

Ambulatory Heart Function and Transplant Patients' Perceptions of Drug–Drug Interactions: A Qualitative Study

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ABSTRACT

Background: Drug–drug interactions (DDIs) can cause adverse drug events, leading to hospitalizations and an increase in the risk of morbidity and mortality. Until now, patients' perceptions of DDIs have represented an understudied area of research.

Objectives: To explore patients' perceptions of DDIs and identify factors important to patients' understanding of their medications.

Methods: Participants were recruited from 2 ambulatory clinics (heart function and transplant) in Vancouver, British Columbia. Participants engaged in key informant interviews and were asked to provide their demographic information, rate their understanding of their own medications, and define a DDI. Afterward, participants were interviewed to gather their perceptions of DDIs and factors important to their understanding of their medications.

Results: A total of 7 patients were recruited. Participants struggled to define a DDI and were unsure if they had ever experienced a DDI. There was a reliance on health care professionals to help manage DDIs. Participants did not identify barriers preventing them from accessing medication information from health care professionals; however, they independently sought medication information found on the internet.

Conclusions: Patients in this study had an incomplete understanding of DDIs and had difficulties differentiating DDIs from side effects of medications. As a result of their limited understanding of DDIs, patients relied on health care professionals to inform and manage their DDIs. Although patients did not identify barriers to accessing medication information, their pervasive use of the internet suggests that there are unidentified barriers preventing patients from speaking directly to their health care professionals regarding their medication therapy.

Keywords: drug interactions, patient perceptions, health care professionals

RÉSUMÉ

Contexte : Les interactions médicamenteuses (IM) peuvent provoquer des événements indésirables, entraînant des hospitalisations et une augmentation du risque de morbidité et de mortalité. Jusqu'à présent, les perceptions des patients concernant les IM représentaient un domaine de recherche sous-étudié.

Objectifs : Explorer les perceptions des patients à l'égard des IM et recenser les facteurs importants pour qu'ils comprennent leurs médicaments.

Méthodes : Les participants ont été recrutés dans deux cliniques ambulatoires (de la fonction cardiaque et de transplantation) à Vancouver, en Colombie-Britannique. Ils ont participé à des entretiens à titre d'informateurs clés et ont été invités à fournir leurs informations démographiques, à évaluer leur niveau de compréhension de leurs médicaments et à définir ce qu'on entend par « IM ». Par la suite, les participants ont été interrogés pour savoir comment ils percevaient les IM et pour recenser des facteurs importants leur permettant de comprendre leurs médicaments.

Résultats : Au total, 7 patients ont été recrutés. Les patients avaient du mal à définir une IM et ne savaient pas s'ils avaient déjà vécu une IM. Ils comptaient ainsi sur les professionnels de la santé pour les aider à les gérer. Les patients n'ont identifié aucun obstacle les empêchant d'accéder aux informations sur les médicaments fournis par les professionnels de la santé; cependant, ils ont, de manière indépendante, cherché des informations sur les médicaments sur Internet.

Conclusions : Les patients de cette étude avaient une compréhension limitée des IM et avaient des difficultés à faire la différence entre les IM et les effets secondaires des médicaments. En raison de cette compréhension limitée, les patients comptaient sur les professionnels de la santé pour les informer et gérer leurs IM. Bien que les patients n'aient pas signalé d'obstacles les empêchant d'accéder aux informations sur les médicaments, leur utilisation systématique d'Internet suggère que des obstacles non identifiés les empêchaient de parler directement à leurs professionnels de la santé au sujet de leur traitement médicamenteux.

Mots-clés : interactions médicamenteuses, perceptions des patients, professionnels de la santé

INTRODUCTION

Drug–drug interactions (DDIs) can alter the efficacy of patients' medication therapy, leading to adverse events, which can cause patient harm. There are 2 categories of DDIs, related to pharmacodynamics and pharmacokinetics. The concept of pharmacodynamics refers to the effect that a drug may have on the body.¹ Pharmacodynamic DDIs can result from one drug antagonizing another drug, thereby reducing the therapeutic effect of one or both of the drugs.² Alternatively, the interacting drugs can have an additive therapeutic effect when combined. In contrast, the concept of pharmacokinetics refers to the effect that the body may have on a drug. Pharmacokinetic DDIs change the absorption, distribution, metabolism, and excretion of one or both of the interacting drugs. DDIs may increase the severity of adverse events or increase the chance of treatment failure.³ In certain applications, prescribers may take advantage of known DDIs by deliberately administering an interacting drug to increase the effects of another drug; for example, cobicistat may be used to boost the effect of protease and integrase inhibitors for the treatment of HIV.⁴

