hospital is your primary study outcome. Your null hypothesis is that there is no difference in adherence at 90 days after discharge between the patients who receive your intervention and the patients who receive usual care, and your alternative hypothesis states that there is a difference in adherence between your intervention and control groups. To evaluate your primary outcome, you decide to perform inferential statistical testing to determine whether you will accept or reject your null hypothesis. On the basis of what is commonly reported in the medical literature, you have decided to use a threshold probability (*p*) value of 0.05 to determine whether your intervention group is statistically different from your control group; that is, if the *p* value associated with your statistical test is less than 0.05, you will reject the null hypothesis and conclude that the difference between your intervention and control groups is statistically significant.

The concept of statistical significance and the use of a threshold *p* value (and corresponding 95% confidence intervals) to determine statistical significance have long been sources of controversy in the research community. If you're a statistics nerd like me, you may have noticed a pair of recent publications regarding the use of statistical significance in research. In the first article, an editorial published in March 2019 and entitled "Scientists rise up against statistical significance", Amrhein and others[2] called for no longer using statistical significance to determine whether there is a difference between groups, because the concept of significance is frequently applied dichotomously, instead of being evaluated on a continuum. The authors stated, "Let's be clear about what must stop: we should never conclude there is 'no difference' or 'no association' just because a *P* value is larger than a threshold such as 0.05 or, equivalently, because a confidence interval includes zero."[2] Instead, the authors suggested using confidence intervals as "compatibility intervals", that is, your point estimate and confidence interval are the most compatible with your data, given the statistical model you have used to calculate your results.[2] Going back to the RCT described above, you conduct your inferential statistical test, and your result is a relative risk of 2.0, with a 95% confidence interval of 1.5–2.5 and a *p* value far below 0.001. Under traditional statistical test reporting, you would conclude that the people in your intervention group were twice as likely as your control group to be adherent to their medication therapy at 90 days after discharge, and that this difference is statistically significant because the confidence interval does not encompass the measure of equivalence of 1. However, if you were to use the proposal set out by Amrhein and others,[2] you would instead state that the values for relative risk, 95% confidence interval, and *p* value most compatible with your data indicate that people who received your intervention were twice as likely to be adherent to their medication 90 days after hospital discharge, and that the risk difference between your treatment and control groups ranged from 1.5 times more likely to 2.5 times more likely to be adherent, given the assumptions of the statistical testing.

In rebuttal to the editorial by Amrhein and others,[2] Ioannidis published an editorial the following month in *JAMA*, entitled "The importance of predefined rules and prespecified statistical analyses: do not abandon significance".[3] In his editorial, Ioannidis emphasized that decisions made in medicine are most often dichotomous, and that more focus is being put on inappropriate claims of finding no statistical difference than on addressing "unwarranted claims of 'difference' and unwarranted denial of refutation", particularly when prespecified rules of statistical testing are not developed or followed by researchers.[3] Instead of banning the concept of statistical significance, Ioannidis emphasized that researchers must focus on both following the rules of statistical testing and ensuring that clinical relevance is applied to decision-making.[3] It is clear that under-

lying both of these editorials is the concern that statistical significance testing and *p* values are often used inappropriately.

What is a *p* value, and what is it not? The American Statistical Association (ASA) defines a *p* value as "the probability under a specified statistical model that a statistical summary of the data (e.g., the sample mean difference between two compared groups) would be equal to or more extreme than its observed value."[4] The key items on which to focus in this definition are the specified statistical model and the data that are used in the statistical test. If we use a *p* value threshold of 0.05 to determine statistical significance, this means that the probability a given result is due to chance is less than 5%, specific to the statistical model and the data used for the test. In an effort to reduce the likelihood of misinterpretation of *p* values, the ASA board of directors published a statement on how *p* values should and should not be used.[4] Although *p* values can be used to determine whether there is evidence against the null hypothesis, as mentioned above, such conclusions are specifically applicable to the data used and the assumptions made to calculate the *p* value.[4] The *p* value does not describe the strength of the effect size or the precision of your result (that is, a smaller *p* value does not reflect a larger effect size or a more precise estimate), nor does it represent the probability that the overall study hypothesis is true or due to chance when applied to the population of interest.[4]

There will likely always be controversy associated with statistical significance and the use of *p* values. There are, however, fundamental consistencies within the editorials by Amrhein and others[2] and Ioannidis[3] and the ASA statement[4] that, if adhered to, will help to minimize the controversy. First, we must ensure that the statistical plan for each study is prespecified, transparent, and applicable to the study data.[2-4] Second, the results of all statistical tests conducted, including point estimates, measures of precision such as confidence intervals, and *p* values, must be reported. Such reporting ensures that we are not selectively reporting certain outcomes and allows for the evaluation of the possibility of type 1 error, that is, finding a statistically significant result where none actually exists, due to a multiplicity of statistical tests.[2-4] Third, we must be realistic when interpreting the results of any study and must avoid over- or under-emphasizing the study results.[2-4] Lastly, clinical decisions should never be based on statistical results alone. We must take into consideration other factors, including the study's validity, the consistency of the study's results with other available information, and the generalizability of the results to the overall population under consideration.[2-4] Following these recommendations will help to ensure the appropriate use of statistical testing in research, so that we can make the best possible clinical decisions for our patients.

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Accordons-nous trop d'importance à la signification statistique?

par Lauren Bresee

Si vous repensez à votre cours d'introduction aux statistiques à l'université, vous vous souvenez peut-être du thème de la vérification des hypothèses, où l'hypothèse nulle précise qu'il n'existe aucune différence entre les groupes d'étude et que l'hypothèse alternative précise quant à elle qu'il en existe une[1]. Aujourd'hui, en tant que pharmacien praticien, vous menez un essai randomisé contrôlé (ERC) pour évaluer si une intervention que vous avez développée aide les patients à mieux respecter leur pharmacothérapie après leur sortie de l'hôpital. Les participants à l'étude seront répartis de manière aléatoire dans un groupe d'intervention ou dans un groupe recevant des soins habituels; le respect de la pharmacothérapie 90 jours après la sortie de l'hôpital constitue votre principal critère de jugement. Votre hypothèse nulle veut qu'il n'y a aucune différence d'observance entre les patients qui reçoivent votre intervention et ceux qui reçoivent des soins habituels 90 jours après leur sortie de l'hôpital; votre hypothèse alternative précise qu'il existe une différence d'observance entre votre groupe d'intervention et les groupes témoins. Pour évaluer votre critère principal, vous menez un test statistique par inférence pour décider si vous allez accepter ou rejeter votre hypothèse nulle. Selon ce que rapporte communément la littérature médicale, vous avez décidé d'utiliser une valeur seuil de probabilité (p) de 0,05 pour déterminer si votre groupe d'intervention est statistiquement différent de votre groupe témoin, c'est-à-dire si la valeur p associée à votre test statistique est inférieure à 0,05, vous rejetterez l'hypothèse nulle et conclurez que la différence entre votre groupe d'intervention et le groupe témoin est significative sur le plan statistique.

Le concept de signification statistique et l'utilisation d'une valeur seuil p (et les intervalles de confiance de 95 % correspondants) pour établir la signification statistique suscitent depuis longtemps la controverse au sein de la communauté scientifique. Si vous êtes féru de statistiques comme moi, vous avez peut-être remarqué quelques publications récentes sur l'utilisation de la signification statistique dans la recherche. Dans le premier article, un éditorial publié en mars 2019 intitulé *Scientists rise up against statistical significance*, Amrhein et collab.[2] appellent à ne plus utiliser la signification statistique pour déterminer s'il existe une différence entre les groupes, parce que le concept est fréquemment appliqué de façon dichotomique au lieu d'être évalué sur un continuum. Les auteurs précisent : « Soyons clairs concernant ce qui doit prendre fin : on ne devrait jamais conclure qu'il n'existe "pas de différence" ou "pas d'association" uniquement parce qu'une valeur P est supérieure à un seuil de 0,05 ou, similairement, parce qu'un intervalle de confiance comprend le zéro »[2]. Au lieu de cela, les auteurs proposent d'utiliser des intervalles de confiance, comme des « intervalles de compatibilité », c'est-à-dire que votre estimation ponctuelle et les limites de confiance sont les plus compatibles avec vos données à cause du modèle statistique que vous avez utilisé pour calculer vos résultats[2]. Pour revenir à l'ERC décrit ci-dessus, vous menez votre test statistique par inférence, et votre résultat donne un risque relatif de 2,0, avec un intervalle de confiance de 95 % de 1,5 à 2,5 et une valeur p bien en dessous de 0,001. En vertu de la déclaration du test statistique traditionnel, vous pourriez conclure que les personnes de votre groupe d'intervention étaient deux fois plus portées que celles de votre groupe témoin à respecter leur pharmacothérapie 90 jours après leur sortie de l'hôpital et que cette différence est statistiquement significative, car l'intervalle de confiance n'englobe pas la mesure d'équivalence de 1. Cependant, si vous deviez utiliser la proposition émise par Amrhein et collab.[2], vous indiqueriez au lieu de cela que les valeurs du risque relatif, de l'intervalle de confiance de 95 % et de la valeur p la plus compatible avec vos données indiquent que les personnes ayant reçu votre intervention étaient deux fois plus portées à respecter leur prise de médicaments 90 jours après leur sortie de l'hôpital et que la différence de risque entre votre groupe de traitement et votre groupe témoin montrait que ce dernier était de 1,5 à 2,5 fois plus enclin à respecter le traitement, étant donné les suppositions du test statistique.

En réplique à l'éditorial d'Amrhein et collab.[2], Ioannidis a publié un éditorial le mois suivant dans le *JAMA*, intitulé *The importance of predefined rules and prespecified statistical analyses : do not abandon significance*[3]. Il souligne dans son article que les décisions prises en médecine sont le plus souvent dichotomiques et qu'on met davantage l'accent sur les « affirmations inappropriées indiquant n'avoir trouvé aucune différence statistique, plutôt que sur les énoncés non fondés

indiquant une différence et un refus sans que ce rejet soit justifié », particulièrement quand les chercheurs ne développent pas ou ne respectent pas les règles des tests statistiques spécifiées au préalable[3]. Au lieu de bannir le concept de signification statistique, Ioannidis soulignait que les chercheurs devaient se concentrer sur le respect des règles des tests statistiques et faire en sorte que la pertinence clinique s'applique à la prise de décision[3]. Il est évident que ces deux éditoriaux portent surtout sur la mauvaise utilisation fréquente de la signification statistique et des valeurs *p*.

Qu'est-ce que la valeur *p* et que n'est-elle pas? L'American Statistical Association (ASA) la définit comme « la probabilité selon un modèle statistique spécifié, qu'un résumé statistique des données (p. ex., l'écart moyen de l'échantillon entre deux groupes de comparaison) serait égal à sa valeur obtenue par l'observation ou plus extrême que cette valeur »[4]. Le modèle statistique spécifié et les données utilisées dans le test statistique sont les éléments clés de cette définition sur lesquels se focaliser. Si on utilise un seuil de valeur *p* de 0,05 pour déterminer la signification statistique, cela signifie que la probabilité que le résultat obtenu soit dû à la chance est inférieure à 5 %, spécifiquement au modèle statistique et aux données utilisées pour le test. Dans le but de réduire la probabilité d'une mauvaise interprétation des valeurs *p*, le conseil d'administration de l'ASA a publié une déclaration sur la bonne et la mauvaise manière d'utiliser les valeurs *p*[4]. Bien qu'elles puissent être utilisées pour déterminer s'il existe des preuves réfutant l'hypothèse nulle, comme nous l'avons mentionné ci-dessus, de telles conclusions sont surtout applicables aux données utilisées et aux suppositions faites pour calculer la valeur *p*[4]. La valeur *p* ne décrit pas la puissance de la taille d'effet ou la précision de votre résultat (c'est-à-dire une valeur *p* plus faible ne reflète pas une plus grande taille d'effet ou une estimation plus précise) et ne représente pas la probabilité que l'hypothèse générale de l'étude soit vraie ou due à la chance lorsqu'elle est appliquée à la population examinée[4].

Une controverse associée à la signification statistique et à l'utilisation des valeurs *p* existera vraisemblablement toujours. Il y a toutefois des concordances fondamentales entre l'éditorial d'Amrhein et collab.[2], celui d'Ioannidis[3] et la déclaration de l'ASA[4] qui, si elles sont respectées, aideront à désamorcer la controverse. Il nous faut tout d'abord nous assurer que le plan statistique de chaque étude soit spécifié au préalable, transparent et applicable aux données de l'étude[2-4]. Deuxièmement, il faut que les résultats de tous les tests statistiques menés, y compris les estimations ponctuelles, les mesures de précision (comme les intervalles de confiance) et les valeurs *p* soient rapportés. De tels rapports permettent d'être sûrs que nous ne reportons pas certains résultats de manière sélective et de tenir compte de l'évaluation de l'erreur de type 1, c'est-à-dire de trouver un résultat significatif d'un point de vue statistique là où il n'en existe aucun, et cela à cause de la multiplicité des tests statistiques[2-4]. Troisièmement, il convient d'être réaliste en interprétant les résultats de toute étude et d'éviter de leur donner trop ou trop peu d'importance[2-4]. Enfin, les décisions cliniques ne devraient jamais se baser uniquement sur les résultats statistiques. Il faut prendre en considération d'autres facteurs, y compris la validité de l'étude, la cohérence de ses résultats par rapport aux informations disponibles et la possibilité de les généraliser à l'ensemble de la population étudiée[2-4]. L'observation de ces recommandations favorisera une utilisation appropriée des tests statistiques dans la recherche, pour que nous puissions prendre les meilleures décisions cliniques possibles pour nos patients.

[Traduction par l'éditeur]

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Measuring Competency of Pharmacy Residents: A Survey of Residency Programs' Methods for Assessment and Evaluation

Steven J Kary, Zack Dumont, Kirsten Tangedal, Jennifer Bolt, and William M Semchuk

ABSTRACT

Background: The Canadian Pharmacy Residency Board (CPRB) specifies the competencies that pharmacy residents must attain and the need for assessment and evaluation. Methods of assessment and evaluation are left to the discretion of individual programs. There is a scarcity of published literature compiling and comparing the strategies used by Canadian residency programs.

Objectives: To determine curricular components used for assessment and evaluation; to describe the tools used by programs; to characterize the scheduling, frequency, and repetition of curricular components; and to determine the individuals or groups involved.

Methods: Coordinators of hospital pharmacy residency programs with CPRB accreditation or accreditation pending were surveyed to collect information about the assessment and evaluation of select CPRB standards.

Results: From the 37 eligible residency programs, 20 unique responses (54%) were received. All respondents were general practice programs (100%) in predominantly multicentre organizations (70%). Programs were similar in terms of assessment components used, with all respondents citing care plan review, direct observation of patient care, journal clubs, creation of project timelines, and ethics submission. The predominant evaluation components were within-department presentations (100%), written manuscripts (95%), drug information rotations (85%), and longitudinal evaluations (75%). Standardized forms (70%–100%) defined by Bloom's taxonomy (65%) and the CPRB "levels and ranges" document (60%) were the principle means used. Assessments for patient care and for provision of education were generally carried out immediately (80% and 95%, respectively), whereas project management skills were assessed predominantly at final evaluation (75%). Self-assessment and assessment by pharmacy team members occurred for every competency, whereas patients (0%–10%) and allied health professionals (5%) were less frequently involved.

Conclusions: The assessment and evaluation strategies reported by programs were congruent. The results provide a summary of national practices and will allow existing and developing programs to examine their approach to assessment and evaluation for alignment with national standards.

RÉSUMÉ

Contexte: Le Conseil canadien de résidence en pharmacie (CCRP) précise les compétences que les résidents en pharmacie doivent acquérir ainsi que le besoin d'observation et d'évaluation. Les méthodes d'observation et d'évaluation sont laissées à la discrétion de chacun des programmes. La littérature publiée qui compile et compare les stratégies utilisées par les programmes en résidence canadiens est rare.

Objectifs : Déterminer les composantes des programmes utilisés pour l'observation et l'évaluation des normes; décrire les outils utilisés par ces programmes; établir l'horaire, la fréquence et la répétition des éléments qui constituent ces programmes et déterminer les personnes ou les groupes concernés.

Méthodes : Les coordinateurs des programmes de résidence en pharmacie hospitalière ayant un agrément ou dont l'agrément est en cours de procédure ont été interrogés afin qu'ils fournissent des informations concernant l'observation et l'évaluation des normes CCRP sélectionnées.

Résultats : Des 37 programmes de résidence admissibles, 20 réponses individuelles (54 %) sont parvenues aux investigateurs. Tous les répondants représentaient des programmes de pratique générale (100 %) dans des organismes majoritairement multicentriques (70 %). Les programmes étaient similaires en termes de points à observer : tous les répondants citaient l'examen des plans de soins, l'observation directe des soins aux patients, les clubs de journaux, la création d'échéanciers pour la réalisation de projets et la proposition de documents sur l'éthique. Les critères d'évaluation prédominants consistaient en des présentations au sein du département (100 %), la rédaction de manuscrits (95 %), des rotations reliées au service d'information pharmacothérapeutique (85 %) et les évaluations longitudinales (75 %). Les formulaires standardisés (70 %–100 %) définis par la taxonomie de Bloom (65 %) et le document *Levels and ranges* (niveaux de performance des compétences) du CCRP (60 %) étaient les ressources de base utilisées. L'observation des soins aux patients et de la formation avait généralement lieu immédiatement (respectivement 80 % et 95 %,), tandis que les compétences en matière de gestion de projet étaient majoritairement évaluées en dernier (75 %). L'auto-observation et l'observation effectué par des membres de l'équipe de pharmacie portaient sur chaque compétence, tandis que les patients (0 % – 10 %) et les autres professionnels de la santé (5 %) participaient plus rarement à cette observation.

Keywords: assessment, evaluation, competency, pharmacy residency, training, professional development

Conclusions : Les stratégies d'observation et d'évaluation rapportées par les programmes concordaient. Les résultats fournissent un résumé des pratiques nationales et permettront aux responsables des programmes existants et en cours d'élaboration d'étudier l'approche de l'observation et de l'évaluation pour l'aligner sur les normes nationales.

Mots-clés : observation, évaluation, compétence, résidence en pharmacie, formation, développement professionnel

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INTRODUCTION

In 2010, the Canadian Pharmacy Residency Board (CPRB) published accreditation standards that implemented the change to a competency-based educational approach for pharmacy residency programs in Canada.[1] The release and adoption of these standards aligned with the evolution of professional education—notably within medicine, social work, and chiropractic care—from a focus on pathways and process to a focus on outcomes or competencies of graduates.[2,3] The CPRB standards have defined competencies that align with current pharmacy practice, and CPRB-accredited programs have adjusted their respective frameworks to ensure these competencies are being achieved.

Within the CPRB accreditation standards for year 1 residencies, as updated in 2018,[4] the core resident competencies describe (3.1) provision of patient care as a member of an interprofessional team, (3.2) management and improvement of medication systems, (3.3) leadership, (3.4) self-management of one's own practice, (3.5) provision of medication- and practice-related education, and (3.6) project management. These competencies align with those described by the National Association of Pharmacy Regulatory Authorities for pharmacists at entry to practice,[5] and they build upon the educational outcomes to be achieved in the first professional degree, as defined by the Association of Faculties of Pharmacy of Canada.[6] Furthermore, they parallel the 4 competencies described by the American Society of Health-System Pharmacists, which reflect the ongoing progression of health-system pharmacy practice.[7]

Despite these definitions of pharmacist competencies, developing the educational processes required to achieve them is complex. The specific activities or curricular components set the course for a resident's progression through a program and form the basis for meaningful assessment.[2] Each competency defined by the CPRB is further delineated to describe the skills, attitudes, and values required to demonstrate success. For example, standard 3.1 defines the components to demonstrate proficiency in evidence-based pharmacy practice in conjunction with other health care professionals. Residents are required to place high priority on selecting and providing appropriate pharmacy services, to demonstrate proficiency in navigating resources, and to establish inter- and intra-professional relationships.[4] The components described within each competency ensure that residency programs can provide relevant assessment and evaluation of residents.

Demonstration of competency through these components is no less complex, and multiple methods are therefore recommended.[8,9] Programs require both appropriate assessment—estimation of a learner's ability, performed longitudinally to guide learning—and evaluation—the summative judgment of an amount or value of competency, occurring at the midpoint or end of an educational or training program.[4,9] CPRB-accredited programs require ongoing formative assessments to aid learning and development of competencies, as well as final evaluations to describe the competencies achieved.[3,4] The CPRB also requires ongoing resident self-assessment of activities, which is to be reviewed with a preceptor.[4] The requirements for "what" but not "how" allow for varied interpretation and implementation by individual programs, and may result in discordance of assessment and evaluation from one program to another.

Appropriate assessment and evaluation are paramount in optimizing learners' capabilities, protecting the public, and providing a basis for learners to progress.[9] Although tools exist to aid in competency assessment,[10] programs must determine their individual needs and implement assessment methods appropriate to those needs. The CPRB has published a "levels and ranges" document to guide programs in their definition of expected levels of competency.[11] Given this flexibility and freedom in the choice of methods to assess and evaluate these competencies, the onus for developing suitable methods lies with individual programs.

There is a lack of published literature pertaining to how CPRB-accredited and accreditation-pending year 1 pharmacy residency programs are assessing the competency of hospital pharmacy residents. Although some programs have shared examples of their assessment tools online,[12] a compilation and comparison of the assessment strategies used by Canadian programs is not currently available.

This study was undertaken to determine the curricular components used for assessment and evaluation of residents' competencies; to describe the tools used for assessment and evaluation; to characterize the scheduling, frequency, and repetition of assessments; and to determine the individuals or groups involved in assessment.

METHODS

A survey focused on assessment and evaluation of specified resident competencies was designed by the authors to determine the methods used by CPRB-accredited and accreditation-pending hospital pharmacy residency programs. The survey questions and response options were determined through analysis of the components of the Regina Qu'Appelle Health Region pharmacy residency program and literature available on the assessment and evaluation of competency. Although the survey was not validated, the content and design were revised before distribution, on the basis of feedback from 2 former residency coordinators and a pharmacist with a background in survey design and implementation, none of whom were otherwise involved in the study.

Survey content reflected the scope of CPRB year 1 standards 3.1, 3.5, and 3.6. These competencies were selected to represent the complete set of standards and were hypothesized to cover a broad range of resident skills and activities and to illustrate perceived similarities (standard 3.1) and differences (standards 3.5 and 3.6) among programs. Standards 3.2, 3.3, and 3.4 were excluded to ensure that the project remained within the scope of a year 1 pharmacy residency project; these standards were not anticipated to provide better examples of congruence or disparity among programs. Respondents were allowed, but not required, to select all applicable answers to each question, and an open response option was made available, to ensure that any unlisted responses could be captured. Respondents were able to provide comments if they wished to elaborate on their response to any question. The survey questions are available in Appendix 1 (https://www.cjhp-online.ca/index.php/cjhp/issue/view/192/showToc).

The survey was distributed electronically via the Research Electronic Data Capture (REDCap) system.[13] REDCap is a secure, web-based application designed to support data capture for research studies hosted on a local server (https://www.project-redcap.org/). Potential participants were identified through the CPRB website, which is updated at least annually and provides contact information for all accredited and accreditation-pending residency programs. The coordinators of the identified residency programs were invited to participate in the survey. If multiple coordinators were involved in an individual program, they were asked to submit a single unified response. Individuals responsible for coordination of multiple programs were asked to submit a separate response for each program. The survey was open from February 19 to March 16, 2018, inclusive, and reminders were sent by e-mail to prospective participants at 2 weeks and 1 week before the survey closing date.

In cases where the number of respondents from each province exceeded the total number of programs known to exist, the data were reviewed independently by 2 of the authors to assess for any duplication of response from individual programs. Where multiple responses were clearly noted for a single program, the most thorough response was used for the analysis.

The data were analyzed descriptively, because of their categorical nature. Results are reported in terms of frequency distributions and medians with interquartile ranges (IQRs). Results from the open responses are reported as "other" and are summarized. Comments from each section of the survey were reviewed for applicability to the results and are highlighted within the Discussion.

RESULTS

Overview of Respondent Programs

A total of 22 responses were received. Following screening for and elimination of duplicates, information from 20 (54%) of the 37 Canadian year 1 programs was included in the analysis. Respondents represented programs in 7 of the 9 provinces with residency programs both large (more than 10 residents accepted annually) and small (10 or fewer residents accepted annually). During the 2017/2018 residency year, 196 residency positions were offered nationally,[14] including the 85 potential positions reported by Quebec Clinical Master's programs. The responses received accounted for 139 (71%) of available positions. All respondents were from general practice residency programs (100%) in predominantly multicentre organizations (70%) (Table 1).

The programs accepted a median of 4 residents (IQR 2–4), with a median of 12 rotations (IQR 9–14) undertaken by each resident annually. Respondents described programs as being predominantly focused on provision of direct patient care, with 17 (85%) of the respondents stating that this aspect constituted 60% or more of the curriculum. The other competencies addressed in the survey made up lesser portions of the programs: medication- and practice-related education and project management skills composed 20% or less of the curriculum in 12 (60%) and 18 (90%) of the programs, respectively. Three respondents (15%) defined medication- and practice-related education as accounting for 80% or more of the curriculum.

Curricular Components Used for Assessment

The curricular components used to assess direct patient care included care plan review (100% of respondents), direct observation of patient care activities (100%), and written documentation of patient care (95%) (Table 2). Respondents also reported discussions with the health care team and the use of a teaching rotation as "other" components of assessment. The components used to assess provision of medication- and practice-related education were journal clubs (100%), response to drug information requests (95%), individual patient education (85%), and preceptorship (85%). Group teaching sessions were used by fewer programs (35%). Assessment of competency in project management was consistently based on creating project timelines, communication with project members, ethics submission, and data collection (100% for all). Additional components cited by

Table 1. Demographic Characteristics of Survey Respondents

Characteristic	No. (%) of Respondents			
	By Individual Responses (*n* = 20)		By Region	
Region				
Western Canada*	8	(40)	8/12	(67)
Eastern Canada†	12	(60)	12/25	(48)
Location of residency				
Multi-centre	14	(70)		
Single centre	6	(30)		
Type of residency				
General practice	20	(100)		
Specialty practice	0	(0)		
No. of residency spots per year (median, IQR)	4	(2–4)		
No. of rotations undertaken per year (median, IQR)	12	(9–14)		

IQR = interquartile range.
*British Columbia, Alberta, Saskatchewan, Manitoba.
†Ontario, Quebec, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador.

Table 2. Curricular Components Used for Assessment of Competencies 3.1, 3.5, and 3.6

Component Used for Assessment	No. (%) of Respondents (*n* = 20)	
Competency 3.1: Provision of patient care		
Care plan review	20	(100)
Direct observation	20	(100)
Written documentation	19	(95)
Case-based lecture	14	(70)
Other*	3	(15)
None	0	(0)
Competency 3.5: Provision of medication- and practice-related education		
Journal clubs	20	(100)
Response to drug information requests	19	(95)
Individual patient education	17	(85)
Preceptorship	17	(85)
Documentation in charts	16	(80)
Group patient teaching	7	(35)
Other†	6	(30)
None	0	(0)
Competency 3.6: Project management skills		
Communication with members	20	(100)
Data collection	20	(100)
Ethics submission	20	(100)
Project timelines	20	(100)
Draft reports	19	(95)
Leading meetings	18	(90)
Other‡	5	(25)

*Discussion with health care team, teaching rotations (based on respondents' open [free-text] responses).
†Case presentations, variety of presentation type requirements, small group teaching sessions, teaching at faculty, workshop facilitation (based on respondents' open [free-text] responses).
‡Presentation to leadership groups, poster preparation, presentations, protocol write up, background research (based on respondents' open [free-text] responses).

5 (25%) of the programs included presentations to leadership groups, poster preparation, protocol write-up, and background research.

Curricular Components Used for Evaluation

The curricular components used for evaluation of direct patient care were longitudinal evaluations (75% of respondents), comprehensive final rotations (45%), and practical skills examinations (25%) (Table 3). Four programs (20%) cited other evaluation components, including a comprehensive oral evaluation, which was used by one of the programs. Provision of medication- and practice-related education was evaluated via departmental or staff presentations in all programs, and additionally through specific rotations: 17 programs (85%) had a drug information rotation and 13 (65%) had a preceptorship rotation. Fewer programs used written education (60%) or other components (25%), such as learning portfolios, presentation slides, and seminars or academic teaching, as curricular components for evaluation. All respondents indicated that a research project was used for demonstration of project management skills; however, 12 programs (60%) additionally used non–research-based projects, such as mini-projects (e.g., audits). Evaluation of competency was predominantly based on written manuscripts (95%), completion of a research project (90%), a separate management project (85%), or a poster presentation of results (75%). Few programs (20%) used an additional publication for evaluation of project management.

Tools Used by Programs for Evaluation

Thirteen programs (65%) reported sharing assessment and evaluation tools with another program (Table 4). The majority of programs (75%) used more than 1 tool to define competency, the most common tools being Bloom's taxonomy[16] (65%) and the CPRB "levels and ranges"[11] document (60%). Most programs used standard evaluation forms for assessment of the 3 competencies; however, the median number of questions on each

Table 3. Curricular Components Used for Evaluation of Competencies 3.1, 3.5, and 3.6

Component Used for Evaluation	No. (%) of Respondents (*n* = 20)	
Competency 3.1: Provision of patient care		
Longitudinal evaluation	15	(75)
Comprehensive rotation	9	(45)
Practical skills exam	5	(25)
Written exam	0	(0)
Other*	4	(20)
None	1	(5)
Competency 3.5: Provision of medication- and practice-related education		
Presentations to department	20	(100)
Drug information rotation	17	(85)
Preceptorship rotation	13	(65)
Written education	12	(60)
Other†	5	(25)
None	0	(0)
Competency 3.6: Project management skills		
Written manuscript	19	(95)
Completion of research project	18	(90)
Management project	17	(85)
Poster presentation	15	(75)
Publication other than research	4	(20)
Other‡	1	(5)

*Comprehensive oral assessment, performance on rotation, review of formative evaluations (based on respondents' open [free-text] responses).
†Learning portfolio, presentation slides, seminars, academic teaching at faculty, preceptor review (based on respondents' open [free-text] responses).
‡Presentation to leadership groups, poster preparation, presentations, protocol write up, background research (based on respondents' open [free-text] responses).

evaluation form ranged from 10 (IQR 3–13) to 20 (IQR 15.5–20), depending on the competency.

Scheduling and Frequency of Assessments

Assessments of standard 3.1 were predominantly carried out immediately (80% of respondents reporting "often" or "always") or within 24 to 48 h (70% "often" or "always") after the provision of patient care. Similarly, assessments of standard 3.5 were carried out immediately or within 24 to 48 h for provision of medication-related education (95% "often" or "always" and 70% "often" or "always", respectively) and practice-related education (85% "often" or "always" and 60% "often" or "always", respectively). Assessments were typically recorded "often" or "always" for midpoint and final evaluations (at least 70% of programs) within these competencies (Figure 1). Assessment of project management skills (standard 3.6) was less frequently undertaken immediately (25% "often" or "always") or within 24 to 48 h (35% "often" or "always"), and these skills were predominantly assessed at the final evaluation (75% "often" or "always") or at additional times specified by the program, including month-end and quarterly, periodically according to the activity schedule, or as set by the project preceptor.

Individuals or Groups Involved in Assessments

Assessment by pharmacy team members, as well as self-assessment by the resident, was used for all 3 competencies (Figure 2). Allied health professionals and patients were rarely involved in assessments of patient care (5% "often" or "always" and 0% "often" or "always", respectively) or assessment of medication-related education (5% "often" or "always" and 10% "often" or

Table 4. Characteristics of Tools Used for Evaluation of Competency

Characteristic	No. (%) of Respondents		Median (IQR)
Tools used/shared with another program			NA
Yes	13	(65)	
No	6	(30)	
I do not know	1	(5)	
Tool(s) used for defining competency[15]			NA
Bloom's taxonomy	13	(65)	
CPRB "levels and ranges" document	12	(60)	
Dreyfus model of skill acquisition	6	(30)	
SOLO taxonomy	4	(20)	
Other*	2	(10)	
Krathwohl's taxonomy	0	(0)	
≥ 2 tools	15	(75)	
Standard evaluation form			No. of questions
3.1: Provision of direct patient care	20	(100)	20 (15.5–20)
3.5: Provision of medication-related education	14	(70)	10 (3–13)
3.5: Provision of practice-related education	17	(85)	10.5 (5.25–13.75)
3.6: Project management skill	18	(90)	12 (10–16)

CPRB = Canadian Pharmacy Residency Board, IQR = interquartile range, NA = not applicable, SOLO = Structure of the Observed Learning Outcome.

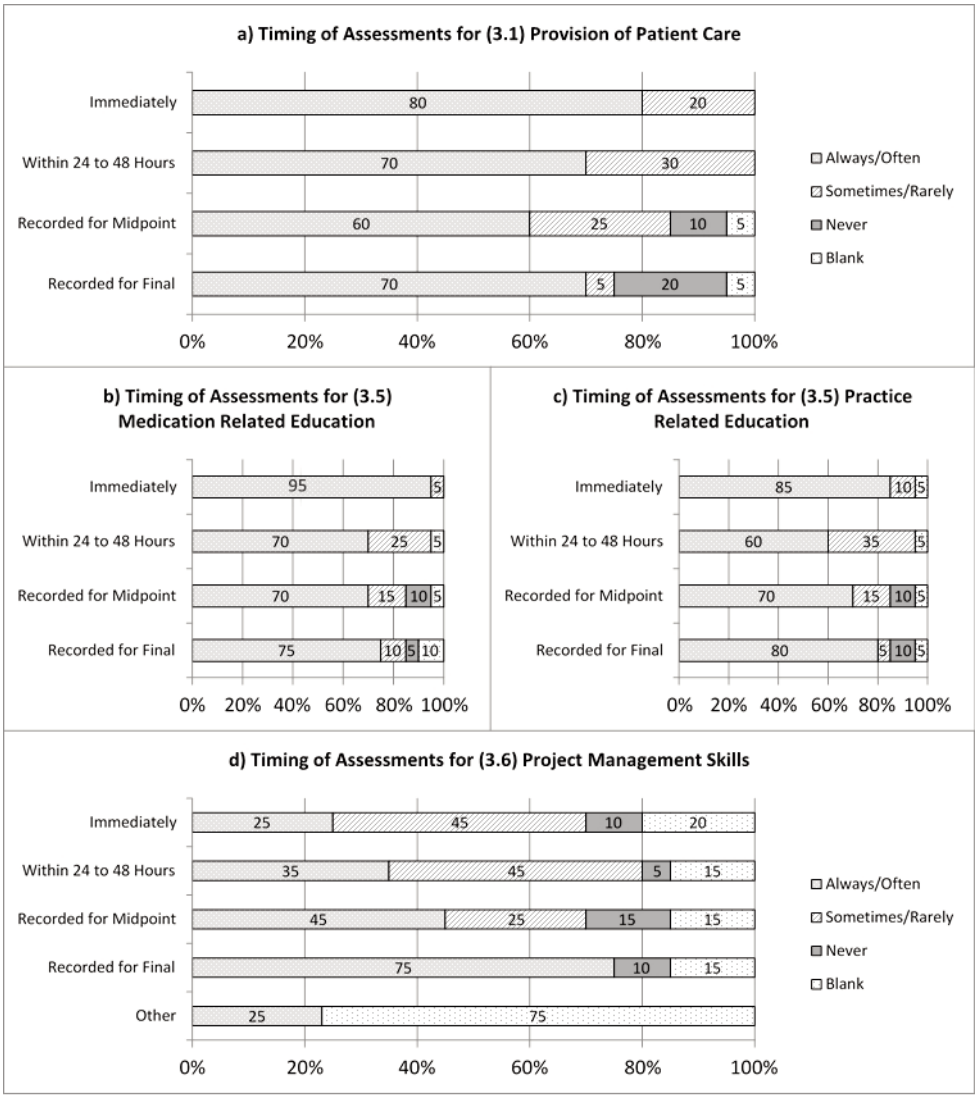

Figure 1. Scheduling of assessment carried out for competencies 3.1, 3.5, and 3.6. The frequency of occurrence (from "never" to "always") for each of the timing domains is represented as a percentage of all respondents. The respondents who chose not to reply to a given question are represented as "blank". Respondents who chose "other" were given the opportunity to provide an open (free-text) response, with the following responses received: "ongoing as components of the project are completed", "month-end and quarterly", "periodic according to activity schedule", "as set by preceptor", "assessment of written work may take 1–2 weeks".

