Demonstration of Pharmacist Impact at a Community-Based HIV/AIDS Hospital

Denise Kreutzwiser, BScH, BScPhm, ACPR, AAHIVP

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Written by:

Denise Kreutzwiser

2015-2016 HIV pharmacy specialty resident,

Toronto General Hospital (University Health Network) and

McGill University Health Centre

in conjunction with the

Leslie Dan Faculty of Pharmacy at the University of Toronto

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Residency research project team members:

- Ann Stewart (Medical Director, Casey House; Department of Family and Community Medicine, Faculty of Medicine, University of Toronto)
- Sharan Lail (Consulting Pharmacist, Casey House; Clinical Pharmacy Specialist/Leader Education, St. Michael's Hospital)
- Soo Chan Carusone (Research Lead, Casey House; Department of Clinical Epidemiology and Biostatistics, McMaster University)
- Nancy Sheehan (Associate Clinical Professor, Faculté de Pharmacie, Université de Montréal; Coordinator, Quebec Antiretroviral Therapeutic Drug Monitoring Program; Pharmacist, Chronic Viral Illness Service, McGill University Health Centre)
- Alice Tseng (HIV Pharmacotherapy Specialist, Immunodeficiency Clinic, Toronto General Hospital; Assistant Professor, Faculty of Pharmacy, University of Toronto)

2015-2016 HIV specialty pharmacy residency advisory committee:
Alice Tseng, Nancy Sheehan, Karen Cameron, Olavo Fernandes, Irving Salit, Sylvie Carle, Joe Cox, and Reina Bendayan

Expert panel:
Alice Tseng, Nancy Sheehan, Alison Wong, and Bertrand Lebouché

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ABSTRACT

Background

Pharmacist impact at a community HIV/AIDS hospital is not well described in the literature.

Objectives

The purpose of this study was to evaluate pharmacist impact at a community HIV/AIDS hospital by characterizing the drug therapy problems (DTPs) identified/addressed by a pharmacist, as well as determine the acceptance rate of the pharmacist's recommendations.

Methods

A retrospective chart review was conducted for patients admitted to a 13-bed community HIV/AIDS hospital between September 1 and October 30, 2015, who underwent pharmacist review. An expert panel of three HIV pharmacists and one HIV physician independently ranked the DTPs for likelihood to cause harm and severity of harm if the DTP was not identified or addressed. Expert panel rankings were reported if at least three of the four panelists independently assigned the same ranking to the DTP.

Results

Sixteen patients were included (87.5% male, median age: 49 years, median number of admission medications: 8, median number of other medical and psychiatric conditions: 5 and 1.5, respectively). At admission, 73.3% had a detectable HIV viral load, 62.5% had a CD4 count below 200 cells/mm^3, and 56.3% were taking antiretroviral therapy. A total of 72

DTPs were identified/addressed in 15 (93.8%) patients (median number of DTPs/patient: 4). Common DTPs were the need for drug monitoring (26.4%), use of a drug without an indication (25.0%), and presence of an untreated indication (15.3%). The pharmacist made 81 recommendations. Physician acceptance rate was 79.0%. As per the expert panel rankings, 9.7% of the DTPs were considered probable to cause harm while 69.4% were considered possible to cause harm. Based on the expert panel ratings, the anticipated DTP severity was classified as severe for 1.4% of the DTPs and moderate for 81.9% of the DTPs.

Conclusions

The high prevalence of DTPs observed in this complex HIV/AIDS population is likely to impact patient outcomes and highlights the need for enhanced pharmacist support services.

INTRODUCTION

The potential for drug therapy problems (DTPs) in patients infected with human immunodeficiency virus (HIV) is high as a result of the chronic nature of antiretroviral (ARV) drug therapy and complexity of HIV pharmacotherapy. The role of a pharmacist caring for HIV infected patients is well defined in Canadian and American guidelines.[1,2] Furthermore, the impact of pharmacists on HIV care has been demonstrated in various healthcare settings including: tertiary hospitals, specialized HIV ambulatory clinics, HIV primary care clinics, and community pharmacies.[1,3-9]

The impact of a pharmacist in a community HIV/AIDS hospital caring for complex patients, however, is not well described in the literature and as such we wished to address this knowledge gap. Casey House is a 13-bed community hospital in Toronto, Ontario, solely dedicated to HIV infected individuals admitted for sub-acute, palliative, or respite care.[10] Casey House started out as an HIV/AIDS hospice focused on end of life care in 1988 and evolved over time into a place of care for patients who are too unwell to manage independently and require a community-based flexible alternative to acute care hospitalization.[11,12] Individuals can be admitted to Casey House for either a general stay (e.g., a stay where the admission duration is not pre-determined) or a respite stay (e.g., a pre-planned 2 week stay to facilitate recovery from surgery, provide care-givers with a break, etc.). An in-depth retrospective chart review conducted by Halman *et al.* of all 83 patients admitted to Casey House in 2008 describes the profile of this vulnerable HIV infected patient population.[11] Patients had a mean of 5.9 medical comorbidities (SD = 2.3) and 1.9 psychiatric disorders (lifetime Axis I diagnoses). Twenty-eight patients (33.7%) had three or more medical diagnoses, 77 patients (92.8%) had two or more Axis I diagnoses, and 16

patients (19.3%) had unstable housing. Seven patients (8.4%) experienced all three of these complexity variables. Patients were on a mean of 11.5 (SD = 5.3) medications at the time of Casey House admission; 74.7% were on ARVs with 55% reporting full adherence.

As demonstrated in a 2014 systematic review by Li and Foisy, the overall medication error rate in hospitalized HIV infected patients ranged from 5.8% to 86%.[13] The wide variation in medication error rate was attributed to differences in study design, duration, and the hospital unit.[13] The most common medication errors pertained to the ARV regimen, dosing, scheduling, drug-drug interactions, and drug-food interactions.[13] Several studies in this systematic review also noted errors related to opportunistic infection (OI) treatment and prevention with common themes being subtherapeutic dosing of *Pneumocystis jirovecii* treatment, continuing OI prophylaxis when it was no longer needed, neglecting to prescribe OI prophylaxis when indicated or providing incomplete OI prophylaxis regimens.[9,14-18] Although medication errors occurred at various points throughout hospitalization and discharge, 27-72% of all detected medication errors occurred in the admission prescribing stage.[13] As highlighted in Li and Foisy's systematic review, intervention studies reported a reduction in medication errors for hospitalized HIV infected patients with timely and accurate medication reconciliations, daily review of medication profiles, clear communication by pharmacists during transitions of care, and involvement of an HIV/infectious diseases clinical pharmacist.[13]

Although an interdisciplinary team cares for Casey House inpatients, there is no part- or full-time pharmacist on this team due to funding constraints. In addition, pharmacy is not involved in the drug distribution process at Casey House. Since mid-2014, a consulting pharmacist with HIV pharmacotherapy expertise has spent 3-4 hours per week assisting with the management of major DTPs.

Given that DTPs are common in hospitalized HIV infected patients and the value of a pharmacist in the provision of HIV care has been demonstrated in many other healthcare settings, this project aims to describe the impact of a clinical pharmacist at Casey House.

METHODOLOGY

Study Design, Setting, and Timeframe

A single-centre retrospective chart review was conducted for patients admitted to Casey House between September 1, 2015 and October 30, 2015 who underwent pharmacist review. This particular timeframe was selected because temporary pharmacist support was available via an agreement with the HIV specialty pharmacy residency program, which is jointly offered by the Toronto General Hospital (Toronto, Ontario) and McGill University Health Centre (Montréal, Québec) in conjunction with the Leslie Dan Faculty of Pharmacy (Toronto, Ontario). In total, pharmacist services were available for approximately 2.5 days/week during the aforementioned timeframe.

Study Objectives

The primary objectives of this study were to characterize the number, types, and clinical significance of the DTPs identified/addressed by a pharmacist for all patients admitted to Casey House in the study timeframe, as well as assess the acceptance rate of the pharmaceutical care recommendations made by the pharmacist. The secondary objectives of this study were to describe the types of patient care services provided by the pharmacist at Casey House in order to capture key services delivered beyond DTP identification and management.

Study Patients

Patients admitted to Casey House prior to September 1, 2015 and who remained as inpatients for some or all of the study timeframe duration were eligible for study inclusion. Patients who were admitted, discharged, and re-admitted to Casey House during the study

timeframe were still considered eligible for study inclusion. Casey House inpatients were excluded from the study if they did not have documented pharmacist review/involvement at some point between September 1, 2015 and October 30, 2015. To identify eligible study patients, an administrative computer-generated list of patients admitted to Casey House during the study timeframe was cross-referenced with the medical charts for these individuals. A patient was deemed appropriate for study inclusion only if documented pharmacist involvement occurred during the aforementioned study timeframe. An eligibility screening template was used to facilitate the process of study inclusion [Appendix 1]. If a patient met the admission timeframe criteria but did not receive pharmacist review during the study timeframe, the reason for lack of pharmacist involvement was recorded if known.

Data Collection

One individual reviewed the medical charts of all patients included in the study and collected data pertaining to demographics, hospitalization details, medical conditions, psychiatric comorbidities, medication use, identified DTPs, and the types of pharmaceutical care services provided to the patient by the pharmacist [Appendix 1]. *A priori* definitions were established to differentiate between the various states of DTPs; an actual DTP was one that was considered clinically significant, a suspected DTP was deemed to occur when the problem was clinically significant but it could not be confirmed that the drug was causing the problem as there could be other possible contributors, and lastly a potential DTP was one that was theoretical in nature. *A priori* descriptions for the types of DTPs and pharmacist's interventions were defined based on a publication by Allenet *et al.*[19] [Appendices 4 and 5].

Expert Panel Assessment

An expert panel comprised of three HIV specialized pharmacists and one HIV specialized physician was formed to determine the importance of the DTPs that were identified and/or addressed by the pharmacist. None of the expert panelists were involved in the direct care of Casey House inpatients. All members of the expert panel signed a confidentiality agreement [Appendix 6] prior to being privy to the abstracted study data [Appendix 2]. All expert panelists were blinded to patient outcomes, as well as the DTP management/intervention recommendations and outcomes of the interventions.

The DTP ranking system used in this study was adapted from previously published methods involving expert panels that ranked medication errors/discrepancies for their potential to cause harm and/or severity.[20-23] For the DTP ranking process, each assessor was asked to independently rate each DTP for the likelihood to cause harm if the DTP had not been identified or addressed [Appendix 3]. If the assessor rated the DTP as unlikely to cause harm, no further rating for clinical impact/type of adverse event was required. If the assessor rated the DTP as possible or probable to cause harm, the assessor completed an additional rating for clinical impact/type of adverse event by selecting one or more of the following anticipated outcomes: potential to cause discomfort/side effect, clinical deterioration, acute care hospitalization, lasting impairment, or death. Each assessor was also asked to independently rate the DTP for severity if the DTP had not been identified or addressed. Only one severity rating per DTP was permitted. Severity rating options were defined *a priori* as: minor (very unlikely to have any adverse effects; no specific management required), moderate (likely to cause some adverse effects or interfere with therapeutic goals but very unlikely to result in death or lasting impairment; close follow-up, dose/treatment adjustment required), or severe (likely to cause death or lasting impairment and/or

necessitates acute care hospitalization). Majority panel rankings were reported (i.e., when at least three of the four panelists independently assigned the same ranking to the DTP).