The overall prevalence of DDIs varies from study to study. In one review article, the authors found that the prevalence of DDIs in hospitals ranged between 15% and 45%.⁵ Another study examining the prevalence of DDIs among hospitalized geriatric patients suggested that DDIs were responsible for 2% to 3% of hospital admissions, and up to 11% of patients were experiencing adverse drug effects that stemmed from DDIs.⁶ The consequences of DDIs put patients at increased risk of hospitalization, morbidity, and mortality, in addition to increasing the costs of health care. For instance, the concurrent use of allopurinol and azathioprine may cause bone marrow suppression, thereby increasing a patient's susceptibility to infection. Another example could be the concurrent use of citalopram and sotalol, which may cause QTc prolongation and increase the risk of a fatal ventricular arrhythmia.⁷

The risk of DDIs increases with the number of medications that a patient is taking. Patients have access to numerous different prescription and nonprescription medications. Polypharmacy, the concurrent use of 5 or more different medications, was found to be common in the elderly population.⁸ The number of drug classes involved in cases of polypharmacy can also be important in relation to DDIs. A drug class is a group of similar medications used to treat a particular medical condition. In 2016, 65.7% of Canadian seniors had medications prescribed from 5 or more different drug classes, 26.5% had medications prescribed from 10 or more drug classes, and 8.4% had medications prescribed from 15 or more drug classes.⁹ The probability of DDIs increases with other risk factors, such as advanced age, comorbidities, narrow therapeutic range of drugs, drug dosage, multiple prescribers, and self-prescribing of medications.¹⁰

Previous research has focused on pharmacists' perceptions of DDIs and the thought processes they apply when assessing DDIs. It has been shown that flagging of DDIs by clinical decision software systems can be excessive and can lead to alert fatigue, which increases the risk of pharmacists missing an important DDI alert.¹¹ In addition, there were discrepancies between the severity ranking of DDIs in a decision software system and actions taken by pharmacists to manage DDIs based on their clinical judgment.¹² Despite the intention of using clinical decision software systems to prevent DDIs, the onus is on the clinician to determine an appropriate course of action.

Patients' perceptions of DDIs have represented an understudied area of research. Evaluating patients' attitudes, beliefs, and interpretations of DDIs can be used to identify possible knowledge gaps and determine ways to improve their understanding of DDIs. There is limited literature examining patients' knowledge of DDIs and their opinions of how health care professionals should help manage their DDIs, what important medication information they seek, and how medication information can be best communicated to them. The objectives of this study were to explore patients' perceptions of DDIs and to identify factors important to patients' understanding of medications.

METHODS

The consolidated criteria for reporting qualitative research (COREQ) were reviewed for transparent data reporting.¹³ We utilized the COREQ checklist to ensure proper reporting of the data and have included detailed answers to each of the checklist items in Appendix 1 (available at <https://www.cjhp-online.ca/index.php/cjhp/issue/view/208>).

Study Population and Recruitment

This qualitative study involved key informant interviews. Convenience sampling was used to recruit English-speaking participants. Recruitment occurred from November 2019 to March 2020; however, further recruitment was stopped because of the COVID-19 pandemic. Participants were primarily recruited from 2 outpatient clinics: an ambulatory renal transplant clinic at St Paul's Hospital and a heart function clinic at Vancouver General Hospital. These clinics were selected because the patients they serve are often taking more medications than the general population, which puts them at higher risk of experiencing DDIs. Patients from other ambulatory clinics could also have been recruited by either clinic's pharmacist through professional interactions. As a result, participants in the study may have shared a unique perspective of DDIs, based on their past experiences, thoughts, and opinions in the context of complex medication regimens.

The role of the pharmacist within each clinic was to identify drug-related problems, provide medication

recommendations, counsel patients about new medications, and answer medication-related questions from health care professionals and patients. For each patient, the physician and the pharmacist were the 2 primary health care professionals responsible for identifying, resolving, and communicating DDI information. Recruitment posters were placed within each clinic. The pharmacist in the heart function clinic did not recruit any participants through professional interactions, but patients coming to this clinic saw the recruitment poster and asked the clinic pharmacist for more information. The pharmacist in the renal transplant clinic recruited stable renal transplant recipients who had undergone transplant within the previous 3 months. In addition, professional interactions involving the renal transplant pharmacist led to recruitment of 1 participant from the ambulatory lung transplant clinic. Potential participants received study information from the clinic pharmacists. Although these clinic pharmacists were responsible for recruitment, they had no role in data collection or analysis of study results.