"always", respectively). Fourteen respondents (70%) indicated that residency coordinators or directors were "always" or "often" involved in assessment of practice-related education. Coordinators and directors were also reported as being "always" or "often" involved in assessment of project management skills in 12 programs (60%). Programs additionally identified project members (85% "often" or "always") and faculty liaisons as being involved in the assessment of project management skills.

DISCUSSION

This study sought to describe how CPRB-accredited and accreditation-pending year 1 pharmacy residency programs assess and evaluate residents in accordance with 3 CPRB competencies: provision of direct patient care, provision of medication- and practice-related education, and demonstration of project management skills.[4] These competencies were selected as it was anticipated that they would highlight similarities and differences

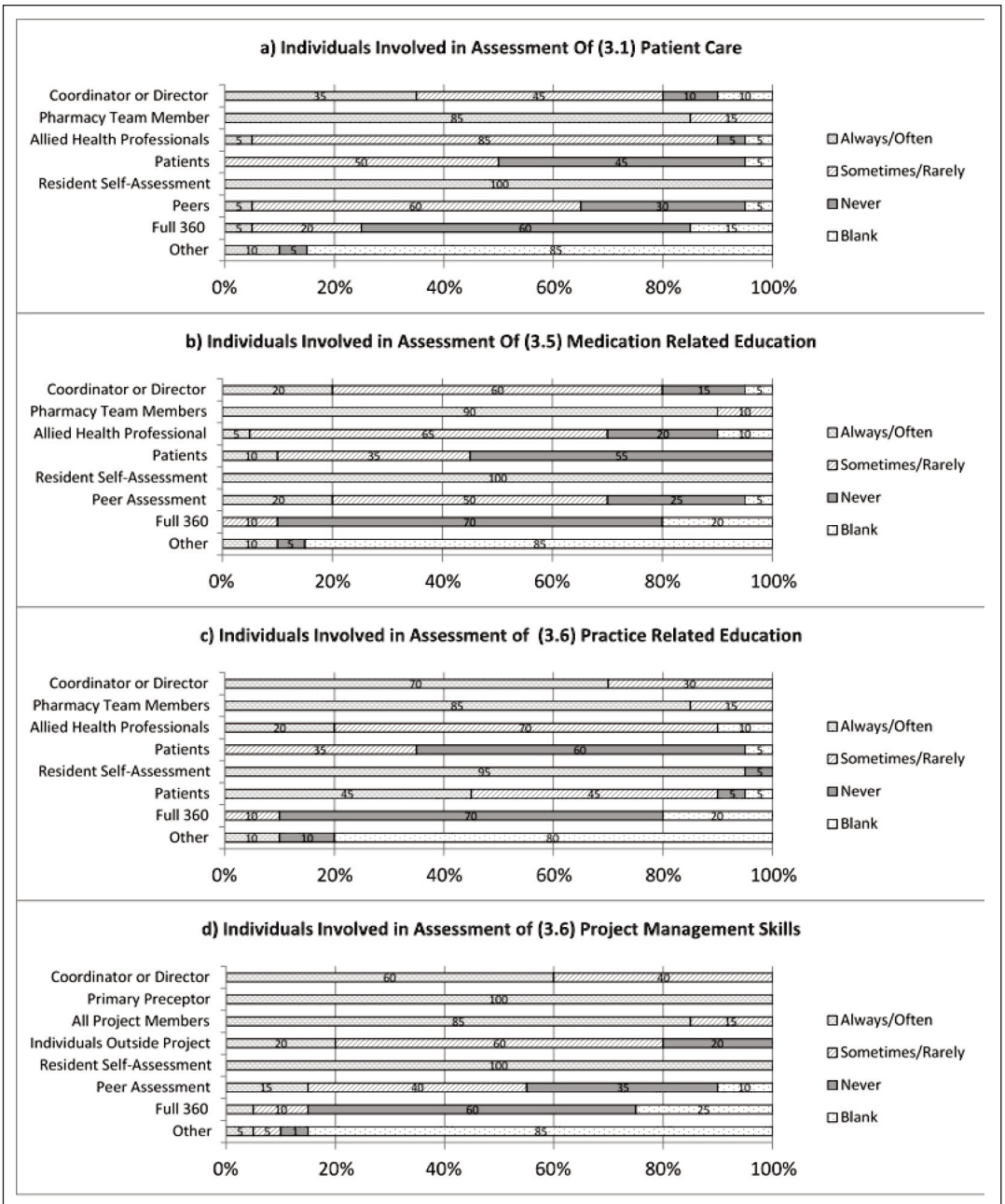

Figure 2. Individuals involved in assessment of competencies 3.1, 3.5, and 3.6. The frequency of occurrence (from "never" to "always") for each individual or group is represented as a percentage of all respondents. The respondents who chose not to reply to a given question are reported as "blank". Respondents who chose "other" were given the opportunity to provide an open (free-text) response, with the following responses received: rotation preceptor, pharmacy technicians during distribution, physician feedback (1 respondent); rotation preceptor (2 respondents); project management assigned to another individual, faculty liaison (1 respondent).

among programs. Patient care was found to be a primary focus (greater than 60% of curriculum) in 85% of respondent programs. Education and project management were anticipated to compose a smaller portion of programs, and the results bore out this assumption, although education was noted to represent 80% or greater of the curriculum in 3 programs. These outliers may reflect a difference among programs, exemplified by the structure of the Quebec Clinical Master's programs as distinct from the structure of residency programs in other provinces. However, there may also be overlap of patient education and provision of patient care as the primary focus of certain programs. The programs were largely congruent in terms of the curricular components used for assessment and the timing of assessment of these 3 competencies. More variability was noted in terms of the curricular components used for evaluation and the individuals involved in assessment of competency.

Identification of the components used for assessment is critical within competency-based education as they facilitate progression of competency development.[17] Many of the curricular components used for assessment of competency in the provision of patient care and the provision of medication- and practice-related education—including care plan review, written documentation, direct observation of patient care, and response to drug information requests—are activities specified within the CPRB accreditation standards.[4] Additionally, these components align with required patient care services specified in US pharmacy residency programs.[7] Case-based lectures, journal clubs, and preceptorship are assessed in many of the Canadian programs, although they are not required. This similarity among components for assessment suggests a common approach to pharmacy practice, and thus to competency development.

All of the respondent programs used a research project for the assessment of project management skills, and the surveyed curricular components were used by at least 90% of respondents (Table 2). Although the CPRB accreditation standards do not mandate a research project for year 1 residencies, a resident must be involved in project development and in data collection, analysis, and interpretation, and must prepare a report suitable for publication in a peer-reviewed journal, activities that together are analogous to the research process.[4] The components for assessment that were reported by survey respondents largely align within the standard for project management, and variability among programs seemed to be reflected only in respondents' free-text comments, which mentioned presentations to leadership groups, poster preparation, protocol write-up, and background research. However, these components were not listed within the options presented to respondents, and it is possible that they were used but not mentioned by other programs; hence, their true frequency within the sample cannot be verified.

Competency-based education places less emphasis on evaluation than on assessment[3,18]; however the curricular components used for evaluation continue to provide a valuable summation of competency achieved.[9] Longitudinal evaluations, used by 75% of programs, represented one of the consistent evaluation processes for provision of patient care. The 2018 CPRB accreditation standards require the ongoing use of longitudinal assessments,[4] which can serve as a foundation for monitoring professional development,[9] but there are few other evaluation requirements in the standards. Correspondingly, an apparent lack of standardization was found among programs in terms of the components used for evaluation. More than half of respondent programs used written education (60%), and just under half used a comprehensive final rotation (45%), whereas a quarter or less used a practical skills exam (25%) or additional publications (20%) for evaluation of competency. However, these components varied substantially across respondents. Although a best practice cannot be defined, the use of multiple methods can help to validate the findings of an evaluation,[9] and programs may benefit from incorporation of additional evaluation components within these competencies.

The use of descriptive assessment tools provides increasing detail and specificity for residents to gain competency.[17] The use of multiple methods to define competency, including Bloom's taxonomy and the "levels and ranges" document (as reported by 75% of respondent programs), demonstrates that qualitative assessment is favoured over quantitative assessment. National standardization and validation of qualitative assessment tools have been suggested in competency-based medical education,[9,18] although these approaches have not been formally implemented in Canadian pharmacy programs. For the competencies surveyed, forms that programs use to assess competency are predominantly standardized within each program (70% to 100%), with 65% of programs sharing their tools with another program. These results reflect the existence of standardized forms at the provincial level in British Columbia and Ontario.[12] It appears that CPRB-accredited pharmacy residency programs are standardizing their approach, although this may not be a consistent national trend. Currently, the CPRB has not implemented formal sharing of assessment tools or standardization of these tools.

To have the desired effect, assessments should be performed frequently,[3,18] although the benefit associated with timing of feedback may vary depending on the focus of the assessment.[19] Assessments done immediately may aid in faster acquisition of knowledge and skill related to specific tasks, whereas a delay in feedback may allow increased automaticity in development of learning strategies and process.[19] Most respondents reported an expectation that assessments would be conducted immediately or within 24 to 48 h for the provision of patient care and for the provision of medication- and practice-related education. Fewer programs assessed these competencies at the midpoint and end of the residency, which may reflect a focus on reinforcing knowledge and skill at the time of acquisition. However, the CPRB accredi-

tation standards continue to recommend midpoint assessments, and they require final assessments.[4] Variation in the timing of assessment of residents' project management skills was noted, which may reflect the time required for review of written documents. Two respondents commented that the timing of assessment for this competency varied according to completion of activities or the schedule of activities that had been laid out.

Involvement of multiple individuals, specifically patients and allied health professionals, has been suggested as essential for successful assessment within competency-based medical education,[9,18] and pharmacy residency programs may benefit from adopting this practice. Assessment for the various competencies largely relied on pharmacy team members, which may reflect the 2010 standards requiring qualified pharmacists or pharmacy technicians to act as preceptors.[1] Only one program reported regular use of allied health professionals in the assessment of patient care. Few programs used allied health professionals (5% "often" or "always") or patients (10% "often" or "always") in the assessment of medication-related education (representing 1% and 2.5% of the total residency spots, respectively). The more recent CPRB standards, released in 2018, identify the need to include patients and health care providers and require their input in the assessment of residents.[4] Patient feedback surveys with a Likert-scale rating, along with review of findings with a preceptor could help to ensure that feedback is specific and meaningful.[20] Additionally, self-assessment remains an essential component of competency-based training, and all of the surveyed programs included self-assessment "often" or "always" for each competency. It has been suggested that self-assessment in isolation is ineffective and potentially dangerous,[18] so it is important to note that the respondent programs did not rely on resident self-assessment in isolation—all of the programs made use of at least one other individual in assessment of each competency.

Implications

This study has provided insight into the assessment and evaluation practices of CPRB-accredited and accreditation-pending pharmacy residency programs in Canada. The alignment and variation among programs may help in identifying areas on which to focus for growth in the tools and methods used, as well as guiding programs currently in development. The results of this study may help inform processes for continuous quality improvement, which are required of all programs.[4] Currently, the CPRB recognizes and publishes information on leading practices, and also provides webinars to aid in program development.[21] Taken together, the results of this survey may help in identifying methods suitable for incorporation into individual programs.

The programs represented in the survey responses were predominantly congruent with respect to assessment and evaluation of competencies, and many of their practices adhered to the accreditation standards. The 2018 CPRB accreditation standards require ongoing incorporation of assessments from multiple individuals, including patients and allied health professionals,[4] methods that were infrequently used by the respondent programs. Most programs will require changes to incorporate assessments by these individuals, and the few programs that have an existing standard in this area may be able to provide guidance as to how this might be achieved.

This study focused on describing how competency assessments and evaluations were being performed at the time of the survey, but did not assess the quality of the assessments by individual programs or the ramifications if competence was not demonstrated through these measures. Additionally, measurement of the outcomes of competency assessments and evaluations and how these outcomes translate into future practice were outside the scope of this study. A framework for the evaluation of competency-based programs was previously described by Baartman and others,[3] and has been applied to a pharmacy residency program in North Carolina for purposes of improvement.[22] The same framework could be applied to Canadian programs to determine the effectiveness of the current approach. Further research should focus on determining best practice and how this might be implemented into the CPRB-accredited pharmacy residency programs.

Limitations

The use of a survey for this study allowed ease of distribution to participants and ease of response, which likely contributed to the relatively high response rate. However, the survey design limited the nature of the responses collected and may have contributed to the high degree of congruence observed among the programs. A semistructured interview or the use of more open-ended questions might have been better ways to achieve more depth and detail about the actual practices of individual programs. Respondents were not required to answer every question, which may have affected interpretation of the overall response for questions with components that were infrequently used. Additionally, the interpretation of response options was subjective and may have varied among individual respondents.

Three of the CPRB-defined competencies were selected to represent assessment and evaluation practices across programs. However, this selection may not be truly representative of practice, as programs may have alignment and variation in the emphasis placed on the other 3 competencies. Although the survey responses were intended to apply to all programs, there may have been bias in the survey design, such that responses may have reflected practices within the Regina Qu'Appelle Health Region pharmacy residency program. Finally, participation in the survey was voluntary, and the findings may reflect programs most interested in the topic rather than being truly representative of all programs.

CONCLUSION

This study showed that the materials and methods used by individual Canadian pharmacy residency programs to assess and evaluate residents' competencies are largely congruent, although some variation exists, particularly with respect to evaluation. These results help to describe the practice landscape among CPRB-accredited pharmacy residency programs with regard to assessment and evaluation. Although a specific best practice was not sought and thus cannot be defined from these findings, the results reported here can help to reinforce current practices. Furthermore, these results help to identify the extent of variability among programs, indicating where efforts could be concentrated if and when it is determined that national alignment is appropriate.

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Contribution of Pharmacy Practice Residents to Resolution of Drug Therapy Problems for Patients: RES-DTP Study

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ABSTRACT

Background: Canadian pharmacy practice residency programs promote development of key competencies for direct patient care resulting in resolution of drug therapy problems (DTPs), which is 1 of 8 national clinical pharmacy key performance indicators. There are no Canadian data on the contribution of residents to resolution of DTPs, including DTPs for priority diseases covered in disease-state education modules (PD-DTPs) or quality indicator DTPs (QI-DPTs), as assessed through application of evidence-based interventions proven to reduce morbidity, mortality, or health resource utilization.

Objective: To describe the contribution of pharmacy practice residents to direct patient care using 3 process-of-care measures: resident-resolved DTPs, PD-DTPs, and QI-DTPs.

Methods: This prospective, observational single-group study was conducted across 5 rotation sites within the authors' health authority from September 2, 2013, to June 13, 2014. The primary outcome was number of DTPs resolved. The secondary outcomes were number of PD-DTPs resolved; number of QI-DTPs resolved; numbers of DTPs, PD-DTPs, and QI-DTPs resolved over time; and residents' satisfaction with electronic tracking of resolved DTPs (in terms of training, usability, efficiency, and time requirements).

Results: Four residents completed a total of twenty-one 4-week rotations and resolved a total of 1201 DTPs. Of these, 620 (52%) were PD-DTPs and 479 (40%) were QI-DTPs. Overall, the number of interventions increased for rotations 1–3, decreased for rotations 4 and 5, and increased again for rotation 6. The median score for all questions in all domains of the satisfaction survey was 4 out of 5 ("agree").

Conclusions: Pharmacy practice residents were resolving DTPs, PD-DTPs, and QI-DTPs for patients and were contributing significantly to direct patient care. On the basis of literature evidence, the number and type of interventions observed in this study would be expected to improve clinical and health economic outcomes for patients.

Keywords: pharmacy resident, clinical care, drug therapy problems, clinical pharmacy key performance indicators

RÉSUMÉ

Contexte : Les programmes de résidence canadiens en pratique pharmaceutique encouragent le développement de compétences clés relatives aux soins directs offerts aux patients. Ces compétences entraîneront la résolution des problèmes de pharmacothérapie (DTP), l'un des huit indicateurs clés nationaux de rendement relatifs à la pharmacie clinique. Il n'existe pas de données canadiennes portant sur la contribution des résidents à la résolution des problèmes de pharmacothérapie, notamment ceux relatifs aux maladies prioritaires (PD-DTP) couverts dans les modules d'éducation sur les problèmes de santé, ou les indicateurs de qualité des DTP (QI-DPT), évalués au moyen d'interventions fondées sur des données scientifiques dont il a été prouvé qu'elles réduisaient la morbidité, la mortalité ou l'utilisation des ressources sanitaires. Dans une étude, les intervenants avaient des opinions divergentes concernant la contribution des résidents à la résolution des DTP, des PD-DTP et des QI-DTP.

Objectif : Décrire la contribution des résidents dans le cadre de la pratique pharmaceutique des soins directs offerts aux patients à l'aide de trois mesures spécifiques du processus des soins : DTP, PD-DTP et QI-DTP résolus par les résidents.

Méthodes : Cette étude prospective par observation portant sur un seul groupe a été menée dans cinq sites de rotation compris dans la sphère d'autorité sanitaire des auteurs, du 2 septembre 2013 au 13 juin 2014. Le résultat principal était le nombre de DTP résolus. Les résultats secondaires étaient les suivants : nombre de PD-DTP résolus; nombre de QI-DTP résolus; nombre de DTP, de PD-DTP et de QI-DTP résolus avec le temps; et la satisfaction des résidents à l'égard du suivi électronique de leurs DTP résolus (en termes de formation, de facilité d'utilisation, d'efficacité et d'exigences en matière de temps).

Résultats : Quatre résidents ont effectué un total de 21 rotations de quatre semaines et ont résolu 1201 DTP. De ceux-ci, 620 (52 %) étaient des PD-DTP et 479 (40 %), des QI-DTP. Les interventions générales ont augmenté de la 1re à la 3e rotation; elles ont diminué à la 4e et à la 5e rotation; elles ont à nouveau augmenté à la 6e rotation. Le score moyen de toutes les questions posées dans l'enquête de satisfaction, tous domaines confondus, était de 4 sur 5 (ou « d'accord »).

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Conclusions : Les résidents en pratique pharmaceutique résolvaient les DTP, les PD-DTP et les QI-DTP des patients et contribuaient de manière significative aux soins directs aux patients. Sur base de la documentation, on pourrait s'attendre à ce que le nombre et le type d'interventions observées dans cette étude améliorent les résultats cliniques et sanitaires des patients.

Mots-clés : résident en pharmacie, soins cliniques, problèmes de pharmacothérapie, indicateurs clés de rendement relatif à la pharmacie clinique

INTRODUCTION

Priority disease states are medical conditions with a high impact on and/or prevalence in the population that account for a disproportionate number of emergency department visits and hospital admissions, prolong length of stay, and increase health care costs.[1-3] Clinical pharmacists can prioritize the care they provide and add value by making evidence-based pharmacotherapy interventions for patients with priority diseases.[4] Two randomized controlled trials showed that hospital pharmacists providing comprehensive proactive clinical care and identifying and resolving drug therapy problems (DTPs) for patients with priority disease states can improve the overall quality of drug therapy, thereby reducing emergency department visits, hospital visits, drug-related readmissions, hospital readmissions, and total cost of care.[5,6] Most importantly, these trials confirmed that pharmacist-resolved DTPs are a useful process measure in continuous quality improvement projects to evaluate clinical pharmacy services, and represent an acceptable surrogate marker for predicting clinical and economic outcomes.

In addition, pharmacist-resolved DTPs have been recommended in the international literature as a clinical pharmacy key performance indicator (cpKPI) for clinical pharmacy services.[7-11] Measuring and reporting cpKPI activities is beneficial to patients, members of the health care team, pharmacy leaders, managers, pharmacists, and pharmacy students to help improve pharmacy practice and the quality of patient care.[11-13]

Canadian pharmacy practice residency programs combine didactic and experiential elements to help the residents developing the necessary competencies to provide evidence-based direct patient care as a member of interprofessional teams, to manage their own practice of pharmacy, to exercise leadership, to demonstrate project management skills, to provide medication- and practice-related education, and to manage and improve medication-use systems in preparation for real-world practice.[14] Identification and resolution of DTPs and provision of other evidence-based clinical activities constitute a major residency development goal that is aligned with the fundamental role of a pharmacist.[15] Currently, there is no Canadian literature capturing the contribution of pharmacy practice residents to cpKPIs in the area of drug therapy interventions (e.g., resolved DTPs).

As the number of experiential rotations for entry-to-practice Canadian pharmacy students increases because of evolving curricula and increasing enrolment, there is more pressure on hospitals to meet the increasing demand for experiential learning practice sites. As employee learners, residents will increasingly need to add value by contributing tangibly to patient care as they evolve through their training. Residents' progress through clinical training entails development of knowledge, skills, abilities, attitudes, and behaviours, as well as the required competencies to identify and resolve a DTP. There is value to using this latter process measure to evaluate pharmacy residents' contributions to and progression in clinical care over the course of the residency.

If it could be confirmed, through observation, that pharmacy practice residents are contributing to clinical care, future development of residency programs and possibly even their expansion would be justified. Conversely, observations showing that pharmacy practice residents are making suboptimal contributions to clinical care would indicate a need for changes to residency training programs. Therefore, the purpose of this study was to describe the contribution of pharmacy practice residents to clinical pharmacy care, using resolved DTPs as an accepted process-of-care measure.

METHODS

Study Design

This was a prospective, observational one-group study that took place across 5 rotation sites within the Interior Health Authority (British Columbia) from September 2, 2013, to June 13, 2014. Ethics approval for the study was obtained from the Interior Health Research Ethics Board and the University of British Columbia Behavioural Research Ethics Board.

Study Population

The Interior Health Pharmacy Practice Residency Program, accredited by the Canadian Pharmacy Residency Board, is delivered at 5 hospitals and ambulatory practice sites across a

single health authority in British Columbia. It consists of 52 weeks of experiential learning, including 30 weeks of direct patient care rotations. All residents must complete core rotations in internal medicine (4 weeks), critical care (4 weeks), infectious diseases (4 weeks), cardiology (4 weeks), and preceptorship skills (2 weeks). Residents are also required to choose 3 elective direct patient care rotations, each of which is 4 weeks in duration. Data about resolved DTPs were collected from all pharmacy practice residents, starting after completion of the first 4-week patient care rotation (internal medicine). Only those residents who consented to participate in an online survey to provide feedback on their perceptions of the DTP tracking experience were included in the study. Resolved DTP data that were un-interpretable or incomplete were excluded.

Clinical Performance Indicator System (DTP Tracker)

In 2009, concurrent with the development of ongoing disease-state education modules for staff professional development, a clinical performance indictor system (DTP Tracker) was developed and implemented to measure clinical pharmacists' effectiveness and efficiency at resolving DTPs for patients. The DTP-related actions captured in the DTP Tracker include discontinuing an unnecessary drug, initiating a new drug, changing a suboptimal or ineffective drug or route, increasing a drug dose, decreasing a drug dose, changing a drug or dose because of an adverse drug reaction (ADR), changing a drug or dose because of a drug interaction, and providing medication adherence strategies. A DTP is deemed to have been resolved if the prescriber accepts the pharmacist's recommendation, with a resultant prescription change, or if the pharmacist provides the patient with medication adherence strategies. According to departmental policy, all pharmacists prospectively capture resolved DTPs in the DTP Tracker (HanDBase software, version 4.8.715, DDH Software, Inc, Wellington, Florida) using an institutional point-of-care device or an institutional desktop version (Microsoft Excel software, version 14.0.7145.5000, Microsoft Corporation, Redmond, Washington). During their residency orientation period before the study, pharmacy practice residents were given initial and ongoing standardized training on use of the DTP Tracker.

For the purposes of the study, a "DTP" was defined as any DTP resolved by a pharmacy practice resident. A priority disease DTP (PD-DTP) was a resolved DTP related to any of the prevalent and high-impact diseases covered in the 8 education modules provided to Interior Health pharmacy staff: heart failure, atrial fibrillation, ischemic heart disease, chronic obstructive pulmonary disease, pneumonia, urinary tract infection, diabetes mellitus, gastroesophageal reflux disease or peptic ulcer disease, and a "general support" disease category for which DTP-related actions included providing venous thromboembolism prophylaxis, immunizations, nicotine replacement therapy, or smoking cessation therapy. A quality indicator DTP (QI-DTP) was a DTP for a priority disease to which the pharmacist could apply an evidence-based intervention that has been proven, in randomized controlled trials or meta-analyses, to improve clinically important outcomes. Any DTP could be subcategorized as a PD-DTP and/or a QI-DTP. For example, any pharmacist-resolved DTP for heart failure would be a PD-DTP, and initiating a β-blocker for heart failure would also be subcategorized as a QI-DTP. According to the organization's process measure data for 2013, clinical pharmacists resolved a total of 29 909 DTPs in that year. Of these, 12 017 (40%) were PD-DTPs and 8682 (29%) were QI-DTPs.

Survey Questionnaire

A nonvalidated 10-question Likert-type questionnaire was developed by the investigators to elicit residents' satisfaction with domains of training, usability, efficiency, and time requirements (Appendix 1). Potential responses ranged from 1 (strongly disagree) to 5 (strongly agree). The survey questionnaire was deployed with SurveyMonkey (San Mateo, California; www.surveymonkey.com).

Outcome Measures

The primary outcome was the total number of DTPs resolved by pharmacy practice residents during 24 weeks of direct patient care rotations from September 2, 2013, to June 13, 2014. Excluded from the analysis were the first 4-week core rotation (internal medicine) and the 2-week preceptorship rotation, the latter because it focused on developing residents' teaching skills rather than providing direct patient care. The secondary outcomes were number of PD-DTPs resolved; number of QI-DTPs resolved; the progression in terms of numbers of DTPs, PD-DTPs, and QI-DTPs resolved by the residents during sequential rotations over time; and feedback from survey respondents about the DTP tracking experience across domains of training, usability, efficiency, and time requirements.

Statistical Analysis

Summary descriptive statistics with median and ranges for ordinal survey data were calculated.

RESULTS

During the study period, all 4 residents consented and participated in the study. DTP data were captured by 1 resident who completed 3 clinical rotations and 3 residents who completed 6 clinical rotations, for a total of twenty-one 4-week rotations with data capture. Pharmacy practice residents resolved a total of 1201 DTPs during the study period. Of these, 620 (52%) were PD-DTPs and 479 (40%) were QI-DTPs. As depicted in Figure 1, the monthly group counts for all DTPs, PD-DTPs, and QI-DTPs increased over time for the first 3 rotations, decreased for rotations 4 and 5, and increased for rotation 6.

Figure 2 illustrates the results for the DTP Tracker satisfaction survey. The median score for all questions was 4 ("agree"). For questions 1 and 2, the response was 4 for all participants; for questions 3 and 4, the response was 3 or 4 for each participant; and for questions 5 through 10, the response was 4 or 5 for each participant. In addition, all residents responded "yes" to a summary question about satisfaction with the DTP Tracker across all 4 domains (data not shown).

Given the variability in progression of resolution of DTPs, PD-DTPs, and QI-DTPs over time (Figure 1), post hoc analyses of totals by individual resident (Table 1) and by rotation (Table 2) were performed. Table 1 shows that 2 of the residents had similar productivity, with the third resident generating slightly lower numbers of resolved DTPs, and the fourth resident (who completed only 3 rotations) having the lowest numbers. Table 2 shows that the numbers of resolved DTPs, PD-DTPs, and QI-DTPs varied depending on the type of rotation. The highest numbers of resolved DTPs were generated during rotations in cardiology, critical care, and community medicine, and the lowest totals were generated in ambulatory care and a remedial medicine rotation.

DISCUSSION

The purpose of this study was to describe the contribution of 4 pharmacy practice residents to clinical pharmacy care, using resolved DTPs as an accepted process-of-care measure. During the twenty-one 4-week rotations, participating residents resolved a total of 1201 DTPs, a median of 346 per resident over 6 months. Of these 1201 resident-resolved DTPs, 620 (52%) were PD-DTPs and 479 (40%) were QI-DTPs (Tables 1 and 2). For perspective, according to DTP Tracker data for January to June 2014, the proportions of DTPs that were PD-DTPs and QI-DTPs were higher for residents than for staff pharmacists: 52% versus 33% for PD-DTPs and 40% versus 23% for QI-DTPs, respectively. The residents accounted for 7% (1201/17 197) of all pharmacist-resolved DTPs, 10% (620/6114) of all PD-DTPs, and 11% (479/4525) of all QI-DTPs in the health authority.

On the basis of the pharmacy practice literature, these numbers of resolved DTPs would be expected to translate into clinical and economic benefits for patients. Gillespie and others[6] demonstrated that 240 pharmacist-resolved DTPs over 6 months translated into a 47% reduction in emergency department visits, a 16% reduction in hospital visits, and an 80% reduction in drug-related readmissions, with a net overall saving of $230/patient. In the Interior Health Authority, the number of resolved DTPs per resident over 6 months was even higher, at a median of 346. Furthermore, 52% of the resident-resolved DTPs in this study were for priority disease states, with 40% involving evidence-based interventions proven to reduced mortality, morbidity, and health resource utilization. In the study by Makowsky and others,[5] 728 pharmacist-resolved DTPs over a 6-month period translated into a 45% increase in the quality of drug therapy for 5 targeted conditions and led to a 20% reduction in 3-month readmission rates. Although that DTP resolution rate was almost double the median number of DTPs resolved by each Interior Health pharmacy practice resident, the pharmacists in the study by Makowsky and others[5] had 5–8 years of experience.

Overall, the pharmacy practice residents in the current study resolved DTPs at a rate and with an importance that would be expected to translate into clinically important benefits, according to our interpretation of the COLLABORATE study.[5] Previous literature indicates that a resolved DTP is a process measure that represents a beneficial change in a patient's medication regimen. More specifically, a PD-DTP is a resolved DTP for a prevalent and impactful disease, and a QI-DTP is a resolved DTP linked to strong guideline recommendations, based on moderate to

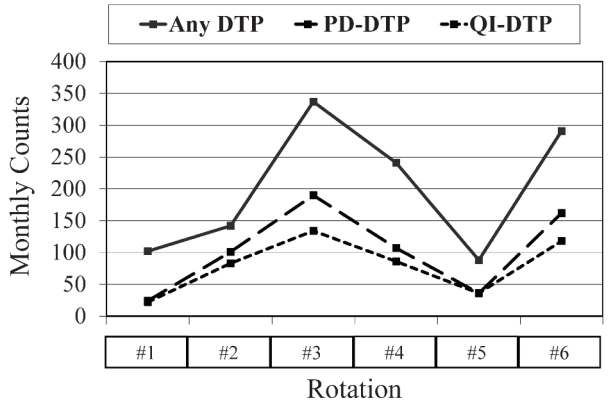

Figure 1. Monthly counts of resident-resolved drug-therapy problems (DTPs), priority disease drug therapy problems (PD-DTPs), and quality indicator drug therapy problems (QI-DTPs) over time, by resident rotation number.

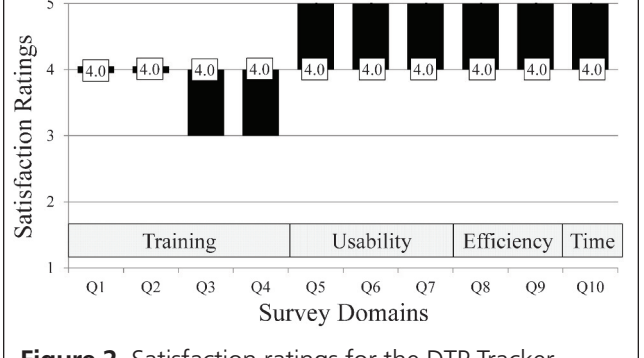

Figure 2. Satisfaction ratings for the DTP Tracker, showing minimum, maximum, and median values. The numbered questions are provided in Appendix 1.

Table 1. Numbers of Drug Therapy Problems, by Resident

	Type of DTP*; No. (%) of DTPs		
Resident	**All DTPs**	**PD-DTPs**	**QI-DTPs**
Resident 1 (6 rotations)	433	240 (55.4)	192 (44.3)
Resident 2 (6 rotations)	426	220 (51.6)	175 (41.1)
Resident 3 (6 rotations)	265	133 (50.2)	96 (36.2)
Resident 4 (3 rotations)	77	27 (35.1)	16 (20.8)

DTP = drug therapy problem, PD-DTP = priority disease drug therapy problem, QI-DTP = quality indicator drug therapy problem.
*For each resident, there were some DTPs categorized as both PD-DTP and QI-DTP. In addition, there were some DTPs not categorized as either PD-DTP or QI-DTP.

Table 2. Numbers of Drug Therapy Problems, by Rotation Type

	Type of DTP*; No. (%) of DTPs		
Rotation	**All DTPs**	**PD-DTPs**	**QI-DTPs**
Cardiology (4 rotations)	360	285 (79.2)	228 (63.3)
Critical care (3 rotations)	297	110 (37.0)	56 (18.9)
Community medicine (4 rotations)	152	54 (35.5)	54 (35.5)
Infectious diseases (3 rotations)	123	58 (47.2)	58 (47.2)
Nephrology (2 rotations)	96	31 (32.3)	19 (19.8)
Cardiac surgery (1 rotations)	94	48 (51.1)	42 (44.7)
Ambulatory care (3 rotations)	54	17 (31.5)	16 (29.6)
Medicine (1 rotation)	25	17 (68.0)	6 (24.0)

DTP = drug therapy problem, PD-DTP = priority disease drug therapy problem, QI-DTP = quality indicator drug therapy problem.
*Within each rotation, there were some DTPs categorized as both PD-DTP and QI-DTP. In addition, there were some DTPs not categorized as either PD-DTP or QI-DTP.

high-quality evidence, that translates into improved quality of medication therapy (outcome measure) and fewer readmissions (health resource utilization measure).[5] In our study, the number of DTPs, PD-DTPs, and QI-DTPs increased during the first 3 rotations, dropped transiently, and then recovered (Figure 1). This pattern may indicate that as the year progressed, residents became more knowledgeable about various disease states and more confident in identifying and resolving DTPs. This progressive increase might also have been due to the residents becoming more efficient in tracking their DTPs as they became more familiar with the device and the tracking process. Finally, the variability in numbers over time might have been due to the low number of rotations for one resident, who did not contribute data after rotation 3, and to the variability in intervention opportunity and yield of DTPs, PD-DTPs, and QI-DTPs for different rotations because of differences in practice settings and practitioners (Table 2). Most of the residents had "lower-yield" rotations scheduled for rotations 4 and 5, which might explain these results. Additionally, reporting bias due to competing duties (e.g., research project work) during rotations 4 and 5 could have influenced the results. It should be noted that the contribution of preceptors to improving the residents' clinical competencies required to independently identify and resolve DTPs was likely variable across rotations, despite standardized tools and processes for competency assessment. In addition, this aspect could not be practically controlled, nor could pertinent data be collected or reported. Finally, the results of the survey concerning DTP Tracker satisfaction (Figure 2) indicated that DTP tracking by residents was well accepted across the domains of training, usability, efficiency, and time. This acceptance would support ongoing use of DTP tracking by residents as a longitudinal process measure for pharmacy practice residents throughout their residency.