Statistical Analysis

Data were analyzed using IBM SPSS Statistics, version 24. Basic descriptive statistics were performed. Percentages were used to describe categorical outcomes while the median, as well as interquartile range depicting the 25th to 75th percentiles, were used to summarize continuous variables. As the DTP rankings were ordinal data, Kendall's coefficient of concordance (*W*) was calculated (with the values corrected for ties) using the R statistics software (version 3.2.3) to determine inter-rater agreement of the four expert panelists who rated the identified DTPs for likelihood to cause harm and degree of severity. Kendall's *W* ranges from 0 (no agreement) to 1 (complete agreement).

Ethical Considerations

Approval for this study was obtained from the HIV Research Ethics Board at the University of Toronto [Appendix 7].

RESULTS

After cross-referencing the study timeframe admission list generated by Casey House administration and the medical charts for these individuals, 16 patients were identified for study inclusion. Figure 1 illustrates study eligibility, inclusion, and exclusion details.

The demographic characteristics for all patients included in this study are summarized in Table 1. The majority of patients were male (87.5%). Median age was 49 years. Median length of stay as an inpatient at Casey House was 49.5 days. No patient had more than one Casey House admission within the study timeframe. Fifteen (93.8%) individuals were admitted for a general stay, while one patient was admitted for a respite stay. The most common reason for Casey House admission was supportive care with a medical (either HIV or non-HIV related) focus and occurred in 43.8% of patients.

Table 2 portrays the medical and psychiatric characteristics of all patients included in the study. Median time since HIV diagnosis was 17.5 years. At admission, 26.7% of patients had an undetectable HIV RNA result (data was unavailable for 1 patient). Ten of the 16 patients (62.5%) had an absolute CD4 count below 200 cells/mm^3 at admission. Median number of medical comorbidities other than HIV infection was 5. The presence of current/prior AIDS defining OIs or malignancy was found in 43.8% and 25.0% of patients, respectively. Three patients (18.8%) either experienced or were experiencing AIDS related wasting. Hepatitis B co-infection was documented in 12.5% of patients, while 18.8% of individuals presently or previously had hepatitis C co-infection. Infection not otherwise captured was documented in 75% of patients. Thrush accounted for the majority of these infections while herpes simplex virus infections, pneumonia, and *tinea* infections represented the next most common types of infection encountered in this group of patients. Pain disorders were common with 43.8% and 12.5% of patients having chronic non-cancer pain

and chronic cancer pain, respectively. Cardiac, respiratory, and renal comorbidities were present in 37.5%, 31.3%, and 18.8%, respectively. Two (12.5%) patients had a history of a non-AIDS defining malignancy. The median number of psychiatric comorbidities was 1.5. Fifty percent of patients were documented to have depression, making this the most common psychiatric condition encountered. Substance abuse/misuse was a known comorbidity in 12.5% of patients, although 31.3% of patients self-reported active substance abuse issues at admission. Seven (53.8%) of the 13 patients with smoking status data available were cigarette smokers.

Table 3 depicts patient medication usage characteristics. Median number of medications taken at admission was 8 (fixed-dose combination products were counted as one medication entity). Nine (56.3%) patients took ARVs at admission. A variety of ARV regimens were used, with no more than two patients using each type of regimen. Six (37.5%) patients had ARV adherence issues at admission. Documentation regarding prior history of ARV non-adherence was available for 15 patients and revealed that 60% of patients had prior ARV non-adherence issues. At admission, 37.5% of patients were taking OI treatment and 37.5% of patients were taking OI prophylaxis. Six (37.5%) patients were taking prescription opioids at admission, with one of these patients taking methadone. None of these patients took buprenorphine/naloxone therapy.

As depicted in Table 4, 93.8% of the patients had DTPs identified or addressed by the pharmacist. A total of 72 DTPs were documented, with 4 being the median number of DTPs identified per patient. As for the state of the DTPs when identified, 65.3% were considered to be actual DTPs while 23.6% were deemed to be potential DTPs and 11.1% were classified as suspected DTPs. Although DTPs were found to occur at all time-points in the admission through discharge process, the majority of DTPs occurred after 72 hours of

hospitalization. Just over half of the DTPs identified (54.2%) pertained to non-HIV/OI medications, while 23.6% and 22.2% of DTPs were related to HIV and OI medications, respectively. The most common type of DTP identified pertained to the need for drug therapy monitoring for efficacy and safety purposes (26.4%) followed by the use of a drug without an indication (25.0%). Eleven (15.3%) DTPs were related to the presence of an untreated indication. Of these 11 DTPs, 6 (54.5%) corresponded to an untreated HIV infection or the presence of an OI prophylaxis/treatment indication while the remaining 5 (45.5%) involved non-HIV/AIDS comorbidities such as hypertension and iron-deficient anemia. Nine (12.5%) DTPs involved an adverse drug reaction. Drug dosing related DTPs were captured as either subtherapeutic dosing (5.6%) or supratherapeutic dosing (4.2%). Overall, drug interactions were found to account for a minimal number of the identified DTPs (8.3%).

A total of 81 DTP management recommendations were made, with the median number of DTP recommendations made being 4 per patient. The majority of DTP management recommendations were fully accepted by the physician (79.0%). Two (2.5%) recommendations were accepted with modification by the physician. In both of these cases, the modification aspect pertained to consulting a specialized physician for assistance to facilitate implementation of the pharmacist's drug therapy recommendations. Two (2.5%) recommendations were considered but deferred for re-assessment at a later point in time. Three (3.7%) recommendations were not accepted by the physician. All three of the unaccepted recommendations were related to laboratory monitoring for efficacy and safety of non-HIV/OI medications. Ten (12.3%) recommendations had 'other' outcomes, such as when a patient changed to palliative status and all medications were stopped and the DTPs became irrelevant. The median number per patient of DTP management/intervention

recommendations that were fully accepted by the physician was 4.

DTP rating results by the expert panel are displayed in Tables 5-7. Majority panel rankings for likelihood to cause harm resulted for 87.5% of the DTPs and revealed that 9.7% of all DTPs were considered probable to cause harm, 69.4% were considered possible to cause harm and 8.3% were ranked as unlikely to cause harm if the DTP was not identified/addressed. The remaining 12.5% of DTPs reflected ranking disagreements between the panelists with respect to the likelihood of harm that would result if the DTPs were not addressed. In most of the panel disagreement cases, 50% of the panelists considered the DTP probable to cause harm while the other 50% of the panelists considered the DTP possible to cause harm. The *W* statistic for ratings pertaining to the likelihood of a DTP to cause harm was 0.658, suggesting a moderate degree of inter-rater agreement. When the expert panel assessed the clinical impact/type of adverse event anticipated to occur from the 69 DTPs considered probable or possible to cause harm, majority panel rankings revealed 53.6% of the 69 DTPs were anticipated to cause discomfort/side effect while 49.3% were expected to cause clinical deterioration and 1.4% were anticipated to cause acute care hospitalization. Majority panel rankings for anticipated degree of severity resulted for 90.2% of the DTPs and revealed that a severe rating was reported for 1.4% of all DTPs, moderate rating for 81.9% of the DTPs, and minor rating for 6.9% of the DTPs. The remaining 9.8% of DTPs reflected severity-ranking disagreements between the panelists. In most of the panel disagreement cases, 50% of the panelists considered the DTP to be of moderate severity while the other 50% of panelists considered the DTP to be of minor severity. The *W* statistic for the DTP severity ratings was 0.569, suggesting a moderate degree of inter-rater agreement.

Tables 8-10 contain several examples of the DTPs identified/addressed by the pharmacist, as well as illustrate how the DTPs were classified, the types of pharmaceutical care recommendations made, and whether or not the physician accepted the pharmacist's recommendation. Results of the expert panel rankings are also included in these examples.

In addition to identifying DTPs, the pharmacist provided the pharmaceutical care services listed in Table 11. The provision of drug information to healthcare providers and/or the patient accounted for more than half of the additional pharmaceutical care services provided.

DISCUSSION

Commentary on Study Objectives and Results

High levels of chronic medical and psychiatric comorbidity, suboptimal ARV uptake, and challenges with ARV adherence indicate complexity is a defining feature of the patients admitted to Casey House**.** The demographic profile of patients admitted to Casey House in 2015 was similar to that described by Halman *et al.*[11] in 2008 and highlights how despite such passage of time and advancements in HIV care, the majority of patients admitted in 2015 still exhibit advanced HIV infection.

DTPs were detected/addressed in 94% of Casey House patients who received pharmacist care, which suggests that the provision of medication-related care at Casey House can be improved. Interestingly, more than 50% of all DTPs involved non-HIV/OI medications. This finding may be reflective of the fact that only 56.3% of patients were taking ARVs at admission. In addition, the high frequency of other medical and psychiatric conditions may have perpetuated the polypharmacy observed in this population. Considering that polypharmacy has been identified as a predictor of non-adherence to ARV therapy,[24] this feature may have influenced which medications were implicated in the DTPs.

Only 6.9% of all DTPs in this study occurred at admission while 66.7% happened at a timepoint beyond 72 hours of hospitalization. This finding is in sharp contrast to the finding by Li and Foisy where prescribing on admission to hospital encompassed the majority of errors. A possible explanation for this discrepancy is that Casey House already has an admission medication reconciliation process in place that is driven by registered nurses and reviewed by physicians. In addition, medication reconciliation on discharge has become standard of care at the local acute care hospitals and further enhances the Casey

House admission medication reconciliation process for patients transferring from acute care. The presence of fewer admission DTPs in this study may also be related to the fact that more than 40% of admitted patients were not taking ARVs at the time of admission. The sub-acute nature of patients admitted to Casey House and median length of stay of 49.5 days are likely factors in why most DTPs were occurring beyond 72 hours of hospitalization. For instance, patients typically undergo admission labwork within the first day or two of admission but these results may not be readily available until after 72 hours of hospitalization and any DTPs related to the labwork would not be identified/confirmed until receipt of the laboratory results. The finding that roughly two-thirds and one quarter of the DTPs were considered to be actual and potential issues, respectively, suggests the pharmacist played both a reactive and proactive role in the medication management process.

In contrast to the systematic review by Li and Foisy, the most common medication problems detected in Casey House patients involved the need for drug monitoring, use of a drug without an indication, and presence of an untreated indication. This difference may be related to the following considerations.