Research ethics board approval to conduct the study was obtained from the University of British Columbia's Behavioural Research Ethics Board, and informed consent was provided by all participants before their interviews.

Interviews

A focus group was initially planned; however, because of the impending COVID-19 pandemic, it was decided to conduct interviews instead. Study participants were given the option of having the interview conducted either in person or over the telephone; ultimately, because of the COVID-19 pandemic, all interviews were done over the phone for safety reasons.

The interviews followed a semi-structured format, and all interviews were audio-recorded. Each interview consisted of 3 parts, and all interviews were conducted by the same investigator (D.P.) (Appendix 2; available at <https://www.cjhp-online.ca/index.php/cjhp/issue/view/208>). The first part of the interview consisted of gathering baseline demographic information. Participants were asked to provide their age, gender, education, number of medical conditions, and current number of medications. The second part of the interview consisted of assessing participants' understanding of their medications and DDIs. Participants were asked to rate their understanding of their medications using a Likert scale from 1 to 5, with 1 being a very poor understanding and 5 being a very good understanding. Participants were then asked to verbally define a DDI.

For the third part of the interview, participants were asked a series of open-ended questions. Because few similar studies are available in the literature, the questions for this part of the interview were developed by the study team based upon our research group's prior qualitative studies.^{11,12} The questions were also reviewed by the ambulatory

clinic pharmacists at St Paul's Hospital and Vancouver General Hospital. The questions first explored participants' perceptions of DDIs (Appendix 2). Next, participants were asked to describe the responsibilities of health care professionals in managing patients' DDIs. Participants were then asked to discuss factors important to the understanding of their own medications and barriers that prevented them from accessing medication information. Lastly, communication of medication information from health care professionals to patients was examined.

Analysis

Qualitative thematic analysis was used to develop major themes from the interviews. Our research philosophy follows an interpretivist approach.¹⁴ The recorded interviews were transcribed verbatim into Word software (Microsoft Corporation). Transcripts were input into NVivo 12 Pro, version 12.6.0.959 (QSR International), a software program used to help with data management. Reflexive journaling was done during the data analysis. Our qualitative approach was suited to uncovering patients' perceptions of DDIs by exploring their understanding of medications. One investigator (D.P.) coded the data. The codes were discussed by the research group to discern emergent patterns. Thematic analysis was done using an inductive approach. Codes and themes that were unclear were discussed by the authors until consensus was reached.

RESULTS

A total of 7 participants were included in the qualitative analysis, 5 men and 2 women. Most of the participants had received postsecondary education. Participants had an average of 3.1 medical conditions and were taking an average of 9.3 medications (Table 1).

Using a Likert scale from 1 to 5, participants rated their understanding of their own medications as good (average 4 out of 5, where 5 was defined as "very good") (Table 2). For purposes of determining participants' understanding of DDIs, the authors pre-established the definition of a DDI as the situation that occurs when one drug increases or decreases the therapeutic effect of another drug. The authors then interpreted each participant's response to determine if it was correct or incorrect, according to the pre-established definition. When asked to define a DDI in their own words, 2 of the 7 participants provided an accurate response:

Okay, so I would define a drug interaction as when the effects of one drug interferes with the effects of another drug. (Participant 3)

A drug interaction ... the effects of one medication might have on the other. Or the, how one medication might amplify the effects of another medication. (Participant 7)

TABLE 1. Characteristics of Study Participants

Interview No.	Clinic	Sex	Age (Years)	Education	No. of Medical Conditions ^a	No. of Medications ^b
1	Heart function	Male	72	Postsecondary	6	10
2	Renal transplant	Male	76	Apprenticeship	3	10
3	Heart function	Female	65	Postsecondary	1	8
4	Other ^c	Male	72	Postsecondary	2	9
5	Renal transplant	Male	66	Diploma	4	7
6	Renal transplant	Male	42	Postsecondary	3	12
7	Renal transplant	Female	49	Postsecondary	3	9

^aMedical conditions were self-reported. The mean number of medical conditions was 3.1 per patient.