To our knowledge, no Canadian literature has captured the contribution of pharmacy practice residents to cpKPIs in the area of drug therapy interventions (e.g., resolved DTPs). Some studies have demonstrated the practice contribution of US entry-to-practice PharmD students and postgraduate residents.[16-19] Taylor and others[16] described the impact of pharmacy faculty, residents, and students (referred to as the education group) on the number and types of interventions at a community hospital. Interventions included discharge counselling and education, provision of formal consultations to physicians, therapeutic recommendations, IV-to-oral conversion, provision of drug information by pharmacists, antibiotic recommendations, follow-up pharmacokinetics, dosage adjustments, and laboratory monitoring.[16] Of the 2873 accepted interventions provided by the education group, the residents contributed 877 (30.5%), while PharmD students contributed 1344 of the total (46.8%).[16] However, the authors did not show breakdowns by specific types of interventions for each group. Maack and others[17] described the contributions of one post-graduate year 1 pharmacy practice resident in an assisted living facility. The interventions were related to ADR/adherence issues, appropriateness of doses, appropriateness of laboratory monitoring, appropriateness of length of therapy, cost issues, drug

contraindications or drug allergies, drug-drug interactions, indications for and appropriateness of all medications, missing drug therapy, responding to requests for patient follow-up visits, and therapeutic duplications.[17] Of the 125 recommendations made by the pharmacy practice resident, 72 (57.6) were accepted.[17] In a systematic review, Mersfelder and Bouthillier[18] showed that PharmD students contributed to direct patient care by providing drug information, recommending therapeutic alternatives/changes, obtaining medication histories, and providing patient education. Individual students made between 1.2 and 16 recommendations to prescribers each week, with an acceptance rate ranging from 32% to 98%.[18] The weekly number of recommendations increased over time, from 1.8 per student in the first week to 6.2 per student in week 5.[18] Finally, Delgado and others[19] described the contribution of pharmacy students and residents to direct patient care in a new practice model. The number of interventions increased from 0.9 to 1.4 per patient-day after learners became involved in providing direct patient care. Although these studies offer a general sense of the clinical activities, recommendations, and acceptance rates for pharmacy students and residents over time, they did not reliably quantify the number, type, and impact of clinical care interventions provided by pharmacy practice residents, or the specific contribution of residents to resolving identified DTPs for patients to improve their drug therapy.

This study had inherent limitations related to its design. Because of the nature of the study, the data collected about resolved DTPs may have been incomplete or inaccurate. Measurement bias may have been present, given that not all residents entered all of their resolved DTPs in the DTP Tracker, and some who delayed data entry may not have recalled or entered all of their DTPs. Given that the study took place over a period when experiential rotations were completed, clinical maturation or proficiency bias could have contributed to differential effects over time, as well as social desirability bias. Given that this study was observational, it is acknowledged that many of these potential biases could not be practically measured or controlled for in the analysis and that they are nondirectional. Furthermore, the investigators were most interested in the real-world impact of residents' contributions to resolution of DTPs, PD-DTPs, and QI-DTPs, and their feedback on the feasibility of the DTP Tracker.

CONCLUSION

This study has demonstrated that pharmacy practice residents at the study institution contributed directly and significantly to clinical care, as measured by resident-resolved DTPs, PD-DTPs, and QI-DTPs for patients. They are implementing evidence-based recommendations on drug therapy for patients with priority disease states and are contributing to a significant proportion of the DTP interventions by all pharmacists in the health authority. Residents' DTP interventions appeared to increase over time but varied by rotation. Based on randomized controlled trials in pharmacy practice, it is our opinion that the magnitude and impact of these resident-resolved DTPs, PD-DTPs, and QI-DTPs would be expected to improve clinical and health economic outcomes for patients. DTP tracking by residents was well accepted, in terms of training, usability, efficiency, and time requirements. Health authorities should use these data to help justify residency program expansion to meet future staffing needs. Future research should focus on describing the contribution of hospital pharmacists and pharmacy practice residents to clinical pharmacy care using the 8 recommended cpKPIs. Such an analysis would provide a more balanced dashboard of quality indicators shown to improve patient outcomes.

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Appendix 1: Questions for a survey about the DTP [Drug Therapy Problem] Tracker.

Training

1. The training information was *relevant* for me to appropriately use the DTP Tracker.
2. I am more *competent* in my knowledge, skills, and abilities to use the DTP Tracker after this training.
3. I am more *confident* in entering data into the DTP Tracker after this training.
4. I am *satisfied* with the training I received for the DTP Tracker.

Usability

5. The DTP Tracker is *easy* to use.
6. The DTP Tracker is *convenient* to use.
7. I am satisfied with the *usability* of the DTP Tracker.

Efficiency

8. The tracking of DTPs *interfered* with other required activities.
9. The DTP Tracker is *efficient* to use.

Time Requirements

10. I am satisfied with the time required to track data in the DTP Tracker.

Note: All questions were answered using a 5-point Likert scale:
1 – strongly disagree
2 – disagree
3 – neutral
4 – agree
5 – strongly agree

ORIGINAL RESEARCH

Physicochemical Stability of Vancomycin at High Concentrations in Polypropylene Syringes

Élise d'Huart, Jean Vigneron, Alexandre Charmillon, Igor Clarot, and Béatrice Demoré

ABSTRACT

Background: In severe infections, high-concentration vancomycin may be administered by continuous infusion. The dosage of vancomycin may reach 60 mg/kg per day.

Objectives: To study the feasibility of preparing high-concentration vancomycin solutions (40 to 83.3 mg/mL), to study the effect of an electric syringe pump on the physical stability of high-concentration vancomycin, and to study the stability of vancomycin 62.5 and 83.3 mg/mL in 0.9% sodium chloride (0.9% NaCl) or 5% dextrose in water (D5W) with storage up to 48 h at room temperature.

Methods: The following sets of syringes were prepared: (1) 4 syringes of vancomycin in 0.9% NaCl for each of 5 concentrations between 40 and 83.3 mg/mL (total 20 syringes); (2) 6 syringes at 83.3 mg/mL in 0.9% NaCl and 6 syringes at 83.3 mg/mL in D5W; and (3) 30 syringes at 83.3 mg/mL in D5W. Visual inspection was performed for all 3 syringe sets, and subvisual inspection for sets 1 and 2 (for periods of 24 h for set 1 and 48 h for sets 2 and 3). One syringe of vancomycin 83.3 mg/mL with each solvent was inserted into an electric syringe pump, and samples from the infusion line and collected after transit through the pump were inspected visually. Chemical stability was evaluated by high-performance liquid chromatography, and physical stability, pH, and osmolality were investigated.

Results: For all sets of syringes, no physical modification was observed over time, nor were any changes observed after transit through the electric syringe pump. In 0.9% NaCl, vancomycin 62.5 and 83.3 mg/mL retained more than 90% of the initial concentration after 48 and 24 h, respectively; however, for the 83.3 mg/mL solution, precipitate was visible after 48 h. In D5W, vancomycin at 62.5 and 83.3 mg/mL retained more than 90% of the initial concentration after 48 h.

Conclusion: It was feasible to prepare high-concentration solutions of vancomycin. The electric syringe pump did not cause any precipitation. Vancomycin in D5W at 62.5 and 83.3 mg/mL was stable over 48 h at room temperature. Precipitation occurred in 0.9% NaCl. D5W is therefore recommended as the solvent for this drug.

Keywords: vancomycin, intensive care unit, high-performance liquid chromatography, stability

RÉSUMÉ

Contexte : En cas d'infection grave, de la vancomycine à forte concentration peut être administrée par perfusion continue à une dose pouvant atteindre 60 mg/kg par jour.

Objectifs : Mener une étude de faisabilité portant sur la préparation de solutions de vancomycine à forte concentration (de 40 à 83,3 mg/mL); étudier l'effet d'un pousse-seringue électrique sur la stabilité physique de la vancomycine à forte concentration; et étudier la stabilité de la vancomycine (62,5 et 83,3 mg/mL) dans une solution de chlorure de sodium à 0,9 % (NaCl à 0,9 %) ou dans une solution aqueuse de dextrose à 5 % (D5W) après 48 h à la température ambiante.

Méthodes : Trois ensembles de seringues ont été préparés : (1) quatre seringues de vancomycine dans une solution de NaCl à 0,9 %, à chacune des cinq concentrations comprises entre 40 et 83,3 mg/mL (20 seringues au total); (2) six seringues à 83,3 mg/mL dans une solution de NaCl à 0,9 % et six seringues à 83,3 mg/mL dans une solution de D5W; et (3) 30 seringues à 83,3 mg/mL dans une solution de D5W. Une inspection visuelle des trois ensembles de seringues et une inspection « sous-visuelle » des ensembles 1 et 2 ont eu lieu (période de 24 h pour l'ensemble 1 et de 48 h pour les ensembles 2 et 3). Une seringue contenant de la vancomycine à 83,3 mg/mL mélangée à chaque solvant a été insérée dans un pousse-seringue électrique, et les échantillons prélevés dans le tube de perfusion et ceux recueillis après leur passage dans la pompe ont été inspectés visuellement. La stabilité chimique a été évaluée par chromatographie liquide à haute performance et la stabilité physique, le pH ainsi que l'osmolalité ont eux aussi été étudiés.

Résultats : Les trois ensembles de seringues n'ont présenté aucune modification physique avec le temps. Aucun changement n'a non plus été observé après le passage dans le pousse-seringue électrique. Dans la solution de NaCl à 0,9 %, la vancomycine à 62,5 et à 83,3 mg/mL a conservé plus de 90 % de sa concentration initiale respectivement après 48 et 24 h. Cependant, le précipité de la solution à 83,3 mg/mL était visible après 48 h. Dans la solution de D5W, la vancomycine à 62,5 et à 83,3 mg/mL a conservé plus de 90 % de sa concentration initiale après 48 h.

Conclusion : La préparation de solutions de vancomycine à forte concentration est faisable. Le pousse-seringue électrique n'a pas causé

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de précipitation. La vancomycine dans la solution de D5W à 62,5 et à 83,3 mg/mL est restée stable pendant plus de 48 h à la température ambiante. Les précipitations se sont produites dans les solutions de NaCl à 0,9 %. On recommande donc la solution de D5W comme solvant pour ce médicament.

Mots-clés : vancomycine, unité de soins intensifs, chromatographie liquide à haute performance, stabilité

INTRODUCTION

Vancomycin is an antibiotic of the glycopeptide family produced by a soil bacterium, *Amycolatopsis orientalis.* Vancomycin kills bacteria in a time-dependent manner, which means that the amount of time the bacteria are exposed to a sufficiently high concentration is key to treatment success.[1] This antibiotic is used to treat a variety of bacterial infections, such as infective endocarditis due to *Staphylococcus* (in penicillin-allergic patients) or methicillin-resistant *Staphylococcus aureus* (MRSA).[2] In infective endocarditis caused by MRSA, the recommended dosage of vancomycin is 30–60 mg/kg daily; for osteoarticular MRSA infections, the recommended dosage is 60 mg/kg daily.[3]

In emergency clinical settings, such as the intensive care unit (ICU), the optimal serum concentration of vancomycin must be achieved rapidly and maintained over time. To avoid fluid overload, ICUs often use a high concentration of drug in a minimal volume of solution. Wysocki and others[4] demonstrated that continuous infusion allowed rapid achievement of the target concentration. In clinical practice, a loading dose can be administered, followed by continuous infusion.[1]

Manufacturers have reported that vancomycin 5 mg/mL in 0.9% sodium chloride (0.9% NaCl) is stable for 48 h at 25°C,[5] but caution that the final concentration should not exceed 10 mg/mL.[6] For patients with body weight about 65 kg, the total daily dose of vancomycin, at the recommended dosage of 60 mg/kg daily, is 4 g. This amount of drug would have to be diluted with 400 mL of solvent to yield a final concentration not exceeding 10 mg/mL. However, for patients with fluid restrictions, this volume is excessive.

Previous studies have evaluated the stability of vancomycin at concentrations exceeding 10 mg/mL. Godet and others[7] determined that vancomycin 41.7 mg/mL in 0.9% NaCl or 5% dextrose in water (D5W) stored in polypropylene syringes at a temperature between 18°C and 25°C was stable for 48 h. Masse and others[8] determined that vancomycin 41.7 mg/mL in water for injection or 0.9% NaCl stored in polypropylene syringes at room temperature was stable for 24 h.

Longuet and others[9] explained that vancomycin at a concentration of 80 mg/mL is often used in electric syringe pumps, but its safety has not been scientifically confirmed. In the authors' hospital, high doses of vancomycin can be administered over 24 h in the ICU, using an electric syringe pump. The total volume is limited to 50 mL (and nurses usually use a final volume of 48 mL), which means that the concentration must be high, for example, 62.5 (3 g of drug in 48 mL of solvent) or 83.3 mg/mL (4 g of drug in 48 mL of solvent).

As reported in a poster presentation, Masse and others[10] studied the physicochemical stability of vancomycin 80 mg/mL in 0.9% NaCl in polypropylene syringes, at 22°C. They used high-performance liquid chromatography (HPLC), visual inspection, particle count, and microbiological stability studies. The authors observed precipitation, with the number of particles (≥ 10 µm) in the unfiltered vancomycin solutions increasing as storage time increased. These authors used an electric syringe pump for a period of 24 h at 22°C, but they did not study the stability of vancomycin 80 mg/mL in D5W.

In the authors' hospital, vancomycin is typically administered by intermittent infusion over 1 h, but high doses of the drug are also administered by continuous infusion in the ICU. The aim of this study was to validate the possibility of preparing highly concentrated solutions for administration by continuous IV infusion. Given the potential risk of precipitation highlighted by Masse and others,[10] our first objective was to determine the feasibility of preparing vancomycin solutions at concentrations between 40 and 83.3 mg/mL in 0.9% NaCl or D5W in polypropylene syringes and to study the effect of an electric syringe pump on the physical stability of vancomycin 83.3 mg/mL in 0.9% NaCl and in D5W. The second objective was to study the stability of vancomycin 62.5 mg/mL and 83.3 mg/mL in 0.9% NaCl or D5W in polypropylene syringes, on the basis of analysis immediately after preparation and after storage for 6, 24, and 48 h at room temperature.

METHODS

Feasibility of Preparing High-Concentration Vancomycin Solutions

Before the stability study, we evaluated the risk of precipitation for vancomycin solutions in 0.9% NaCl or D5W at various concentrations between 40 and 83.3 mg/mL in polypropylene syringes at room temperature.

The first set of test solutions consisted of 4 syringes of vancomycin in 0.9% NaCl at each of 5 concentrations—40, 50, 58.8, 71, and 83.3 mg/mL—prepared and stored at room temperature. The second set consisted of 12 syringes of vancomycin 83.3 mg/mL—6 syringes in 0.9% NaCl and 6 syringes in D5W—prepared from 1-g vials of vancomycin. For the preparation of 3 syringes with each solvent, we used a

polycarbonate spike adaptor (ChemoClave Universal Vented Vial Spike, ICU Medical Inc, San Clemente, California) to reconstitute the vancomycin; for the other 3 syringes, we used a needle and air intake. The third set consisted of 30 syringes of vancomycin 83.3 mg/mL in D5W, to study physical compatibility.

All syringes in each set were visually inspected by 2 technicians against a white background with the unaided eye. In addition, the subvisual aspect of the first 2 sets of syringes was investigated by evaluation of turbidity with a UVmc2 spectrophotometer (SAFAS Monaco), with absorbance determined at 350, 410, and 550 nm.[11] For the first set of syringes, visual and subvisual inspections were performed after preparation and after storage for 8, 15, and 24 h. For the second set of syringes, visual and subvisual inspections were performed after preparation and after storage for 24 and 48 h. For the third set of syringes, visual inspection only was performed after storage for 6, 16, 24, and 48 h at room temperature.

To determine the influence on the solution (before administration) of an electric syringe pump with infusion line, incorporating a 0.22-µm filter (Agilia Injectomat, Fresenius Kabi), a syringe containing vancomycin 83.3 mg/mL in 0.9% NaCl (final volume 48 mL) was inserted into the pump. We added an extension for infusion (Doran International; 160 cm, VR = 1.334 mL, diameter = 1.0 × 3.0 mm; batch 261801P), with a 0.2-µm filter (Codan France; batch K73791-1), onto the syringe. The same process was repeated for a syringe containing vancomycin 83.3 mg/mL in D5W. The flow rate was 25 mL/h. Vancomycin samples collected from the infusion line underwent visual evaluation.

Stability Study: Preparation of Test Solutions

To assess the stability of vancomycin, solutions were prepared at 2 concentrations (62.5 and 83.3 mg/mL) in 0.9% NaCl or D5W; a total of 3 syringes were prepared for each combination of concentration and solvent (i.e., total of 12 syringes). For each syringe with concentration 62.5 mg/mL, 3 vials of vancomycin 1 g (Sandoz; batch EC0107) were each reconstituted with 16 mL of 0.9% NaCl (Easyflex 0.9% NaCl 500 mL, MacoPharma; batch 18B01B) or D5W (Easyflex D5W 500 mL, MacoPharma; batch 17I12D) and then combined for a total of 48 mL for each solvent. For each syringe with concentration 83.3 mg/mL, 4 vials of vancomycin 1 g were each reconstituted with 12 mL of 0.9% NaCl or D5W and then combined for a total of 48 mL for each solvent. Each 48-mL volume of drug was transferred to a polypropylene syringe (BD Plastipak, 50-mL Luer-lock syringes; batch 1803236) for storage at room temperature (20°C to 25°C), without protection from light.

Stability Study: Determination of Chemical Stability

HPLC Assay

The vancomycin solutions were analyzed by a stability-indicating reverse-phase HPLC method with photodiode array detection.[8]

The HPLC system consisted of an Elite LaChrom VWR/Hitachi plus autosampler, a VWR photodiode array detector L-2455, and a VWR L-2130 HPLC pump. Data were acquired and integrated with EZChrom Elite software (VWR). The column used contained LiChrospher 100 RP-18 gel carrier in a LiChroCART 125-4 cartridge, 12.5 cm long with 5-µm particle size (Merck). The mobile phase consisted of 0.1 mol/L buffer (8% acetonitrile [VWR Chemicals; batches D7G058267G and D5N045046A] and 92% monopotassium phosphate [Merck; batch AM09735277618]), adjusted to pH 3.5 with orthophosphoric acid 85% (VWR Chemicals; batch 15D200503). Water for chromatography was obtained from a reverse osmosis system (Millipore Iberica).

The flow rate was set at 1.5 mL/min, with an injection volume of 10 µL. The detection wavelength was set at 220 nm. The temperature of the injector was set at 15°C and that of the column oven at 30°C. The calibration curve was constructed from plots of peak area versus concentration. The linearity of the method was evaluated for 5 concentrations (50, 75, 100, 125, and 150 µg/mL).

For preparation of the standard curve, a solution of vancomycin 1 mg/mL was prepared from 100.0 mg of precisely weighed drug (vancomycin 125 mg, Sandoz; batch DA0012) diluted in 100.0 mL of the mobile phase. Further dilution of this 1 mg/mL solution with the mobile phase was used to generate solutions suitable for creating standard curves. The intra-day reproducibility was evaluated as recommended by the Q2 (R1) guideline of the International Conference on Harmonisation,[12] using 3 determinations for each of 3 concentrations: 50, 100, and 150 µg/mL. To evaluate inter-day precision, the 3 concentrations (50, 100, and 150 µg/mL) were assayed 3 times on each of 3 different days. To demonstrate the specificity of the method and the absence of interaction between vancomycin and the solvent, solutions of 0.9% NaCl and D5W were analyzed by HPLC.

The stability-indicating capability of the assay was evaluated by analyzing vancomycin solutions that had been subjected to forced degradation. For acidic degradation, 1 mL of a 400 µg/mL vancomycin solution (vancomycin 125 mg, Sandoz; batch DA0012) was diluted with 1.0 mL of hydrochloric acid (HCl) 1.0 mol/L (VWR Chemicals; batch 17110005), stored at room temperature (20°C to 25°C) for 16 h, neutralized with 1.0 mL of sodium hydroxide (NaOH) 1.0 mol/L (VWR Chemicals; batch 17110003), and then diluted with 1.0 mL of the mobile phase to obtain a theoretical concentration of 100 µg/mL. For alkaline degradation, 1 mL of a 400 µg/mL vancomycin solution was diluted with 1.0 mL of NaOH 1.0 mol/L, stored at room temperature (20°C to 25°C) for 60 min, neutralized with 1.0 mL of HCl 1.0 mol/L, and then diluted with 1.0 mL of the mobile phase to obtain a theoretical concentration of 100 µg/mL. For oxidative degradation, 1 mL of a 400 µg/mL vancomycin solution was diluted with 1.0 mL hydrogen peroxide (H_2O_2) 3.0% or 30.0% (both concentrations prepared from 30% H_2O_2; Merck, batch K48743810713), stored at room temperature (20°C to 25°C) for 1 h, and then diluted with 2.0 mL of the mobile phase

to obtain a theoretical concentration of 100 µg/mL. For heat degradation, a solution of 100 µg/mL vancomycin was exposed to a temperature of 80°C for 6 h.

The photodiode array detector could evaluate the ultraviolet (UV) spectrum of the chromatographic column effluent every 0.4 s, which allowed evaluation of the UV purity of each eluting peak. Variations in the UV spectrum over the elution profile of the peak of interest would indicate that the peak was contaminated, that the analytical method did not separate vancomycin from its degradation products, and that the method was therefore unsuitable.[13]

The stability of the diluted sample in the autosampler was also evaluated. Solutions of vancomycin diluted in ultrapure water were stored in the autosampler at 15°C. Vancomycin concentration was evaluated at various times up to 24 h.

At each analysis time, 5 mL of solution was removed from each syringe (62.5 mg/mL or 83.3 mg/mL). Each sample was then diluted with the mobile phase to obtain a theoretical concentration of 100 µg/mL (the middle of the standard curve). For each syringe, samples were prepared in triplicate for analysis by reverse-phase HPLC immediately after initial preparation and after 6, 24, and 48 h of storage. Total run time for HPLC was set at 15 min.

Chemical stability was defined as not less than 90.0% of the initial vancomycin concentration in relation to the evolution of potential degradation products.[12,14]

Measurement of pH

The pH of each solution (i.e., every syringe representing each combination of concentration and solvent) was measured with a Bioblock Scientific pH meter after initial preparation and after 6, 24, and 48 h of storage. The pH values were considered acceptable if they did not vary by more than 1.0 pH unit from the initial measurement.[14]

Osmolality

Osmolality was measured for each syringe at each analysis time using an osmometer (Roebling). Before each measurement, the osmometer was calibrated with a quality control solution (300 mOsm/kg) provided by the manufacturer.

Stability Study: Determination of Physical Stability

Physical stability was defined as the absence of particulate formation, haze, colour change, or gas evolution.[11] The samples from the stability study were visually inspected, with the unaided eye, against a white or black background by 2 technicians (working independently) after initial preparation and after storage for 6 h, 24 h, 48 h, and 5 days. The subvisual aspect was assessed, after manual agitation, with a UVmc2 spectrophotometer (SAFAS Monaco), with absorbance evaluated at 350, 410, and 550 nm.[11]

RESULTS

Feasibility of Preparing High-Concentration Vancomycin Solutions

No change in appearance of the solutions was visible at any analysis time for any combination of concentration and solvent. Similarly, there were no differences in the visual appearance of syringes prepared with a needle and air intake or with a spike adaptor. The maximum variation in turbidity between the time of syringe preparation and assay time (for solutions in the first 2 sets of syringes) was less than 0.04 absorbance units (AU) at 350 nm, less than 0.02 AU at 410 nm, and less than 0.02 AU at 550 nm.

After use of the electric syringe pump, no precipitate was observed for vancomycin 83.3 mg/mL in 0.9% NaCl or D5W.

Stability Study: Determination of Chemical Stability

HPLC Assay

The calibration curve was linear, and the coefficient of determination was 0.9995. The equation for the calibration curve was $y = 68080.757x - 339239.933$. The intra-day precision, expressed as relative standard deviation, was between 0.22% and 1.37%. The intermediate precision, expressed as relative standard deviation, was 2.48% at 50 µg/mL, 1.70% at 100 µg/mL, and 2.33% at 150 µg/mL.

For the evaluation of stability in the autosampler, solutions were stable, with a degradation rate less than 1%.

The stability-indicating capability of the assay was tested under various conditions of forced degradation. More specifically, the UV spectral purity of the vancomycin peak in chromatograms of the degraded samples was compared with the spectrum of the undegraded sample of vancomycin obtained at time 0. A sample chromatogram of vancomycin without forced degradation is presented in Figure 1, with retention time of 7.19 min, and a chromatogram of vancomycin after alkaline degradation in Figure 2. The mass balance and retention of degradation products relative to the pure vancomycin peak are presented in Table 1. After forced degradation, the extent of degradation was 25% under acidic conditions, 23% under alkaline conditions, and 14% with heating. No degradation occurred under oxidative conditions.

The various conditions tested allowed good separation and detection of degradation products. The extent of degradation was about 20%, the limit recommended in a guideline developed by the Société Française de Pharmacie Clinique (French Society of Clinical Pharmacy) and the Groupe d'Évaluation et de Recherche sur la Protection en Atmosphère Contrôlée (Evaluation and Research Group on Protection in Controlled Atmosphere).[14]

The percentage of vancomycin remaining in solutions with original concentration 62.5 or 83.3 mg/mL in 0.9% NaCl or D5W after storage at room temperature (20°C to 25°C) for various periods is shown in Table 2.

During the stability study, none of the degradation products that appeared with forced degradation were observed. Peaks 3, 9,

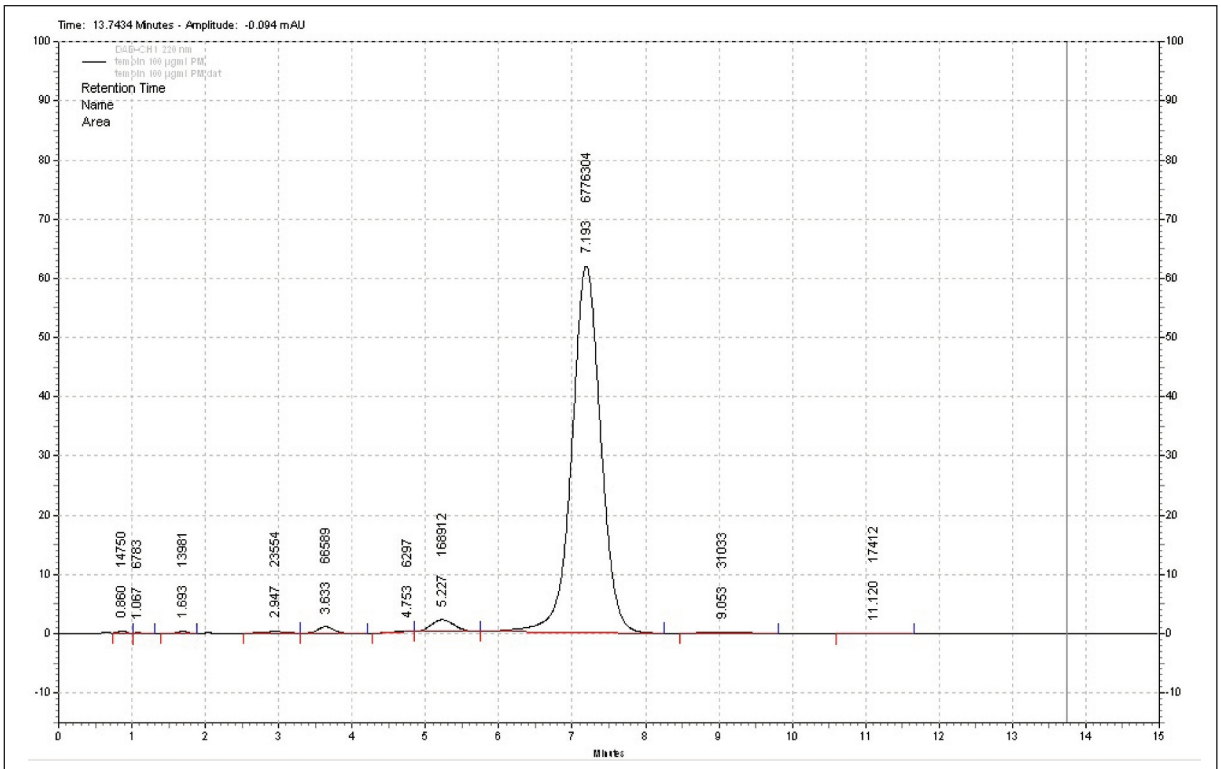

Figure 1. Chromatogram of vancomycin 100 µg/mL without degradation.

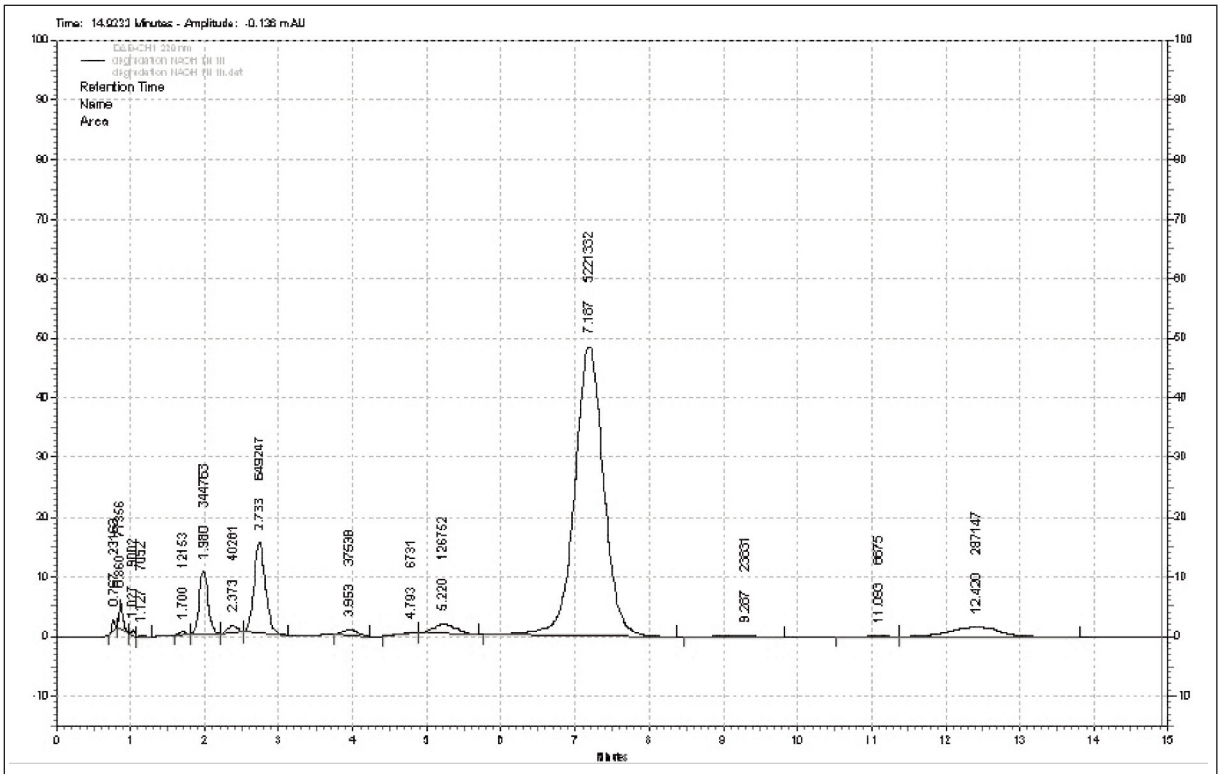

Figure 2. Chromatogram of vancomycin 100 µg/mL after alkaline degradation (sodium hydroxide 1.0 mol/L, 1 h).

Table 1. Mass Balance of Vancomycin Solutions after Various Methods of Forced Degradation

Peak no.	Retention time (min)	Relative retention	Mass Balance, as Area under the Curve (AUC)*			
			Without degradation	Acidic (1.0 M HCl for 16 h)	Alkaline (1.0 M NaOH for 60 min)	Heat (80°C for 4 h)
Original solution of vancomycin	7.19	1.00	6 776 304	5 083 649	5 221 332	5 807 582
1	0.86	0.12	14 750	37 974	–	20 173
2	1.06	0.15	6 783	–	–	–
3	1.69	0.24	13 981	13 154	12 153	9 990
4	1.98	0.28	–	21 855	344 763	–
5	2.07	0.29	–	–	–	9 509
6	2.37	0.33	–	–	40 281	–
7	2.74	0.38	–	12 884	–	252 400
8	2.96	0.41	23 554	–	–	–
9	3.63	0.51	66 589	20 029	37 538	788 716
10	5.23	0.73	168 912	135 190	126 752	155 835
11	9.05	1.26	31 033	–	–	–
12	9.29	1.29	–	–	23 831	–
13	9.45	1.31	–	–	–	138 086
14	11.12	1.55	17 412	1 148 901	8 675	–
15	12.42	1.73	–	–	287 147	–
Total mass balance			7 119 318	6 473 636	6 102 472	7 182 291
% degradation				25%	23%	14%

*A dash indicates that the peak was not present.

Table 2. Stability of Vancomycin in 0.9% Sodium Chloride (NaCl) and 5% Dextrose in Water (D5W)

Solvent and Concentration	Time; % of Initial Concentration (Mean ± SD)*			
	0 h	6 h	24 h	48 h
NaCl 0.9%				
62.5 mg/mL				
Syringe 1	100.00 ± 2.01	100.84 ± 1.53	101.71 ± 1.79	100.50 ± 0.59
Syringe 2	100.00 ± 0.51	98.58 ± 0.87	100.07 ± 0.58	99.52 ± 1.65
Syringe 3	100.00 ± 0.92	99.87 ± 1.21	100.41 ± 0.10	98.44 ± 0.63
83.3 mg/mL				
Syringe 1	100.00 ± 2.00	100.32 ± 1.94	96.84 ± 0.58	ND
Syringe 2	100.00 ± 2.09	99.09 ± 0.47	99.89 ± 1.47	ND
Syringe 3	100.00 ± 0.30	98.78 ± 0.19	98.36 ± 0.85	ND
5% dextrose in water				
62.5 mg/mL				
Syringe 1	100.00 ± 0.59	98.47 ± 0.68	97.05 ± 1.04	91.79 ± 2.57
Syringe 2	100.00 ± 0.37	99.67 ± 1.29	98.59 ± 1.02	94.91 ± 1.31
Syringe 3	100.00 ± 0.46	99.80 ± 0.52	99.05 ± 1.11	97.02 ± 0.40
83.3 mg/mL				
Syringe 1	100.00 ± 2.13	102.08 ± 0.12	89.21 ± 3.49	100.97 ± 0.60
Syringe 2	100.00 ± 1.97	99.69 ± 0.91	98.24 ± 1.42	101.61 ± 0.21
Syringe 3	100.00 ± 0.56	100.52 ± 0.64	100.54 ± 0.50	100.35 ± 0.80

ND = not determined (because a precipitate was present), SD = standard deviation.
*Drug concentration in samples measured at time 0 were designated as 100%. Each reported value is the mean of triplicate samples.

and 10, with relative retention 0.24, 0.51, and 0.73, respectively, were consistently observed immediately after preparation and after storage for 24 and 48 h.