Firstly, the terminology employed must be taken into account. Our study focused on DTPs, while Li and Foisy summarized the published literature pertaining to medication errors. Neither our team nor Li and Foisy provided *a priori* definitions of DTP or medication error, respectively. Although DTPs and medication errors reflect overlapping medication mismanagement concepts, they are not the exact same entity. For example, Cipolle *et al.* define a DTP as "any undesirable event experienced by a patient that involves, or is suspected to involve, drug therapy, and that interferes with achieving the desired goals of therapy and requires professional judgment to resolve."[25] A medication error, meanwhile, is defined by the National Coordinating Council for Medication Error Reporting and

Prevention as "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing, order communication, product labeling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use."[26] Thus, the terminology employed may have influenced the types of medication mismanagement issues reported on.

Secondly, Li and Foisy noted medication error variability in the published literature because of differences in study design and methods to define/identify errors and determine causality. By extension of this observation, it is likely that the classification system used to define/identify medication mismanagement issues in Casey House patients also contributed to variability in the type of DTPs detected in our study. Allenet *et al.*'s ten DTP category descriptions[19] were used in this study, rather than the more widely known seven DTP category descriptions by Cipolle *et al.,*[25] because they focus solely on medication problems and are able to separate the problem from the cause of the problem. For example, Allenet *et al.,* consider 'failure to receive a drug' as a problem and describe patient non-compliance as one of the reasons why this DTP may occur. In contrast, Cipolle *et al.* consider adherence as the DTP category when a patient is unable or unwilling to take a drug as instructed and thereby indicate the medication problem is not separate from the cause of the problem. As the primary study objective was to describe the types of DTPs addressed at Casey House, the validated DTP classification and intervention instrument designed by Allenet *et al.* was considered to align better with the needs of this study. Interestingly, just over a quarter of the DTPs in this study pertained to the need for drug monitoring for efficacy and safety purposes while none of the drug-related problems described in Li and Foisy's review article

involved drug monitoring. A probable explanation for this discrepancy is that Allenet *et al.* specifically list the need for drug monitoring as a DTP category and thus, this data was captured in our study. Cipolle *et al.,* however, do not consider the need for drug monitoring to be a specific DTP category and thus, the need for drug monitoring is potentially not investigated and therefore, not reported in other studies.

Thirdly, the types of DTPs detected may represent a combination of the uniqueness of DTP reporting in this study, complexity of patients admitted to Casey House, and use of a drug distribution process that does not involve pharmacy. For example, this study reported all DTPs detected in Casey House patients rather than just focusing on HIV related DTPs. In addition, this study considered HIV infected patients regardless of whether or not they were prescribed ARVs. The length of stay at Casey House and lack of measures in place to flag longer than necessary medication courses are drivers for why 'drug without an indication' accounted for one quarter of all DTPs in this study. With a median length of stay at Casey House greater than 1.5 months, far longer than that of HIV infected patients admitted to acute care hospitals,[27] ample opportunity existed to investigate the indication for each drug a patient was taking at admission or during their hospital stay, perform laboratory investigations if needed to confirm whether the drug therapy indication was still present, as well as institute a medication taper or discontinue a drug that was no longer indicated and monitor for patient response to drug removal. A common reason for longer than necessary treatment courses was the initiation of anti-infective drugs without specification of treatment duration and realization that a patient was still taking an anti-infective drug beyond the recommended treatment duration and resolution of their health problem. Typically, hospital pharmacy systems will employ automatic stop dates or re-assessment dates for anti-infective drugs as a reminder for healthcare providers to review treatment and prevent overuse of

anti-infective agents. Such a feature was not is place at Casey House at the time this study was done, but should be considered as a strategy to optimize anti-infective stewardship and reduce medication costs related to the use of longer than necessary treatment durations.

Considering that at admission nearly two-thirds of patients in this study had an absolute CD4 count below 200 cells/mm^3 with only 37.5% taking OI prophylaxis and 56.3% on ARVs, it is not surprising that the majority of 'untreated indication' DTPs pertained to the treatment of HIV/opportunistic infections or prevention of opportunistic infections. This study was not designed to address the underlying reasons why suboptimal ARV uptake occurred in this population. A potential hypothesis, however, is that the high levels of chronic medical and psychosocial morbidity observed may be insufficiently addressed via traditional healthcare models and therefore, interfering in the ability of some of these individuals to succeed on ARV therapy. Halman *et al.* have called for comprehensive HIV program planning with interventions that can flexibly adapt to meet the multidimensional and complex needs of this vulnerable group of patients.[11] Going forwards, increased focus on Halman *et al.*'s recommendations may be needed to address the underlying reasons for suboptimal HIV treatment uptake and maintenance.

The opportunity to improve DTP identification/management at Casey House is also demonstrated by the finding that the majority of DTPs ranked by the expert panelists were rated as being possible to cause harm if not identified/addressed. As such, a modest effort focused on improving the identification and management of common DTPs is anticipated to make a substantial difference in a patient's overall medication experience at Casey House. Given the complicated structural and psychosocial barriers encountered by many Casey House patients, improved management of DTPs related to ARV non-adherence and suboptimal uptake are not necessarily something that can be addressed by the pharmacist.

Such situations typically require collaboration with an interdisciplinary team and multiple community resources in order to be successful.

As the expert panelists anticipated discomfort/side effect or clinical deterioration would account for most of the clinical impact/adverse events in cases where harm was considered possible or probable, this finding demonstrates that the more serious events (e.g., acute care hospitalization, lasting impairment, or death) were anticipated to occur in very low numbers. Furthermore, as the majority of DTPs ranked by the expert panelists were moderate in terms of their severity rating, one may conclude that the Casey House physician and nursing team is currently successful at preventing, identifying and addressing the most severe DTPs. When reflecting on the expert panel severity ratings, it is important to note that only one DTP was considered by all four panelists to be severe if unaddressed; this particular DTP was one in which a patient with advanced HIV infection and a long history of ARV non-adherence was admitted for ARV re-initiation. Assistance with selecting an effective and sustainable ARV regimen was needed but given this patient's specific situation and failure of prior attempts to achieve sustained ARV adherence, a collaborative team approach was used when addressing this DTP with the pharmacist contributing just one part of the overall patient care effort.

As the most common DTPs identified were the need for drug monitoring and use of a drug without an indication, it is not surprising that drug monitoring and drug discontinuation were the two most common pharmaceutical care recommendations made by the pharmacist. An interesting discovery is that nearly 20% of the pharmacist's interventions did not fall under one of the seven pre-defined management categories. This finding suggests the intervention categories were insufficiently comprehensive. Based on the interventions classified under the 'other' category, more descriptive results would have been

achieved if the DTP intervention categories were expanded to include: adherence support, no management change at present but re-assess the DTP in a week, consultation with/referral to another healthcare provider, and communication at discharge with the patient's community pharmacist.

According to a 2008 mini-review by Viktil and Blix, prescriber acceptance rates in the published literature have ranged from 41-96% for pharmacist recommendations and the highest prescriber acceptance rates occur when pharmacists attend rounds with physicians and make recommendations for interventions at the ordering or prescribing stages.[28] When pharmacist recommendations pertaining solely to the care of HIV infected patients are considered, a prescriber acceptance rate of 85% and greater has been observed.[15,17,29-32] The finding that 79% of the pharmacist's recommendations were fully accepted by a physician indicates the prescriber acceptance rate in our study was within the limits of what has been reported for pharmacist recommendations, but was lower than what has been reported for the HIV positive population. During the study timeframe, the pharmacist attended weekly interdisciplinary team rounds but the option of making recommendations during the medication prescribing process was limited because she was only available 2.5 days per week. Although some DTPs may have been adverted and more drug information questions asked and addressed if the pharmacist had an increased presence at Casey House during the ordering or prescribing stages, a drastic change in acceptance rate of the DTP management recommendations is unlikely because only three (3.7%) pharmacist recommendations were not accepted by the physician and ten (12.3%) pharmacist recommendations were classified as 'other' because the pre-determined DTP recommendation outcome categories insufficiently captured the various outcomes of the pharmacist's recommendation. Few DTP recommendation outcomes would have fallen under the 'other' category if the pre-

determined outcome categories were expanded to capture recommendations that were no longer applicable due to patient-specific factors/wishes (e.g., refusal to take medication) or a change in the direction of care (e.g., a switch from active treatment to palliative care). An oversight in the pre-determined DTP recommendation outcome categories was that every option, aside from 'other', assumed the physician was the individual contemplating the recommendation. As such, whenever the healthcare provider best positioned to address the DTP was the community pharmacist or a nurse, the outcome, regardless of what it was, fell under the 'other' category.

Recommendations for Optimizing Medication Management at Casey House

One of the most successful strategies reported to reduce ARV medication errors in hospitalized HIV infected patients is the multipronged approach implemented by Daniels *et al.* that was tailored specifically to address the types of medication errors commonly discovered at their site.[33] Their intervention strategy included distribution of an educational pocket-sized card about common ARVs to the hospital's healthcare professionals, the addition of alerts and built-in defaults to the pharmacy's computer order-entry system to flag potential drug interactions and incorrect dosages, updates to the formulary to include co-formulated products, and medication profile review at admission, daily throughout hospitalization, as well as at discharge by a clinical pharmacist trained in infectious diseases. Error rates decreased from 49/68 (72%) to 12/78 (15%) 7 months after implementation of the aforementioned interventions. A similar multidimensional strategy is recommended to optimize medication management at Casey House. Key areas of focus should include: staff education, an improved drug distribution and administration system, and the provision of enhanced pharmacist support services.

A preliminary strategy to improve medication management would be to direct Casey

House physicians and nurses to a guidebook created by Pittman and Foisy that provides a step-by-step framework on the assessment of ARV therapy in HIV hospitalized patients.[34] Staff education sessions could be held at Casey House to further expand on the various elements discussed within this guidebook. This option may be particularly useful in the interim when limited pharmacist services are available.

To minimize DTPs related to drug monitoring needs and untreated indications, a staff education initiative along with revision of the physician order forms are recommended. A pocket-card could be provided to all Casey House physicians and nurses highlighting common HIV medication monitoring recommendations (e.g., check HIV viral load 2-8 weeks after ARV initiation/modification; for patients taking ARVs with a detectable HIV viral load, repeat the HIV viral load every 4-8 weeks until it is below 200 copies/mL, and thereafter, every 3 to 6 months; renal monitoring guidance for patients taking tenofovir disoproxil fumarate, etc.). This pocket-card could also summarize the CD4 count cutoff recommendations for both primary and secondary OI prophylaxis therapy. At present, physician orders are handwritten on fairly basic and non-specific forms. As implementation of computerized physician order entry is not yet underway at Casey House, another interim measure could be to revamp the physician order form to include mandatory fields at the top of the page for age, allergies, weight, serum creatinine/creatinine clearance, as well as date and result of the most recent HIV viral load and CD4 count/percentage. Inclusion of these fields could aid the prescriber in performing a more systematic review of key efficacy and safety parameters during the medication ordering stage and remind the team to assess for primary and/or secondary OI prophylaxis if the CD4 count is below 200 cells/mm^3.