^bIncludes prescription and nonprescription medications. The mean number of medications was 9.3 per patient.

^cPatient was recruited from an ambulatory lung transplant clinic.

TABLE 2. Patients' Self-Reported Understanding of Medications

Aspect of Knowledge	Result (n = 7)	
Understanding of medications ^a	Mean ± SD 4 ± 1	
Definition of a drug–drug interaction ^b	Correct 2	Incorrect 5

^aPatients were asked to self-report their understanding of their own medications using a Likert scale (1 = very low, 3 = average, 5 = very good).

^bPatients were asked to define a drug–drug interaction in their own words. The patient's definition was compared with the authors' predetermined definition and was designated as correct or incorrect.

In contrast, 5 of the 7 participants provided a vague definition, as in the following examples:

My understanding of it is that where drugs that have conflicting properties are prescribed or taken at the same time. So that, one ... the interaction between the two of them is detrimental to the patient. (Participant 5)

Drug interaction is, could possibly fatal or harmful to patients. (Participant 6)

No new emerging themes were identified following the last interviews, so it was concluded that data saturation had been achieved. Three themes were identified from the patient interviews: an incomplete understanding of DDIs, a strong reliance on health care professionals to identify and manage DDIs, and a lack of inquiry by patients about their DDIs.

In terms of the first theme, the interviews showed that participants had an incomplete understanding of DDIs and often equated them with side effects (Appendix 3, available at <https://www.cjhp-online.ca/index.php/cjhp/issue/view/208>). Participants were unsure whether adverse events in their past had been caused by a DDI, had been a side effect

from one or more medications, or had occurred because of their medical condition.

Well I don't know what interaction if any is causing [my symptoms] or if it's something totally separate. (Participant 1)

I think I had a drug ... I'm not positive if drug interaction, but I was taking allopurinol and candesartan when my kidney function was declining, and I had quite a bit of rash, and some changes in my blood work. (Participant 7)

When asked to provide examples of concerning outcomes of minor and moderate DDIs, participants conveyed that central nervous system side effects, such as headache, and gastrointestinal side effects, such as nausea, abdominal pain, and diarrhea, were most important to them.

... [a] minor [drug interaction] might be like an inconvenience where I don't know, like, that your quality of life reduced. Like it may, the drug may, the interaction of the drugs may affect some daily living activity, to a certain extent like maybe being more tired, little bit more dizzy or a little bit more abdominal cramping or something like that. (Participant 3)

[a] moderate [drug interaction] would be pain that doesn't seem to wanna go away. (Participant 5)

The second overarching theme was that patients relied heavily on health care professionals to identify and manage DDIs. Participants believed these professionals should inform patients of DDIs and provide an action plan to mitigate associated risks.

I would expect it be explained to me, what the interaction is ... telling me what happened, the reason it's happened, and what they plan [to do] about it ... (Participant 5)

... they should find an alternative to one or both of the medication ... contact me for sure and let me know if I should stop taking one or both of them. (Participant 7)

Both the pharmacist and the physician were thought to be integral to the management of DDIs, given their respective backgrounds.

I think the physician who's prescribing, as well as the pharmacy who fills my prescription. Assuming that you go to the same pharmacy and they have a record of what you're taking. (Participant 7)

Pharmacists were thought to have the pharmacological knowledge to detect DDIs.

But I still feel that the pharmacist would have more knowledge [than physicians] because [pharmacists are] more specialized in drugs... (Participant 1)

The doctors and the pharmacists ... They're the two professions that I recognize to be an expert in the field. As such they should be responsible. (Participant 2)

In comparison, physicians were thought to be responsible for the medications being prescribed to patients.

I would expect the prescribing physician would know what [the drug interactions] are ... (Participant 4)

The doctor should be aware of the, all the medication the patient has been taking. So he won't be able or she won't be able to mix and match the medication that interact each other. (Participant 6)

The third main theme was that patients did not specifically seek information related to DDIs. In terms of medication counselling, patients were most concerned about and wanted to have additional information with respect to the side effects of medications.

... potential or possible side effects that they should be letting the patient know that. (Participant 4)

... well, number one thing is probably understanding the side effects of the drugs that I'm taking. (Participant 6)

DDI information was considered to be an important counselling point for only 2 participants.

Just like for instance, as far as interactions. The likelihood, okay the likelihood of an interaction is like, you know 0.5% or 0.05% or common or you know. What's the prevalence of interactions with these medications, you know. (Participant 3)

Yeah and what I should be, what I should not be taking to interact with my current prescriptions.