Measurement of pH

No significant change in pH was observed during the stability studies. For vancomycin 62.5 and 83.3 mg/mL in NaCl 0.9%, mean pH was 3.57 (standard deviation [SD] 0.02) and 3.54 (SD 0.02), respectively, over the course of the stability study. For vancomycin 62.5 mg/mL and 83.3 mg/mL in D5W, mean pH was 3.26 (SD 0.16) and 3.32 (SD 0.14), respectively, over the course of the stability study.

Osmolality

No significant change in osmolality was observed during the stability studies. Osmolality was slightly lower in solutions using 0.9% NaCl as the solvent than in solutions using D5W. With 0.9% NaCl, osmolality was 337–351 mOsm/kg at 62.5 mg/mL and 362–378 mOsm/kg at 83.3 mg/mL. With D5W, osmolality was 363–383 mOsm/kg at 62.5 mg/mL and 379–409 mOsm/kg at 83.3 mg/mL.

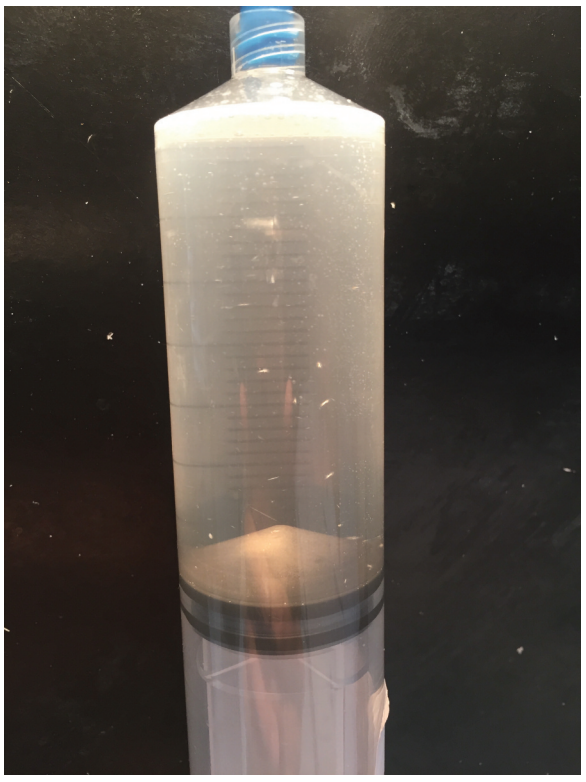

Figure 3. Appearance of vancomycin 83.3 mg/mL in 0.9% sodium chloride, after storage in syringe for 48 h.

Stability Study: Determination of Physical Stability

After storage for 48 h, precipitate was observed in syringes of vancomycin 83.3 mg/mL in 0.9% NaCl (Figure 3). These syringes were stored for an additional 3 days; upon visual inspection after a total of 5 days of storage, an extensive white precipitate was visible in all 3 syringes (Figure 4).

Solutions of vancomycin 83.3 mg/mL in D5W were slightly yellow in colour, but remained clear, with no precipitate, after 5 days of storage.

To confirm the absence of risk of precipitation at 83.3 mg/mL in D5W, a batch of 30 syringes at this concentration in this solvent was prepared and inspected visually by 2 technicians after 6, 16, 24, and 48 h of storage at room temperature. No precipitation or visual modification was observed at any observation time.

In terms of subvisual inspection, mean absorbance values for the 3 wavelengths (350, 410, and 550 nm) after the various storage periods are presented in Table 3.

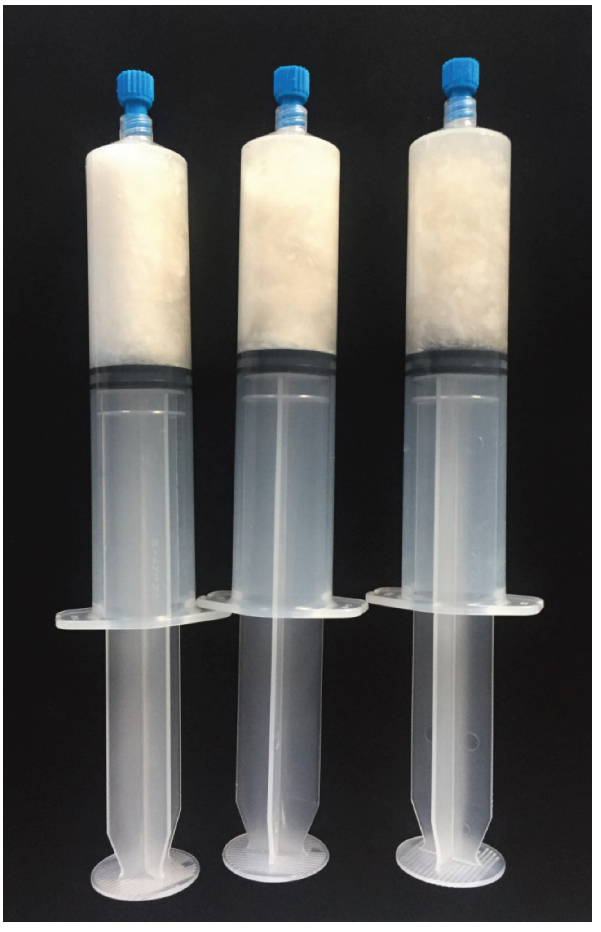

Figure 4. Appearance of vancomycin 83.3 mg/mL in 0.9% sodium chloride, after storage in syringes for 5 days.

Table 3. Absorbance Values for Vancomycin Solutions during Stability Study

Wavelength and Solution	Storage Time; Absorbance (Mean ± SD) 0 h	6 h	24 h	48 h
350 nm				
NaCl 0.9%				
62.5 mg/mL	0.09 ± 0.00	0.10 ± 0.00	0.11 ± 0.01	0.12 ± 0.00
83.3 mg/mL	0.14 ± 0.00	0.13 ± 0.00	0.15 ± 0.00	ND
D5W				
62.5 mg/mL	0.08 ± 0.01	0.08 ± 0.01	0.10 ± 0.00	0.11 ± 0.00
83.3 mg/mL	0.12 ± 0.00	0.13 ± 0.00	0.15 ± 0.00	0.17 ± 0.01
410 nm				
NaCl 0.9%				
62.5 mg/mL	0.03 ± 0.00	0.03 ± 0.00	0.04 ± 0.01	0.05 ± 0.00
83.3 mg/mL	0.05 ± 0.00	0.05 ± 0.00	0.06 ± 0.00	ND
D5W				
62.5 mg/mL	0.03 ± 0.00	0.03 ± 0.01	0.04 ± 0.00	0.05 ± 0.00
83.3 mg/mL	0.04 ± 0.00	0.04 ± 0.00	0.07 ± 0.00	0.08 ± 0.01
550 nm				
NaCl 0.9%				
62.5 mg/mL	0.01 ± 0.00	0.01 ± 0.00	0.01 ± 0.00	0.02 ± 0.00
83.3 mg/mL	0.02 ± 0.00	0.02 ± 0.00	0.02 ± 0.00	ND
D5W				
62.5 mg/mL	0.01 ± 0.00	0.01 ± 0.01	0.01 ± 0.00	0.01 ± 0.00
83.3 mg/mL	0.01 ± 0.00	0.01 ± 0.00	0.03 ± 0.00	0.03 ± 0.00

D5W = 5% dextrose in water, NaCl 0.9% = sodium chloride 0.9%, ND = not determined (because a precipitate was present), SD = standard deviation.

DISCUSSION

Vancomycin is most commonly administered by continuous infusion with an electric syringe pump.[15] For some indications, the dose of vancomycin can be elevated, meaning that a higher concentration is required, given the volume limit of 48 mL in syringes used with this type of pump. Masse and others[10] observed a precipitate in vancomycin solutions at 80 mg/mL in 0.9% NaCl stored in polypropylene syringes at 22°C (they did not study the stability of vancomycin in D5W).

In the first phase of this work, before performing the stability study, we tested the physical stability of 3 sets of vancomycin solutions (in 0.9% NaCl or D5W) in polypropylene syringes stored for 24 or 48 h at room temperature, but noted no visual or subvisual changes. Furthermore, the electric syringe pump did not cause any precipitate to form.

Stability in D5W

Diluted in D5W and stored at room temperature (20°C to 25°C), vancomycin solutions at 62.5 mg/mL and 83.3 mg/mL retained more than 90.0% of the initial concentration after 48 h.

At a concentration of 62.5 mg/mL and after storage for 48 h, syringe 1 retained 91.79% of the initial concentration with a standard deviation (SD) of 2.57%. This SD value is related to the low value obtained for 1 of the 3 samples prepared for this syringe. At a concentration at 83.3 mg/mL and after storage for 24 h, syringe 1 retained slightly less than 90% of the initial concentration, but after storage for 48 h, the value was more than 90%. We assume that these results are related to a technical problem, probably due to the 2 dilutions required to obtain the target (theoretical) concentrations.

During 48 h of storage at room temperature, no degradation products, no change of pH, and no visible modifications were observed for vancomycin solutions at 62.5 or 83.3 mg/mL in D5W.

Stability in 0.9% NaCl

Diluted in 0.9% NaCl and stored at room temperature (20°C to 25°C), vancomycin solutions at 62.5 mg/mL and 83.3 mg/mL retained more than 90.0% of the initial concentration after 48 h and 24 h, respectively. Barbault and others[16] studied the stability of vancomycin eye drops 50 mg/mL in 0.9% NaCl in glass vials. They concluded that the eye drops were stable for 15 days at 25°C, with the appearance of new peaks on the chromatogram after 7 days of storage.

The 3 syringes of vancomycin 83.3 mg/mL in 0.9% NaCl precipitated after 48 h of storage, in contrast to the 62.5 mg/mL solutions, which did not show any physical modification during the stability study. These results are discrepant with the results in the first stage of this study, described above. When we evaluated the potential risk of precipitation for vancomycin between 40 and 83.3 mg/mL, we observed no visible precipitate. The risk of precipitation for vancomycin 80 mg/mL was demonstrated by Masse and others,[10] who observed the formation of precipitates after 12 h of storage. They used an electric syringe

pump over 24 h at 22°C. In our study, mechanical pumping did not cause precipitation.

However, it must be kept in mind that the formation of precipitates can be influenced by excipients present in the product; for example, the vancomycin used in this study (from Sandoz) contained mannitol, sodium hydroxide, and hydrochloric acid. Therefore, the results cannot be extrapolated to products containing other excipients.

CONCLUSION

In the first part of this study, which investigated the feasibility of high-concentration solutions of vancomycin, solutions with concentrations between 40 and 83.3 mg/mL in 0.9% NaCl and D5W showed no visual or subvisual modification over 48 h of storage at room temperature. In addition, mechanical pumping by means of an electric syringe pump did not cause the precipitation of vancomycin at these high concentrations.

Vancomycin in D5W at concentrations of 62.5 mg/mL and 83.3 mg/mL was physically and chemically stable over a period of 48 h at room temperature. These stability data provide additional knowledge to assist intensive care services in daily practice. Vancomycin in 0.9% NaCl at a concentration of 62.5 mg/mL was physically and chemically stable over a period of 48 h at room temperature; at a concentration of 83.3 mg/mL, the solution was physically and chemically stable over a period of 24 h. Therefore, for high concentrations of vancomycin, D5W is recommended as the solvent.

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Validation of a Weight Threshold–Based Vancomycin Dosing Protocol for Patients Undergoing Intermittent Hemodialysis

Lu Xuan (Lisa) Sun, Kang-Wei (David) Liu, Stephanie Lynch, Mielen Mistry, Heather Wise, and Eduard Iliescu

ABSTRACT

Background: Patients receiving intermittent hemodialysis (IHD) are at high risk of acquiring gram-positive infections, which are often treated with IV vancomycin. Despite frequent use of vancomycin in the IHD setting, there is variability in dosing and monitoring practices among clinicians at the study institution. There is also a paucity of evidence regarding optimal vancomycin dosing to achieve target pre-IHD serum concentration.

Objectives: The primary objective was to compare the percentage of treatment courses with a serum vancomycin concentration between 15 and 20 mg/L, measured before the third IHD session, before and after implementation of a weight threshold–based dosing protocol. The secondary objectives were to compare the percentage of treatment courses with a pre–third IHD vancomycin concentration between 10 and 22 mg/L and the number of vancomycin measurements per treatment day, before and after protocol implementation.

Methods: This quasi-experimental, single-centre study included inpatients and outpatients who underwent IHD and received at least 2 IV doses of vancomycin, with vancomycin being measured in an appropriately drawn sample before the third IHD session. Before protocol implementation, vancomycin dosing was at the clinician's discretion (usual care). After protocol implementation, each patient received a loading dose of 1000, 1500, or 2000 mg and a maintenance dose of 500, 750, or 1000 mg, depending on body weight.

Results: The percentage of treatment courses with a pre–third IHD vancomycin concentration between 15 and 20 mg/L was greater after implementation of the protocol than with usual care, but the difference was nonsignificant (44% [8/18] versus 20% [3/15], $p = 0.27$). However, the percentage of treatment courses with a pre–third IHD vancomycin concentration between 10 and 22 mg/L was significantly higher after protocol implementation (94% [17/18] versus 53% [8/15], $p = 0.012$). There was no difference in the median number of vancomycin measurements per treatment day before and after protocol implementation (0.133 versus 0.125, $p = 0.99$).

Conclusions: At the study institution, the likelihood of achieving recommended vancomycin concentration increased (relative to previous practice) after implementation of a simplified vancomycin dosing protocol for patients undergoing IHD.

RÉSUMÉ

Contexte : Les patients recevant une hémodialyse intermittente (HDI) présentent un risque élevé de contracter des infections à Gram positif, souvent traitées à l'aide de vancomycine par intraveineuse (IV). Malgré l'utilisation fréquente de la vancomycine dans les environnements d'HDI, les pratiques portant sur le dosage et le suivi varient entre les cliniciens de l'institution où l'étude s'est déroulée. Il existe également peu de données probantes sur la dose optimale de vancomycine permettant d'atteindre la concentration sérique cible avant l'HDI.

Objectifs : L'objectif principal visait à comparer le pourcentage de traitements à la vancomycine, dont la concentration sérique se situait entre 15 et 20 mg/L, lors de la mesure prise avant la troisième séance de HDI, avant et après la mise en place d'un protocole de dosage basé sur le poids. Les objectifs secondaires visaient à comparer le pourcentage de traitements, dont la concentration de vancomycine mesurée avant la troisième séance d'HDI était comprise entre 10 et 22 mg/L, et le nombre de mesures de vancomycine par jour de traitement, avant et après la mise en place du protocole.

Méthodes : Cette étude quasi expérimentale, menée dans un seul centre, comprenait des patients hospitalisés et ambulatoires ayant subi une HDI et reçu au moins deux doses de vancomycine par IV et dont un échantillon prélevé de manière appropriée avant la troisième séance d'HDI a permis de mesurer la vancomycine. Avant la mise en place du protocole, le dosage de vancomycine était laissé à la discrétion du clinicien (soins habituels). Après sa mise en place, chaque patient recevait une dose de charge de 1000, 1500 ou 2000 mg et une dose de maintenance de 500, 750 ou 1000 mg selon sa masse corporelle.

Résultats : Le pourcentage de traitements dont la concentration de vancomycine mesurée avant la troisième séance d'HDI était comprise entre 15 et 20 mg/L était plus élevé après la mise en place du protocole qu'après les soins habituels, mais la différence n'était pas significative (44 % [8/18] contre 20 % [3/15], $p = 0{,}27$). Cependant, le pourcentage de traitements dont la concentration de vancomycine mesurée avant la troisième séance d'HDI était comprise entre 10 et 22 mg/L était significativement plus élevé après la mise en place du protocole (94 % [17/18] contre 53 % [8/15], $p = 0{,}012$). Le nombre moyen de mesures de vancomycine par traitement n'avait pas varié entre le jour précédant et le jour suivant la mise en place du protocole (0,133 contre 0,125, $p = 0{,}99$).

Keywords: vancomycin, dialysis, therapeutic drug monitoring, serum concentration, drug levels, dosing protocol

Conclusions : Dans l'institution où l'étude s'est déroulée, la probabilité d'atteindre la concentration de vancomycine recommandée avait augmenté après la mise en place d'un protocole simplifié de dosage de vancomycine pour les patients recevant une HDI comparativement à une pratique antérieure.

Mots-clés : vancomycine, dialyse, suivi thérapeutique pharmacologique, concentration sérique, concentrations du médicament, protocole de dosage

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INTRODUCTION

Infection is the second leading cause of death among patients receiving intermittent hemodialysis (IHD), with most infections being related to vascular access.[1] In patients receiving IHD, *Staphylococcus aureus* is the leading pathogen, accounting for 27% to 39% of all cases of bacteremia.[2] The risk of infection with invasive methicillin-resistant *S. aureus* (MRSA) is 100-fold higher in patients receiving IHD than in the general population; thus, vancomycin use is frequently warranted.[3]

There is a lack of evidence to support definitive recommendations on optimal targets for serum vancomycin concentration in the IHD population. Available evidence suggests that in the general population, exposure to vancomycin at serum trough concentrations less than 10 mg/L can produce *S. aureus* strains with characteristics similar to vancomycin-intermediate *S. aureus*.[4] Therefore, the 2009 guideline of the Infectious Diseases Society of America (IDSA) recommended that serum trough concentrations of vancomycin be consistently maintained above 10 mg/L to prevent the development of resistance.[4] For bacteremia and complicated infections, such as osteomyelitis, meningitis, hospital-acquired pneumonia, and infective endocarditis caused by MRSA, the IDSA guideline further recommended targeting vancomycin trough concentrations between 15 and 20 mg/L.[4] Trough concentrations within this range should achieve a ratio of area under the curve to minimum inhibitory concentration (AUC/MIC) of at least 400 in most patients, provided that the pathogen's MIC is no greater than 1 mg/L. More specifically, for patients receiving IHD, most studies have targeted pre-IHD vancomycin concentrations of either 10–20 mg/L or 15–20 mg/L.[5-12] These targets have also been adopted at the Kingston Health Sciences Centre (KHSC), where this study was conducted, with the latter being used for all patients with MRSA infection. However, recently published literature has suggested that a value of 18.6 or higher for the ratio of pre-IHD concentration to MIC is a predictor of positive clinical outcomes in treating MRSA bacteremia.[13] In view of susceptibility data from Ontario, where the MIC of vancomycin for MRSA ranges between 0.5 and 1 mg/L, a target between 9.3 and 18.6 mg/L for pre-IHD vancomycin concentration may be reasonable.[14]

An upper threshold for optimal pre-IHD vancomycin targets has not been well defined in existing guidelines, nor has a threshold been explicitly reported in the literature. In the general population, vancomycin use has been linked to nephrotoxicity, especially at high trough concentrations.[3] On the basis of extrapolation from existing studies, high pre-IHD vancomycin concentrations are avoided at KHSC in an effort to preserve any residual renal function, which is associated with greater patient survival.[15]

The optimal sampling time for pre-IHD measurement of vancomycin has been poorly defined, and suggested approaches vary considerably in clinical practice. The half-life of vancomycin in patients with stage 5 chronic kidney disease can reach 180 h and is highly dependent on residual renal function in patients receiving IHD, making it difficult to routinely obtain true steady-state concentrations.[16] The draft 2019 update of the IDSA guideline suggests measuring vancomycin concentration no less than once weekly; however, it does not offer specific recommendations on sampling time in relation to timing of the dialysis session.[17] At KHSC, samples are routinely drawn before the third IHD session, to ensure that a vancomycin concentration is obtained within the first week of therapy.

Dosing of vancomycin in the setting of IHD varies considerably both in the studies reported in the literature and in practice. For much of the existing literature evaluating vancomycin dosing protocols, multiple vancomycin measurements were required to establish the dosing regimen for each patient, thus limiting their practicality.[7,10,12,18] Zelenitsky and others[5] and Maxson and others[6] evaluated fixed weight-based dosing protocols, but they were unable to achieve therapeutic targets in many patients. The draft 2019 IDSA guideline update offers specific suggestions for both intradialytic and post-IHD loading and maintenance doses.[17] However, variability in medication administration practices for KHSC inpatients may hinder the ability to prescribe and administer the appropriate dose as per guideline recommendations. A standardized dosing approach for both outpatients and inpatients is therefore preferable at KHSC.

The purpose of this study was to standardize vancomycin dosing in the setting of IHD by building upon previously

investigated vancomycin dosing protocols. The goal was to evaluate the efficacy of a simplified weight threshold–based vancomycin IHD dosing protocol (Table 1) at KHSC using a pragmatic approach to both dosing and monitoring of vancomycin.

Table 1. Weight Threshold–Based Dosing Protocol

Weight*	Loading Dose (mg)	Maintenance Dose (mg)
< 70 kg	1000	500
70–100 kg	1500	750
> 100 kg	2000	1000

*Dry weight.

METHODS

Study Design and Population

The study was approved by the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board before data collection. It was a quasi-experimental study at an academic tertiary care hospital, with retrospective chart review of patients in the pre-intervention period, followed by prospective evaluation of the dosing protocol during the post-intervention period.

The study included inpatients and outpatients receiving IHD at KHSC and selected satellite hemodialysis units, who received at least 2 IV doses of vancomycin and for whom vancomycin concentration was measured in an appropriately drawn sample before the third IHD session. Concentration values as measured in samples drawn up to 12 h before the third IHD session were included. Pre-intervention treatment courses were identified from a historical cohort of patients who underwent IHD from October 1, 2016, to April 30, 2017, and post-intervention treatment courses were identified prospectively from October 1, 2017, to April 30, 2018. Treatment courses were excluded if continuous renal replacement therapy or peritoneal dialysis was used after initiation of vancomycin therapy, before the sample was drawn for measurement of pre–third IHD vancomycin concentration. In the post-intervention period, treatment courses that did not follow the dosing protocol were excluded. Most of the patients in both groups received IHD 3 or 4 times weekly. All patients underwent dialysis with high-flux membranes (FX HDF 800 [Fresenius Medical Care, Homburg, Germany] or Exeltra 170 [Baxter Healthcare Corporation, Deerfield, Illinois]).

Data Collection

Eligible treatment courses were identified through electronic patient care and pharmacy systems. Lists of patients receiving both IHD and vancomycin were generated from the pharmacy system, and administration of specific vancomycin doses was confirmed through medication administration records.

Vancomycin Dosing Protocol and Blood Sampling for Determination of Vancomycin Concentrations

During the pre-intervention period, vancomycin dosing in patients receiving IHD was based on a combination of individual clinician discretion and previous institutional vancomycin dosing guidelines. The previous institutional guidelines recommended a loading dose of 20 mg/kg rounded to the nearest 250 mg, followed by an initial maintenance dose of 500 mg administered either after IHD (inpatients) or during the remaining 30 min of dialysis (outpatients). The maintenance dose was subsequently adjusted as needed by increments or decrements of 250 mg on the basis of pre-IHD concentrations targeted between 8 and 20 mg/L. These previous guidelines did not recommend a specific sampling time for pre-IHD vancomycin concentrations.

During the post-intervention period, vancomycin dosing was based on weight thresholds, whereby patients with body weight less than 70 kg received a loading dose of 1000 mg, followed by a maintenance dose of 500 mg; patients with body weight between 70 and 100 kg received a loading dose of 1500 mg, followed by a maintenance dose of 750 mg; and patients with body weight greater than 100 kg received a loading dose of 2000 mg, followed by a maintenance dose of 1000 mg (Table 1). For inpatients, the loading and maintenance doses could be given either after dialysis or during dialysis, timed to end with the dialysis session. In all outpatients, the loading and maintenance doses were administered during dialysis and were timed to end with the dialysis session. Vancomycin was administered at a rate of 1000 mg/h. Samples were drawn for pre-IHD measurement of vancomycin concentration before the third dialysis session.

Protocol Implementation

During protocol implementation, the proposed loading and maintenance doses were pre-populated in the patient care system of the outpatient hemodialysis unit, with corresponding weight ranges shown in brackets, to facilitate selection of the appropriate doses during prescribing by computerized physician order entry. The institutional vancomycin dosing and monitoring guidelines were updated with the study dosing protocol. This served to facilitate prescribing of IV vancomycin within the paper-based system for inpatients receiving IHD. Pharmacists reviewed inpatient vancomycin orders and intervened as needed to ensure that the dosing protocol was followed, as clinically appropriate. Education was also provided to the physicians and other staff implicated in this study through in-person presentations and e-mail communications. Reference cards detailing the weight threshold–based dosing protocol were also circulated to hemodialysis units.

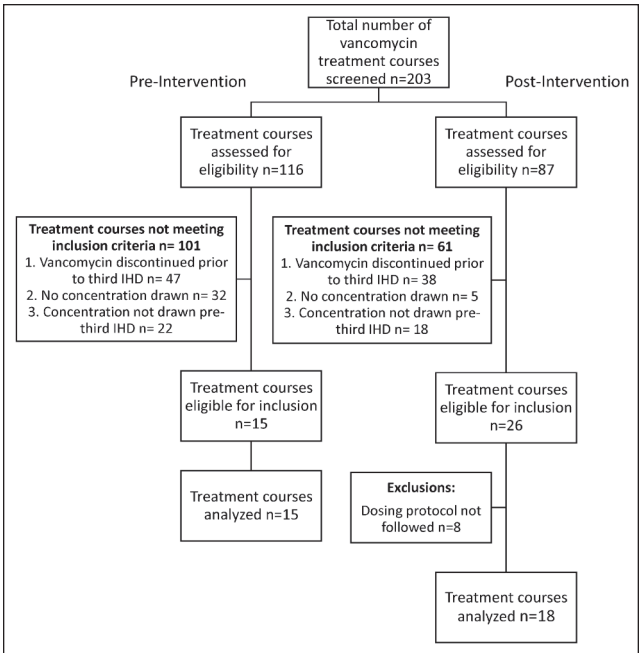

Figure 1. Vancomycin treatment courses in patients receiving intermittent hemodialysis (IHD) in the 2 study periods: pre-intervention (October 1, 2016, to April 30, 2017) and post-intervention (October 1, 2017, to April 30, 2018).

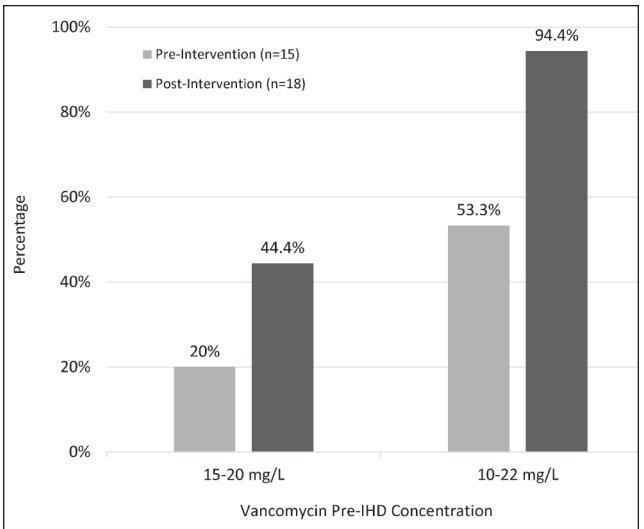

Figure 2. Percentage of treatment courses with vancomycin concentration within target range, for samples measured before the third intermittent hemodialysis (IHD) session, comparing the pre-intervention and post-intervention groups (for vancomycin between 15 and 20 mg/L, $p = 0.27$; for vancomycin between 10 and 22 mg/L, $p = 0.012$).

Study Outcomes

The primary outcome was the difference in percentage of treatment courses with pre–third IHD vancomycin concentrations between 15 and 20 mg/L, before and after protocol implementation. Secondary outcomes were the differences between the 2 groups in the percentage of treatment courses with pre–third IHD vancomycin concentrations between 10 and 22 mg/L, as well as the number of samples drawn for measurement of vancomycin concentration per day of vancomycin treatment while receiving IHD. The upper limit of 22 mg/L was selected a priori, after taking into consideration the lower clinical concern about high vancomycin concentrations in this patient population among KHSC nephrologists and information in the existing literature.[5] It was hypothesized that the new dosing protocol would result in more frequent attainment of vancomycin concentration within the desired range, which would lead clinicians to order fewer pre-IHD measurements of vancomycin concentration and hence create potential resource savings.

Statistical Analysis

Analysis was performed with IBM SPSS version 24.0 (IBM Corporation, Armonk, New York). For study outcomes involving proportions of treatment courses with vancomycin concentration reaching the target ranges, the Fisher exact test was used to evaluate the difference between the pre-intervention and post-intervention groups. The number of measurements per day of vancomycin treatment was analyzed with the Mann-Whitney U test. A p value less than 0.05 was considered statistically significant.

RESULTS

A total of 203 vancomycin treatment courses were screened for inclusion in this study. Fifteen treatment courses (from 14 unique patients) in the pre-intervention group and 18 treatment courses (from 16 unique patients) in the post-intervention group were included for analysis (Figure 1). In the post-intervention group, 8 treatment courses were excluded because the study dosing protocol was not followed. Baseline characteristics were similar between the 2 groups, as was the distribution between inpatients and outpatients (Table 2). The median loading dose was significantly higher in the post-intervention group than in the pre-intervention group (19.36 mg/kg and 13.33 mg/kg, respectively, $p = 0.012$). The median maintenance dose was similar for the 2 groups (9.68 mg/kg and 9.62 mg/kg, respectively). In most cases (29 of 33 [88%]), samples for pre–third IHD vancomycin measurement were drawn within an hour before the start of dialysis.

In terms of the primary outcome, pre–third IHD vancomycin concentrations between 15 and 20 mg/L were achieved in 8 (44%) of 18 treatment courses after implementation of the simplified dosing protocol, compared with 3 (20%) of 15 treatment courses before the intervention ($p = 0.27$) (Figure 2). In terms of the secondary outcomes, pre–third IHD vancomycin

Table 2. Baseline Characteristics

Characteristic	No. (%) of Treatment Courses*†	
	Pre-implementation (*n* = 15)	Post-implementation (*n* = 18)
Age (years) (median)	68	62
Body weight‡		
< 70 kg	4 (27)	2 (11)
70–100 kg	8 (53)	10 (56)
> 100 kg	3 (20)	6 (33)
Sex, male	9 (60)	10 (56)
Inpatients	10 (67)	9 (50)
Dose of vancomycin (mg/kg) (median and IQR)		
Loading	13.33 (10.42–19.23)	19.36 (15.81–19.75)
Maintenance	9.62 (7.08–13.33)	9.68 (7.91–9.88)

*For the pre-implementation group, the 15 treatment courses involved a total of 14 patients. For the post-implementation group, the 18 treatment courses involved a total of 16 patients. As such, some patients were double-counted in the proportions reported here.
†Except where indicated otherwise.
‡Dry weight.

concentrations between 10 and 22 mg/L were achieved in 17 (94%) of 18 treatment courses after the intervention, compared with 8 (53%) of 15 treatment courses before the intervention ($p = 0.012$). The median number of samples drawn for measurement of vancomycin concentration per treatment day was similar between the pre- and post-intervention groups (0.133 versus 0.125, $p = 0.99$).

The spread between pre- and post- intervention groups in terms of pre–third IHD vancomycin concentration is illustrated in Figure 3. The median vancomycin concentration achieved was 10.4 (interquartile range [IQR] 8.1–16.1) mg/L in the pre-intervention group and 13.6 (IQR 11.4–17.1) mg/L in the post-intervention group. Among all treatment courses included in the post-intervention group, the highest vancomycin concentration achieved was 21.2 mg/L.

The spread between groups in terms of the pre–third IHD vancomycin concentration was further examined by separating the data according to the 3 weight threshold categories outlined in the dosing protocol (Figure 4). For vancomycin courses in the pre-intervention group for patients weighing 70 kg or more, 18% (2/11) and 45% (5/11) of pre–third IHD vancomycin concentrations were within the target ranges of 15–20 and 10–22 mg/L, respectively. Correspondingly, in the post-intervention group, 50% (8/16) and 94% (15/16) of pre–third IHD vancomycin concentrations were within the target ranges of 15–20 and 10–22 mg/L, respectively. No supratherapeutic concentrations, defined as a concentration greater than 22 mg/L, were observed in any weight category within the post-intervention group.

DISCUSSION

The results of this study demonstrated the feasibility of a pragmatic, weight threshold–based vancomycin dosing protocol for patients receiving IHD. The study data revealed a numerically higher percentage of treatment courses with pre-IHD vancomycin concentrations between 15 and 20 mg/L, and a statistically significantly higher percentage of treatment courses with pre-IHD vancomycin concentrations between 10 and 22 mg/L, after implementation of the weight threshold–based dosing protocol. The results of this study were consistent with those of the study conducted by Zelenitsky and others,[5] in which approximately 90% of measured values for pre-IHD vancomycin concentration after administration of a loading dose and at least one maintenance dose were within the range of 10 to 22 mg/L, and approximately 40% of the measured values were between 15 and 20 mg/L.

The dosing and monitoring of vancomycin in the setting of IHD remains challenging. Patients with differing clinical presentations, such as admission status, severity of infectious disease, and baseline residual renal function, have been studied, often with each study evaluating slightly different dosing, timing of vancomycin administration, and concentration sampling times.[5-7,9,11,18,19] In addition, several studies have evaluated only loading doses.[8,16] For these reasons, it is difficult to synthesize a dosing and monitoring strategy that can be conveniently applied to routine clinical practice.