Recommendations for a Pharmacist Position at Casey House

Funding for the majority of Casey House's inpatient operating costs comes from the Ontario Ministry of Health and Long-Term Care (MOHLTC) via the Toronto Centre Local Health Integration Network.[10] Individual, community, and corporate donor support is used to supplement the care and services provided to Casey House patients.[10] Funding for the consulting pharmacist services is not provided by the MOHLTC, but rather the Casey House donation fund. The sustainability of this funding arrangement fully depends on the availability of continued donations and the competing needs of other essential Casey House services that are not funded by the MOHLTC. Consequently, reliance on donations to fund clinical pharmacist support for this complex patient population is not an ideal long-term solution. Integrating the findings from this study into a MOHLTC funding application for clinical pharmacist support is recommended.

During this study, clinical pharmacist time was equivalent to a 0.45 full-time-equivalent position. The pharmacist aimed to achieve all eight Canadian consensus clinical pharmacy key performance indicators (medication reconciliation on admission and at discharge, pharmaceutical care planning, assessment and management of drug therapy problems, participation at inter-professional patient care rounds, patient education during hospital stay and at discharge, and provision of bundled patient care interventions)[35] for each patient. Due to the complexity of Casey House patients and time constraints, only 16/29 (55%) patients admitted to Casey House received documented pharmacist involvement during the study timeframe. Priority was given to the most complicated/ill patients, as well as focusing on DTP identification and management. Although 13/29 admitted patients did not receive documented pharmacist care during the study timeframe, these patients were considered to be of lower pharmacist priority mostly based on their reason for admission or

timing related considerations. As the pharmacist at Casey House was unfamiliar with all patients at the beginning of the study timeframe, it is anticipated that the continued presence of the pharmacist at Casey House would result in increased familiarity with the patients, especially those frequently admitted to Casey House, and this would facilitate the ability to review more admitted patients over time.

If a pharmacy managed drug distribution service was in place whereby electronic medication administration records could highlight proper medication administration (e.g., take with food, do not co-administer with magnesium, separate administration from antacids/iron by "X" hours, etc.) and provide either duration of use comments or automatic stop dates for anti-infective drugs, it is anticipated that many DTPs would be averted and the time available for clinical pharmacist services maximized. After reviewing all 72 DTPs observed in this study, it is anticipated 35 (49%) DTPs could have been detected by a non-HIV specialized distribution pharmacist during the medication ordering phase or upon discharge prescription preparation if a pharmacy managed drug distribution service was in place. The distribution pharmacist, however, would have needed to refer 9/35 (26%) DTPs to a clinical pharmacist for further investigation before DTP management recommendations could be made.

If a pharmacy managed drug distribution service were to be instituted, a 0.5 full-time-equivalent clinical pharmacist position would likely be sufficient to optimize pharmaceutical care services at Casey House. Hiring an upper year pharmacist co-op student to support the clinical and distribution pharmacists is also recommended as an economical way to enhance medication management at Casey House while also building on Casey House's reputation as a unique teaching site for healthcare providers.

Study Limitations

A major limitation of this project is the retrospective design and lack of a comparator group. Inconsistent, abbreviated or missing documentation may have introduced room for information bias and misinterpretation. A prospective study comparing a cohort of patients who received pharmacist care against a cohort of patients who did not receive pharmacist care would have provided more robust data. Such a design, however, would have been unethical considering that consulting pharmacist involvement was standard of care at Casey House for the management of major DTPs.

In addition, sampling bias may have been present given that 13/29 (45%) patients admitted to Casey House during the study timeframe did not receive documented pharmacist care during the study timeframe. In an ideal situation, all patients would have received pharmacist care during the study timeframe. However, resource and time constraints meant that priority for pharmacist review was given to the most complicated/ill patients. This aspect may have, in turn, selected for sicker patients with more DTPs and thereby overestimated the median number of DTPs per patient at Casey House.

Another limitation is that the pharmacist who provided pharmaceutical care services to Casey House patients during the study timeframe was also the individual primarily responsible for designing and conducting the study, as well as collecting and analyzing the data. This was an unfunded study and as such, resources were limited. Ideally, the pharmacist providing patient care would have been separate from the research team performing the study. Such a strategy would have mitigated a Hawthorne effect by the pharmacist. All physicians at Casey House were aware of this research study. Although these physicians could have altered their medication management practices during the study timeframe due to their awareness of being observed, it is unlikely such a Hawthorne effect

occurred because only one of the four physicians was privy to the finer details of the study and all four physicians provided care on a rotating basis.

Although evaluation of DTP clinical significance was strengthened via involvement of an expert panel consisting of four HIV specialist providers, the expert panelists were only required to independently rank each DTP. A methodological limitation was that the panelists were not required to achieve a formal DTP ranking consensus after independently rating each DTP. To compensate for this limitation and bring meaning to the panelists' rankings, only ratings where at least three of the four panelists reached the same conclusion are reported. Another flaw was that the categories for likelihood to cause harm were not defined *a priori*. As a result, the expert panelists were left to independently interpret the definitions for 'unlikely', 'possible', and 'probable'; variability in panelist interpretation may have occurred.

Future Considerations

Due to the short study timeframe and difficulty in following patients post-discharge, this study was unable to track and analyze key patient outcomes (e.g., impact on HIV viral load/CD4 count, effect on length of Casey House stay and hospital re-admission rates, etc.) related to the pharmacist's interventions. Numerous studies, however, have demonstrated a beneficial impact of HIV specialized pharmacists on achieving improved ARV adherence, higher rates of viral suppression, greater increases in CD4 counts, and reducing pill burden/dosing frequency in HIV infected individuals.[8,36-40]

Despite the breadth of pharmaceutical care studies conducted in HIV infected individuals, very few studies have provided an economic analysis of pharmacist impact in this particular patient population.[41] Our study, like many others, was not designed to analyze pharmacist impact from a cost-effectiveness perspective. Some insight into the impact a

pharmacist at Casey House could have on drug cost-containment was, however, garnered from one specific DTP addressed by the pharmacist. In this case, the pharmacist recommended extensive modification of a patient's ARV regimen and noted that in addition to the clinical and safety benefits of modifying the ARV regimen, $16,400 in ARV drug costs could be saved in one year. Although this is just one example, it suggests the presence of a clinical pharmacist on the Casey House team is likely to generate a return on investment and warrants the opportunity to test out this hypothesis.

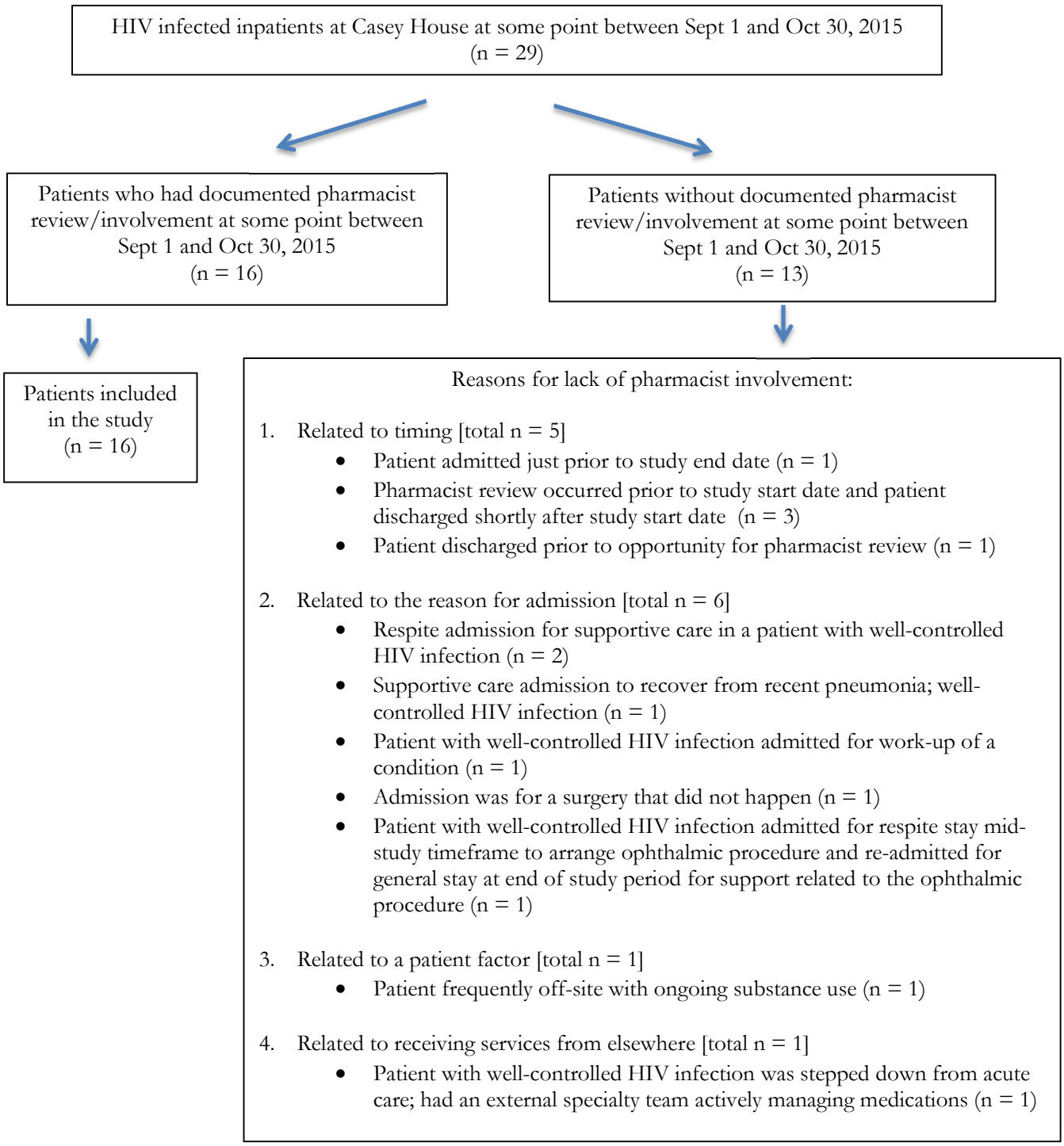
Should funding be arranged for a clinical pharmacist position, a follow-up study investigating the aforementioned aspects could be conducted as part of a quality assurance evaluation and to help the Casey House team understand the overall reach and durability of their efforts.

CONCLUSION

A high prevalence of DTPs was observed in this complex HIV/AIDS population. Expert panel ratings suggest the majority of DTPs were likely to adversely affect patient outcomes if not identified/addressed. The 79% physician acceptance rate of pharmacist recommendations suggests a clinical pharmacist with HIV experience makes an impact in this setting. Our findings highlight the need for enhanced pharmacist services at Casey House. In order to ensure the provision of sustainable pharmacist services at Casey House, funding support from the MOHLTC should be pursed. Overall, a multipronged strategy is recommended to optimize medication management with additional key features focusing on staff education, as well as an improved drug distribution and administration system.