Like for example with my anti-rejection, I should not be consuming any grapefruit at all or something like that. (Participant 6)

Overall, the participants did not believe there were any barriers preventing them from accessing medication information.

I don't know if there any barriers to access the information. (Participant 2)

I have no barriers when I go looking for information. (Participant 4)

In addition, they expressed that they could readily find medication information online.

You know, in today's world of technology, as long as you're going to the right places on the internet, there's all kind of information out there ... (Participant 4)

There's, there's information readily available as long as you know where to look on the internet. (Participant 5)

DISCUSSION

The results of this study indicate that patients may have a limited understanding of DDIs and the impact that DDIs could have on their health. Although study participants perceived a greater-than-average understanding of their own medications (where "average" was defined as 3 on a 5-point Likert scale), testing of their knowledge of DDIs indicated only limited understanding. For example, participants associated DDIs with gastrointestinal and central nervous system side effects. In fact, participants were more aware of medication side effects than of DDIs. Their inability to distinguish a DDI from a medication side effect suggested that they do not understand the ramifications of DDIs. During the interviews, participants were uncertain whether they had experienced a DDI in the past because they did not know what to expect as an outcome of a DDI. Given participants' limited understanding of DDIs, they were therefore reliant on health care professionals to help manage their DDIs.

Health care professionals such as physicians and pharmacists have medication knowledge that can be used in managing a patient's DDIs. In complex cases involving patients with multiple comorbidities who are taking numerous medications, it becomes difficult, even for experienced clinicians, to ascertain if a patient's symptoms are due to deterioration of their medical condition, medication side effects, or DDIs. It would be unrealistic and potentially dangerous to expect patients to self-manage their DDIs, as many do not have a background in pharmacotherapeutics. However, similar to counselling patients to recognize key side effects of their medications, it may be important for

patients to be made aware of and told how to recognize key DDIs that could pose a risk to their health. When selecting an over-the-counter product, a patient who is cognizant of the risk of DDIs might check with their pharmacist to determine if the product can be safely taken with their current medications. For example, patients who are taking warfarin should be aware that their risk of bleeding will increase if they take nonsteroidal anti-inflammatory drugs. Pharmacists have been identified as having a major role in detecting and preventing adverse drug events, including DDIs.¹⁵ During medication counselling involving DDIs, pharmacists may counsel patients to avoid certain medication combinations or modify doses of medications affected by DDIs, and they may provide education so that patients can self-monitor for adverse effects. Pharmacists can also help mitigate DDIs by adjusting the administration times of medications. For example, to improve absorption of doxycycline, pharmacists could counsel patients to separate the administration time of antacids, calcium, and iron products from the administration time of doxycycline. To enhance patients' understanding of DDIs, pharmacists could provide specific DDI handouts tailored to each patient's medication profile, reinforce important DDI information at subsequent visits, and check for patients' understanding of DDIs at each visit.

Medication counselling by a pharmacist or a physician may be instrumental in a patient's understanding of their medications.¹⁶ Patients have different perspectives when it comes to the importance of DDIs affecting their health. In a focus group study involving patients, physicians, and pharmacists, the authors evaluated what patients wanted to know about their medications.¹⁷ The results suggested that patient-important factors during medication counselling provided by health care professionals included wanting to know about medication side effects and risks, duration of therapy, cost, different treatment options, and whether the medication was indicated for the particular patient.¹⁷ Patients also wanted to know about possible DDIs and contraindicated medications that could affect their medical therapy.¹⁷ Similarly, in a mixed-methods qualitative study examining pharmacy quality assurance, most participants thought that DDI information constituted important safety counselling points.¹⁸ In contrast to the unavoidable side effects of medications, DDIs are preventable. However, in this study, participants were primarily interested in understanding the side effect profile of their medications. Only 2 (29%) of the 7 participants wanted to know more about DDIs that could affect their medication therapy. Our results were comparable to those of another study based on interviews with 600 patients or caregivers at community pharmacies, which found that when starting new medications, "31.7% of participants wanted to know about drug interactions with prescription and non-prescription medications".¹⁹ Furthermore, in a survey study of 5014 patients receiving statin therapy, 76% were "not at all concerned" or "not very