During development of the study's dosing protocol and monitoring plan, studies by Zelenitsky and others[5] and Maxson and others[6] were closely examined. Zelenitsky and others[5] prospectively evaluated a dosing protocol derived from Monte Carlo simulations. Patients with body weight less than 70 kg, between 70 and 100 kg, and greater than 100 kg received loading doses of 1000, 1250, and 1500 mg, respectively, and maintenance doses of 500, 750, and 1000 mg, respectively, infused during the last hour of dialysis. This protocol delivered mean loading and maintenance doses of 16 and 9.1 mg/kg, respectively. We

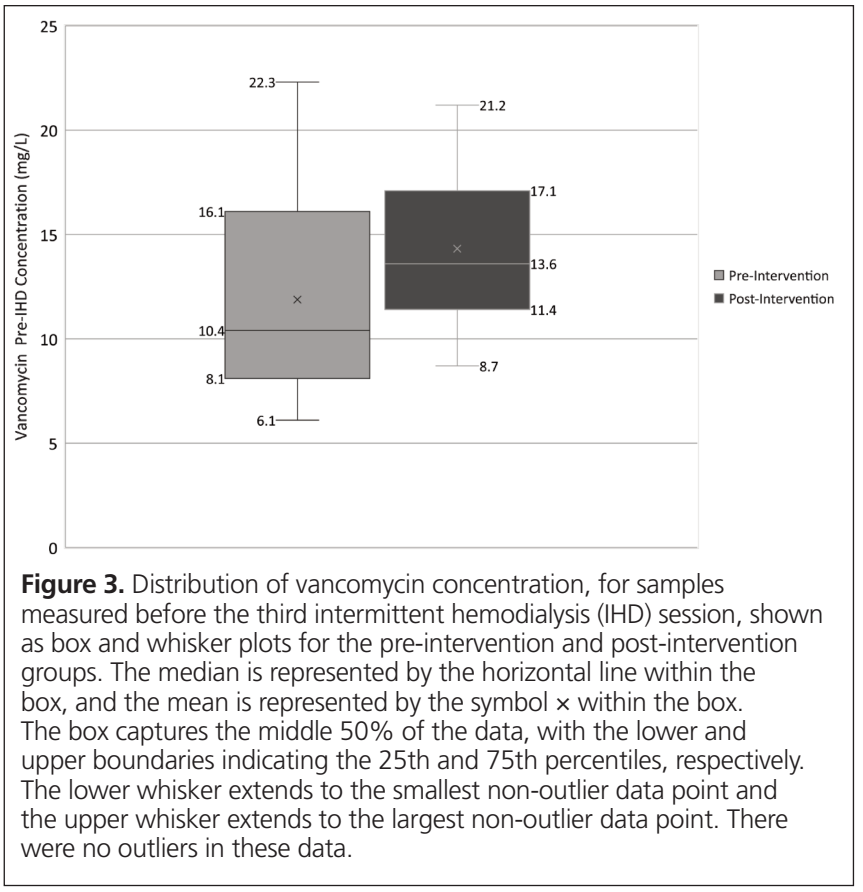

Figure 3. Distribution of vancomycin concentration, for samples measured before the third intermittent hemodialysis (IHD) session, shown as box and whisker plots for the pre-intervention and post-intervention groups. The median is represented by the horizontal line within the box, and the mean is represented by the symbol × within the box. The box captures the middle 50% of the data, with the lower and upper boundaries indicating the 25th and 75th percentiles, respectively. The lower whisker extends to the smallest non-outlier data point and the upper whisker extends to the largest non-outlier data point. There were no outliers in these data.

hypothesized that the loading doses might have been too low, as 76.9% of pre–second IHD (post-load) concentration values were between 10 and 20 mg/L, with only 34.6% between 15 and 20 mg/L. However, the maintenance doses used appeared to be adequate, as a considerable percentage of pre-IHD measurements between the third and seventh sessions were in the ranges of 10–22 mg/L (89.7%) and 15–22 mg/L (62.1%). Conversely, Maxson and others[6] examined a fixed loading dose of 20 mg/kg, followed by a weight-based maintenance dose up to 1250 mg, administered after dialysis in hospital inpatients. This dosing strategy resulted in a mean maintenance dose of 13.8 mg/kg. Pre-IHD concentration of vancomycin over 20 mg/L was observed in more than 50% of patients with body weight above 75 kg.

Building on these 2 studies, we designed a weight threshold–based vancomycin dosing protocol for both loading and maintenance doses at KHSC. The loading dose was capped at 2000 mg in the current study, as there is a lack of evidence examining intradialytic administration of vancomycin beyond the last 2 h of the dialysis session.[20] The maintenance doses were selected on the basis of dosing strategies and resulting pre-IHD vancomycin concentrations in previous studies,[5,6,9-11] with emphasis on those by Zelenitsky and others[5] and Maxson and others.[6] Overall, patients in the post-intervention group of the current study received a significantly higher loading dose, whereas the maintenance dose was comparable between the pre- and post-intervention groups (Table 2). The higher loading dose did not result in supratherapeutic pre-IHD vancomycin concentration (> 22 mg/L) across weight categories. Despite variability among inpatients and outpatients with regard to volume status, acute disease state, residual renal function, or patient adherence to IHD therapy, the study's weight threshold–based dosing protocol resulted in more patients achieving target pre-IHD vancomycin concentration, and therefore represents a reasonable and practical approach to vancomycin dosing for patients receiving IHD at KHSC.

In this study, we examined vancomycin concentration as measured in samples drawn before the third IHD session. With acknowledgement that a steady state would not likely be achieved before treatment completion, the pre–third IHD vancomycin concentration nevertheless provides useful information, reflecting the contribution of both loading and maintenance doses to the observed concentration and ensuring the availability of a vancomycin concentration within the first week of treatment to direct subsequent dosing.[4,5]

One of the study's secondary outcomes attempted to capture potential cost savings, by determining whether there was a reduction in the number of pre-IHD vancomycin measurements

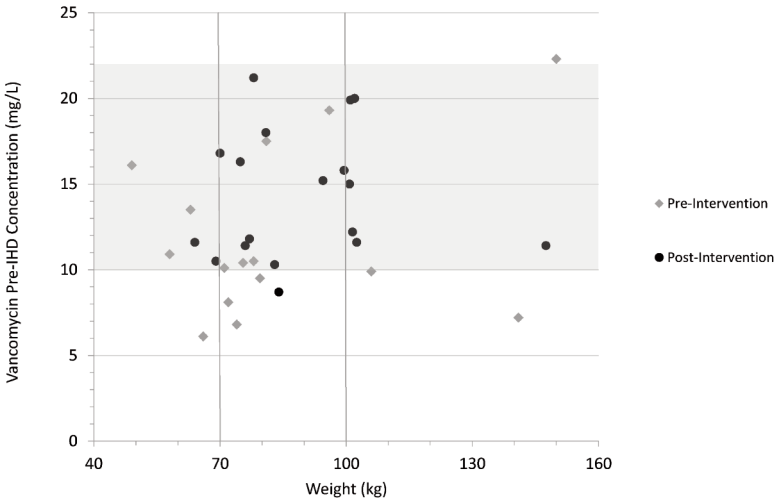

Figure 4. Scatter plot of vancomycin concentration, for samples measured before the third intermittent hemodialysis (IHD) session, by body weight. The pre-intervention (n = 15) and post-intervention (n = 18) data points are shown within 3 weight categories: < 70 kg, 70–100 kg, and > 100 kg. For post-intervention treatment courses in patients with body weight less than 70 kg, the pre-IHD concentrations were 10.5 and 11.6 mg/L (2 data points). For post-intervention treatment courses in patients between 70 and 100 kg, the pre-IHD concentrations ranged from 8.7 to 21.2 mg/L (10 data points), with a median of 15.5 mg/L. For post-intervention treatment courses in patients with body weight more than 100 kg, the pre-IHD concentrations ranged from 11.4 to 20 mg/L (6 data points), with a median of 13.6 mg/L.

required for ongoing monitoring after implementation of the protocol. However, there was no difference in the median number of vancomycin measurements obtained per day of vancomycin therapy before and after protocol implementation. We hypothesize that this result was largely due to the education provided about the study protocol, which may have improved clinicians' awareness of the requirement for regular monitoring of vancomycin concentration, which may not have been occurring routinely during the pre-intervention period.

This study had several limitations that should be considered. Potential confounders that may influence vancomycin concentration could not be completely controlled, including patients' residual renal function, vancomycin administration time relative to IHD, duration of each IHD session, the interdialytic interval, and dialysis vintage. Moreover, the small sample size may have limited the statistical power of the study and generalizability of the results. The study was performed at a single centre and therefore results may not be generalizable to other institutions, because of differences in clinical practice that may affect the dosing, administration, and monitoring of vancomycin therapy in patients receiving IHD. Lastly, pre-IHD vancomycin concentration represents a surrogate for clinical outcomes such as clinical or bacteriological cure. However, the main goal of this study was to validate the effect of the dosing protocol in achieving desired pre-IHD vancomycin concentration.

Despite differences between patients, the smaller spread in pre-IHD vancomycin concentration after implementation of the dosing protocol demonstrated more reliable attainment of concentrations within the target range (Figure 3). In patients weighing more than 70 kg, the high proportion of pre-IHD vancomycin concentrations within the target range provides relative confidence in the applicability of the study's dosing protocol to this patient population (Figure 4). The totality of study results is hypothesis-generating, and future studies could be designed to evaluate higher maintenance doses, such as 750 and 1000 mg for weight categories of less than 70 kg and 70–100 kg, respectively, while keeping the loading dose unchanged.

CONCLUSION

This study demonstrated that a fixed, weight threshold–based dosing protocol was effective and practical in achieving target pre-IHD vancomycin concentrations for both inpatients and outpatients undergoing IHD. The percentage of treatment courses with pre-IHD vancomycin concentrations between 10 and 22 mg/L was significantly higher after implementation of the protocol. Extension of the study duration, to increase patient

enrolment and capture more patients with extremes of weight, may help to further validate this dosing protocol and identify areas where potential changes may be required.

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Cross-Sectional Evaluation of Surface Contamination with Antineoplastic Drugs in Canadian Health Care Centres

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ABSTRACT

Background: Surfaces in health care centres are often contaminated with traces of antineoplastic drugs. Such contamination should be limited as much as possible, to reduce workers' exposure.

Objectives: The primary objective was to monitor environmental contamination with 9 antineoplastic drugs in oncology pharmacy and patient care areas of Canadian health care centres. The secondary objective was to explore the use of sodium hypochlorite as a cleaning agent for cyclophosphamide contamination.

Methods: This cross-sectional evaluation was conducted from January to April 2018. Twelve standardized sites were sampled at each participating centre: 6 in the oncology pharmacy and 6 in patient care areas. Six of the antineoplastic drugs (cyclophosphamide, ifosfamide, methotrexate, gemcitabine, 5-fluorouracil, and irinotecan) were quantified by ultra-performance liquid chromatography – tandem mass spectrometry. For the other 3 antineoplastic drugs (docetaxel, paclitaxel, and vinorelbine), samples were screened for contamination but not quantified. The effect of using sodium hypochlorite as a cleaning agent was evaluated with a Kolmogorov-Smirnov test for independent samples.

Results: Of 202 Canadian centres invited, 79 participated. A total of 887 surface samples were analyzed, 467 from pharmacy areas and 420 from patient care areas. Cyclophosphamide was the drug most often found as a contaminant (32.2% [286/887] of samples positive, 75th percentile of measured contamination 0.0017 ng/cm², 90th percentile 0.021 ng/cm²). The front grille inside the hood (80.8% [63/78] of samples positive for at least one antineoplastic drug), treatment chair armrest (78.9% [60/76]), storage shelf in pharmacy (61.5% [48/78]), and floor in front of the hood (60.3% [47/78]) were the most frequently contaminated surfaces. Cleaning with a sodium hypochlorite solution was highly variable. Among centres that reported using sodium hypochlorite to clean armrests on patient chairs, the concentration of cyclophosphamide was lower (0.00866 versus 0.0300 ng/cm², $p = 0.014$).

Conclusions: Despite growing awareness and implementation of new safe-handling guidelines, surfaces in health care centres were contaminated with traces of many antineoplastic drugs. Providing centres with attainable goals (e.g., 75th to 90th percentile relative to other similar centres) would help in identifying the sampling sites where improvements are needed and in achieving lower surface contamination.

RÉSUMÉ

Contexte : Les surfaces dans les centres de santé sont souvent contaminées par des traces de médicaments antinéoplasiques. Une telle contamination devrait être limitée autant que faire se peut afin de réduire l'exposition des employés à ces produits.

Objectifs : L'objectif principal consistait à mesurer la contamination environnementale provenant de neuf médicaments antinéoplasiques dans la section de la pharmacie oncologique et celle des soins offerts aux patients dans des centres de soins de santé canadiens. L'objectif secondaire consistait à explorer l'action nettoyante de l'hypochlorite de sodium pour éliminer la contamination par la cyclophosphamide.

Méthodes : Cette évaluation transversale a été menée de janvier à avril 2018. Des échantillons ont été prélevés dans douze endroits standardisés de chaque centre participant : six dans la section de la pharmacie oncologique et six dans celle des soins donnés aux patients. La présence de six des médicaments antinéoplasiques examinés (cyclophosphamide, ifosfamide, méthotrexate, gemcitabine, 5-fluorouracil et irinotécan) a été quantifiée par chromatographie liquide à haute performance (HPLC) avec spectrométrie de masse en tandem. Quant aux trois autres échantillons de médicaments antinéoplasiques (docetaxel, paclitaxel et vinorelbine), ils ont été analysés pour rechercher la présence d'une contamination qui n'a pas été quantifiée. L'action nettoyante de l'hypochlorite de sodium a été évaluée à l'aide d'un test de Kolmogorov-Smirnov pour les échantillons indépendants.

Résultats : Sur 202 centres canadiens invités à participer à l'étude, 79 ont répondu à l'invitation. L'analyse a porté sur 887 échantillons de surfaces des lieux sélectionnés : 467 dans la section de la pharmacie et 420 dans la section des soins donnés aux patients. La cyclophosphamide était le médicament contaminant le plus souvent décelé (32,2 % d'échantillons positifs [286/887], 75e percentile de contamination mesurée 0,0017 ng/cm², 90e percentile 0,021 ng/cm²). La grille frontale à l'intérieur de la hotte de laboratoire (80,8 % des échantillons [63/78] étaient positifs pour au moins un médicament antinéoplasique), l'accoudoir de la chaise du patient (78,9 % [60/76]), l'étagère de stockage dans la pharmacie (61,5 % [48/78]) et le sol en face de la hotte (60,3% [47/78]) étaient les surfaces le plus souvent contaminées. L'usage d'une solution d'hypochlorite de sodium pour le nettoyage variait grandement d'un centre à l'autre. Dans les centres qui indiquaient utiliser cet agent

Keywords: environmental monitoring, surface contamination, antineoplastic drugs, cyclophosphamide, health care centres, pharmacy

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pour nettoyer les accoudoirs des chaises du patient, la concentration de cyclophosphamide sur les accoudoirs était moins élevée (0,00866 contre 0,0300 ng/cm², p = 0,014).

Conclusions : Malgré la prise de conscience et la mise en place croissantes de nouvelles lignes directrices en matière de manipulation sécuritaire, les surfaces de certains endroits des centres de santé sont contaminées par des traces de nombreux médicaments antinéoplasiques. La fixation d'objectifs atteignables pour les centres (p. ex., entre le 75e et le 90e percentile par rapport aux autres centres similaires) aide à déterminer les sites d'échantillonnage où des améliorations sont nécessaires et à diminuer la contamination des surfaces.

Mots-clés : contrôle environnemental, contamination des surfaces, médicament antinéoplasique, cyclophosphamide, centres de santé, pharmacie

INTRODUCTION

Surfaces in health care centres are often contaminated with traces of antineoplastic drugs, notably cyclophosphamide, gemcitabine, and 5-fluorouracil,[1,2] Surfaces in centres that handle larger quantities of antineoplastic drugs are generally more contaminated.[2] All types of surfaces have been documented as being potentially contaminated, from hood surfaces and drug administration areas to pencils and telephones.[1,2] The causes of this contamination are varied, with inadequate drug handling and spills being the more obvious sources. Other important sources of contamination are health care workers themselves, who inadvertently carry traces of antineoplastic drugs on their hands or gloves.[3] Patients treated with these drugs are also an important source of contamination, notably because of contaminated excreta. Over time, working practices have improved worldwide, and many authors have documented a substantial reduction in surface contamination.[2,4,5] Despite these improvements, trace contamination continues to occur, and few centres are able to avoid all contamination.

Effective and frequent surface cleaning is of the utmost importance to reduce the risk of exposure to these drugs. However, no single cleaning agent can completely remove all antineoplastic drugs from a surface.[6-8] Furthermore, no health-based exposure limit has been determined for antineoplastic drugs. Thus, centres strive to reduce as much as possible workers' potential exposure. Performing regular environmental monitoring is recommended by many Canadian organizations.[9-11] To help in compliance with this recommendation, many groups have proposed thresholds based on environmental monitoring data for a particular region or country.[2,12,13] Comparison of a health care centre's data with these reference values can help the centres to target apparently problematic surfaces.

The primary objective of this study was to monitor environmental contamination by 9 antineoplastic drugs in oncology pharmacy and patient care areas of Canadian health care centres. The secondary objective was to explore the use of sodium hypochlorite as a cleaning agent for cyclophosphamide contamination.

METHODS

Participating Centres

This cross-sectional evaluation involved a voluntary sample of centres from across Canada. Directors of pharmacy departments in Canadian centres with at least 50 acute care beds were contacted by e-mail on December 8, 2017, with an invitation to participate in a study of surface contamination with antineoplastic drugs (total of 202 directors from the following 11 provinces and territories, listed in alphabetical order: 12 in Alberta, 23 in British Columbia, 13 in Manitoba, 8 in New Brunswick, 2 in Newfoundland and Labrador, 3 in Northwest Territories, 9 in Nova Scotia, 62 in Ontario, 2 in Prince Edward Island, 62 in Quebec, and 6 in Saskatchewan). One reminder was sent by e-mail.

Participating centres applied their local policies and procedures for compounding, administration, surface cleaning, waste management, and any other aspects of drug handling. The pharmacy directors provided data describing their practices for the period April 2017 to March 2018.

Sampling and Analysis

At each centre, surface sampling was conducted on a single day between January and April 2018. Each centre paid for analysis of its samples.

Twelve standardized sampling sites were used: 6 in oncology pharmacy areas and 6 in patient care areas. Any samples from sites that did not match the prespecified sites were excluded from analysis. The 12 sites were selected to represent potential exposure of workers from these areas and to allow comparison with previous studies conducted annually since 2010.[2] For health care centres located close to the authors' institution, samples were collected by

a single research assistant (D.H.). For centres at locations remote from the authors' institution, samples were collected by an employee at each participating centre. To reduce variability, these employees were trained using a video, descriptions, and photographs of the standardized sampling sites and procedures. Sampling technique and analytical procedures were the same as those previously reported.[2] Sites were sampled at the end of a workday or in the morning, before surfaces were cleaned.

The following 6 antineoplastic drugs were quantified: cyclophosphamide, ifosfamide, methotrexate, gemcitabine, 5-fluorouracil, and irinotecan. Samples were also screened for the following 3 antineoplastic drugs, but these drugs were not quantified: docetaxel, paclitaxel, and vinorelbine. These 9 drugs were chosen for our study because they are among the most frequently used in Quebec and because a cost-effective analytical method existed. Quantification and detection of antineoplastic drugs in sampling extracts were performed by ultra-performance liquid chromatography – tandem mass spectrometry (Acquity UPLC chromatographic system coupled with Xevo TQ-S tandem mass spectrometer; Waters Corporation, Milford, Massachusetts). Chromatography was carried out on a C18 Acquity UPLC HSS T3 column (2.1 × 100 mm, 1.8 µm; Waters Corporation). All tests were performed at the Institut national de santé publique du Québec, with the same equipment. The limits of detection and quantification are presented in Table 1. The limit of detection was used as the reporting limit.

Data Analysis

The proportion of positive samples was calculated. A sample was considered positive for a particular drug if the value was above the limit of detection and if the quantifier peak was within the maximum tolerance of the mean calibrator for confirmatory criteria (signal/noise ratio > 3, retention time ±0.02 min, quantifier/qualifier ion ratio ±20%). Descriptive statistical analyses (which generated percentiles) were carried out with SPSS software (IBM Statistics for Windows version 20.0, IBM Corporation, Armonk, New York). For the purpose of calculations, values that fell between the limit of detection and the limit of quantification were assigned a value corresponding to the limit of quantification divided by 2,[14] and values that fell below the limit of detection were assigned a value corresponding to the limit of detection divided by 2.[15]

Subanalyses were performed to explore the effect on cyclophosphamide concentration of cleaning with a sodium hypochlorite solution. The following practices were also evaluated: antineoplastic drug usage, removal of outer packaging, cleaning of vials after receipt, use of closed-system drug transfer devices, and priming of antineoplastic IV tubing in the pharmacy. Results were compared with a Kolmogorov-Smirnov test for independent samples. A p value less than 0.05 was considered statistically significant.

Table 1. Limits of Detection and Quantification

Antineoplastic Drug	Limit of Detection (ng/cm²)	Limit of Quantification (ng/cm²)
Cyclophosphamide	0.0010	0.0033
Docetaxel	0.30	0.30
5-Fluorouracil	0.0400	0.1400
Gemcitabine	0.001	0.001
Ifosfamide	0.004	0.0055
Irinotecan	0.0030	0.006
Methotrexate	0.0020	0.0060
Paclitaxel	0.04	0.1200
Vinorelbine	0.01	0.0120

Communication of Results

After completion of the study, each participating centre was given access to a secure website from which they could retrieve their 2018 results, as well as historical results, if they had participated in sampling in previous years. Sites with values higher than the global Canadian 75th and 90th percentiles were highlighted with a colour code (orange for values between the 75th and 90th percentiles and red for values above the 90th percentile), so that centres could target their corrective measures to surfaces with the most contamination (Figure 1).

RESULTS

Overall, 79 centres from 4 provinces were recruited in 2018 (Table 2). A total of 15 centres had participated in all 8 studies since 2010, and all of these used more than 250 g of cyclophosphamide annually.

In the current study, samples from a total of 887 surfaces were analyzed: 467 in pharmacy areas and 420 in patient care areas. An additional 61 samples were excluded from the analysis because the sampling locations did not match the standardized sampling sites or sampling was not completed. The 3 drugs used in the largest quantities (cyclophosphamide, gemcitabine, and 5-fluorouracil) were also the ones most often detected on surfaces (Table 3).

The proportion of samples with a positive result for at least 1 antineoplastic drug was similar in pharmacy areas (46.9%) and patient care areas (42.4%) (Table 4). The front grille inside the hood (80.8% [63/78]), armrest of patient treatment chair (78.9% [60/76]), storage shelf in pharmacy (61.5% [48/78]), and floor in front of the hood (60.3% [47/78]) were the most frequently contaminated sites, and the contaminating drugs were found at higher concentrations (Table 4).

Cleaning with a sodium hypochlorite solution was highly variable among participating centres. Few centres used this cleaning solution on the armrests of patient treatment chairs (16.0% [12/75]), whereas it was more commonly used on the floor in front of the hood (39.5% [30/76]) and on the front grille of the hood (79.7% [63/79]). The concentration of sodium

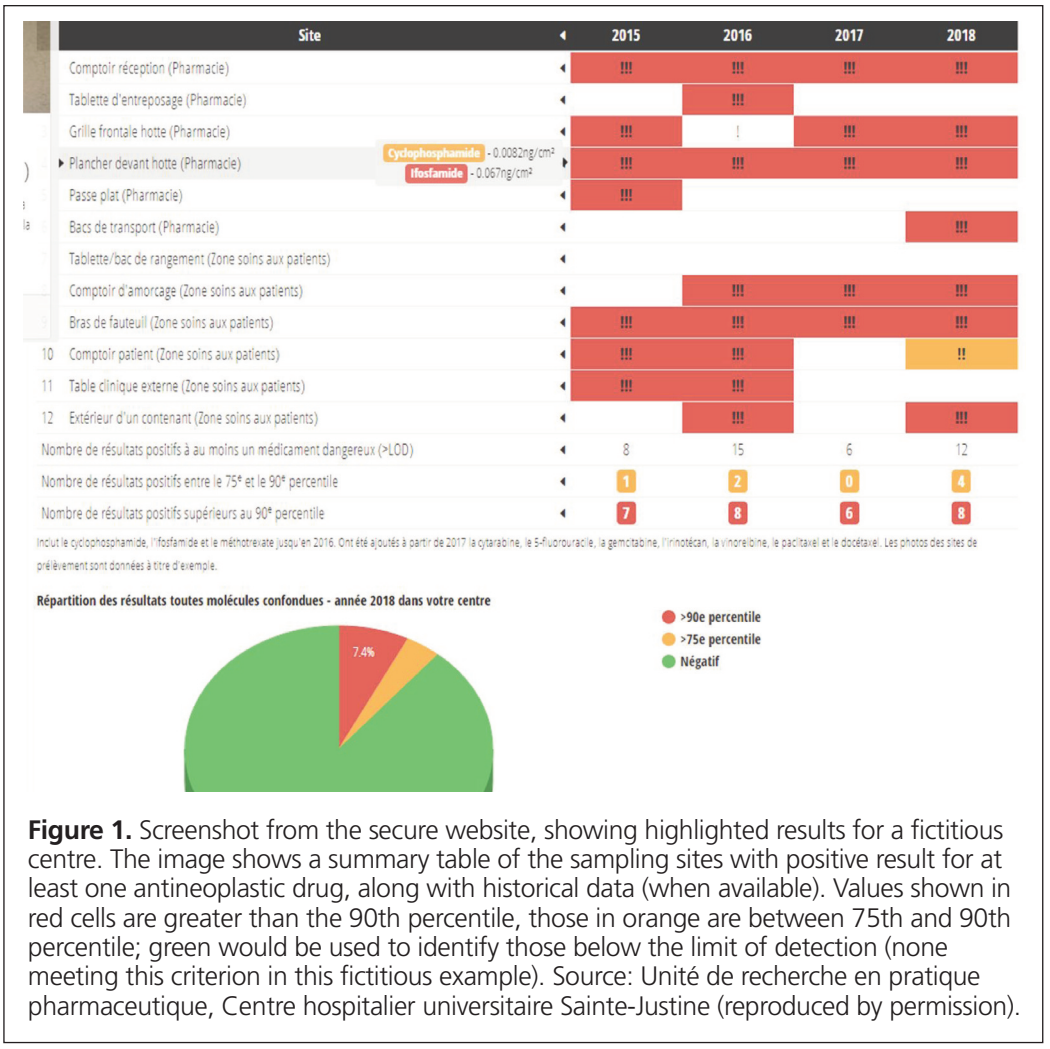

Figure 1. Screenshot from the secure website, showing highlighted results for a fictitious centre. The image shows a summary table of the sampling sites with positive result for at least one antineoplastic drug, along with historical data (when available). Values shown in red cells are greater than the 90th percentile, those in orange are between 75th and 90th percentile; green would be used to identify those below the limit of detection (none meeting this criterion in this fictitious example). Source: Unité de recherche en pratique pharmaceutique, Centre hospitalier universitaire Sainte-Justine (reproduced by permission).

hypochlorite varied between 0.6% and 10%, with concentrations in the range of 2% to 2.4% being the most common (e.g., for front grille of the hood, this concentration was used by 87.5% [49] of the 56 centres reporting these data). The frequency of cleaning with sodium hypochlorite was also highly variable, from many times a day to once a year. For example, monthly cleaning of the front grille of the hood with sodium hypochlorite was reported by 36 (57.1%) of 63 centres. Centres that reported cleaning a particular surface with a sodium hypochlorite solution tended to have lower cyclophosphamide concentrations on that surface than did centres not performing such cleaning, although the difference was significant only for the armrest of patient treatment chairs (Table 5).

The centres with the greatest use of cyclophosphamide had the highest level of contamination: those that reported using 250 g or more of this drug per year had higher concentrations of cyclophosphamide than those that reported using less than 250 g (75th percentile 0.0060 ng/cm^2 versus less than limit of detection; $p < 0.001$). Centres that used a closed-system drug transfer device for at least 90% of drug preparations did not have lower contamination (75th percentile of cyclophosphamide 0.0017 ng/cm^2 versus 0.0029 ng/cm^2, $p = 0.20$), nor did the centres that primed at least 90% of their lines in the pharmacy (0.0017 versus 0.0037, $p > 0.99$). Centres that removed the outer packaging and those that cleaned vials upon receipt tended to have lower surface contamination, but this difference was significant only for cleaning vials upon receipt (0.0017 versus 0.0084, $p = 0.026$).

DISCUSSION

In this study, nearly half of surfaces sampled in 79 Canadian centres were contaminated with 1 of the 9 antineoplastic drugs analyzed, and one-third were contaminated with cyclophosphamide. Contamination was mostly found on front grilles inside hoods, armrests of patient treatment chairs, storage shelves, and floors in front of the hoods. The 75th percentile of cyclophosphamide concentration was 0.0017 ng/cm², and the 90th percentile was 0.021 ng/cm². There was high variability in methods among centres that used sodium hypochlorite cleaning solutions for decontamination.

Table 2. Characteristics of Participating Centres

Characteristic	No. (%) of Centres (*n* = 79)	
Province		
Quebec	64	(81.0)
Ontario	9	(11.4)
New Brunswick	5	(6.3)
Manitoba	1	(1.3)
Participation in previous multicentre surveillance studies by same research team		
0–7 studies	64	(81.0)
8 studies	15	(19.0)
Size of oncology clinic		
No. of inpatient beds		
< 15	57	(72.2)
≥ 15	21	(26.6)
Data missing	1	(1.3)
No. of outpatient stretchers, chairs, beds		
< 15	48	(60.8)
≥ 15	30	(38.0)
Data missing	1	(1.3)
Antineoplastic preparations/year		
< 4000	32	(40.5)
≥ 4000	40	(50.6)
Data missing	7	(8.9)
Cyclophosphamide used/year (g)		
< 250	38	(48.1)
≥ 250	40	(50.6)
Data missing	1	(1.3)
Removal of outer packaging upon receipt		
Yes	68	(86.1)
No	11	(13.9)
Cleaning of vials after receipt		
Yes	64	(81.0)
No	15	(19.0)
Use of closed-system drug transfer device*		
Yes	26	(32.9)
For ≥ 90% of preparations	17	NA
For < 90% of preparations	9	NA
No	53	(67.1)
Priming of antineoplastic IV tubing		
In pharmacy (for ≥ 90% of preparations)	59	(74.7)
In health care unit (for ≥ 90% of preparations)	18	(22.8)
Other†	2	(2.5)

NA = not applicable (proportion not calculated for this subgroup).
*The following devices were used: ChemoClave System (ICU Medical Inc, San Clemente, California), *n* = 18; Phaseal (Becton, Dickinson and Company, Franklin Lakes, New Jersey), *n* = 4; Equashield (EquaShield Medical, Port Washington, New York), *n* = 2; Tevadaptor (Teva Medical, Petha Tikva, Israel), *n* = 1; and Texium (BD, Franklin Lakes, New Jersey), *n* = 1.
†For 2 centres, neither the pharmacy nor the health care unit performed ≥ 90% of priming.

Environmental Contamination in Canadian Hospitals

These results were similar to those obtained in 2017: the proportion of contaminated samples remained constant, and the same sites were the most frequently contaminated.[2] The 75th percentile of cyclophosphamide concentration declined, from 0.0040 to 0.0017 ng/cm², which confirms previous observations that practices improve over the years.[2,4,5] Although Dugheri and others[5] observed a reduction over time in the proportion of positive samples (from 11.7% in 2010 to 1% in 2017), the reduction that we observed was not as marked, for instance, from 52% of samples positive for cyclophosphamide in 2008–2010[16] to 32% in the current study. This difference may be partly explained by differences in sampling sites, study methods, and handling practices.

Effect of Cleaning

Considering the importance of surface cleaning in the elimination of persistent traces of antineoplastic drugs, we explored the effect of cleaning with a sodium hypochlorite solution. This cleaning solution was chosen for investigation because it has previously been shown as the most effective cleaning agent for a variety of antineoplastic drugs.[6,7] We hypothesized that surfaces with more thorough routine cleaning might have lower residual contamination, leading to less contamination at the end of the workday. However, the aim of the current study was not to test cleaning efficacy, especially given that surfaces were sampled after a workday, before cleaning. Even surfaces that have been cleaned may be contaminated with antineoplastic drugs immediately after cleaning.[8] The cleaning practices of centres that did not use sodium hypochlorite were not investigated.

There was tremendous variability in cleaning practices with sodium hypochlorite. Some centres used this solution for daily cleaning, but it was mostly used on a weekly or monthly basis, to perform more thorough cleaning. Indeed, the Ordre des pharmaciens du Québec recommends monthly deactivation of the hood with sodium hypochlorite followed by thiosulfate, in addition to daily cleaning with water and detergent and disinfection with alcohol.[11] The armrests of patient treatment chairs were seldom cleaned with sodium hypochlorite, perhaps because a disinfecting product is often prioritized for use when oncology patient care areas are cleaned.[8] Centres that did use sodium hypochlorite to clean treatment chair armrests had significantly lower contamination. This promising result will need to be confirmed by further studies. The concentration of sodium hypochlorite used for cleaning was also variable. Preliminary results have suggested that less concentrated solutions are equivalent in effectiveness, and using more dilute solutions would help to alleviate the disadvantages of sodium hypochlorite, notably its corrosive action on some surfaces and the unpleasant odour for workers and patients.[17]

The other working practices that were evaluated led to results similar to those reported previously.[2] The centres that used more antineoplastic drugs had greater levels of surface contamination, but the other practices were not associated with significantly lower concentrations of cyclophosphamide. Conflicting results were obtained for centres that removed the outer packaging and those that cleaned the vials upon receipt, given that the difference was

Table 3. Surface Contamination and Reported Annual Use of Antineoplastic Drugs

Antineoplastic Drug	No. (%) of Positive Samples (*n* = 887)		Contamination (ng/cm²)*			Reported Use (g/year)†	
			75th percentile	90th percentile	Max	Median	Max
Cyclophosphamide	286	(32.2)	0.0017	0.021	2.4	251	1 900
Gemcitabine	167	(18.8)	<0.001	0.0043	8.5	302	3 210
5-Fluorouracil	74	(8.3)	<0.0400	<0.0400	210	1756	10 660
Ifosfamide	47	(5.3)	<0.004	<0.004	3.0	12	2 800
Methotrexate	37	(4.2)	<0.0020	<0.0020	2.6	4.35	5 997
Irinotecan	19	(2.1)	<0.0030	<0.0030	0.33	47.75	1 560
Paclitaxel	5	(0.6)	NA	NA	NA	40.35	604
Vinorelbine	1	(0.1)	NA	NA	NA	3	280
Docetaxel	0	(0)	NA	NA	NA	10	390

Max = maximum, NA = not applicable (drug not quantified).
*For all drugs, the minimum level of contamination was below the limit of detection.
†Based on data for 78 centres.

Table 4. Contamination by Sampling Site

Sampling Site	No. (%) Positive for ≥ 1 Antineoplastic Drug		No. (%) Positive for Cyclophosphamide		Cyclophosphamide Concentration (ng/cm²)		
					75th percentile	90th percentile	Maximum
Pharmacy areas							
Front grille of hood (*n* = 78)	63	(80.8)	50	(64.1)	0.022	0.19	1.3
Floor in front of hood (*n* = 78)	47	(60.3)	43	(55.1)	0.015	0.11	0.78
Storage shelf (*n* = 78)	48	(61.5)	36	(46.2)	0.0042	0.015	0.082
Trays used for drug delivery (*n* = 78)	24	(30.8)	8	(10.3)	<0.0010	0.0017	0.026
Service hatch or counter for post-preparation validation (*n* = 78)	22	(28.2)	11	(14.1)	<0.0010	0.019	0.039
Shipment reception counter (*n* = 77)	15	(19.5)	6	(7.8)	<0.0010	<0.0010	0.07
Subtotal (*n* = 467)	219	(46.9)	154	(33.0)	0.0034	0.020	1.3
Patient care areas							
Armrest on patient treatment chair (*n* = 76)	60	(78.9)	56	(73.7)	0.030	0.098	1.1
Exterior surface of antineoplastic drug container (*n* = 68)	29	(42.6)	17	(25.0)	0.0014	0.032	2.4
Counter used for priming or validation (*n* = 75)	24	(32.0)	17	(22.7)	<0.0010	0.0017	0.0091
Counter in patient room (*n* = 58)	25	(43.1)	19	(32.8)	0.0017	0.018	0.068
Counter in outpatient clinic (*n* = 71)	20	(28.2)	14	(19.7)	<0.0010	0.0017	0.055
Storage shelf (*n* = 72)	20	(27.8)	9	(12.5)	<0.0010	0.0017	0.79
Subtotal (*n* = 420)	178	(42.4)	132	(31.4)	0.0017	0.022	2.4
Total (pharmacy and patient care areas) (*n* = 887)	397	(44.8)	286	(32.2)	0.0017	0.021	2.4

significant only for the latter. The low concentrations measured on surfaces and the descriptive approach of this study limit the generalizability of these findings.