FIGURES

Figure 1: Study enrolment based on inclusion and exclusion criteria



TABLES

Table 1: Patient demographics (total n = 16)

Demographic Characteristic	Result*
Age (years)	49.0 (39.8-67.8)
Gender	
Male	14 (87.5%)
Female	2 (12.5%)
Weight at admission (kg)	55.5 (49.9-78.56)
Type of admission:	
General stay	15 (93.8%)
Respite stay	1 (6.3%)
Reason for admission:	
Supportive care/medical focus	7 (43.8%)
Antiretroviral adherence support	3 (18.8%)
Supportive care/medical focus + antiretroviral adherence support	3 (18.8%)
End of life care	1 (6.3%)
Other	2 (12.5%)
First admission during study timeframe:	
Yes	16 (100%)
Length of stay as inpatient (days)	49.5 (35.3-72.8)

* continuous data are presented as median (interquartile range, 25-75 percentiles)

Table 2: Patient medical and psychiatric characteristics

Characteristic	Result*
Time since HIV diagnosis (years)	17.5 (9.3-24.8)
CD4 nadir (n = 6 instead of 16; data unavailable for 10 patients)	
Below 200 cells/mm^3	5 (83.3%)
200-500 cells/mm^3	1 (16.7%)
HIV RNA at admission (n=15 instead of 16; data unavailable for 1 patient):	
Detectable (40 copies/mL or above)	11 (73.3%)
Undetectable (less than 40 copies/mL)	4 (26.7%)
Absolute CD4 count at admission:	
Below 200 cells/mm^3	10 (62.5%)
200-500 cells/mm^3	4 (25.0%)
Above 500 cells/mm^3	2 (12.5%)
Number of medical comorbidities other than HIV infection	5.0 (5.0-11.3)
Frequency of current or prior AIDS defining conditions:	
Opportunistic infection	7 (43.8%)
Malignancy	4 (25%)
Wasting	3 (18.8%)
Frequency of viral hepatitis co-infection:	
Hepatitis C co-infection (current or prior)	3 (18.8%)
Chronic hepatitis B co-infection	2 (12.5%)
Frequency of non-AIDS related medical conditions:	
Infection (other than AIDS defining or viral hepatitis)	12 (75.0%)
Pain disorder	
chronic non-cancer pain	7 (43.8%)
chronic cancer pain	2 (12.5%)
Cardiac disease	6 (37.5%)
Respiratory disease	5 (31.3%)
Kidney disease	3 (18.8%)
Non-AIDS defining malignancy (current or prior)	2 (12.5%)
Other condition not otherwise captured	14 (87.5%)
Number of psychiatric comorbidities	1.5 (0.3-2.0)
Frequency of the following psychiatric conditions:	
Depressive disorder	8 (50.0%)
Substance abuse/misuse	2 (12.5%)
Cognitive disorder including dementia	2 (12.5%)
Anxiety disorder	1 (6.3%)
Bipolar disorder	1 (6.3%)
Schizophrenia disorder	1 (6.3%)
Post traumatic stress disorder	1 (6.3%)
Other psychiatric disorder	2 (12.5%)
Active substance abuse at admission	5 (31.3%)
Marijuana	3 (18.8%)
Cocaine or crack	2 (12.5%)
Alcohol	1 (6.3%)
Morphine	1 (6.3%)
Benzodiazepines	1 (6.3%)
Cigarette smoker at admission (n = 13 instead of 16; data not documented for 3 patients)	7 (53.8%)

Note: n = 16 patients unless otherwise specified in the table

* continuous data are presented as median (interquartile range, 25-75 percentiles)

Table 3: Patient medication usage characteristics

Characteristic	Result*
Total number of medications** taken at admission	8.0 (6.3-13.5)
Taking antiretroviral medication at admission	9 (56.3%)
Type of antiretroviral regimen at admission (n = 9 for patients taking antiretrovirals at admission) 2 NRTIs + PI regimen 2 NRTIs + NNRTI regimen 2 NRTIs + INSTI regimen Other antiretroviral combination regimen	 1 (11.1%) 2 (22.2%) 2 (22.2%) 4 (44.4%)
Antiretroviral adherence issues at admission	6 (37.5%)
Prior history of antiretroviral non-adherence (n = 15; data on 1 patient unavailable)	9 (60.0%)
Taking opportunistic infection treatment at admission	6 (37.5%)
Taking opportunistic infection prophylaxis at admission	6 (37.5%)
Taking prescription opioids at admission	6 (37.5%)
Type of opioid at admission (n = 6 for patients taking opioids at admission) Methadone Buprenorphine/naloxone therapy Other:	 1 (16.7%) 0 (0%) 6 (100%)

Note: n = 16 patients unless otherwise specified in the table
* continuous data are presented as median (interquartile range, 25-75 percentiles)
** fixed-dose combinations were counted as one medication

Legend:
NRTIs = nucleos(t)ide reverse transcriptase inhibitors, PI = protease inhibitor, NNRTI = non-nucleoside reverse transcriptase inhibitor, INSTI = integrase strand transfer inhibitor

Table 4: Drug therapy problem (DTP) descriptions

Characteristic	Result*
Number of patients with DTPs	15 (93.8%)
Number of DTPs identified	72
Of the 15 patients with DTPs, number of DTPs identified per patient	4.0 (2.0-7.0)
Timepoint DTP occurred:	
Beyond 72 hours of hospitalization	48 (66.7%)
Within 42-72 hours of admission	12 (16.7%)
Upon discharge	7 (9.7%)
Admission	5 (6.9%)
DTP pertains to:	
Non - HIV/opportunistic infection medication	39 (54.2%)
HIV medication	17 (23.6%)
Opportunistic infection treatment/prevention medication	16 (22.2%)
State of DTP when identified:	
Actual	47 (65.3%)
Potential	17 (23.6%)
Suspected	8 (11.1%)
DTP categorization:	
Drug monitoring needed	19 (26.4%)
Drug without an indication	18 (25.0%)
Untreated indication	11 (15.3%)
Adverse drug reaction	9 (12.5%)
Subtherapeutic dosage	4 (5.6%)
Supratherapeutic dosage	3 (4.2%)
Drug interaction	6 (8.3%)
Combination to be avoided	5 (6.9%)
Use with caution	1 (1.4%)
Combination contraindicated	0 (0%)
Improper administration	4 (5.6%)
Failure to receive drug	4 (5.6%)
Non-conformity to guidelines or contraindication	3 (4.2%)
Number of DTP management/intervention recommendations made	81
Of the 15 patients with DTPs, number of DTP management/intervention recommendations made per patient	4.0 (2.0-10.0)
Recommended DTP management/intervention categorization:	
Drug monitoring	21 (25.9%)
Drug discontinuation	20 (24.7%)
Dose adjustment	9 (11.1%)
Addition of a new drug	6 (7.4%)
Drug administration mode optimization	4 (4.9%)
Drug switch	4 (4.9%)
Change of administration route	1 (1.2%)
Other	16 (19.8%)
Outcomes of the DTP recommendations	
Accepted by physician	64 (79.0%)
Not accepted by physician	3 (3.7%)
Accepted with modification by physician	2 (2.5%)
Considered, but deferred for re-assessment	2 (2.5%)
Other	10 (12.3%)
Of the 15 patients with DTPs, number of recommendations fully accepted by physician per patient	4.0 (2.0-5.0)

* Continuous data are presented as median (interquartile range, 25-75 percentiles)

Table 5a: Majority panel drug therapy problem rating results for likelihood to cause harm

Rankings	Drug Therapy Problem (DTP) Rating for Likelihood to Cause Harm if DTP was NOT identified or addressed (n = 72 drug therapy problems)		
	Unlikely to cause harm	**Possible to cause harm**	**Probable to cause harm**
All 4 raters reached the same rating conclusion	3/72 (4.2%)	30/72 (41.7%)	3/72 (4.2%)
3 of the 4 raters reached the same rating conclusion	3/72 (4.2%)	20/72 (27.8%)	4/72 (5.6%)
Overall DTP likelihood of causing harm based on ratings where at least 3 of the 4 raters reached the same conclusion	6/72 (8.3%)	50/72 (69.4%)	7/72 (9.7%)

Table 5b: Non-majority panel drug therapy problem rating results for likelihood to cause harm

Drug Therapy Problem (DTP) Rating for Likelihood to Cause Harm if DTP was NOT identified or addressed (n = 72 drug therapy problems)		
50% panelists → unlikely 50% panelists → possible	**50% panelists → possible 50% panelists → probable**	**25% panelists → unlikely 25% panelists → possible 50% panelists → probable**
2/72 (2.8%)	6/72 (8.3%)	1/72 (1.4%)

Table 6: Majority panel drug therapy problem rankings for clinical impact/type of adverse event

	Discomfort/ Side effect	Clinical deterioration	Acute care hospitalization	Lasting impairment	Death
Clinical impact/ type of adverse event anticipated if the DTP was not identified/addressed. Results are based on ratings where at least 3 of the 4 panelists reached the same conclusion*	37/69 (53.6%)	34/69 (49.3%)	1/69 (1.4%)	0 (0%)	0 (0%)

**Raters could select more than one clinical outcome per DTP. The denominator is 69 because 3 of the DTPs were considered by all 4 panelists to be unlikely to cause harm and therefore ranking the clinical impact/type of adverse event anticipated was not applicable.*

Table 7a: Majority panel drug therapy problem rating results for severity

Rankings	Drug Therapy Problem (DTP) Rating for Severity if DTP was NOT identified or addressed (n = 72 drug therapy problems)		
	Minor	**Moderate**	**Severe**
All 4 raters reached the same rating conclusion	2/72 (2.8%)	46/72 (63.9%)	1/72 (1.4%)
3 of the 4 raters reached the same rating conclusion	3/72 (4.2%)	13/72 (18.1%)	0/72 (0%)
Overall DTP severity based on ratings where at least 3 of the 4 raters reached the same conclusion	5/72 (6.9%)	59/72 (81.9%)	1/72 (1.4%)

Table 7b: Non-majority panel drug therapy problem rating results for severity

Drug Therapy Problem (DTP) Rating for Severity if DTP was NOT identified or addressed (n = 72 drug therapy problems)		
50% panelists → minor 50% panelists → moderate	**50% panelists → moderate 50% panelists → severe**	**25% panelists → minor 50% panelists → moderate 25% panelists → severe**
4/72 (5.6%)	2/72 (2.8%)	1/72 (1.4%)

Legend for Tables 7a and 7b:
Minor = very unlikely to have any adverse effects; no specific management required
Moderate = likely to cause some adverse effects or interfere with therapeutic goals but very unlikely to result in death or lasting impairment; close follow-up, dose/treatment adjustment required
Severe = likely to cause death or lasting impairment and/or necessitates acute care hospitalization

Table 8: Examples of actual drug therapy problems identified/addressed by the pharmacist