concerned" about DDIs with other medications, suggesting that for the majority of patients, the desire to understand DDIs remains low.²⁰ Given the results from these studies and ours, it remains unclear whether patients were simply not interested in DDIs or if they were not concerned about the implications of DDIs because of their low baseline knowledge of DDIs. Patients' inability to recognize the importance of DDIs may be the result of incomplete understanding of DDIs arising from insufficient medication counselling by health care professionals. During counselling, patients may be told to avoid certain drugs or foods but may not be specifically told that the reason for the recommendation could be the risk of a DDI. In a South Korean questionnaire study, the authors found a gap between patients' expectations and perceptions during medication counselling at community pharmacies.²¹ The largest gaps were related to counselling about adverse drug reactions, DDIs, and past drug allergies. Poor communication between health care professionals and patients may be contributing to patients' uncertainty of what exactly constitutes a DDI and if they have truly experienced a DDI in the past or not.

Medical and medication information is available through various sources. Numerous professionals, including physicians, pharmacists, nurses, and dietitians, are involved in the health care of ambulatory clinic patients. Participants in this study, all of whom were recruited from ambulatory clinics, felt confident when assessing their own understanding their medications, perhaps because of consistent follow-up and access to different health care professionals involved in their care. Their self-confidence in understanding their medications may also have been bolstered by the ready availability of medication information on the internet, a feature of the current digital age. Although it was an underexplored area in our study, most participants acknowledged using the internet to find supplemental medication information. Some online sources of health information are reliable, such as government and hospital websites, as well as websites with the Health on the Net certification.²² However, concerns remain about websites with different levels of readability and reliability, which may lead to misinterpretation of information.^{23,24} It is particularly concerning that patients may be interpreting medication information from online sources without speaking to a health care professional; this suggests that there were barriers preventing patients from speaking directly to their care providers about their medication therapy. Although not explored specifically in this study, possible barriers to speaking with health care professionals may include patients' negative experiences with such professionals in the past, as well as patients feeling embarrassed, neglected, or dismissed when they have asked questions. Health care professionals failing to sufficiently address patients' questions or concerns because of time constraints, patients forgetting to ask questions during their clinic

visits, and patients requiring more time to process and formulate questions may be other reasons why patients turn to the internet to find medication information.

Our study had several limitations. First, it was a small study involving key informant interviews with 7 participants. Second, all of the participants in this study were ambulatory clinic patients who had many health care professionals actively involved in their care. Such patients are often routinely followed over the course of months to years by physicians, pharmacists, and nurses, who can support a patient's understanding of medications. As a result, this study may not be applicable to inpatients or patients in the community who are not attending an ambulatory clinic. Finally, because this was a qualitative study, the analysis and interpretations of results may be subjective. Nonetheless, we believe that our data are rich in content from the unique perspective that each participant provided. Future studies may assess the use of different educational interventions during medication counselling to promote patients' understanding of clinically important DDIs. A future project could also explore physicians' and pharmacists' attitudes and perceptions when communicating DDIs to patients, to gain insight and improve the communication of medication information.

CONCLUSION

In our study, patients did not fully understand the concept of DDIs, how DDIs might affect their medication therapy, and the potential negative health outcomes that DDIs may cause. Although some patients wanted to be informed of DDIs, they relied heavily on their physician and pharmacist to manage interactions. Participants reported that during medication counselling, they felt that DDI information was not as important as understanding the side effects caused by medications. Health care professionals play an important role in promoting the health literacy of patients. Rather than only counselling patients on what medications or foods to avoid because of DDIs, they could play a more active role in promoting why it is important for patients to understand DDIs. Patients could be counselled to monitor for the adverse effects of DDIs and report them to a health care professional. To increase overall DDI knowledge, patients could also be counselled to understand the difference between DDIs and side effects of medications, and how DDIs can affect their medication therapy and their health.

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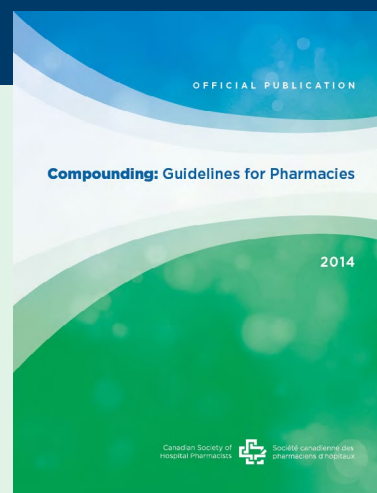
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