Contaminated Surfaces to Be Targeted for Action

Centres that participated in our study could access their own results through a study-specific website and could easily identify the surfaces with the greatest contamination, through colour coding (see Figure 1). These are the sites that should be prioritized for corrective measures. We agree with others that this pragmatic method is helpful for centres looking to reduce surface contamination.[12,13] Considering the improvements that we have observed over the years (since 2010), our approach is to update the target values each year. In addition, target values should be established at the regional level, taking into account differing regulations and working practices. For instance, the 90th percentiles for cyclophosphamide and gemcitabine obtained for Canada in 2018 were 0.021 and 0.0043 ng/cm², respectively, whereas Sottani and others[12] reported 90th percentiles in Italian hospitals of 3.6 and 0.9 ng/cm², respectively.

In addition to prioritizing surfaces according to threshold values, failure mode and effects analysis could be conducted to identify and score the risks of occupational exposure. Le and

Table 5. Effect of Cleaning with Sodium Hypochlorite Solution

Surface Cleaned*	Cyclophosphamide Concentration (ng/cm²), as 75th Percentile	*p* Value†
Armrest on patient treatment chair‡		0.014
Cleaned with sodium hypochlorite (*n* = 12)	0.00866	
Not cleaned with sodium hypochlorite (*n* = 63)	0.0300	
Front grille of hood		0.59
Cleaned with sodium hypochlorite (*n* = 63)	0.0205	
Not cleaned with sodium hypochlorite (*n* = 16)	0.130	
Floor in front of hood‡		0.90
Cleaned with sodium hypochlorite (*n* = 30)	0.00833	
Not cleaned with sodium hypochlorite (*n* = 46)	0.015	

*Grouped results for any cleaning frequency and use of sodium hypochlorite solution with any concentration.
†Kolmogorov-Smirnov test for independent samples (2 groups).
‡Some centres did not report their cleaning practice for specific surfaces: for armrest of patient treatment chair, *n* = 4; for floor in front of hood, *n* = 3.

others[18] used this approach to rank their corrective measures and succeeded in reducing their risk score over 5 years. They implemented a specific training program, posted the requirements for personal protective equipment, and reviewed cleaning practices.

Strengths and Limitations

For each participating centre, sampling occurred at the end of a single workday and might not represent the risk of exposure on all days. The results obtained from the 79 centres were comparable to those obtained in previous years, which supports the conclusion that they are representative of surface contamination in Canadian health care centres. For centres remote from the authors' location, sampling was not done by the same research assistant, which might have biased the results; however, care was taken to train staff members at these locations, in an attempt to ensure uniformity of the sampling technique. Participation was voluntary, and each centre paid for its own analyses, which might have introduced participation bias. Most of the participating centres were from Quebec, so the results are more representative of practice in that province. In a previous study, we showed that there was no significant difference between Quebec and other Canadian provinces in terms of contamination of health care centres.[19] The standards of the National Association of Pharmacy Regulatory Authorities[20] were directly inspired by the Quebec standards[11]; therefore, as these standards are adopted by each province, improvements may be observed in the future.

The sampling method had good limits of detection, which were comparable to other published methods.[21] The chemical analysis was not blinded.

Not all working practices were investigated; for example, we did not inquire about the use of other cleaning agents. Although these preliminary results are interesting, they should be interpreted with caution, and the usefulness of sodium hypochlorite as a cleaning agent must be confirmed in other studies. No methods were applied to control for type 1 error associated with conducting multiple statistical tests.

CONCLUSION

Contamination of surfaces with antineoplastic drugs persists in Canadian health care centres. Over the past few years, improvements have been observed, but trace contamination occurred each year. Attainable goals based on results from many similar centres (e.g., 75th and 90th percentiles of concentration) can help facilities to identify the specific sampling sites where attention is needed to attain the least possible contamination and reduce the risk of workers' exposure. Optimizing cleaning methods may help in achieving this objective.

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ON THE FRONT COVER

Autumn in London, Ontario

This issue's cover photograph was one of several taken by Linda Hooper during a walk home from the London Health Sciences Centre, University Hospital, where she works as a Drug Information Specialist. Linda used her iPhone 5 to capture the image. Being from Northern Ontario, Linda has a deep appreciation for the fall colours and enjoys the opportunity to walk home when the weather permits."I like to think that most everywhere is within walking distance if you have the time, and I like to make the time!"

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

Newer Oral Antihyperglycemics: From *Seinfeld* to *Breaking Bad*

In a previous Research Letter,[1] we aired our grievances regarding dipeptidyl peptidase-4 (DPP-4) inhibitors by likening them to the popular television show *Seinfeld*. Similar to the trivial yet humorous experiences of Jerry and his friends, DPP-4 inhibitors basically do nothing with respect to clinically meaningful outcomes. Our meta-analysis of 3 large randomized controlled trials (RCTs) demonstrated that, compared with placebo, DPP-4 inhibitors have no effect on major adverse cardiovascular events (defined as cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke with or without unstable angina), all-cause mortality, or hospital admission for heart failure in patients with type 2 diabetes mellitus who had or were at risk for cardiovascular disease. Since then, additional cardiovascular outcome trials involving DPP-4 inhibitors have been published.

Updating our previous search to January 2019, we identified 60 new articles, of which 2 RCTs met the same inclusion criteria as we used previously.[1] One trial compared omarigliptin with placebo in 4202 patients (mean age 64 years, 70% men) with type 2 diabetes and cardiovascular disease over a median of 1.8 years.[2] The CARMELINA trial compared linagliptin with placebo in 6979 patients (mean age 66 years, 63% men) with type 2 diabetes and cardiovascular disease over a median of 2.2 years.[3] We updated our meta-analysis using a Mantel-Haenszel fixed-effect model when statistical heterogeneity was low (defined as $I^2 < 50\%$) and a random-effects model when statistical heterogeneity was high (defined as $I^2 \geq 50\%$) (Review Manager, version 5.3, Cochrane Collaboration).

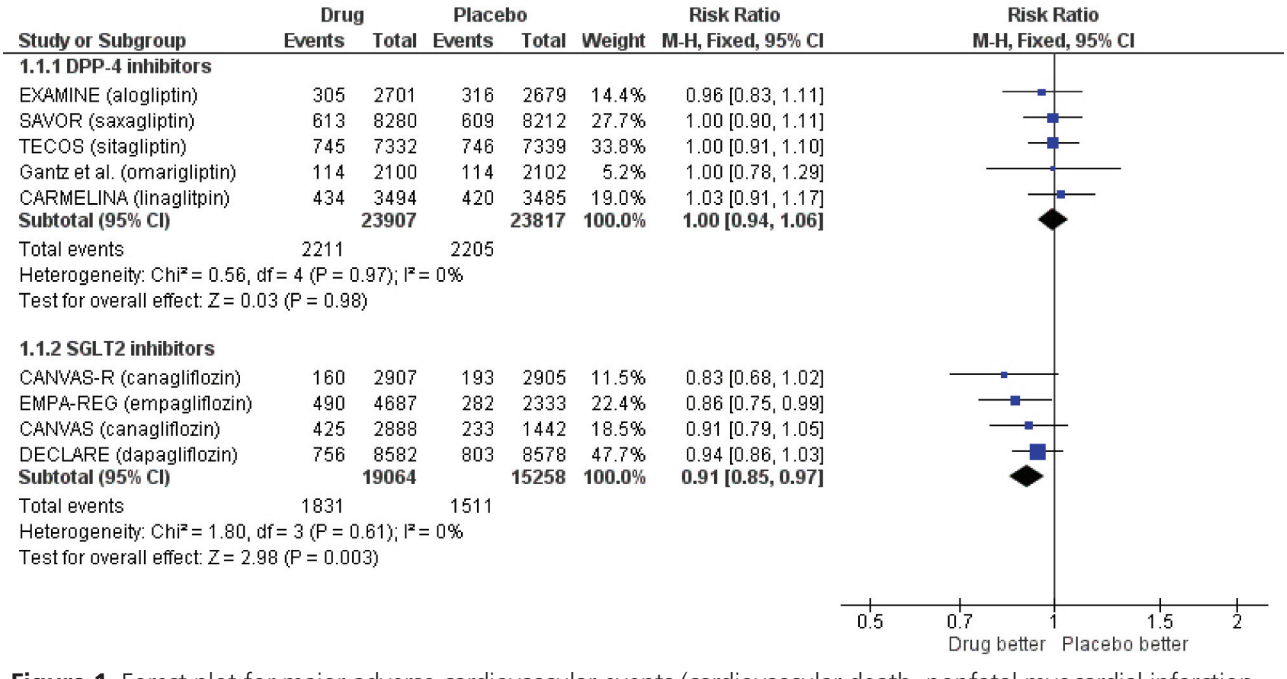

Figure 1. Forest plot for major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or unstable angina) in patients receiving dipeptidyl peptidase-4 (DPP-4) inhibitors and sodium glucose cotransporter-2 (SGLT2) inhibitors. EXAMINE trial for alogliptin = White and others,[4] SAVOR trial for saxagliptin = Scirica and others,[5] TECOS trial for sitagliptin = Green and others,[6] trial for omarigliptin = Gantz and others,[2] CARMELINA trial for linagliptin = Rosenstock and others,[3] CANVAS and CANVAS-R trials for canagliflozin = Neal and others,[8] EMPA-REG trial for empagliflozin = Zinman and others,[7], DECLARE trial for dapagliflozin = Wiviott and others.[9] CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.

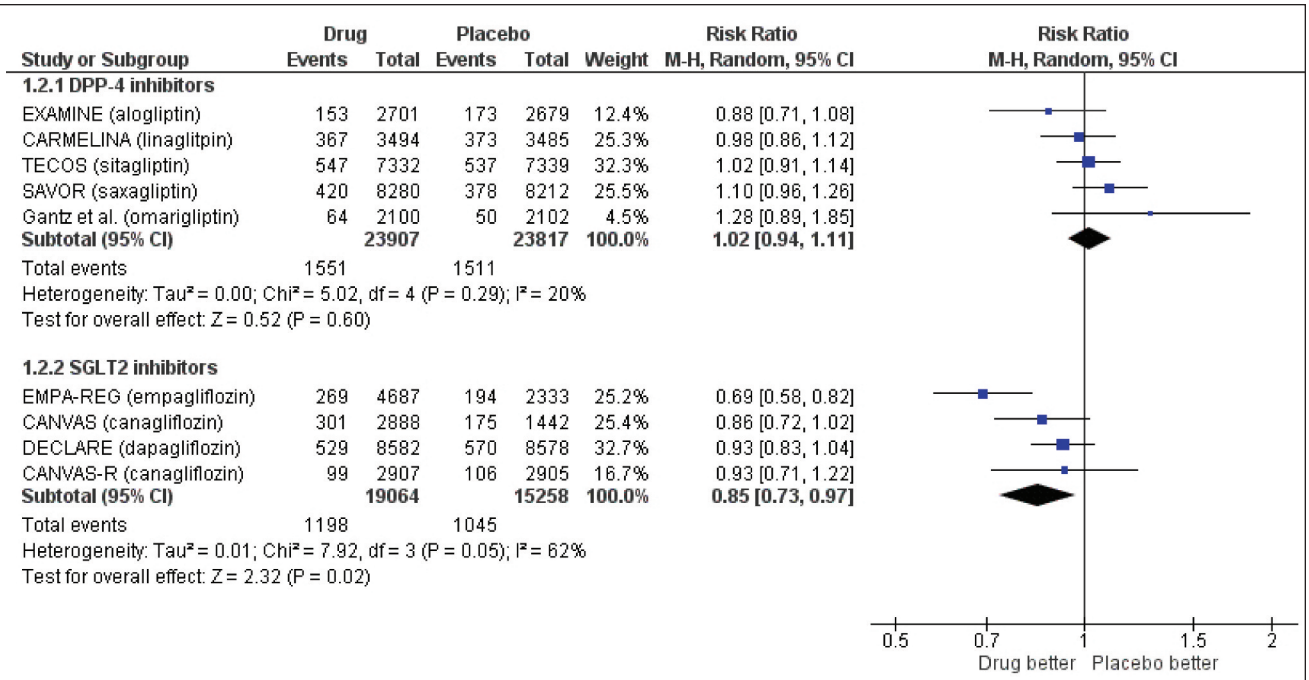

Figure 2. Forest plot for all-cause mortality in patients receiving dipeptidyl peptidase-4 (DPP-4) inhibitors and sodium glucose cotransporter-2 (SGLT2) inhibitors. EXAMINE trial for alogliptin = White and others,[4] CARMELINA trial for linagliptin = Rosenstock and others,[3] TECOS trial for sitagliptin = Green and others,[6] SAVOR trial for saxagliptin = Scirica and others,[5] trial for omarigliptin = Gantz and others,[2] EMPA-REG trial for empagliflozin = Zinman and others,[7], CANVAS and CANVAS-R trials for canagliflozin = Neal and others,[8] DECLARE trial for dapagliflozin = Wiviott and others.[9] CI = confidence interval, df = degrees of freedom, M-H = Mantel-Haenszel.

The overall results from the fixed-effect and random-effects models were similar. As with our previous analysis, there was no significant difference in major adverse cardiovascular events (risk ratio [RR] 1.00, 95% confidence interval [CI] 0.94–1.06; Figure 1), all-cause mortality (RR 1.02, 95% CI 0.94–1.11; Figure 2), or hospital admission for heart failure (RR 1.04, 95% CI 0.95–1.15). These data corroborate our previous conclusion that DPP-4 inhibitors represent the *Seinfeld* of oral antihyperglycemics.

Another class of oral antidiabetic drugs—the sodium glucose cotransporter-2 (SGLT2) inhibitors—has now emerged, with more promising evidence. We searched PubMed using the terms "sodium glucose cotransporter-2 inhibitors" and "cardiovascular disease" for the period December 2008 to January 2019 using the same inclusion criteria.[1] Of the 54 articles identified, 3 RCTs were included, all of which had enrolled patients with type 2 diabetes who had or were at risk for cardiovascular disease.[7-9] The EMPA-REG OUTCOME trial compared empagliflozin with placebo in 7020 patients (mean age 63 years, 71% men).[7] The CANVAS/CANVAS-R trials compared canagliflozin with placebo in 10 142 patients (mean age 63 years, 64% men).[8] The DECLARE-TIMI 58 trial compared dapagliflozin with placebo in 17 160 patients (mean age 64 years, 63% men).[9] Median follow-up was 3.1 to 4.2 years. We performed a meta-analysis with these trials (n = 34 322), which showed that SGLT2 inhibitors significantly reduced major adverse cardiovascular events (RR 0.91, 95% CI 0.85–0.97; Figure 1) and hospital admission for heart failure (RR 0.71, 95% CI 0.62–0.80). These appear to be class effects. All-cause mortality was significantly lower with the SGLT2 inhibitors (RR 0.85, 95% CI 0.73–0.97; Figure 2), but the substantial heterogeneity (I^2 = 62%) and more pronounced effect with empagliflozin suggest that this effect may be unique to that agent. These results are consistent with another recent meta-analysis.[10]

However, despite these encouraging results, SGLT2 inhibitors may be "breaking bad". We are not referring here to criminality, as with Walter White on the hit television drama of the same name, but rather to the inconsistent efficacy and unexpected adverse events associated with these agents. Much like a pizza on a roof, we believe these concerns cannot be ignored. Although they have not been encountering *Breaking Bad*–style violence, patients taking SGLT2 inhibitors are unexpectedly experiencing fractures and undergoing amputations. A recent meta-analysis of the aforementioned trials showed an increased risk of amputations with SGLT2 inhibitors (hazard ratio [HR] 1.26, 95% CI 1.06–1.51), although these results had substantial heterogeneity (I^2 = 79%) and were primarily driven by canagliflozin.[10] Fractures were numerically higher with SGLT2 inhibitors (HR 1.08, 95% CI 0.98–1.20), with moderate heterogeneity (I^2 = 42%), and this result was again primarily driven by canagliflozin. In addition, diabetic ketoacidosis was significantly higher with SGLT2 inhibitors (HR 2.20, 95% CI 1.25–3.87).

On the basis of these analyses, we emphatically recommend SGLT2 inhibitors over DPP-4 inhibitors in the management of type 2 diabetes. The cardiovascular efficacy data must be respected. However, as with any new class of medications, SGLT2 inhibitors have the potential to "break bad". With inspiration from Walter White, if that's true, and if we don't know whether any of these agents are more harmful than the others, then maybe our best course would be to tread lightly. Even though future studies are needed to refine their net clinical effect, using SGLT2 inhibitors remains far removed from wearing a black porkpie hat and adopting the pseudonym "Heisenberg". Despite possibly "breaking bad" for some non-cardiovascular outcomes, at least the SGLT2 inhibitors have some measurable clinical benefit, which is more than can be said for the DPP-4 inhibitors.

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ARTICLE DE SYNTHÈSE

Utilisation des jeux d'évasion en santé : une revue de littérature

par Amélie Chabrier, Suzanne Atkinson, Pascal Bonnabry et Jean-François Bussières

RÉSUMÉ

Contexte : Il existe différentes stratégies pédagogiques permettant l'apprentissage, tant en milieu universitaire qu'en milieu professionnel. Parmi toutes ces stratégies, on note l'émergence de simulation ayant recours au concept de jeu d'évasion.

Objectif : L'objectif était de recenser les modalités entourant l'utilisation, la conception et la réalisation de jeux d'évasion dans le domaine de la santé.

Sources des données : Les recherches sur Pubmed, Embase et CINAHL ont été effectuées jusqu'au 3 décembre 2018.

Sélection des études : Toutes les études portant sur la conception ou la réalisation de jeux d'évasion dans le domaine de la santé, en anglais et en français, ont été incluses.

Extraction des données : Le pays, la population cible, la conception, la réalisation, la méthode d'évaluation et les résultats ont été extraits.

Synthèse des données : Sept résumés de communication affichée et neuf articles ont été inclus. Douze jeux d'évasion ont été réalisés aux États-Unis. Ils sont utilisés en médecine (n = 5), en pharmacie (n = 4), en sciences infirmières (n = 4) ainsi que dans d'autres disciplines (n = 3), principalement dans un cadre pédagogique universitaire (n = 12) mais aussi professionnel (n = 4). Leurs objectifs visaient à améliorer les connaissances (n = 8), à augmenter l'intérêt et la motivation des participants pour un sujet précis (n = 2) et à améliorer la cohésion et la communication dans une équipe (n = 2). Dix des jeux d'évasion décrits dans les articles étaient basés sur un scénario orienté vers la clinique. Dix équipes ont réalisé un débriefing avec les participants, une équipe n'en a pas fait et cinq articles ne mentionnaient pas cette information.

Conclusion : Il existe peu de données entourant l'utilisation de jeux d'évasion en santé. Il est trop tôt pour juger de l'efficacité de cette approche. Toutefois, l'intérêt grandissant justifie l'instauration d'une veille documentaire pour suivre l'évolution et mieux comprendre la place de ce type de stratégie dans l'apprentissage en santé.

Mots clés : stratégie pédagogique, simulation, jeux d'évasion, pharmacie

ABSTRACT

Background: Many different teaching strategies are used to promote learning in an academic or professional environment. Among these can be noted the emergence of simulation, based on the concept of escape games.

Objective: To identify methodologies relating to the use, design, and implementation of escape games in health care.

Data Sources: The Pubmed, Embase, and CINAHL databases were searched up to December 3, 2018.

Study Selection: All studies focusing on the design or development of escape games in the health care field (published in English or French) were included.

Data Extraction: For each study, the country, target population, design, development, method of evaluation, and results were extracted for analysis.

Data Synthesis: Seven poster abstracts and 9 published articles were included. Twelve escape games were developed in the United States. They were used in medicine (n = 5), pharmacy (n = 4), nursing (n = 4) and other fields (n = 3), mainly within academic teaching contexts (n = 12) but also in professional settings (n = 4). Their goals were to improve knowledge (n = 8), to increase participants' interest and motivation regarding a specific topic (n = 2), and to improve cohesion and communication within a team (n = 2). Ten of the escape games described in the articles were based on a clinical scenario. Ten of the research teams held debriefings with participants, and one did not; 5 articles did not report information about debriefing.

Conclusions: Few data exist concerning the use of escape games in the health care setting, and it is too early to judge the efficiency of this approach to learning. However, growing interest justifies systematic monitoring of the literature to follow the evolution of such strategies and to better understand their place in health care education.

Keywords: teaching strategy, simulation, escape games, pharmacy

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INTRODUCTION

Il existe différentes stratégies pédagogiques permettant l'apprentissage.

Messier définit une stratégie pédagogique comme une « série d'opérations qui vise l'atteinte d'objectifs pédagogiques dans le cadre d'une situation pédagogique. L'enseignant doit la choisir ou la concevoir et la mettre en œuvre dans le cadre d'une situation pédagogique réelle. Plus spécifiquement, on peut différencier des "méthodes" (p. ex. : apprentissage par problèmes, apprentissage coopératif) et des "techniques" (p. ex. : jeu de rôles, ateliers) au sein même du concept global de stratégies pédagogiques »[1]. Le Bureau de l'environnement numérique d'apprentissage de l'Université de Montréal définit la stratégie pédagogique comme « un ensemble d'opérations agencées en vue de favoriser l'atteinte d'un but. Dans ce cas, la stratégie pédagogique est composée d'un principe intégrateur qui décrit le plan général et d'un scénario d'évènement d'apprentissage qui explicite l'agencement et l'articulation des opérations »[2]. Ainsi, il existe de nombreuses stratégies pédagogiques.

Dans le domaine de la santé, il existe plusieurs stratégies d'apprentissage, notamment la conférence, le débat, l'étude de cas, l'évaluation par les pairs, l'exercice, l'exposé, la lecture dirigée, le projet, la publication, la résolution de problème, la simulation, le jeu sérieux, le stage ou encore le travail en équipe.

Selon la Haute Autorité de santé (HAS), la « simulation en santé correspond à l'utilisation d'un matériel (comme un mannequin ou un simulateur procédural), de la réalité virtuelle ou d'un patient standardisé pour reproduire des situations ou des environnements de soin, dans le but d'enseigner des procédures diagnostiques et thérapeutiques et de répéter des processus, des concepts médicaux ou des prises de décision par un professionnel de santé ou une équipe de professionnels »[3]. L'HAS décrit différentes techniques de simulation en santé, comme le « patient standardisé », les « simulateurs de patients » ou encore les « jeux sérieux ». Ces derniers ont pour objectifs d'être divertissants et d'y ajouter « une intention sérieuse, de type pédagogique, informative, communicationnelle ou d'entrainement avec des ressorts ludiques »[4]. Ainsi, la simulation peut inclure différents types de stratégies (p. ex. simulation clinique avec scénario[5], simulation avec chambre des erreurs[6], simulation avec jeu en ligne[7] et jeu présenté sous la forme de questionnaire[8]). Les jeux d'évasion ayant les mêmes intentions que les jeux sérieux, ils peuvent être considérés comme une technique de simulation. Olszewski et collab. ont publié en 2017 une revue de littérature sur l'utilisation des jeux sérieux dans l'éducation médicale sans commenter les jeux d'évasion[9]. On note l'émergence de simulations ayant recours au concept de jeu d'évasion dans la littérature scientifique.

Le grand dictionnaire terminologique définit le jeu d'évasion comme étant un « jeu immersif qui est construit autour d'un scénario et dont le but est généralement de sortir d'un lieu donné dans une limite de temps préétablie en résolvant des énigmes. Généralement, le jeu d'évasion se joue en groupe et est supervisé par un maître de jeu dont le rôle peut être d'assurer le bon déroulement du jeu, de donner des indices aux joueurs ou de jouer le rôle d'un personnage faisant partie du scénario »[10].

On trouve de plus en plus de jeux d'évasion dans la société. La première mention du recours à un jeu d'évasion remonte à 2007 au Japon et à 2012 aux États-Unis[11,12]. Ces jeux ludiques sont élaborés pour développer notamment un esprit d'équipe, favoriser le développement de nouveaux rôles et faciliter la collaboration. Dans le milieu de la santé, les jeux d'évasion font leur apparition à partir de 2017.

Afin de réaliser nous-mêmes un jeu d'évasion à visée éducative dans notre établissement de santé, nous nous sommes intéressés à l'utilisation des jeux d'évasion dans le domaine de la santé.

METHODE

Il s'agit d'une revue de littérature.

L'objectif principal était de recenser les modalités entourant l'utilisation, la conception et la réalisation de jeux d'évasion dans le domaine de la santé afin de développer un jeu d'évasion par la suite.

Sources de données

À partir de la stratégie de recherche, nous avons recherché les articles pertinents dans Pubmed [("escape" [All Fields] AND room[All Fields]) OR ("escape" [All Fields] AND game[All Fields])], Embase [« Escape room » OR « escape game »] et CINAHL [« Escape room » OR « escape game »] publiés jusqu'au 3 décembre 2018. Une recherche manuelle complémentaire a été menée à partir de la liste bibliographique des articles retenus et sur Google Scholar.

Critères d'inclusion et d'exclusion

Les études incluses portaient sur la conception ou la réalisation de jeux d'évasion dans le domaine de la santé, tant en milieu universitaire qu'en milieu professionnel (c.-à-d. hôpital). Seuls les textes en anglais et en français ont été inclus. Étant donné le nombre limité d'articles publiés, les abrégés de communications affichées dans les bases de données consultées ont également été inclus. Les lettres à l'éditeur et les commentaires en ont été exclus.

Analyse

Les articles, sélectionnés de façon indépendante au moyen de la stratégie de recherche, ont été déterminés sur la base du titre par une assistante de recherche et par un pharmacien chercheur. Par la suite, les doublons ont été éliminés. Pour finir, les articles ont été retenus sur la base du résumé structuré selon le même processus. Un chiffrier a été établi (Excel, Microsoft, Seattle, WA, ÉUA) afin de recueillir les données pertinentes de chaque article,

soit auteur, revue, année de publication, pays, type d'étude, type d'enquête, questionnaire, référentiel, participants, joueurs, superviseurs, durée, local, scénario, nombre d'énigmes, indices, coût, débriefing, taux de réussite, temps moyen de sortie du jeu d'évasion pour les équipes ayant réussi le jeu d'évasion dans le temps imparti, taux de réponses, résultats du questionnaire, type de participation, durée de la conception, nombre de concepteurs, connaissances nécessaires, approbation du sujet, consentement des participants, les limites et les commentaires.

À partir de la constitution du chiffrier détaillé, un tableau de synthèse a été produit.

Seules des statistiques descriptives et des analyses qualitatives ont été effectuées.

RESULTATS

Conformément à la stratégie de recherche mise en place, 40 articles et résumés de communication affichée (nommés ci-dessous « articles ») ont été sélectionnés et 16 ont été retenus[13-28]. De ces 16 articles, neuf étaient des articles et sept, des résumés de communication affichée. La figure 1 représente la cartographie de sélection des articles.

La majorité des jeux d'évasion (n = 12) a été réalisée aux États-Unis et principalement dans le domaine de la médecine (n = 5), de la pharmacie (n = 4), des sciences infirmières (n = 4) ou d'autres disciplines (n = 3).

Les jeux d'évasion étaient généralement utilisés dans un cadre pédagogique universitaire (n = 12) mais aussi en milieu professionnel (n = 4). Les jeux d'évasion avaient généralement pour objectif d'améliorer les connaissances (n = 8), d'augmenter l'intérêt et la motivation des participants sur un sujet précis (n = 2) ou d'améliorer la cohésion et la communication dans une équipe (n = 2). Quatre articles ne donnaient pas cette information. Les jeux d'évasion se réalisaient dans différents locaux, comme la chambre d'un patient (n = 3), un amphithéâtre / une salle de classe (n = 3), une salle de simulation (n = 2) ou encore dans une salle d'évasion commerciale (n = 1). Sept articles ne mentionnaient pas cette information.

La participation aux jeux d'évasion était obligatoire (n = 4), volontaire (n = 3) ou n'était pas mentionnée (n = 9) dans les études retenues.

Dix des jeux d'évasion décrits dans les articles étaient basés sur un scénario orienté vers la clinique, cinq ne possédaient pas de scénario clinique et un ne le précisait pas. La majorité des jeux étaient réalisés selon un scénario linéaire simple (n = 4), c'est-à-dire que la première énigme permet de découvrir la seconde et ainsi de suite jusqu'à l'énigme finale. Les scénarios pouvaient être convergents simples (n = 1), c'est-à-dire que les énigmes peuvent être résolues dans un ordre aléatoire pour découvrir l'énigme finale ou être un mélange de scénario linéaire et convergent simple (n = 1). Dix articles ne précisaient pas cette information. Six articles donnaient des indices, les autres (n = 10) ne mentionnaient pas cette information.

Seuls trois articles indiquaient le coût relatif à la conception du jeu d'évasion, les prix variant de 12 à 200 USD. Un autre article indiquait un faible coût de conception du jeu, et les autres (n = 12) ne mentionnaient pas cette information.

Le nombre total de participants allait de 7 à 213, répartis en groupes de deux à quatorze participants. Trois articles indiquaient le temps que prenait la conception. Il variait entre 6 et 20 heures. Un autre article annonçait un temps de conception considérable sans préciser le temps réel consacré à la seule conception[13].

La durée des jeux évoquée variait de 30 à 80 minutes avec une moyenne d'une heure. Les jeux comportaient généralement entre 5 et 12 énigmes à résoudre pour atteindre entre 3 et 10 objectifs différents. Certains auteurs proposaient une succession de salles avec des thèmes différents au cours d'un même jeu.

À la fin du jeu d'évasion, dix équipes ont réalisé un débriefing avec les participants, une équipe n'en a pas fait et cinq articles ne donnaient pas cette information.

Deux articles retenus testaient les connaissances avant et après

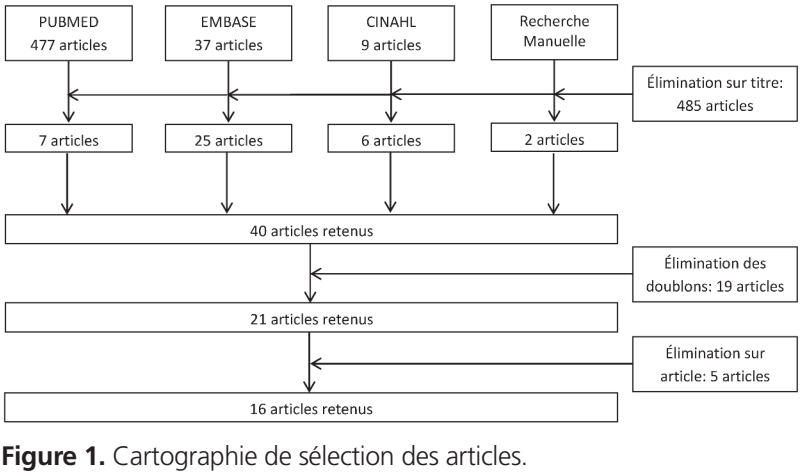

Figure 1. Cartographie de sélection des articles.

Tableau 1 (partie 1 de 11). Profil des résumés et des articles décrivant les modalités entourant la conception et la réalisation de jeux d'évasion dans le domaine de la santé

Profil*	Objectifs	Méthode†	Réalisation du jeu‡	Résultats§	Commentaires**
Jeux d'évasion réalisés en milieu universitaire					
Hermanns et al.[14] *Journal of Nursing Education and Practice* 2017 États-Unis Article : étude descriptive, quantitative	Décrire l'utilisation d'une stratégie de jeu basée sur une salle d'évasion pour aider les étudiants à en savoir d'avantage sur les médicaments du système cardiovasculaire dans un cours de pharmacologie Décrire la perception qu'ont les étudiants de leur expérience avec le jeu d'évasion pour apprendre les médicaments cardiovasculaires	Enquête post. au jeu Référentiel utilisé pour réaliser les énigmes : SM	Participants : Étudiants en sciences infirmières Joueurs : 145 répartis en groupes de 4 ou 5 personnes Superviseur : professeur de la faculté Durée du jeu d'évasion : 60 min Local : amphithéâtre Scénario : non clinique, avec des superhéros Nombre d'énigmes : SM Indices donnés en cours de jeu : SM Coût : SM Débriefing : oui	Taux de réussite au jeu d'évasion : SM Temps moyen de sortie du jeu d'évasion : SM Taux de réponses à l'enquête : 82 % Résultats du questionnaire : • le jeu est une activité d'apprentissage précieuse : 74,8 % • apprentissage au cours du jeu : 72,2 % • augmentation de la compréhension par le jeu : 52,9 %	Type de participation : SM Temps de conception : SM Nombre de concepteurs du jeu : SM Connaissances particulières nécessaires pour ce jeu : oui Approbation du projet : conseil d'administration de l'université Consentement des participants : SM
Cain[15] *Current Pharmacy Teaching and Learning* 2019 États-Unis Article	Fournir une preuve de concept que les jeux d'évasion peuvent se faire dans une grande salle de classe Déterminer les degrés d'engagement et de plaisir des élèves qui participent au jeu d'évasion	Enquête post. au jeu Questionnaire constitué de 5 questions; réponses cotées de 1 (fortement en désaccord) à 5 (fortement d'accord) Référentiel utilisé pour réaliser les énigmes : enseignement sur les ressources humaines de l'université	Participants : étudiants en pharmacie Joueurs : 141 répartis en groupes de 5 ou 6 personnes Superviseur : professeur de la faculté (2), résident (1) Durée du jeu d'évasion : 45 min Local : amphithéâtre Scénario : non clinique, linéaire Nombre d'énigmes : 10 Indices donnés en cours de jeu : oui (autant que souhaité) Coût : 12 USD Débriefing : oui (10 min)	Taux de réussite au jeu d'évasion : 100 % Temps moyen de sortie du jeu d'évasion : SM Taux de réponses à l'enquête : SM Résultats du questionnaire : • préférence par rapport à un cours classique : 91 % • plus de participation à la discussion et la résolution de problème dans le jeu : 84 % • jeu apprécié : 89 % • collaboration de l'équipe : 93 % • tous les membres ont participé activement au jeu : 91 %	Type de participation : obligatoire au sein d'un enseignement universitaire Temps de conception : 18 h 45 Nombres de concepteurs du jeu : SM Connaissances particulières nécessaires pour ce jeu : oui Approbation du projet : SM Consentement des participants : SM Alternance d'énigmes réelles et informatiques Jeu d'évasion testé au préalable par des étudiants

Suite à la page 392

Tableau 1 (partie 2 de 11). Profil des résumés et des articles décrivant les modalités entourant la conception et la réalisation de jeux d'évasion dans le domaine de la santé

Profil*	Objectifs	Méthode†	Réalisation du jeu‡	Résultats§	Commentaires**
Gómez-Urquiza et al.[13] *Nurse Education Today* 2019 Espagne Article : étude descriptive transversale, quantitative et interventionnelle	Mesurer la satisfaction des étudiants à utiliser un jeu d'évasion en tant que jeu d'enseignement pour les aider dans leur processus d'apprentissage et leur préparation des examens Évaluer l'impact d'un jeu d'évasion sur la motivation des étudiants à étudier	Enquête post. au jeu disponible en ligne avec rappel 7 jours plus tard Questionnaire constitué de 6 questions; réponses cotées de 1 (fortement en désaccord) à 5 (fortement d'accord) selon l'échelle de Likert Référentiel utilisé pour réaliser les énigmes : aucun	Participants : étudiants en sciences infirmières Joueurs : 105 répartis en groupes de 5 personnes Superviseur : professeur de la faculté Durée du jeu d'évasion : 30 min Local : salle de classe Scénario : non clinique Nombre d'énigmes : SM Indices donnés en cours de jeu : oui (2) Coût : faible (non chiffré) Débriefing : non	Taux de réussite au jeu d'évasion : 66,5 % Temps moyen avant le retrait du jeu d'évasion : 27 min 24 sec Taux de réponses à l'enquête : 84,76 % Résultats du questionnaire : • le jeu aide à avoir de meilleures connaissances : 4,8/5 • les participants ont aimé jouer : 4,6/5 • le jeu aide à réussir les examens : 4,6/5 • utilisation des connaissances dans le jeu : 4,7/5 • augmenter le nombre de jeux dans l'enseignement : 4,8/5	Type de participation : volontaire Temps de conception : considérable, non chiffrée Nombre de concepteurs du jeu : SM Connaissances particulières nécessaires au jeu : non Approbation du projet : SM Consentement des participants : oui

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le jeu d'évasion, les autres (n = 14) évaluaient la perception que les participants avaient du jeu.

