Article details: 2015-0087	
Title	Emergency department use by persons with HIV in Ontario: a population-based cohort study
Authors	Ryan Ng MSc, Claire E. Kendall MD PhD, Ann N. Burchell PhD, Ahmed M. Bayoumi MD MSc, Mona R. Loutfy MD MPH, Janet Raboud PhD, Richard H. Glazier MD MPH, Sean Rourke PhD, Tony Antoniou PhD
Reviewer 1	Patrick Fleming
Institution	University of Toronto, Division of Dermatology
General comments and author response	Comment #1: "Thank for the opportunity to review this interesting manuscript. This is a well-designed population-based study addresses utilization of the emergency department by HIV-positive patients in Ontario, Canada. It has a robust sample size and uses sophisticated statistical analysis. Its population-based nature allows for a high level of external validity. Although it is apparently the first large-scale study in Canada, similar studies have been published in the United States." Response: We thank the reviewer for this comment. Comment #2: "Study hypothesis is clearly stated and a rationale for the study is provided." Response: We thank the reviewer for this comment. Comment #3: "findings generated in the United States are of limited generalizability to the Canadian context because Canadians have access to universally insured and publicly-financed health care; consequently, emergency room use should not be influenced by health insurance status." This statement is somewhat speculative. My understanding is that Americans who present to the emergency department still receive a bill (which would be much higher than for the equivalent primary care visit). Is there any published data to support this?" Response: We are unclear about this comment, as the statement seems to reiterate our view that insurance status is a determinant of emergency room in the United States. We have not made any changes to the manuscript regarding this point, but welcome clarification if we have misinterpreted the comment. Comment #4: "The authors should provide reference number of their ethics application." Response: Because of the process by which projects conducted at the Institute for Clinical Evaluative Sciences are reviewed by the Research Ethics Board of Sunnybrook, a reference number is not available. Accordingly, we have not made any changes to the manuscript regarding this point. We have uploaded a letter detailing this process as well as a copy of the approval for Editorial review. Comment #5: " Although CTAS is likely an acceptable maker of severity and has been used in other studies, has this been validated? This should be stated." Response: CTAS has not been validated. We have added this as a limitation to our work (page 15). Comment #6: " How was the regression model constructed? E.g. backwards vs. forward elimination. Were any regression diagnostics computed e.g. Goodness-of-fit tests, etc." Response: Because we wanted to adjust for all determinants of emergency room use, we included all relevant covariates in the model. We compared the fit of several different models used for the analysis of rates and counts, including poisson, zero-inflated, hurdle, and negative binomial models. We have not made any changes to the manuscript in this regard, but could do so if the editors felt this was warranted. Comment #7: "Results are clearly presented. The confidence intervals are fairly tight reflecting the large sample size." Response: We thank the reviewer for this comment. Comment #8: " The discussion clearly answers the authors previously stated research question." Response: We thank the reviewer for this comment. Comment #9: " Our study suggests that developing community-based interventions that promote access to outpatient-based mental health care, substance use treatment, oral health…" The results of this paper certainly suggest that HIV-infected patients certainly utilize the emergency department for the above conditions. However, there is no data

	in the manuscript pertaining to the effectiveness of preventative interventions in reducing non-urgent visits to the emergency department nor is any relevant literature for this populated cited. The authors should consider rephrasing the above conclusion." Response: We agree, and have modified this statement to read "Further research examining whether community-based interventions that promote access to outpatient mental health care, substance use treatment and oral health can reduce potentially preventable emergency room visits among persons with HIV is warranted" (page 10). Comment #10: "Were there any data on subgroups available among HIV-infected patients (e.g. intravenous drug users or men who have sex with me)? This would add to the discussion and help when targeting interventions in the future and enriched the discussion." Response: Our databases do not contain information regarding mode of HIV acquisition. We have added this as a limitation of our work (page 14). Comment #11: " In contrast, skin and soft tissue infections accounted for the majority of these episodes in persons with HIV, possibly reflecting complications of injection drug use among susceptible…" I did not identify the data indicating the