	Drug Therapy Problem (DTP) Example	DTP Classification	Expert Panel DTP Rankings		DTP Management/ Intervention Recommendation	Outcome of DTP Recommendation
			Likelihood of Harm if DTP Not Addressed	Severity Rating if DTP Not Addressed		
1.	A patient who started ARVs immediately after his HIV diagnosis 6 months ago had his last HIV viral load test 2 months post-ARV initiation (result: 600 copies/mL). Just prior to Casey House admission, patient had a brief course of a drug known to lower the level of one of his ARVs. Although admitted to Casey House for the past 3 months, no HIV viral load was done within the past 4 months and no undetectable HIV viral load had ever been obtained.	Drug monitoring needed	Probable x 1 panelist; possible x 3 panelists	Moderate x 4 panelists	Drug monitoring needed	Accepted by physician
2.	Elderly patient with declining cognitive function and a long-standing history of ranitidine 150 mg BID use but no clear reason for use. Ranitidine can have minor anticholinergic effects in the elderly, which may worsen cognitive function.	• Drug without indication • Adverse drug reaction	Possible x 4 panelists	Moderate x 4 panelists	Drug discontinuation	Accepted by physician
3.	A patient with a history of chronic, normocytic anemia admitted on an iron supplement. Iron studies at admission revealed no current indication for use.	Drug without indication	Possible x 2 panelists; unlikely x 2 panelists	Moderate x 2 panelists; minor x 2 panelists	Drug discontinuation	Accepted by physician
4.	Patient taking magnesium oxide 420 mg orally TID. No actual indication. Patient's admission serum magnesium level was just above the upper limit of normal.	• Drug without indication • Supratherapeutic dosage	Possible x 3 panelists; unlikely x 1 panelist	Moderate x 3 panelists; minor x 1 panelist	Drug discontinuation	Accepted by physician
5.	Ciprofloxacin was prescribed to an asymptomatic patient based on a urine sample done to follow-up on prior hematuria. A positive urine culture in an asymptomatic, non-pregnant adult is not an indication for antibiotics.	Drug without indication	Possible x 3 panelists; unlikely x 1 panelist	Moderate x 3 panelists; minor x 1 panelist	Drug discontinuation	Accepted by physician
6.	Patient taking fluconazole for the last 18 days for oral thrush. No fluconazole stop date, nor recent thrush re-evaluation. Fluconazole is usually used for 7-14 days to treat oral thrush.	Drug without indication	Possible x 4 panelists	Moderate x 4 panelists	Drug discontinuation	Accepted by physician
7.	A patient with a long history of non-compliance to HIV care and ARVs was admitted for ARV re-initiation. A regimen with a high resistance barrier that was suitable for the patient's resistance history and could be tied to his daily methadone was needed.	Untreated indication	Probable x 4 panelists	Severe x 4 panelists	Addition of a drug	Accepted by physician

Drug Therapy Problem (DTP) Example		DTP Classification	Expert Panel DTP Rankings		DTP Management/ Intervention Recommendation	Outcome of DTP Recommendation
			Likelihood of Harm if DTP Not Addressed	Severity Rating if DTP Not Addressed		
8.	A patient with a CD4 count less than 50 cells/mm^3 was recently prescribed ARVs but was taking intermittently (by self-choice). No OI prophylaxis was considered or offered.	Untreated indication	Possible x 4 panelists	Severe x 1 panelist; moderate x 3 panelists	Other *(focus on ARV adherence first; re-assess OI prophylaxis in 1 week)*	Other *(recommendation not addressed as patient began refusing medications)*
9.	A patient with multiple comorbidities and prior history of hypertension was not taking anti-hypertensives. Blood pressure readings revealed elevated results. Patient taking a darunavir/ritonavir based regimen. Physician requested assistance selecting an anti-hypertensive that could be used safely with patient's ARVs and in the setting of renal failure.	Untreated indication	Probable x 3 panelists; possible x 1 panelist	Moderate x 4 panelists	Addition of a drug	Accepted by physician
10.	An 82 kg patient was prescribed pyrazinamide 1500 mg/day (18.3 mg/kg/day). Pyrazinamide is dosed as 20-25 mg/kg/day or as 2000 mg/day for weight of 76-90 kg.	Subtherapeutic dosage	Possible x 3 panelists; unlikely x 1 panelist	Moderate x 3 panelists; minor x 1 panelist	Dosage adjustment	Accepted by physician
11.	A patient with a CD4 count less than 50 cells/mm^3 and prior history of CNS toxoplasmosis was prescribed sulfamethoxazole 800 mg/trimethoprim 160 mg once daily. Although adequate for *Pneumocystis jirovecii* prophylaxis, the recommended dose for secondary *Toxoplasmosis gondii* prophylaxis at the time was sulfamethoxazole 800 mg/trimethoprim 160 mg BID.	Subtherapeutic dosage	Possible x 3 panelists; unlikely x 1 panelist	Severe x 1 panelist, moderate x 2 panelists, minor x 1 panelist	Dose adjustment	Accepted by physician
12.	Elderly patient taking ASA 325 mg/day for secondary cardiovascular risk reduction. Doses above 81 mg/day are not more efficacious but may increase bleeding risk.	Supratherapeutic dosage	Possible x 4 panelists	Moderate x 4 panelists	Dose adjustment	Accepted by physician
13.	A patient receiving hypercalcemia treatment was also prescribed a multivitamin containing 200 mg calcium carbonate. Supplemental calcium use limits the impact of hypercalcemia treatment.	Adverse drug reaction	Probable x 1 panelist; possible x 3 panelists	Moderate x 4 panelists	Drug discontinuation	Accepted by physician
14.	Patient prescribed ciprofloxacin 250 mg at 10AM and 10PM while taking 900 mg ferrous fumarate at 10PM. Ciprofloxacin should be given at least 2 hours before or 6 hours after iron supplements to mitigate a chelation interaction. Patient very unlikely to agree to medication administration separation.	Drug interaction – combination to be avoided	Probable x 2 panelists, possible x 1 panelist, unlikely x 1 panelist	Moderate x 3 panelists; minor x 1 panelist	Drug discontinuation *(stop iron supplement while receiving ciprofloxacin)*	Accepted by physician

Drug Therapy Problem (DTP) Example		DTP Classification	Expert Panel DTP Rankings		DTP Management/ Intervention Recommendation	Outcome of DTP Recommendation
			Likelihood of Harm if DTP Not Addressed	Severity Rating if DTP Not Addressed		
15.	Patient concurrently prescribed raltegravir and Milk of Magnesia. Coadministration is not recommended (a potential chelation interaction can reduce raltegravir levels).	Drug interaction – combination to be avoided	Probable x 1 panelist; possible x 3 panelist	Moderate x 4 panelists	Drug discontinuation	Accepted by physician
16.	Darunavir 800 mg once daily and ritonavir 100 mg once daily were prescribed, but given as darunavir 800 mg HS and ritonavir 100 mg QAM. Ritonavir boosts the darunavir concentration; these drugs should be given at the same time.	Improper administration	Probable x 4 panelists	Moderate x 4 panelists	Administration mode optimization	Accepted by physician
17.	A patient with prior MI was taking six ARV drugs. Genotype history review revealed some ARVs, including abacavir, had limited efficacy potential due to the presence of drug resistance. BID darunavir/ritonavir was prescribed but no darunavir mutations were present. Unnecessary exposure to BID darunavir/ritonavir may increase the risk of harm from metabolic side effects. Safety concerns with abacavir are also present given the unresolved controversy about abacavir and MI risk. The ARV regimen was also unnecessarily expensive.	• Non-conformity to guidelines or contraindication • Adverse drug reaction	Possible x 3 panelists and unlikely x 1 panelist	Moderate x 3 panelists; minor x 1 panelist	• Drug discontinuation • Addition of a new drug • Dose adjustment • Drug monitoring	All recommendations accepted by physician
18.	Patient with extensive Kaposi sarcoma in his mouth was prescribed ARVs but was unable to swallow pills due to large size. Patient refused crushed pills. Speech language pathologist recommended regular liquid diet. No feeding tube in place. Patient had oncology appointment scheduled in 6 days time to assess whether Kaposi's sarcoma was treatable.	Failure to receive drug	Possible x 4 panelists	Severe x 2 panelists; moderate x 2 panelists	• Drug discontinuation *(stop ARVs until a reliable administration route is obtained)* • Change ARV administration route *(arrange for feeding tube to give ARVs)*	Both recommendations accepted by a physician

Legend: ARV = antiretroviral, BID = twice daily, TID = three times a day, OI = opportunistic infection, CNS = central nervous system, ASA = acetylsalicylic acid, HS = at bedtime, QAM = every morning, MI = myocardial infarction

Table 9: Examples of potential drug therapy problems identified/addressed by the pharmacist

	Drug Therapy Problems (DTP) Example	DTP Classification	Expert Panel DTP Rankings		DTP Management/ Intervention Recommendation	Outcome of DTP Recommendation
			Likelihood of Harm if DTP Not Addressed	Severity Rating if DTP Not Addressed		
1.	A patient was taking ethambutol for the past 5 months. No ophthalmology review prior to ethambutol initiation, nor documented monitoring for visual side effects was found. Risk factors for vision related issues were: ethambutol ~15mg/kg/day for more than 2 months and renal insufficiency.	Drug monitoring needed	Possible x 4 panelists	Moderate x 4 panelists	Drug monitoring	Accepted by physician
2.	Patient with a long history of ARV adherence difficulties was just re-started on her prior ARV regimen, which contained maraviroc. Unclear if maraviroc is still a useful option for this patient as maraviroc is only indicated for CCR5 tropic HIV infection and HIV tropism can change as the virus reproduces and mutates over time. No recent tropism result found.	Drug monitoring needed	Possible x 3 panelists; unlikely x 1 panelist	Moderate x 3 panelists; minor x 1 panelist	Drug monitoring	Accepted by physician
3.	Patient had increased use of acetaminophen for anti-pyretic purposes related to IRIS. Patient also taking medications that can have negative impacts on liver function (pyrazinamide, isoniazid, rifampin, and efavirenz). Last LFTs were checked prior to efavirenz initiation and a pyrazinamide dose increase.	Drug monitoring needed	Possible x 4 panelists	Moderate x 4 panelists	Drug monitoring	Accepted by physician
4.	A patient taking pyrazinamide for the past 6 weeks for tuberculosis lymphadenitis had no documented stop date or reference to treatment duration. Pyrazinamide is usually only taken for the first 8 weeks of tuberculosis lymphadenitis therapy.	Drug without indication*	Possible x 3 panelists; unlikely x 1 panelist	Moderate x 3 panelists; minor x 1 panelist	Drug discontinuation *(when 8 weeks of treatment completed)*	Accepted by physician
5.	Upon acute care hospital discharge, a patient was prescribed a 2-week prednisone course for hypercalcemia treatment. Casey House team was querying if a prednisone taper was needed.	Drug without indication**	Possible x 4 panelists	Moderate x 4 panelists	Drug monitoring	Accepted by physician
6.	Patient with CD4 count less than 50 cells/mm^3 and history of sulfa allergy was prescribed dapsone for *Pneumocystis jirovecii* prophylaxis. No toxoplasma IgG antibody result; if toxoplasma IgG antibody is positive, dapsone monotherapy is inadequate for primary *Toxoplasma gondii* prophylaxis	Untreated indication	Possible x 4 panelists	Moderate x 4 panelists	Drug monitoring	Accepted by physician