Par ailleurs, deux projets ont reçu l'approbation d'un comité universitaire, trois d'un comité hospitalier et pour un article, le comité d'éthique de la recherche n'a pas jugé nécessaire d'évaluer le projet et de décerner une approbation. Les autres études n'ont pas donné cette information (n = 8). Deux articles retenus indiquent que les participants ont signé un consentement.

Deux équipes ont essayé le jeu d'évasion avec des étudiants avant de le lancer à grande échelle. Les autres (n = 14) ne mentionnaient pas de tests préalables.

Le tableau 1 présente le profil des résumés et des articles décrivant les modalités entourant la conception et la réalisation de jeux d'évasion dans le domaine de la santé.

DISCUSSION

Cette revue de littérature met en évidence un nombre limité d'articles portant sur la conception et l'utilisation des jeux d'évasion, une nouvelle stratégie pédagogique dans le domaine de la santé, tant dans le cadre de l'enseignement en milieu universitaire que dans celui de la pratique professionnelle.

Les articles recensés donnent des exemples concrets de conception et d'utilisation de jeux d'évasion et constituent une première base de données pour la réalisation d'initiatives similaires. Dans plusieurs cas, les jeux d'évasion ont pour objectif le renforcement de compétences transversales (p. ex. leadership, communication, travail en équipe, esprit critique)[13-28]. D'autres visent davantage des connaissances (p. ex. diabète, chirurgie vasculaire, empoisonnement, maladies infectieuses). Notre revue montre que plusieurs études ne décrivent pas forcément de démarche très structurée pour la création du jeu. Il semble important d'établir des objectifs spécifiques d'apprentissage, de déterminer des éléments de contenus ciblés pour la tenue du jeu (c.-à-d. éléments de connaissances précis à acquérir), de proposer un scénario réaliste comportant une séquence d'énigmes ainsi qu'une trame logique qui soutient le scénario dans un lieu donné. Les jeux d'évasion comportent généralement quelques énigmes qui permettent aux

Tableau 1 (partie 3 de 11). Profil des résumés et des articles décrivant les modalités entourant la conception et la réalisation de jeux d'évasion dans le domaine de la santé

Profil*	Objectifs	Méthode†	Réalisation du jeu‡	Résultats§	Commentaires**
Eukel et al.[16] *American Journal of Pharmaceutical Education* 2017 États-Unis Article	Concevoir un jeu éducatif augmentant les connaissances en gestion du diabète parmi les étudiants en pharmacie de troisième année Évaluer la perception du jeu des étudiants en pharmacie	Enquête ant. et post. au jeu, réalisée la semaine avant et immédiatement après le jeu Questionnaire constitué de 23 questions « vrai/faux » Référentiel utilisé pour réaliser les énigmes : cours de la faculté portant sur le diabète	Participants : étudiants en pharmacie Joueurs : 83 répartis en groupes de 5 personnes Superviseur : professeur de la faculté Durée du jeu d'évasion : 75 min Local : SM Scénario : clinique, linéaire Nombre d'énigmes : 5 Indices donnés en cours de jeu : oui (4) Coût : 75 USD Débriefing : SM	Taux de réussite au jeu d'évasion : SM Temps moyen de sortie du jeu d'évasion : SM Taux de réponse à l'enquête : 95 % Résultats du questionnaire : • le jeu d'évasion m'a permis de voir les choses différemment : 4,3/5 • le jeu m'a permis d'apprendre de mes pairs : 4,4/5 • le jeu est efficace pour en savoir plus sur le diabète : 4,3/5 • le jeu est efficace pour obtenir de nouvelles connaissances sur le diabète : 4,2/5 • meilleur apprentissage avec le jeu qu'avec une conférence didactique : 4/5 • le jeu est efficace pour apprendre les produits relatifs au diabète : 4,3/5 • le jeu a permis d'impliquer activement mes coéquipiers dans l'apprentissage proposé : 4,4/5 • sentiment de stress / dépassement empêchant l'apprentissage : 3,7/5 • la partie non éducative du jeu m'a empêché d'apprendre des choses sur le diabète : 3,4/5 • propension à utiliser différentes sources pour apprendre de nouvelles choses : 3,8/5 • en général, les jeux, tous types confondus, sont appréciés : 4,2/5	Participation obligatoire dans le cadre d'un enseignement universitaire Temps de conception : 20 h (participation des étudiants) Nombres de concepteurs du jeu : SM Connaissances particulières nécessaires pour ce jeu : oui Approbation du projet : par le conseil institutionnel de la faculté Consentement des participants : oui Jeu conçu pour atteindre 17 objectifs d'apprentissage

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Tableau 1 (partie 4 de 11). Profil des résumés et des articles décrivant les modalités entourant la conception et la réalisation de jeux d'évasion dans le domaine de la santé

Profil*	Objectifs	Méthode†	Réalisation du jeu‡	Résultats§	Commentaires**
Nelson et al.[17] *Annals of Emergency Medicine* 2017 États-Unis Résumé	Proposer un jeu d'évasion à la place d'une présentation magistrale standard dans le cadre d'une journée de conférences	Référentiel utilisé pour réaliser les énigmes : SM	Participants : résidents en médecine Joueurs : répartis en groupes de 6-8 personnes; 8 groupes ont participé Superviseur : SM Durée du jeu d'évasion : 80 min Local : centre de simulation Scénario : clinique, multiple Nombre d'énigmes : 5 Indices donnés en cours de jeu : SM Coût : SM Débriefing : SM	Taux de réussite au jeu d'évasion : SM Temps moyen de sortie du jeu d'évasion : SM Taux de réponses à l'enquête : SM Résultats du questionnaire : SM	Type de participation : SM Temps de conception : SM Nombres de concepteurs du jeu : SM Connaissances particulières nécessaires pour ce jeu : oui Approbation du projet : SM Consentement des participants : SM

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participants de franchir, une à une, les étapes du jeu. Par exemple, la résolution d'une énigme permet de déverrouiller un cadenas qui donne accès à un nouvel indice. La plupart des auteurs évoquent le caractère ludique comme incitatif à l'utilisation de ce type d'activité afin de créer un intérêt auprès du public cible, d'encourager la participation et possiblement d'obtenir des gains en termes de connaissances et de compétences. Toutefois, les données recueillies ne permettent pas de comparer le taux de participation aux jeux d'évasion par rapport à d'autres stratégies pédagogiques. Presque tous les jeux recensés comportaient une évaluation, tantôt des perceptions (n = 14), tantôt des connaissances (n = 2). Si le jeu d'évasion est utilisé à des fins pédagogiques, nous pensons essentiel de recourir à un outil de mesure pour vérifier l'acquisition de connaissances, le changement de perception ou la satisfaction.

La majorité des jeux d'évasion développés se sont déroulés dans un cadre pédagogique en milieu universitaire, mais certains jeux ont été menés en milieu professionnel. Nous pensons que le milieu universitaire est plus propice à la mise en place de ce type de stratégie, parce qu'il dispose généralement d'experts et de ressources pédagogiques pour soutenir le développement de tels jeux et qu'il a le recul nécessaire par rapport aux nombreuses stratégies pédagogiques. En milieu professionnel, les ressources sont principalement consacrées à la prestation de soins et il n'y a pas forcément d'experts pour le développement de telles activités.

À notre avis, il est important de concevoir un jeu dont le temps requis demeure réaliste par rapport aux contraintes des participants. Il ne faut pas négliger le temps supplémentaire requis pour la présentation de l'activité et des consignes de même que le temps au terme du jeu pour la conclusion et le débriefing, s'il est envisagé.

Les données recueillies laissent entendre que la mise en place d'un jeu d'évasion est peu coûteuse (< 100 USD / initiative) et qu'elle requiert peu de temps (< 20 heures de conception / initiative). Les données n'incluent pas les coûts associés aux ressources humaines nécessaires, tant pour la conception que pour la participation. Si un jeu est réalisé durant le temps de travail, il semble raisonnable de considérer l'ensemble des coûts humains associés à la conception et la participation au jeu. De même, le temps moyen de conception calculé dans notre revue nous apparaît inférieur à ce que représente la mise en place complète d'un jeu d'évasion. À la lecture des différents articles, la mise en place d'un jeu d'évasion devrait comporter une phase de conception théorique, une phase de test préalable et une phase de réalisation. En général, un tel jeu requiert un animateur qui donne des consignes au départ, fournit des indices en cours de route à l'aide d'un moyen de communication et participe à la conclusion suivie d'un débriefing de l'activité. À la lumière des données

Tableau 1 (partie 5 de 11). Profil des résumés et des articles décrivant les modalités entourant la conception et la réalisation de jeux d'évasion dans le domaine de la santé

Profil*	Objectifs	Méthode†	Réalisation du jeu‡	Résultats§	Commentaires**
Korenoski et al.[18] *Clinical Toxicology* (50th North American Congress of Clinical Toxicology) 2018 États-Unis Résumé	Illustrer comment un jeu d'évasion peut être utile pour l'enseignement et l'application des connaissances de la pharmacie Évaluer l'efficacité d'un jeu d'évasion sur la confiance et la compétence des étudiants pour appliquer les recommandations de traitement lors d'une urgence toxicologique	Enquête ant. et post. au jeu d'évasion Questionnaire constitué de 5 questions dont certaines sont cotées selon une échelle de Likert allant de 1 à 5 Référentiel utilisé pour réaliser les énigmes : SM	Participants : étudiants en pharmacie Joueurs : 22 répartis en groupes de 3 ou 4 personnes Superviseur : professeur de la faculté Durée du jeu d'évasion : SM Local : SM Scénario : clinique Nombre d'énigmes : SM Indices donnés en cours de jeu : SM Coût : SM Débriefing : SM	Taux de réussite au jeu d'évasion : SM Temps moyen avant la sortie du jeu d'évasion : SM Taux de réponses à l'enquête : 100 % Résultats du questionnaire : • réussite > 70 % du questionnaire sur les connaissances du cas 1, ant. au jeu : 18 %, post. au jeu : 82 % • réussite > 70 % du questionnaire sur les connaissances du cas 1 : ant. au jeu : 0 %, post. au jeu : 68 % • confiance dans la gestion d'un cas de toxicologie : ant. au jeu ≤ 2/5 et post. au jeu 100 %, ≥ 3/5 pour 95 % • amélioration des connaissances : 95 % • satisfaction du jeu : 95 % • souhait d'intégrer leur jeu dans le cursus : 91 %	Type de participation : SM Temps de conception : SM Nombre de concepteurs du jeu : SM Connaissances particulières nécessaires pour ce jeu : oui Approbation du projet : SM Consentement des participants : SM Réalisation de 2 cas cliniques différents

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rapportées dans les études, nous pensons que la conception et la réalisation d'un jeu d'évasion représentent des coûts plus importants que ceux notés dans les articles et qu'il est important de déterminer les conditions gagnantes permettant la tenue du jeu durant une période de temps suffisante pour amortir les coûts ou de le répéter à intervalles réguliers et de rejoindre une population suffisante.

En outre, nous pensons que les stratégies pédagogiques de type ludique comportent un intérêt parce qu'elles offrent une approche d'apprentissage interdisciplinaire différente et qu'elles peuvent susciter de l'intérêt et de la participation[23]. Toutefois, nous pensons que de tels jeux doivent être encadrés, planifiés et bien gérés pour espérer des résultats utiles. Dans cet esprit, le centre interprofessionnel de simulation des hôpitaux universitaires de Genève insiste sur l'importance du débriefing en simulation. On considère que « le débriefing peut "faire ou défaire" une séance de simulation, il peut être considéré comme le "cœur et l'esprit" de l'apprentissage en simulation »[29]. Dans un jeu d'évasion, tous les participants ne sont pas forcément exposés à tous les éléments du contenu; selon la dynamique d'équipe, certains participants tireront davantage profit des éléments de contenu partagés. Le débriefing, qui peut inclure un aide-mémoire, est essentiel pour

Tableau 1 (partie 6 de 11). Profil des résumés et des articles décrivant les modalités entourant la conception et la réalisation de jeux d'évasion dans le domaine de la santé

Profil*	Objectifs	Méthode†	Réalisation du jeu‡	Résultats§	Commentaires**
Kinio et al.[19] *Journal of Surgical Education* 2019 Canada Étude prospective éducationnelle Article	Mettre en œuvre un jeu d'évasion sur le thème de la chirurgie vasculaire Évaluer l'impact d'un jeu d'évasion sur la chirurgie vasculaire sur la motivation, la satisfaction et l'engagement sur les CAN MEDS	Enquête post. au jeu lors du débriefing Référentiel utilisé pour réaliser les énigmes : 6 articles du *NEJM* portant sur la chirurgie vasculaire et les compétences définies par le Collège royal des médecins et chirurgiens du Canada	Participants : étudiants en médecine Joueurs : 13 répartis en groupes de 3 ou 4 personnes Superviseur : 2 organisateurs Durée du jeu d'évasion : 60 min Local : salle de simulation ressemblant à une chambre de patient Scénario : clinique Nombre d'énigmes : SM Indices donnés en cours de jeu : SM Coût : SM Débriefing : oui	Taux de réussite au jeu d'évasion : 75 % Temps moyen de sortie du jeu d'évasion : 56,8 min Taux de réponses à l'enquête : 92,3 % Résultats du questionnaire : • augmentation de la compréhension grâce au jeu : 75 % • format « jeu d'évasion » approprié au test des connaissances : 92 % • la collaboration et la communication sont essentielles au jeu : 100 % • les étudiants ont un plus grand intérêt pour la chirurgie vasculaire à la suite de ce jeu : 92 % • expérience appréciée : 100 %	Participation volontaire (sollicitation par courriel) Temps de conception : SM Nombres de concepteurs du jeu : SM Connaissances particulières nécessaires pour ce jeu : oui Approbation du projet : par le comité d'éthique de l'hôpital Consentement des participants : SM Les participants devaient se préparer au jeu en lisant des articles scientifiques sur le sujet abordé Répartition des documents à lire dans le groupe plutôt que lecture individuelle de tous les documents Test sur les connaissances du groupe et non individuelles

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résumer les apprentissages ciblés, le tout effectué en veillant à ce que que le partage ne nuise pas à la pérennité du jeu auprès d'autres participants.

Cette revue de littérature comporte des limites. Seuls les articles en anglais et en français ont été retenus dans le domaine de la santé. Bien que la revue comporte trois bases de données, Google Scholar et une recherche manuelle, la consultation d'autres bases de données pourrait être utile (p. ex. Web of Science, Scopus). Cette étude recense un faible nombre d'études, neuf des 16 études incluses étaient des résumés de communication affichée de congrès et comportaient très peu de détails décrivant le jeu et sa portée. Seules quatre études ont été réalisées en milieu professionnel. D'autre part, la plupart des études recensaient la perception qu'avaient les participants de l'activité plutôt que l'amélioration des connaissances au moyen de cette activité ludique. Ce nombre limité d'études ne permet pas de tirer des conclusions sur les modalités d'utilisation, de conception et de réalisation de jeux d'évasion dans le domaine de la santé, mais seulement d'apporter des informations sur ce qui se fait présentement afin d'aiguiller de futures équipes souhaitant développer un jeu d'évasion. Compte tenu de l'émergence de cette approche pédagogique, il est probable que plusieurs articles seront publiés au cours des prochaines années. Il serait utile de répéter une telle revue de littérature d'ici trois à cinq ans, afin de pouvoir inclure un plus grand nombre d'expériences.

Tableau 1 (partie 7 de 11). Profil des résumés et des articles décrivant les modalités entourant la conception et la réalisation de jeux d'évasion dans le domaine de la santé

Profil*	Objectifs	Méthode†	Réalisation du jeu‡	Résultats§	Commentaires**
Cotner et al.[20] *Open Forum Infectious Disease* 2018 États-Unis Résumé	Décrire la conception et la mise en œuvre du jeu d'évasion comme activité d'apprentissage dans le cadre d'un cours facultatif en pharmacie, consacré aux maladies infectieuses en pharmacie	Enquêtes ant. au jeu, post. au cas et post au jeu envoyées électroniquement Réponses au questionnaire cotées de 1 (pas du tout) à 7 (beaucoup) Référentiel utilisé pour réaliser les énigmes : cours de la faculté	Participants : étudiants en pharmacie Joueurs : SM Superviseur : SM Durée du jeu d'évasion : SM Local : SM Scénario : clinique Nombre d'énigmes : SM Indices donnés en cours de jeu : SM Coût : SM Débriefing : SM	Taux de réussite au jeu d'évasion : SM Temps moyen de sortie du jeu d'évasion : SM Taux de réponses à l'enquête : 100 % Résultats du questionnaire : • score moyen des connaissances : ant. au jeu : 90,5 %; post. au cas : 82,1 % et post. au jeu : 90,5 % • préférence pour le jeu comme outil d'apprentissage : 94,7 % • meilleur apprentissage avec le jeu d'évasion : 57,9 % • perception positive des deux activités	Type de participation : obligatoire Temps de conception : SM Nombres de concepteurs du jeu : SM Connaissances particulières nécessaires pour ce jeu : oui Approbation du projet : SM Consentement des participants : SM
Gordon[21] Society for Academic Emergency Medicine 2017 États-Unis Résumé	Donner aux étudiants un enseignement sur les empoisonnements chez les enfants	Référentiel utilisé pour réaliser les énigmes : SM	Participants : étudiants dans le domaine de la santé Joueurs : SM Superviseur : professeurs et résidents Durée du jeu : SM Local : SM Scénario : clinique, linéaire Nombre d'énigmes : 5 Indices donnés en cours de jeu : oui Coût : SM Débriefing : oui	Taux de réussite au jeu d'évasion : SM Temps moyen de sortie du jeu d'évasion : SM Taux de réponses à l'enquête : SM Résultats du questionnaire : NA	Type de participation : SM Temps de conception : SM Nombres de concepteurs du jeu : SM Connaissances particulières nécessaires pour ce jeu : oui Approbation du projet : SM Consentement des participants : SM Jeu réalisé pour aborder 3 objectifs d'apprentissage

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Tableau 1 (partie 8 de 11). Profil des résumés et des articles décrivant les modalités entourant la conception et la réalisation de jeux d'évasion dans le domaine de la santé

Profil*	Objectifs	Méthode†	Réalisation du jeu‡	Résultats§	Commentaires**
Wu et al.[22] *Medical Education* 2018 États-Unis Résumé	Évaluer si les étudiants utilisaient dans le jeu les cinq compétences de leadership apprises et si cela avait un impact positif sur les relations dans l'équipe	Enquête post. au jeu Réponses au questionnaire cotées de 1 (pauvre) à 5 (excellent) Référentiel utilisé pour réaliser les énigmes : SM	Participants : étudiants en médecine Joueurs : 28 répartis en groupes de 7-10 personnes Superviseur : SM Durée du jeu : 60 min Local : SM Scénario : SM Nombre d'énigmes : SM Indices donnés en cours de jeu : SM Coût : SM Débriefing : oui	Taux de réussite au jeu d'évasion : SM Temps moyen de sortie du jeu d'évasion : SM Taux de réponses à l'enquête : 93 % Résultats du questionnaire : • activité excellente : 92 % • utilisation des 5 compétences de leadership au cours du jeu : 28 % • utilisation de ≥ 3 compétences de leadership dans le jeu : 100 % • recommandations du jeu aux autres étudiants : 100 %	Type de participation : SM Temps de conception : SM Nombres de concepteurs du jeu : SM Connaissances particulières nécessaires pour ce jeu : SM Approbation du projet : SM Consentement des participants : SM
Friedrich et al.[23] *Journal of Interprofessional Care* 2018 États-Unis Article	Décrire un programme interprofessionnel spécifique aux soins de santé utilisant un jeu d'évasion pour encourager la communication et le travail en équipe des étudiants Évaluer la perception de l'activité des jeux d'évasion par les étudiants Autoévaluer la communication et les compétences de travail en équipe des étudiants	Enquête post. au jeu envoyée par courriel Questionnaire constitué de 6 questions cotées de 1 (fortement en désaccord) à 7 (fortement d'accord) selon une échelle de Likert Référentiel utilisé pour réaliser les énigmes : SM	Participants : Étudiants en formation médicale et paramédicale Joueurs : 181 répartis en groupes de 8 personnes au maximum Superviseur : professeurs et étudiants de la faculté Durée du jeu : 45 min Local : chambre de patient Scénario : clinique, linéaire Nombre d'énigmes : 7 Indices donnés en cours de jeu : SM Coût : SM Débriefing : oui (20 min)	Taux de réussite au jeu d'évasion : SM Temps moyen de sortie du jeu d'évasion : SM Taux de réponses à l'enquête : 78 % Résultats du questionnaire : • le jeu augmente le travail d'équipe et la communication : 79,5 % • le jeu améliore les capacités individuelles à communiquer en équipe : 77,7 % • le débriefing aide à mieux comprendre la dynamique d'équipe et la communication : 84,5 % • le débriefing aide à mieux comprendre la contribution de chacun au travail d'équipe et la communication : 86,6 % • le jeu est un élément important du cursus : 76,1 %	Participation obligatoire Temps de conception : SM Nombres de concepteurs du jeu : 5 Connaissances particulières nécessaires pour ce jeu : non Approbation du projet : exemptée par le comité d'examen de l'université Consentement des participants : SM Étude pilote réalisée au préalable avec 30 participants

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Tableau 1 (partie 9 de 11). Profil des résumés et des articles décrivant les modalités entourant la conception et la réalisation de jeux d'évasion dans le domaine de la santé

Profil*	Objectifs	Méthode†	Réalisation du jeu‡	Résultats§	Commentaires**
Seto[24] *Journal canadienne de médecine d'urgence* 2018 Canada Résumé	Utiliser le jeu d'évasion comme simulation non clinique pour favoriser le travail en équipe	Référentiel utilisé pour réaliser les énigmes : enseignement de la faculté « Team Scheme domains »	Participants : étudiants en médecine Joueurs : répartis en groupes de 5 personnes Superviseur : étudiants en médecine Durée du jeu : 30 min Local : SM Scénario : non clinique Nombre d'énigmes : 8 Indices donnés en cours de jeu : SM Coût : SM Débriefing : oui (15 + 45 min)	Taux de réussite au jeu d'évasion : SM Temps moyen de sortie du jeu d'évasion : SM Taux de réponses à l'enquête : NA Résultats du questionnaire : NA	Type de participation : SM Temps de conception : SM Nombres de concepteurs du jeu : 10 Connaissances particulières nécessaires pour ce jeu : non Approbation du projet : SM Consentement des participants : SM
Jeux d'évasion réalisés en milieu professionnel					
Zhang et al.[25] *Cureus* 2018 États-Unis Article	Utiliser un jeu d'évasion en tant qu'activité de développement de l'esprit d'équipe	Enquête post. au jeu validée et adaptée à partir d'une étude précédente Questionnaire constitué de 18 questions Référentiel utilisé pour réaliser les énigmes : aucun	Participants : résidents et membres de l'université de l'unité d'urgence d'un hôpital Joueurs : 10 regroupés en un seul groupe Superviseur : auteur Durée de la salle d'évasion : 60 min Local : salle d'évasion commerciale Scénario : non clinique Nombre d'énigmes : 10-12 Indices donnés en cours de jeu : oui (3) Coût : SM Débriefing : oui	Taux de réussite au jeu d'évasion : 100 % Temps moyen de sortie du jeu d'évasion : 46 min Taux de réponses à l'enquête : 100 % Résultats du questionnaire : • similitude entre le service des urgences et le jeu d'évasion : 100 % • similitude des interactions sociales et interprofessionnelles : 90 % • bonne appréciation du débriefing : 100 % • souhait d'un débriefing plus structuré avec une rétroaction formative : 50 %	Participation volontaire (sollicitation par courriel) Temps de conception : NA Nombres de concepteurs du jeu : 5 Connaissances particulières nécessaires pour ce jeu : non Approbation du projet : par le comité d'administration de l'hôpital Consentement des participants : SM

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Tableau 1 (partie 10 de 11). Profil des résumés et des articles décrivant les modalités entourant la conception et la réalisation de jeux d'évasion dans le domaine de la santé

Profil*	Objectifs	Méthode†	Réalisation du jeu‡	Résultats§	Commentaires**
Adams et al.[26] *Journal for Nurses in Professionnal Development* 2018 États-Unis Article	Intégrer la pensée critique, le travail d'équipe et la communication dans une stratégie d'apprentissage pour adultes Évaluer la capacité de rétention des infirmières lors des cours	Enquête post. au jeu Questionnaire constitué de 6 questions Référentiel utilisé pour réaliser les énigmes : programme de résidence des infirmières	Participants : résidents en sciences infirmières et infirmiers expérimentés Joueurs : 213 répartis en groupes de 6-14 personnes Superviseur : responsable du développement professionnel du personnel infirmier Durée du jeu : 60 min Local : chambre de patient Scénario : clinique Nombre d'énigmes : SM Indices donnés en cours de jeu : oui Coût : 200 USD Débriefing : oui	Taux de réussite au jeu d'évasion : 100 % Temps moyen de sortie du jeu d'évasion : 35 min Taux de réponses à l'enquête : 100 % Résultats du questionnaire : • participation à un jeu d'évasion avant le jeu : 44 % (infirmières expérimentées) / 20 % (résidents en science infirmières) • satisfaction vis-à-vis du jeu : 100 % / 97 % • le jeu permet d'améliorer la pratique : 94 % / 80 % • le jeu permet de montrer ses connaissances : 100 % / 91 % • le jeu m'a donné confiance pour effectuer les tâches qui étaient proposées : 100 % / 95 % • la sortie du jeu s'est faite en utilisant mes connaissances : 100 % / 92 %	Type de participation : SM Temps de conception : SM Nombres de concepteurs du jeu : SM Connaissances particulières nécessaires pour le jeu : oui Approbation du projet : le comité d'examen institutionnel de l'hôpital Consentement des participants : SM Jeu réalisé pour aborder 10 objectifs d'apprentissage Variation de la taille des groupes Différentes chambres de patients utilisées ont nécessité des adaptations du jeu Transmissions des énigmes entre les différentes équipes

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Tableau 1 (partie 11 de 11). Profil des résumés et des articles décrivant les modalités entourant la conception et la réalisation de jeux d'évasion dans le domaine de la santé

Profil*	Objectifs	Méthode†	Réalisation du jeu‡	Résultats§	Commentaires**
Connelly et al.[27] *Journal of Nursing Education* 2018 États-Unis	Développer une technique de recrutement du personnel infirmier dans un milieu rural à l'aide d'un jeu d'évasion	Enquête post. au jeu Questionnaire constitué de 2 questions Référentiel utilisé pour réaliser les énigmes : SM	Participants : Étudiants qui ne sont pas en sciences infirmières Joueurs : 7 répartis en groupes de 2-4 personnes Superviseur : professeur Durée du jeu : 15 min par salle, 4 salles Local : divers Scénario : clinique, linéaire (3), multiple (1) Nombre d'énigmes : SM Indices donnés en cours de jeu : oui (utilisation d'un avertisseur sonore) Coût : SM Débriefing : oui (méthode plus-delta)	Taux de réussite au jeu d'évasion : SM Temps moyen de sortie du jeu d'évasion : SM Taux de réponses à l'enquête : SM Résultats du questionnaire : • le jeu est une expérience appréciée • le jeu a eu un impact positif sur la prise en considération d'une carrière en soins infirmiers	Type de participation : SM Temps de conception : 6 h Nombres de concepteurs du jeu : SM Connaissances particulières nécessaires pour ce jeu : non Approbation du projet : SM Consentement des participants : SM
Styling et al.[28] *Canadian Journal of Respiratory Therapy* 2018 Canada Résumé	SM	Enquête ant. et post. au jeu (1 mois) Référentiel utilisé pour réaliser les énigmes : Pratiques organisationnelles requises (Agrément Canada)	Participants : Équipe interprofessionnelle Joueurs : 134 Superviseur : SM Durée du jeu : SM Local : simulation de chambre de patient Scénario : clinique Nombre d'énigmes : SM Indices donnés en cours de jeu : SM Coût : SM Débriefing : SM	Taux de réussite au jeu d'évasion : SM Temps moyen de sortie du jeu d'évasion : SM Taux de réponses à l'enquête : SM Résultats du questionnaire : • augmentation de la notion de sécurité du patient : 89 % • le jeu est une excellente activité d'équipe : 100 % • souhait d'avoir d'autres jeux pour les nouvelles priorités d'apprentissage : 100 %	Type de participation : SM Temps de conception : SM Nombres de concepteurs du jeu : SM Connaissances particulières nécessaires pour ce jeu : oui Approbation du projet : SM Consentement des participants : SM

Ant. = antérieure, post. = postérieure, NA = non applicable, SM = sans mention.
*Auteur, revue, année de publication, pays, type d'étude.
†Type d'enquête, questionnaire, référentiel.
‡Participants, joueurs, superviseurs, durée, local, scénario, nombre d'énigmes, indices, coût, débriefing.
§Taux de réussite, temps moyen de sortie, taux de réponses, résultats du questionnaire.
**Type de participation, temps de conception, nombre de concepteurs, connaissances nécessaires, approbation du sujet, consentement des participants, autres.

CONCLUSION

Il existe peu de données entourant l'utilisation de jeux d'évasion en santé. Il est trop tôt en ce moment pour juger de l'efficacité de ce type d'approche. Toutefois, l'intérêt grandissant justifie qu'une veille documentaire soit instaurée et qu'une recension des écrits soit répétée pour en suivre l'évolution et mieux comprendre la place de ce type de stratégie dans l'apprentissage en santé.

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Discharge Medication Reconciliation for Patients Being Discharged to a First Nations Reserve*

Jaris Swidrovich

INTRODUCTION

The Canadian Patient Safety Institute defines medication reconciliation as "a formal process in which healthcare providers work together with patients, families, and care providers to ensure that accurate, comprehensive medication information is communicated consistently across transitions of care".[1] Following the medication reconciliation process is known to result in fewer adverse drug events and, therefore, positive health outcomes for patients.[1] In 2010, Accreditation Canada, a nonprofit organization dedicated to health care improvement, mandated Canadian hospitals to have an established medication reconciliation program in at least one clinical area in order to become accredited.[2] Certainly, Canadian hospitals face a number of challenges in meeting this accreditation standard, including the need for adequate staff and resource allocation. However, geographic, jurisdictional, and cultural differences contribute added complexity for patients coming from and being discharged to First Nations reserves, because registered First Nations persons and recognized Inuit are medically insured by the federal government, rather than by the provincial governments, which cover all nonregistered First Nations and non-Inuit persons.[3] Caught between the federal and provincial health systems and accessing care in both municipalities (under provincial jurisdiction) and reserves (under federal jurisdiction), First Nations and Inuit individuals are subject to drastic service and funding inequities, which have direct impacts on all of the social determinants of health and health care services.[4] The Calls to Action of the Truth and Reconciliation Commission of Canada stress the importance of closing the gaps in health outcomes between Indigenous (First Nations, Métis, and Inuit) and non-Indigenous people in Canada.[5] Pharmacists, the most accessible of health care professionals and often ranked as the most trusted, are uniquely and ideally situated in Canada's health care system to both respond to and proactively prevent inequities in the health outcomes experienced by Indigenous people in Canada.[6,7] In particular, discharge medication reconciliation performed by hospital pharmacists is likely to contribute to positive health outcomes for all hospitalized patients, including First Nations individuals being discharged to a reserve.[8]

About 50% of all First Nations people in Canada live on reserve.[9] Few pharmacies exist on reserves across Canada, leaving the people of most reserves with no option but to use the services of a pharmacy in a nearby city, town, or community. In addition, some reserves have contracts with particular pharmacies that will dispense and ship medications to the reserve at a certain frequency. As such, it is possible, and indeed common, for many First Nations people living on reserve to never interact with a pharmacist face-to-face. Despite the criticality of relationships in Indigenous communities and in health service delivery to First Nations people, it may be difficult for pharmacies and pharmacists to provide relationship-based care to First Nations individuals living on reserves without a pharmacy, especially in circumstances where the First Nations patient and the pharmacist have limited interactions. Conversely, in an acute care environment, there is significant opportunity to ensure that First Nations individuals coming from and/or being discharged to a reserve receive care from a pharmacist.

The objective of this article is to bridge a gap in the literature by highlighting unique challenges experienced when providing medication reconciliation services for patients coming from and/or being discharged to a First Nations reserve and to offer practical suggestions for hospital pharmacists to use in their care of such individuals (summarized in the form of a checklist in Box 1).

*This article intentionally uses gender-inclusive language (e.g., "themselves" instead of "him/herself") to be inclusive of non-binary and Two Spirit individuals.

Box 1. Discharge Medication Reconciliation Checklist for Patients Being Discharged to a Reserve

Complete medication assessment

Have *all* medications and medicines been *assessed*?

Patient may not be eligible for or may not have access to provincial comprehensive medication assessment program by community pharmacist.

Is or will the patient be taking any *traditional First Nations medicines*?

Is there any published information about the traditional medicine(s)?

Are any precautions required with co-administration of traditional medicines and the patient's other medications?

Has *enough supply* been prescribed to ensure no gaps in therapy?

Have the patient's *family* and/or friends been included in the assessment and education (with the patient's permission)?

Community pharmacy

Does the reserve have a *contract* with a particular community pharmacy?

What is the *delivery schedule* of the pharmacy that services the reserve?

Can/should the hospital send an interim supply of medications home with the patient?

Does the pharmacy have the required *stock* to send an interim supply for the patient?

Medication insurance coverage

Does the patient have a First Nations *status card* (and therefore an NIHB billing number)?

Does the patient have *other medication coverage* (e.g., work insurance plan, through spouse or parent, social assistance)?

Will any medication(s) require *prior approval* through NIHB? If yes, check NIHB formulary to ensure the medication(s) are listed.

Provision of physician services on the reserve

What is the *schedule* for physician services to the reserve?

Does the discharge medication quantity and/or number of refills need to be increased?

Language services

Are language services required to ensure that the patient understands the discharge medication plan?

Are there any written materials about the medications and/or disease state available in the patient's primary language?

Interprofessional and community collaboration

Do any other professionals or community members need to be consulted to ensure seamless care?

NIHB = Non-Insured Health Benefits.

PRACTICE DESCRIPTION AND IMPLICATIONS

Complete Medication Assessment

Hospital pharmacists not only have the opportunity and ability to establish a relationship with First Nations patients coming from and/or being discharged to a reserve but can also provide such patients with comprehensive and quality care. Instead of the typical concentrated focus on medications that have been newly started, stopped, and/or adjusted during the hospitalization, medication reconciliation for a First Nations person coming from and/or being discharged to a reserve should involve critical attention to all medications that the person is taking. Often, status First Nations individuals are ineligible for provincially funded medication review programs (e.g., Saskatchewan Medication Assessment Program) because health care for First Nations people with a status card (and for "recognized Inuit") is federally funded. As such, it is unrealistic to expect that a status First Nations person will receive a complete and comprehensive medication assessment from a community pharmacist in the absence of a federal reimbursement structure through the Non-Insured Health Benefits (NIHB) program.

When participating in the best possible discharge medication reconciliation process for a First Nations individual being discharged to a reserve, pharmacists should first check whether a best possible medication history (BPMH) was completed on admission to hospital. The BPMH is a systematic process of interviewing the patient/family and reviewing at least one other reliable source of information to obtain and verify information about all medications (prescribed and nonprescribed) that a patient is using.[1] Completion of a BPMH is critical, as the information obtained may differ from what appears in the patient's records.[1] It is important to note that prescriptions filled by a First Nations person that were billed to the federal NIHB program may not appear on provincial medication record databases if the individual did not also, at the time of dispensing, present a provincial health card along with their prescription and status card. As such, due diligence must be exercised when conducting a BPMH for First Nations patients, particularly as it relates to prescription medications that may not appear in provincial databases.

Although it is not unusual for family members, friends, and/or other visitors to be included in a hospital pharmacist's interactions with any hospitalized patient, the intentional inclusion of such individuals in interactions with First Nations patients coming from and/or being discharged to a reserve is encouraged—with the patient's permission, of course. *Wahkotowin* (the Cree word for "kinship") is a common

characteristic of First Nations' world view and family life. Additionally, the concept of health and wellness is not limited to the individual alone but also includes others who are close to the individual. In the setting of medication reconciliation processes, more complete medication and health information is likely to be obtained with the inclusion of individuals who are close to the First Nations patient in terms of relationships and connectedness. As such, engagement with the people, family, and community around and close to a First Nations patient is considered as important in the discharge medication reconciliation process as engagement with the patient themself.

Although population-wide generalizations cannot be made, there is often a greater likelihood that on-reserve First Nations individuals (relative to First Nations persons growing up and/or living off-reserve) will use, or at least have a strong appreciation for, traditional medicines and traditional approaches to health and wellness. Therefore, the use of traditional medicines and/or practices should be considered in the discharge medication reconciliation processes for an individual being discharged to a reserve. Traditional First Nations medicines and the practices related to understanding and disseminating knowledge about their use are not often (if ever) indexed and recorded in the ways that Western medications and practices are documented. As such, trying to retrieve information about traditional First Nations medicines and practices from the common and typical sources familiar to pharmacists may yield minimal or no results. Furthermore, few traditional First Nations medicines are indexed in alternative resources, such as the Natural Medicines Comprehensive Database (https://naturalmedicines.therapeuticresearch.com/), so pharmacists should be prepared to conduct discharge medication reconciliation without the information and literature about such medicines that would typically be available for mainstream prescription and nonprescription medications.[10]

Community Pharmacy

If the patient does not already have a regular pharmacy (either one where they can pick up their own medications or one that will deliver medications to the reserve), the hospital pharmacist is encouraged to determine whether the reserve to which the patient is being discharged has a contract with a particular community pharmacy. If, after conversation with the patient, the pharmacist has been unable to determine the contract status of the patient's reserve, it may be necessary to make a phone call to either the reserve's health centre or Band Office, the most appropriate contacts for all reserves. Upon determining which pharmacy will dispense the patient's medications, the hospital pharmacist should contact that pharmacy for the fax number to which discharge medication reconciliation information and the prescription(s) may be sent. Additionally, it is suggested that the hospital pharmacist inquire whether the pharmacy has the necessary stock for the patient's prescriptions and confirm the dates and times when the pharmacy makes deliveries to the reserve, to ensure that the patient will receive all needed medications on time, without any gaps in therapy. Occasionally, it may be most convenient and economical to send the patient home to their reserve with some of the hospital's stock of medication, rather than keeping the patient in hospital while their contracted community pharmacy acquires, dispenses, and delivers the medications.

Medication Insurance Coverage

When confirming insurance coverage for medications, the contracted pharmacy will, of course, need the patient's NIHB number and information regarding any other medication coverage (e.g., through work, parent, or spouse). If the NIHB program will be the payer, or partial payer, of the person's prescriptions, the hospital pharmacist should first review the NIHB formulary online, because this formulary is not always consistent with a particular province's formulary. Furthermore, "limited use" medications on the NIHB formulary may not be consistent with provincial practices regarding which medications require special/prior approval. An NIHB requirement for prior approval for any of the patient's medications may cause a significant delay in either the discharge date for the patient or the date when the medications are dispensed to the patient at no cost. Once again, it may be most convenient and economical, for both the patient and the hospital, to discharge the patient home to reserve with enough supply from the hospital's stock to ensure there are no gaps in medication therapy while the prior approval process is adjudicated, which may take a few days.

Provision of Physician Services to the Reserve

The timing and frequency of physician services to reserve communities must also be considered during the discharge process. Physician services are rarely offered 7 days a week, and in many cases occur as infrequently as 1 day or 1 half-day every 1 to 2 weeks. For patients whose future care will require a physician's monitoring and/or intervention, the hospital pharmacist should collaborate with hospital and/or community prescribers to ensure the patient is discharged with a sufficient quantity of medication and any necessary refills to avoid potential gaps in pharmacotherapy that could arise because of infrequent provision of physician services to the reserve community. If the patient does not know the frequency of physician services to the community, a phone call to the reserve's health centre or Band Office may be warranted.

Language Services

Beyond both the expected and less familiar logistical tasks to consider for First Nations individuals being discharged from hospital to a reserve, ethnocultural differences should also be considered. Pharmacists should seek or be aware of ethnoculturally appropriate services, information, and supports that may be of benefit for First Nations patients. For example, it may be necessary

to arrange language services for the patient and/or family, not only during the hospital stay but also for all discharge processes and discharge teaching. Given that many First Nations individuals living on reserve may have minimal to no access to a pharmacist, and given that access to a pharmacist who speaks the individual's First Nations language may be even more limited, discharge medication reconciliation and medication teaching activities should include interpretation services as needed. Collaboration with speakers of the First Nations languages commonly spoken by the patients and communities often seen within a particular hospital is also encouraged, to help in the development of written and/or verbal medication information in the particular languages, especially for high-risk medications (e.g., warfarin).

Interprofessional and Community Collaboration

In the spirit of interdisciplinarity, pharmacists may collaborate with other health professionals when performing discharge medication reconciliation processes for individuals being discharged to a reserve. If the hospital has its own First Nations health service, the pharmacist is encouraged to request the service to participate in the admission and discharge of all First Nations individuals. Such specialized health services often have Elders on staff, as well as health navigators, language keepers, social workers, and others with particular expertise. For hospitals with no such service, the pharmacist and other members of the health care team are encouraged to consider which culturally relevant services might be available for the patient after discharge to the reserve, if the patient so desires.

If the discharged patient will need daily transportation to and from a community pharmacy (e.g., for daily witnessed dosing of methadone), consultation with a health navigator or social worker may be required to make the necessary arrangements. Notably, pharmacists should be aware of the stigma associated with the term "social worker" in some (though not all) First Nations communities. More specifically, for some First Nations people and communities, the term "social worker" is associated with traumatic situations and events, such as the residential school system and the Sixties Scoop, when social workers apprehended children, often without the permission of the family or First Nations authorities. Only through engagement with the patient, family, community, health care team, and local social workers themselves will pharmacists be able to ascertain whether there is any concern with using this term.

CONCLUSION

Despite being experts in medication reconciliation on admission to, transfer between, and discharge from hospitals, pharmacists should be cognizant of the unique experiences of First Nations patients coming from and/or being discharged to a reserve. Positive interactions with health care providers such as pharmacists and a better understanding of their role in improving patient outcomes can encourage First Nations individuals to consider becoming health care providers themselves. First Nations patients will continue to be admitted from and discharged to reserves, so a focus on the unique features described in this article is likely to improve the patient outcomes of and reduce disparities for First Nations patients.

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Should Medical Devices Be Regulated as Rigorously as Drugs?

THE "PRO" SIDE

The term "medical device" applies to a broad set of product categories, ranging from simple, low-risk devices, such as tongue depressors, to complex, high-risk devices that are implanted or sustain life, such as drug-eluting cardiac stents, implantable pacemakers, and deep-brain stimulators. Such devices are intended to be used for diagnosis, prevention, monitoring, treatment, or alleviation of disease and do not achieve their primary intended action by pharmacological, immunological, or metabolic means.[1] At present, medical devices are increasingly integrated into pharmacy practice. For instance, with the availability of medication delivery systems (e.g., insulin pumps) and combination products (e.g., drug-eluting stents), pharmacists are in a position to provide education, to assist in implementing appropriate adjunctive pharmacotherapy when needed, and to support decision-making about where and when to use the devices.[2] Moreover, pharmacists may also be involved in choosing medical devices during the procurement process, monitoring the efficacy of medical devices once they are in use, and managing and reporting adverse events associated with these products.[3] Therefore, it is important for pharmacists to have a good understanding of the regulation of medical devices.

The regulation of medical devices varies greatly around the world. Some countries, such as the United States, countries within the European Union, Japan, and China, have adopted a tiered, risk-based approach. In these countries, regulatory departments prioritize the limited resources available, focusing regulatory measures on high-risk products. As such, various products are subject to different standards and enforcement activities, depending on the level of risks, as determined by the regulatory authority. In other areas of the world, regulatory requirements for premarketing assessment of medical devices are minimal or low. Moreover, regulatory systems may also differ vastly in terms of their classification of medical devices, risk-based regulation, and premarket evaluation, which results in different levels of assurance concerning safety and effectiveness.[4] For example, one study showed that medical devices approved first in the European Union, which was known to have a less stringent regulatory system for these products, were associated with a greater risk of postmarketing safety alerts and recalls than products approved first in the United States.[5]

Many clinicians and patients believe that current methods of regulation and enforcement within and across countries are not fit for the purpose of safety assurance.[6,7] The medical device market has become globalized, and the number of reports about adverse events associated with medical devices leading to serious complications or even death is on the rise. There have been reports of medical devices being brought to market without sufficient independent assessment of safety and efficacy to safeguard patients.[8,9] Even in the United States, with its relatively strict regulatory environment, more than 80 000 deaths and 1.7 million injuries have been potentially linked to medical devices during the past decade.[10] In April 2019, the US Food and Drug Administration finally stopped the sale of vaginal mesh (which had been approved in 2002 as a class II "moderate risk" medical device) after tens of thousands of patients reported serious complications, including intense pain and bleeding, after implantation.[11] The stringency of the approval process for higher-risk products, which may require only bench-testing data and perhaps some clinical study, and the delay in responding to new findings about adverse events have been repeatedly questioned.[12]

There have been calls for more robust regulatory measures for medical devices, but objections to tougher oversight have been intense. Some manufacturers argued that more rigorous regulations will increase the costs of development, manufacturing, and service for the industry and ultimately for health care providers and patients, limiting access to the devices themselves and to innovative development.[13,14] This debate continued, without any major impact on the regulatory systems, until recently, when the results of a global investigation into medical device misadventures revealed numerous cases of malfunction, injury, or even death associated with devices that had been approved for sale by regulatory authorities.[15] It was then concluded and recognized that health authorities around the world had failed to protect patients from poorly assessed medical devices. In light of increased public attention and concerns, some countries have finally stepped up their regulation of medical devices. In Australia, the Therapeutic Goods Administration has announced an action plan that strategically aims to improve how new devices get to market, to strengthen the postmarket monitoring of devices, and to provide more information to patients about the devices they use.[16] Other countries, such as the United States, France, Canada, Italy, Germany, the United Kingdom, the Netherlands, and India, have also announced new actions and measures in attempts to close the gaps in the risk management of medical devices.[17]

Pharmacists have come to appreciate the importance to our patients of stringent regulation through lessons learned from the history of pharmaceutical regulation. Sadly, this history reminds us that laws and regulations protecting public health are rarely proactive, but instead are usually enacted following public health disasters. The sulfanilamide tragedy of the 1930s was the trigger for enactment, in 1938, of the US *Food, Drug and Cosmetic Act*.[18] The thalidomide disaster of the 1960s prompted governments around the world to raise the safety standards for pharmaceuticals.[18] The rofecoxib incident of the early 2000s led to calls for the reinforcement of pharmacovigilance to identify rare and severe adverse events as early as possible.[19] Given what is known about how previous health disasters have shaped the current regulatory landscape for pharmaceutical products, the need for a system of independent assessment of medical devices by regulatory agencies, one that continues to evolve and develop according to technological advancements and patients' needs, is indisputable.

What is worthy of further discussion is the repositioning of regulatory systems for medical devices and how to achieve the goals of protecting and promoting public health and optimizing clinical outcomes for individual patients.[20] Historically, the fundamental job of regulatory agencies was to protect the general public from the "harm" of medical devices by keeping substandard and/or unsafe products off the market. However, the vast and rapid development of medical devices and the increasing needs of patients have shifted the paradigm toward a more proactive role for regulators. These agencies are now expected to promote public health by also facilitating innovations so that safer, more effective, and more economical medical devices can become accessible as quickly as possible. These goals are challenging, given the advancement of new technologies and the increasing complexity of product design. To address the challenges, the discipline of regulatory science should be better applied to support scientific regulation of these products.[21] Apart from developing new tools, methodologies, standards, models, and approaches to assessing the efficacy, safety, quality, and patient benefits of medical devices, there should also be a focus on alignment among industry, research institutes, payers, consumer advocacy groups, and other stakeholders, so that capacity can be built across different sectors for the development, implementation, and effective execution of guidelines and care pathways. Regulatory science also emphasizes the collection and leveraging of real-world data for regulatory decision-making, especially for high-risk medical devices. For this, pharmacists, as part of the multidisciplinary team supporting better regulation of medical devices, should have an increasing role to play in clinical vigilance, through monitoring medical device efficiency and managing and reporting any adverse events associated with such devices.

In summary, a reliable regulatory system and greater regulatory transparency about medical devices are important to protecting public health and the health of individual patients. Pharmacists have a growing role to play in supporting the scientific regulation of medical devices.

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THE "CON" SIDE

Perfection is achieved, not when there is nothing more to add, but when there is nothing left to take away
—Antoine de Saint-Exupery, Airman's Odyssey

Around the world, the regulation of drugs is currently more rigorous than the regulation of medical devices, and at the jurisdictional level, the United States (US) has more stringent regulation of medical devices than the European Union (EU). However, this situation is about to change. In 2020, in response to the outcry about the notorious PIP breast implant scandal that occurred in France in 2010, the EU will be implementing a new medical device regulation, which will require more extensive clinical evidence than is now the case.[1] The company implicated in the scandal produced about 2 million sets of silicone breast implants over a period of 20 years using unapproved materials; these implants had abnormally high rates of rupture, and 30 000 French women were advised to have their implants removed.[2] Clearly, more safety assessments are needed, but medical device regulation will need a unique approach, different from that applied to drug regulation.

In the context of regulation, there are distinct differences between drugs and medical devices. The history of drug and medical device regulation in the US is a good example to elucidate these differences. In that country, the Food and Drug Administration (FDA) is the federal regulatory agency for both drugs and medical devices. The present drug regulatory system began in 1938 in response to the notorious Elixir sulfanilamide tragedy of 1937, which caused mass poisoning and more than 100 deaths.[3,4] Before 1938, animal testing and premarketing clinical studies were not required by law, and the company responsible for this tragedy performed none.[4] The *Food, Drug and Cosmetic Act*, enacted in 1938, was the first step in making animal safety tests compulsory; with significant amendments enacted later, extensive clinical data evaluations to demonstrate the safety and efficacy of new drugs became a requirement for FDA approval.[3,4] In contrast to this 8-decade history of drug regulation, the first clear regulation of medical devices in the US occurred in 1976, driven by rapid innovations in medical technology that convinced FDA officers to review certain new devices for premarketing safety and efficacy.[3] In the 1960s, the argument was made that several medical devices, such as contact lenses and copper-7 intrauterine devices for contraception, should be regulated as "new drugs", and FDA officers soon recognized that a clearer definition and a distinct regulatory system were required for medical devices, to avoid the unnecessary costs of regulation for medical devices with no obvious adverse effects.[3] The central principle behind the 1976 amendments for medical devices was that "No single form of regulation, such as drug-like premarket approval, would fit all medical devices."[3] Therefore, medical devices were to be regulated differently.

Unlike the situation for drug regulation, which requires that rigorous clinical trials be applied to virtually all new drugs (except drugs for emergency use and orphan drugs used by small numbers of patients),[5-7] not all new medical devices require clinical data. New devices are first classified according to their level of risk. In the US and the EU, 3 classes are used, with class I having low risk (e.g., dressings and gauges) and class III having high risk (e.g., heart valves and cardiac pacemakers). The Australian regulatory authority, the Therapeutic Goods Administration (TGA), has specified an additional class for active implantable medical devices (AIMDs), which also carry high risk; examples include implantable defibrillators and cardiac pacemakers.[8] No clinical data are required for class I devices, whereas all class III and AIMD devices require clinical trials.[7,8] Within class II, clinical evidence is required only for those devices having medium risk.[7,8] To apply the same standard of regulation to all medical devices as is currently applied to drugs would be to suggest that devices such as dressings and gauges require clinical trial evidence similar to that required for a new class of medicines. Such regulation would involve unnecessary costs and inappropriate use of resources (on the part of manufacturers, regulators, and hospitals/patients). Instead of imposing additional clinical evidence requirements for low-risk devices, perhaps it would be better to invest effort in scientific evidence and expert review processes to ensure accurate identification of low-risk devices.

Before 2017, the clinical evidence requirements for class II devices differed between the US and the EU, with US regulation being more rigorous. About 75% of class II devices in the US required clinical evidence, whereas manufacturers in the EU were exempt from the requirement for clinical data if the devices had substantial similarity to previous "predicate" devices.[7] The strict US regulations prevented the outcry about PIP breast implants

that occurred in the EU from extending to the US. Medical devices introduced in the EU earlier than in the US have also shown higher risk of postmarketing safety issues.[9] However, the safety risks of medical devices are not necessarily directly associated with the safety and efficacy of the products themselves. One study compared the factors contributing to adverse events between medicines and non-AIMDs, and demonstrated distinct causes between these 2 types of adverse events.[10] User challenges, design problems, and lack of effective training were identified as 3 major causes of adverse events with medical devices, but all of these are difficult to evaluate in premarketing clinical trials.[10] Imposing new and more burdensome clinical trial requirements to evaluate the safety and efficacy of certain medical devices may not be as effective as implementing strategies such as increased user training and better customer service.[10,11] Rigorous evaluation of medical devices is needed to minimize the risk of harm to users; however, such evaluation should be conducted by experts who can distinguish data that are essential for safety and effectiveness evaluation from data that are "nice to have".[11] Furthermore, the advent of digital medical devices poses new and unique challenges to regulators, including cybersecurity risks.[12] These devices include stand-alone software, such as electronic health record systems, or software incorporated into various types of equipment, such as blood glucose monitors and computed tomography scanners, which can be vulnerable to cyberattacks leading to malfunction.[12] Assessment of cybersecurity risk cannot be evaluated by the FDA alone through traditional means of safety evaluation (e.g., clinical trials); rather, it requires transparent reporting of cybersecurity features and continual collaboration among regulators, manufacturers, health care providers, cybersecurity researchers, and government agencies.[12]

Excessive regulation could also pose more harm to the medical device industry through direct impacts on patients. It has already been predicted that the new EU medical device regulation will incur an additional 10%–15% in the cost of medical device development, which will be reflected in higher sale prices.[1] This regulation will also lead to higher financial risks for small and medium-sized companies, which constitute most of the medical device industry. For example, in Germany, 80% of medical device companies are small or medium-sized.[1] Increasing the approval burden will extend the product development cycle, cost, and approval time, making investments unattractive and possibly driving the industry to shift resources to improving existing products rather than generating truly innovative ideas.[11] FDA data have shown that applications for breakthrough approvals are low.[11]

The primary goal of regulating medical devices is to ensure their safety and efficacy, yet it is also important to encourage innovations to bring benefit to patients. Given the distinct differences between medical devices and drugs, regulatory authorities need to take a unique approach to the regulation of devices, one that focuses on balancing the evaluation of safety and efficacy with innovation, rather than adopting the models of rigorous assessment that are used for drugs. Studies investigating current medical device regulation have identified several key issues: lack of transparency in reporting the reasons for medical device safety alerts and recalls,[13] lack of regulation of user behaviour,[14] lack of high-quality postmarketing surveillance,[10] and lack of incorporation of real-world evidence into regulatory decision-making.[15] Improvements to medical device regulation are needed, but the simple approach of applying rigorous regulation, as is the case for drug regulation, will not be the solution.

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Documentation in the Patient's Medical Record by Clinical Pharmacists in a Canadian University Teaching Hospital: Correction

A recent article[1] in the *Canadian Journal of Hospital Pharmacy* concerned documentation by clinical pharmacists in patients' medical records. As a result of errors in processing the manuscript for publication, the definition for "minimal documentation" was worded incorrectly (with incorrect data being reported for this category of results), an incorrect version of Figure 1 was published, and some text was omitted from the paragraph describing strengths and limitations of the study. We sincerely apologize for any inconvenience caused by these errors.Corrections are provided here.

ABSTRACT—Results: The opening sentences of this paragraph should read as follows (correction indicated in bold):

> A total of 779 patient charts from 4 inpatient units were included in the analysis. Of these, **131 (16.8%)** were considered to have minimal documentation **(at least 1 suggestion or verbal order without a note in the progress section)**, 432 (55.5%) had sufficient documentation (at least 1 note written during the patient's hospitalization), and 81 (10.4%) had extensive documentation (appropriate number of notes in relation to duration of hospitalization).

METHODS—Outcomes (paragraph 2):

The definition of minimal documentation should read as follows, with omission of reference to a composite end point:

> "Minimal" documentation was defined as at least 1 suggestion or verbal order recorded in the prescription section of the patient's medical record, without any note in the progress section of the patient's medical record. ~~This composite end point was intended to represent any visible indication of the pharmacist's activity in the patient record.~~

RESULTS—paragraph 1:

The summary statement of results and updated table should read as follows (corrections indicated in bold):

> The numbers of patients' medical records with minimal, sufficient, and extensive documentation were **131 (16.8%)**, 432 (55.5%) and 81 (10.4%), respectively (Table 1).

Table 1. Level of Documentation and Interventions Included in Patients' Medical Records

Characteristic	No. (%) of Records* (*n* = 779)	
Level of documentation†		
Extensive	81	(10.4)
Sufficient	432	(55.5)
Minimal	**131**	**(16.8)**
Intervention documented in the prescription section		
Verbal orders		
Records with ≥ 1 verbal order	142	(18.2)
No. of verbal orders per record (median and IQR)	1	(1–2)
Suggestions		
Records with ≥ 1 suggestion	369	(47.4)
No. of suggestions per record (median and IQR)	1	(1–2)
Verbal orders and/or suggestions		
Records with ≥ 1 verbal order or suggestion (or both)	426	(54.7)

IQR = interquartile range.
*Except where indicated otherwise.
†Extensive documentation was defined as presence of ≥ 1 admission, follow-up, or discharge note for hospital stays ≤ 2 days; an admission note and a discharge note for hospital stays of 3–6 days; or an admission note, a follow-up note, and a discharge note for hospital stays ≥ 7 days. Sufficient documentation was defined as presence of ≥ 1 note in medical section of patient's medical record, regardless of the patient's length of stay in hospital. **Minimal documentation was defined as ≥ 1 suggestion or verbal order recorded in the prescription section of the patient's medical record, without any note in the progress section of the patient's medical record.**

A corresponding summary statement of results also appears in the first paragraph of the Discussion, where the same correction is required (i.e., number of records with minimal documentation was 131 [16.8%]).

The correct version of Figure 1 (next page) details the study results according to clinical unit of the hospital.

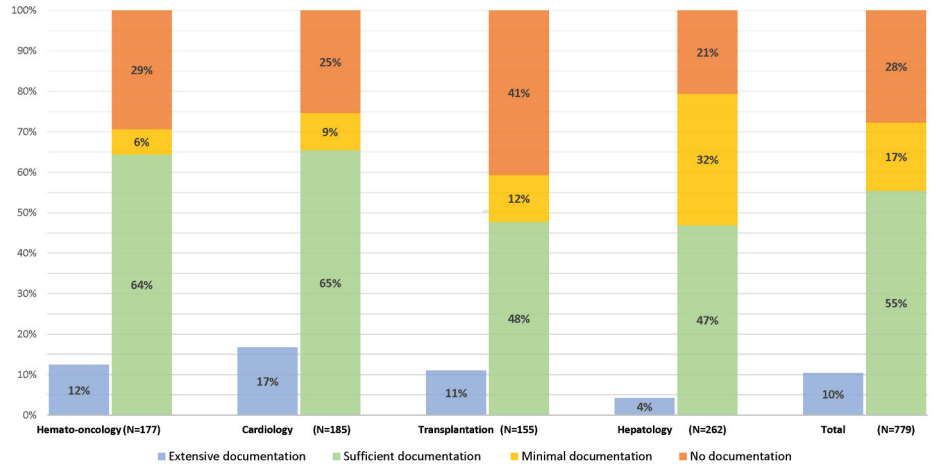

Figure 1. Level of documentation in patients' medical records, by clinical unit. **Charts categorized as having extensive documentation are included in the count of charts with sufficient documentation; the other categories are mutually exclusive.**

DISCUSSION—Strengths and Limitations

Some text was inadvertently omitted from the paragraph describing strengths and limitations of the study. The complete paragraph is presented here:

> This study had both strengths and limitations. The data in this study were obtained retrospectively and objectively thereby avoiding self-reported documentation like others studies.[2,3] Collection of the data by 2 pairs of students may have introduced observation bias. To limit such bias, 10% of all records were double-checked and corrected, if appropriate, by the other team of students. The patients' medical records were handwritten and although the observers were vigilant, some data may have been missed (e.g., if pharmacists did not identify themselves adequately in the record or if the quality of the handwriting was poor). However, the large number of records analyzed (with exclusion of only 1 record) may have compensated for these limitations. Another limitation was the absence of testing for interindividual variability between clinical pharmacists. However, the goal of the study was not to identify differences among pharmacists, but rather to determine tendencies and trends, in order to ameliorate the practice of a group of pharmacists. Only 4 types of specialized clinical units were included in the study, which might have affected the external validity in relation to less specialized clinical units (e.g., internal medicine, emergency and other nonteaching hospitals with fewer resources. These specialized clinical units were chosen for 3 reasons: ease of retracing patients followed by pharmacists, presence of students for 2 of every 4 months, and presence of the clinical pharmacist on the unit every weekday during the duration of the study. Because the objective of the study was to quantify pharmacists' documentation in patients' medical records, the impact of pharmacists' notes on patient care could not be evaluated. Although the acceptance rate was unknown, the clinical pharmacists were proactive in proposing drug changes either through verbal orders or suggestions in more than 50% of the records. Finally, the statistical analysis did not control for multiplicity.

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La coopération, la concurrence et les liens qui nous unissent

par Zack Dumont

On considère souvent la coopération et la concurrence comme étant en opposition. Le désir d'une personne de coopérer avec d'autres pourrait cacher son désir de concurrence et vice-versa. Il existe également des questions relatives au contexte et à l'échelle : lorsque les enjeux sont mineurs, la personne qui s'entend généralement bien avec les autres aura peut-être tendance à s'engager dans une concurrence amicale. Tant que les intentions sont bonnes, les deux approches sont méritoires. Somme toute, la concurrence est un important facteur d'innovation, et peut-être le plus important qui soit. Par contre, quand il s'agit d'accomplir de grandes choses, la coopération a permis à l'humanité de réaliser des exploits.

Au-delà des débats sur les thèmes du marché et de la justice sociale, je vous invite instamment à observer les proportions que prennent actuellement la concurrence et la coopération dans notre monde. À l'échelle globale, j'observe une concurrence acharnée qui règne autour de l'émotion, du temps, de l'argent, de l'énergie, des suffrages et bien plus encore. La coopération est rarement érigée en modèle et à peine encouragée. La concurrence effrénée est capable de semer la division. Alors je pose la question suivante : où est l'équilibre?

Je ne veux pas présenter une fausse dichotomie. Comme c'est souvent le cas, la réalité présente différentes nuances de gris, de pour et de contre, et l'approche est primordiale. Dans un éditorial figurant ailleurs dans ce numéro, Bresee aborde l'interprétation des valeurs de *p* dans la recherche (*J. Can. Pharm. Hosp*. 2019; 72 [5] : 341-2). On nous rappelle que les valeurs de *p* continuent d'être utilisées pour créer des dichotomies dans l'esprit des lecteurs de littérature scientifique, autrement dit : « oui, une intervention est bénéfique » ou elle ne l'est pas. L'éditorial compare et met en contraste des philosophies opposées qui sont présentées dans deux publications récentes : la première souligne l'inefficacité et les dangers du seuil arbitraire de la valeur de *p*; l'autre s'appuie sur ce seuil comme mécanisme naturel à l'œuvre dans la prise de décision en matière de soins de santé. Les deux arguments sont convaincants. Plutôt que de prendre parti, Bresee trouve un terrain d'entente et fait émerger une position commune. La concurrence permet d'approfondir notre compréhension, et la coopération favorise de plus grandes découvertes. Dans les soins de santé, les opinions et les prises de position abondent. En remettant en question l'idée qu'elles sont en porte-à-faux et en trouvant un point de convergence grâce à une empathie mutuelle, nous dépassons les différences et ce sont les patients qui en profiteront. C'est une voie plus difficile, mais les patients le méritent.

Dans ce numéro, nous apprenons davantage sur la population des Premières Nations du Canada, pour qui la communauté des soins de santé indique un processus de bilan comparatif des médicaments dépareillé (*J. Can. Pharm. Hosp*. 2019; 72[5]: 403-6). Heureusement, l'auteur, Swidrovich, fait part de solutions pratiques pour faciliter les efforts de leadership des pharmaciens de première ligne. L'article me rappelle l'engagement pris par la Société canadienne des pharmaciens d'hôpitaux (SCPH) en octobre 2018, visant à répondre au rapport de la Commission de vérité et réconciliation. Dans les mois à venir, les membres du personnel et les bénévoles de la SCPH mettront de côté la concurrence et coopéreront avec d'autres organismes pour créer quelque chose plus grand que n'importe quel plan stratégique, tableau de bord équilibré ou résultat financier.

Je vois ces efforts comme des signes que les prestataires de soins de santé s'affranchiront des tendances mondiales, ils s'efforceront d'élargir les cercles de la coopération en taille et en nombre et de réduire les domaines dans lesquels persiste la concurrence nuisible et non productive. La SCPH est le forum qui nous permet de nous rassembler et aucun autre cercle ne peut mieux représenter vos intérêts professionnels spécifiques. Étant donné le déséquilibre actuel de la concurrence auquel j'ai fait allusion un peu plus tôt, choisissons ensemble la coopération. Et encourageons les autres à se joindre à nous.

Ensemble, nous coopérerons. Nous lutterons, non les uns contre les autres, mais contre la maladie et l'inégalité. Nous nous efforcerons de voir les choses en adoptant la perspective des autres. Nous découvrions des liens qui unissent.

[Traduction par l'éditeur]

Zack Dumont, B. S. P. , A, C. P. R., M. S. (Pharm.), est devenu président désigné et agent de liaison interne de la Société canadienne des pharmaciens d'hôpitaux lors de la réunion du conseil qui a suivi son élection à l'Assemblée générale annuelle d'octobre 2019.

Cooperation, Competition, and Ties That Bind

Zack Dumont

Cooperation and competition are often considered at odds with one another. A person's desire to cooperate with others may hinder the drive to compete, and vice versa. There are also matters of context and scale: perhaps when the stakes are low, a friendly competitive streak emerges in someone who would usually aim to get along with others. As long as intentions are true, both approaches have merit. After all, competition is considered an important—perhaps the most important—driver of innovation. Conversely, when it comes to getting big things accomplished, cooperation has afforded humanity great success.

Topical debates about markets and social justice aside, I urge you to consider current proportions of competition and cooperation in our world. On a global level, I see relentless competition for everyone's emotion, time, money, energy, votes, and more. Cooperation is rarely modelled, and hardly encouraged. Unbridled competition may be driving us apart. Where is the balance?

I do not mean to present a false dichotomy. As is often the case, in reality there are shades of grey, pros and cons, and perspective is paramount. In an editorial elsewhere in this issue, Bresee tackles the interpretation of *p* values in research (*Can J Hosp Pharm*. 2019;72[5]:339-40). We're reminded that *p* values continue to be used to create dichotomies for consumers of scientific literature—put simply, "yes, an intervention is beneficial", or not. The editorial compares and contrasts opposing philosophies presented in 2 recent publications: the first highlighting the ineffectiveness and dangers of the *p* value's arbitrary cutoff, the other leaning on this cutoff as a natural mechanism in health care decision-making. Both arguments are compelling. Rather than taking sides, Bresee finds common ground, and a unified position emerges. The competition drove our understanding deeper, and the cooperation found something greater. In health care, opinions and positions abound. When we challenge the notion that they are at odds with one another, using empathy to come together, we rise above the differences, and patients will stand to benefit. It's the more challenging road, but patients deserve it.

Also in this issue of the journal, we learn more about Canada's First Nations population, for whom the health care community has designed a mismatched medication reconciliation process (*Can J Hosp Pharm*. 2019;72[5]:403-6). Thankfully, the author, Swidrovich, shares practical solutions to facilitate leadership efforts by front-line pharmacists. The article reminds me of the commitment that the Canadian Society of Hospital Pharmacists (CSHP) made in October 2018, to address the Truth and Reconciliation Commission report. In the coming months, CSHP staff and volunteers will put aside competition and will cooperate with other organizations to produce something bigger than any strategic plan, balanced score card, or bottom line.

I see these efforts as signs that health care providers will shrug off global trends, strive to expand circles of cooperation (in both size and number), and shrink domains in which nonproductive, potentially harmful competition persists. CSHP is our forum for coming together, and there is no more fitting circle to represent your unique professional interests. Given the modern imbalance of competition to which I alluded earlier, let's go all-out in opting for cooperation. Encourage others to join us.

Together, we'll cooperate. We'll compete, not among ourselves, but with disease and inequality. We'll fight to see things from others' perspectives. We'll find the ties that bind.

Zack Dumont, BSP, ACPR, MS(Pharm), became President Elect and Internal Liaison for the Canadian Society of Hospital Pharmacists at the Board meeting following his election during the Annual General Meeting in October 2019.

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