Legend: ARV = antiretroviral, CCR5 = chemokine receptor type 5, IRIS = immune reconstitution inflammatory syndrome, LFTs = liver function tests, IgG = immunoglobulin G

* Classified as 'drug without indication' because if not identified the drug may have been prescribed for too long

** Classified as 'drug without indication' because no taper was indicated and if not assessed the drug may have been prescribed for too long

Table 10: Examples of suspected drug therapy problems identified/addressed by the pharmacist

Drug Therapy Problems (DTP) Example		DTP Classification	Expert Panel DTP Rankings		DTP Management/ Intervention Recommendation	Outcome of DTP Recommendation
			Likelihood of Harm if DTP Not Addressed	Severity Rating if DTP Not Addressed		
1.	A patient had a generalized tonic-clonic seizure despite having a therapeutic valproic acid level. Patient was taking quetiapine 25 mg HS; indication was unclear but suspected to be treatment of insomnia. Quetiapine is not recommended for insomnia because risks outweigh benefits. Patient's ARV regimen included darunavir/ritonavir, which can increase quetiapine levels significantly via CYP 3A4 inhibition. Higher quetiapine doses have been associated with seizures.	• Drug without indication • Drug interaction – use with caution • Adverse drug reaction	Possible x 4 panelists	Moderate x 4 panelists	Drug discontinuation	Accepted with modification *(physician accepted the recommendation but referred patient to a neurologist and family doctor to further confirm indication and pursue quetiapine discontinuation)*
2.	A patient with active osteomyelitis of the jaw and radiation induced osteonecrosis of the jaw was taking alendronate. Although uncommon, bisphosphonates have been associated with osteonecrosis of the jaw. Risks of continued alendronate therapy deemed to outweigh benefit for this particular patient's situation.	Adverse drug reaction	Probable x 2 panelists; possible x 2 panelists	Severe x 2 panelists; moderate x 2 panelists	Drug discontinuation	Accepted by physician
3.	Concurrent use of darunavir/ritonavir BID with budesonide 200 mcg/formoterol 6 mcg one inhalation BID for COPD for at least the past 5 months. A CYP 3A4 mediated interaction can increase budesonide levels and the risk of adverse steroid effects.	Drug interaction – combination to be avoided	Possible x 4 panelists	Moderate x 4 panelists	• Drug switch • Drug monitoring	Other for both recommendations *(patient changed to palliative status, all active treatment and related drugs stopped, DTP no longer an issue)*

Legend: ARV = antiretroviral, HS = at bedtime, BID = twice daily, COPD = chronic obstructive pulmonary disease, CYP = cytochrome P450

Table 11: Additional pharmaceutical care services provided for patients

Pharmaceutical Care Service Provided	Result (# and % of patients receiving the service)
Best possible medication history/medication reconciliation	5 (31.3%)
Adherence optimization efforts	3 (18.8%)
Medication counseling	5 (31.3%)
Drug information services	9 (56.3%)
Drug coverage assistance	3 (18.8%)
Discharge prescription assistance	1 (6.3%)

APPENDICES

Appendix 1- Overall study data collection template

Appendix 1
Data Collection Form: Subject ID #: 15 – 0 _____

Study Inclusion Criteria: (must answer **YES** to both criteria before proceeding with data collection)		
HIV-infected inpatient at Casey House at some point between Sept 1, 2015 and Oct 30, 2015	✎ Yes	✎ No
Pharmacist review/involvement occurred at some point between Sept 1, 2015 and Oct 30, 2015	✎ Yes	✎ No
		If known, indicate reason for no pharmacist review/involvement: ✎ Patient left against medical advice prior to opportunity for pharmacist review ✎ Patient discharged prior to opportunity for pharmacist review ✎ Patient died prior to opportunity for pharmacist review ✎ Other: _____

Pharmaceutical Care Activities Provided by Pharmacist for this Patient	**Checkmark below if response is yes**
Best possible medication history collection/ medication reconciliation	
Adherence optimization efforts	
Patient medication counseling	
Provision of drug information responses	
Drug coverage assistance	
Other (list details):	

Drug Therapy Problem (DTP) Summary	
Total # of DTPs identified for this patient	
Total # of pharmaceutical care recommendations by pharmacist for this patient	
Total # of pharmacist recommendations accepted for this patient	

Appendix 1
Data Collection Form: Subject ID #: 15 – 0 _____

Demographics

Type of Casey House (CH) admission	General admission Respite admission	
Reason for CH admission	Supportive care/medical focus Supportive care/psychosocial focus Antiretroviral (ARV) adherence support End of life care Caregiver relief Other: _____	
Date of CH admission	Sept _____, 2015 Oct _____, 2015 Other: _____	
First admission during study timeframe?	Yes No: This patient was a re-admission with their previous admission date being _____	
Age (years) at admission		
Gender	Male Female Trans: (M to F) or (F to M)	
Ethnicity	Caucasian African-American Asian Aboriginal Inuit Hispanic Other	
Total # of medical comorbidities other than HIV infection		
Type of medical comorbidities (as per physician discharge summary)	*Category* AIDS defining opportunistic infection (OI) AIDS-defining malignancies Other AIDS-defining illness Cardiac disease Respiratory disease/condition Liver disease (eg HCV/HBV infection) Kidney disease Non-AIDS defining malignancies Infection not otherwise captured Pain disorder: acute or chronic pain cancer or non-cancer pain Other:	*Specify Details*
Total # of psychiatric comorbidities		
Type of psychiatric comorbidities (as per consulting psychiatric documentation and/or physician discharge summary)	Substance abuse/misuse disorder Cognitive disorder including dementia Depressive disorder Anxiety disorder Bipolar disorder Schizophrenia disorder Post traumatic stress disorder Adjustment disorder Other psychiatric disorder:	
Time duration since HIV diagnosis	_____ months / years	
CD4 nadir	_____cells/mm^3	
Taking ARVs at admission?	✎ Yes **If yes,** were other ARV regimens taken aside from the regimen at CH admission? Yes/No **If yes,** how many prior ARV regimens has patient had? _____	✎ No **If no,** is patient ARV treatment naïve at admission? Yes/No

Appendix 1

Data Collection Form: Subject ID #: 15 – 0 _____

ARV adherence issues at time of admission?	✎ Yes	✎ No
Prior history of ARV non-adherence?	✎ Yes	✎ No
Taking OI treatment at admission?	✎ Yes	✎ No
Taking OI prophylaxis at admission?	✎ Yes	✎ No
Taking opioids at admission? Methadone maintenance therapy Methadone for pain Suboxone (buprenorphine/naloxone) maintenance Other: _____	✎ Yes ✎ Yes ✎ Yes ✎ Yes ✎ Yes	✎ No ✎ No ✎ No ✎ No ✎ No
Active substance abuse at admission Self-reported substance abuse Determined by urine drug screen	✎ Yes ✎ Yes ✎ Yes	✎ No ✎ No ✎ No
Type of substance abused	Alcohol Heroin Cocaine Morphine Hydromorphone Benzodiazepines Amphetamines Marijuana Other (list details):	
Cigarette smoker at admission	✎ Yes	✎ No
HIV viral load at admission	Target not detected (< 40 copies/ml) or _____ copies/mL	
Absolute CD4 count & CD4% at admission	_____cells/mm^3 _____ %	
Weight at time of admission	_____ lbs/kg	
Serum creatinine at time of admission	_____ umol/L	
Estimated CrCl at admission (using Cockcroft Gault equation)	At actual weight: _____mL/min	
Total # of medications prescribed at admission (this includes regularly scheduled and only PRN medications that are actually being used on day of admission)		
Admission medications		
Date of Discharge:	_____ or Still admitted at time of chart review (circle if correct)	

Appendix 1
Data Collection Form: Subject ID #: 15 – 0 _____

Drug Therapy Problems Identified by the Pharmacist

DTP # _____. Name and doses of medications involved: Context and Problem: Suggested Management/Intervention:	
Timepoint DTP occurred at:	Admission to CH Within 24-72 hours of admission After 72 hours of hospitalization Upon discharge
DTP pertains to:	HIV medication OI medication Non-HIV/OI medications being used for other comorbidity management: CV meds; Pain meds; Respiratory meds; Antimicrobial meds; Chemotherapy meds Other (specify):_____
State of the DTP as determined by pharmacist at time of documentation	Actual DTP Suspected DTP Potential DTP
DTP category (circle) *See Appendix 1 of Allenet et al. Pharm World Sci (2006) 28:181-188 for details describing these drug related problems further.*	1.1 Non conformity to guidelines or contraindication 1.2 Untreated indication 1.3 Subtherapeutic dosage 1.4 Supratherapeutic dosage 1.5 Drug without indication 1.6 Drug interaction • Use with caution • Combination to be avoided • Combination contraindicated 1.7 Adverse drug reaction 1.8 Improper administration 1.9 Failure to receive drug 1.10 Drug monitoring
Recommended DTP Management/Intervention (circle) *See Appendix 2 of Allenet et al. Pharm World Sci (2006) 28:181-188 for details describing the types of pharmacist interventions.*	2.1 Addition of a new drug 2.2 Drug discontinuation 2.3 Drug switch 2.4 Change of administration route 2.5 Drug monitoring 2.6 Administration mode optimization 2.7 Dose adjustment
Outcome of the DTP Intervention Recommendation	1. Accepted by physician 2. Accepted with modification by physician 3. Not accepted by physician 4. Considered, but deferred for re-assessment at a later point in time 5. Recommendation not addressed because patient died or left against medical advice (circle) before physician review occurred 6. Other (list details): _____

*Actual DTP = clinically significant; Suspected DTP = clinically significant but unable to confirm it is due to the drug at that time as there may be other possible contributors; Potential DTP = theoretical

Appendix 2: Template for data provided to the expert panel

REB Appendix 2
Abstracted Data Spreadsheet Provided to the Expert Panel:!
CH Study ID #: 15 – 0 _____

!

Type of Casey House (CH) admission	General admission Respite admission
Reason for CH admission	Supportive care/medical focus Supportive care/psychosocial focus Antiretroviral (ARV) adherence support End of life care Caregiver relief
First admission vs. re-admission during study timeframe	First admission Re-admission
Age (years) at admission	
Gender	Male Female Trans: (M to F) or (F to M)
Ethnicity	Caucasian African-American Asian Aboriginal Inuit Other
Total # of medical comorbidities other than HIV infection	
Type of medical comorbidities	AIDS defining opportunistic infection (OI) AIDS-defining malignancies Other AIDS-defining illness Cardiac disease Respiratory disease/condition Liver disease (in particular HCV or HBV infection) Kidney disease Non-AIDS defining malignancies Infection not otherwise captured Pain disorder: acute or chronic pain cancer or non-cancer related pain Other:
Total # of psychiatric comorbidities	
Type of psychiatric comorbidities	Substance abuse/misuse disorder Cognitive disorder including dementia Depressive disorder Anxiety disorder Bipolar disorder Schizophrenia disorder PTSD Adjustment disorder Other psychiatric disorder:
Time duration since HIV diagnosis	_____ months / years
CD4 nadir	_____cells/mm^3
Taking ARVs at admission?	Yes No **If yes,** has patient taken other ARV regimens aside from the regimen at CH admission? Yes/No **If no,** is patient ARV treatment naïve at admission? Yes/No
ARV adherence issues at time of admission?	Yes No
Prior history of ARV non-adherence?	Yes No

REB Appendix 2

Abstracted Data Spreadsheet Provided to the Expert Panel:!

CH Study ID #: 15 – 0 _____

!

Taking OI treatment at admission?	Yes	No
Taking OI prophylaxis at admission?	Yes	No
Taking opioids at admission? Methadone maintenance therapy Methadone for pain Suboxone (buprenorphine/naloxone) maintenance Other: _____	Yes Yes Yes Yes Yes	No No No No No
Active substance abuse at admission Self-reported substance abuse Determined by urine drug screen	Yes Yes Yes	No No No
Type of substance abused	Alcohol Heroin Cocaine Morphine Hydromorphone Benzodiazepines Amphetamines Marijuana Other (list details):	
Cigarette smoker at admission	Yes	No
HIV viral load at admission	Target not detected (< 40 copies/ml) or _____ copies/mL	
Absolute CD4 count & CD4% at admission	_____cells/mm^3 _____ %	
Weight at time of admission	_____ kg	
Estimated CrCl at admission (using Cockcroft Gault equation)	At actual weight: _____mL/min At IBW: _____mL/min	
Total # of medications prescribed at admission (this includes regularly scheduled and only PRN medications that are actually being used on day of admission)		

!

!

! !

REB Appendix 2

Abstracted Data Spreadsheet Provided to the Expert Panel:!

CH Study ID #: 15 – 0 _____

!

DTP # _____. Name and doses of medications involved: Context and Problem:
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DTP # _____. Name and doses of medications involved: Context and Problem:

!

Appendix 3: Template for expert panel rating of drug therapy problems

Appendix 3
Expert Panel's Drug Therapy Problem (DTP) Rating Form:
Subject ID # 15- 0_____

For DTP # _____/ DTP Details_____

DTP Severity Ranking (check most accurate response):

- ○ minor (very unlikely to have any adverse effects; no specific management required)
- ○ moderate (likely to cause some adverse effects or interfere with therapeutic goals but very unlikely to result in death or lasting impairment; close follow-up; dose/treatment adjustment required)
- ○ severe (likely to cause death or lasting impairment and/or necessitates hospitalization)

Likelihood of Causing Harm if the DTP was not identified and addressed (check most accurate response):

- ○ Unlikely to cause harm
- ○ Possible to cause harm
- ○ Probable to cause harm

If above response was possible or probable to cause harm, please answer the next question.

Clinical Impact/Type of Adverse Event if the DTP was not identified and addressed (check all applicable responses):

- ○ potential to cause discomfort/side effect
- ○ potential to cause clinical deterioration
- ○ potential to cause hospitalization
- ○ potential for lasting impairment
- ○ potential for death

Appendix 4: Description of the types of drug therapy problems

(Appendix 1 in Allenet *et al.*[19])

	DRP	Description
1.1	Non conformity to guidelines or contra-indication	*Non conformity of the drug choice compared to the Formulary:* An equivalent is available on the formulary *Non conformity of the drug choice compared to guidelines:* Another drug has a better benefit/risk ratio or a better cost/efficacy ratio according to current guidelines *There is a physio-pathologic contra-indication for the present drug:* for example: the patient is asthmatic and was prescribed beta-blockers
1.2	Untreated indication	*Valid indication without drug prescription* *A new symptom is not being treated* *A drug is missing after patient transfer* *The patient was not given any pre-medication or prophylactic treatment* *A synergic or corrective drug should be added to the ongoing treatment*
1.3	Subtherapeutic dosage	*Dose too low* in this specific case (daily dose) *Length of the treatment too short.* (for example: antibiotic prescription for 5 days instead of 10 days)
1.4	Supratherapeutic dosage	*Supratherapeutic dose:* Dose too high in this specific case There is a risk for accumulation of the drug *Duplicate prescription:* a same active substance is prescribed several times (for example: oral acetaminophen and the oral association of dextropropoxyphen/acetaminophen)
1.5	Drug without indication	*No justified indication for the drug* *The drug is prescribed for too long* (for example: antibiotics prescribed for 15 days) *Therapeutic redundancy*: prescription of two different molecules from the same therapeutic class
1.6	Drug interaction	*A drug interferes with another drug* and can lead to a non adapted pharmacological impact (over or under expressed) *Level according to the French "Red Book" Vidal©* *Interaction reported but not documented in the Vidal©* (specify bibliographic references)
1.7	Adverse drug reaction	*The patient presents an adverse drug reaction with an adequate dosage* (clinical, biological, or kinetic effect)
1.8	Improper administration	The drug is adequate but the mode of administration is not adapted *An other route may be more effective or less costly for the same effectiveness* *The mode of administration is not adequate* (reconstitution, dilution, length of administration) *Inappropriate drug form* *Incomplete formulation* (dosage missing, etc.) *Inappropriate timing of administration*
1.9	Failure to receive drug	*Physicochemical incompatibility between several injectable drugs:* there is a risk of precipitation between drugs during infusion *Patient's non-compliance*
1.10	Drug monitoring	*The patient is not suitably or sufficiently followed-up*: lab tests, kinetics, symptoms (glycemia, EKG, blood pressure, blood concentration of specific drugs, etc.)

Appendix 5: Description of the pharmacist's interventions

(Appendix 2 in Allenet et al.[19])

	Intervention	Description
2.1	Addition of a new drug	*Addition of a drug to the ongoing treatment*
2.2	Drug discontinuation	*Discontinuation of a drug without any substitution*
2.3	Drug switch	*Switch from the currently administered drug to another drug* Substitution for a generic drug or a therapeutic equivalent (according to the local formulary) Switch following a validated protocol Switch for another drug better adapted to the case
2.4	Change of administration route	*Parenteral/oral switch* Alternative drug with equivalent effectiveness and possible oral administration Alternative oral form of a parenteral drug with the same bioequivalence *Choice of a route of administration better adapted to the case*
2.5	Drug monitoring	*Drug monitoring*: INR, kalemia, kinetics, symptoms, etc *Discontinuation/Request for a new lab test* *Discontinuation/request for a new dosage of a specific drug*
2.6	Administration mode optimisation	*Timing of administration* Distribution of doses according to food intake, to drug–food, drug–drug interactions (without modification of the dose) Information on the drug regimen (for example: take on an empty stomach, take during meals, take in the standing position, etc.) *Data on administration procedure* (for example: mode of reconstitution, of dilution, length of infusion, etc.)
2.7	Dose adjustment	*Dose adjustment for a drug with a narrow therapeutic index*, according to its blood level, to renal and hepatic data, or other lab test *Dose adjustment according* to the patient's weight, age, clinical status *Prolongation of treatment*

Appendix 6: Expert panel confidentiality agreement

2015-2016 HIV Pharmacy Specialty Residency Research Project:
Demonstration of Pharmacist Impact at a Community-Based HIV/AIDS Hospital

Expert Panelist Confidentiality Agreement

I, _____, agree that as an expert panelist for the 2015-2016 HIV Pharmacy Specialty Residency research project I will keep all information stemming from the cases evaluated throughout this residency project completely confidential.

_____ _____
Signature Date

_____ _____
Witness Date

Appendix 7: Research ethics board approval letter

UNIVERSITY OF TORONTO

OFFICE OF THE VICE-PRESIDENT, RESEARCH AND INNOVATION

PROTOCOL REFERENCE # 32083

October 6, 2015

Dr. / Mr. / Ms. Community Researcher
SPECIAL - COMMUNITY-BASED RESEARCH
DIVN OF V-P RESEARCH

Dr. Ann Stewart
SPECIAL - COMMUNITY-BASED RESEARCH
DIVN OF V-P RESEARCH

Dear Dr. Community Researcher and Dr. Ann Stewart,

Re: Your research protocol entitled, "Demonstration of pharmacist impact at a community-based HIV/AIDS hospital"

ETHICS APPROVAL	**Original Approval Date: October 6, 2015** **Expiry Date: October 5, 2016** **Continuing Review Level: 1**

We are writing to advise you that the HIV Research Ethics Board (REB) has granted approval to the above-named research protocol, for a period of **one year**. Ongoing research under this protocol must be renewed prior to the expiry date.

Any changes to the approved protocol or consent materials must be reviewed and approved through the amendment process prior to its implementation. Any adverse or unanticipated events in the research should be reported to the Office of Research Ethics as soon as possible.

Please ensure that you submit an Annual Renewal Form or a Study Completion Report 15 to 30 days prior to the expiry date of your current ethics approval. Note that annual renewals for studies cannot be accepted more than 30 days prior to the date of expiry.

If your research is funded by a third party, please contact the assigned Research Funding Officer in Research Services to ensure that your funds are released.

Best wishes for the successful completion of your research.

Yours sincerely,

Raj Maharaj
REB Co-Chair

Darrell Tan, M.D., Ph.D.
REB Co-Chair

Dario Kuzmanovic
REB Manager

OFFICE OF RESEARCH ETHICS
McMurrich Building, 12 Queen's Park Crescent West, 2nd Floor, Toronto, ON M5S 1S8 Canada
Tel: +1 416 946-3273 ● Fax: +1 416 946-5763 ● ethics.review@utoronto.ca ● http://www.research.utoronto.ca/for-researchers-administrators/ethics/

List of Abbreviations

AIDS = acquired immunodeficiency syndrome

ARV = antiretroviral

ASA = acetylsalicylic acid

BID = twice daily

CCR5 = chemokine receptor type 5

CH = Casey House

CNS = central nervous system

COPD = chronic obstructive pulmonary disease

CrCl = creatinine clearance

CYP = cytochrome P450

DTP = drug therapy problem

HBV = hepatitis B virus

HCV = hepatitis C virus

HIV = human immunodeficiency virus

HS = at bedtime

INSTI = integrase strand transfer inhibitor

IgG = immunoglobulin G

IQR = interquartile range

IRIS = immune reconstitution inflammatory syndrome

LFTs = liver function tests

MI = myocardial infarction

NNRTI = non-nucleoside reverse transcriptase inhibitor

NRTI = nucleoside reverse transcriptase inhibitor

OI = opportunistic infection

PI = protease inhibitor

QAM = every morning

TID = three times daily

W = Kendall's coefficient of concordance

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