number of injection drug users in the manuscript. It would be helpful to provide this or cite relevant studies indicating the proportion of users that make up similar HIV-infected populations." Response: We have added a reference to the proportion of people with HIV in Ontario for whom injection drug use was the mode of HIV acquisition to page 14. Comment #12: " A general discussion of other potential bias in the limitations section would enhance the manuscript. E.g. information bias – could there have been differential misclassification of CTAS status. Might there be ascertainment bias – e.g. could diagnoses such as cellulitis be overcalled in HIV-infected patients? Was there any missing data?" Response: We agree, and have added these possibilities to pages 14 and 15 of our manuscript. With respect to missing data, this occurred for the neighborhood income quintile variable among patients without available postal code data. We have added a 'missing' category for the neighborhood income quintile variable to Tables 1 and 4. Comment #13: " rationale for interventions to strengthen access to comprehensive primary care, community-based mental health and drug and alcohol treatment services for persons with HIV" I am not sure if the data can allow the authors to conclude that increased access to such services to reduce emergency department use (although would be quite intuitive). Consider softer wording for such conclusions." Response: We agree, and have modified this sentence (page 15).
Reviewer 2	Shane Smith
Institution	Royal Canadian Medical Service
General comments and author response	Comment #1: " This is a retrospective cohort study using administrative databases to survey rates of emergency department (ED) utilization among a population with HIV. The authors have chosen a control sample by frequency matching with HIV-negative adults on age, sex, and census division. The results confirm the authors' hypothesis that people with HIV in Ontario have higher rates of ED visits than those without HIV. This is very useful contribution to the literature on caring for Canadians with HIV. Population-based data from the United States (authors' reference number 14) is not directly applicable to the Canadian context, where universal health care would be expected to mitigate some of the disparities in access encountered in the US." Response: We thank the reviewer for this comment. Comment #2: "The results presented in Supplemental Table 1 (reasons for emergency department visits) show that, in particular, infectious diseases (including cellulitis) and mental health complaints (including substance abuse), are more common causes for presentation to the ED among those with HIV than those without. As the authors have included in their discussion (paragraphs 1 and 5), these data suggest specific areas for targeted preventative outpatient health care in this population. I think the authors should consider including Supplemental Table 1 more prominently in the body of the paper, instead of only summarizing it in the results section. This table will be of

	particular interest to clinicians providing primary and emergency care to this population." Response: Because there are already five tables and one figure in the manuscript, we have elected to keep reasons for admission as a supplemental Table. However, we will defer to the Editors regarding the most appropriate placement of this table if the manuscript is ultimately published CMAJ Open. Comment #3: "A secondary hypothesis, which forms an underlying assumption of this paper, is that patients in the HIV cohort inappropriately or excessively accessed emergency services because primary care options were not accessible. This assumption makes common sense, and is in line with other medical literature (ex. authors' reference number 1). The present study was not designed to test this hypothesis. However, since much of the authors' discussion depends upon this assumption, they should more directly address how their data does (or does not) support it." (see response below) Comment #4: "The HIV cohort accessed the emergency department at twice the rate of the control group. However, they also accessed primary care at twice the rate. How does this fit with the authors' discussion about inadequate access to primary care?" Response: Comments #3 and #4 address a similar issue, namely the assertion that higher rates of emergency department use in HIV are related to inadequate primary care access. We agree with the reviewer that our findings do not directly support this claim. In light of these and earlier comments reflecting that clinicians may be more cautious in their treatment of patients with HIV, we have made changes to the conclusion of the abstract and page 14 of the Interpretation section. Comment #5: "Although the HIV cohort had more visits initially triaged as low acuity, they required more hospitalizations following assessment, at all levels of acuity. Admission is probably a reasonable indicator that an emergency department visit was "necessary". Is the use of triage level to define "potentially avoidable" visits in this population therefore unjustified?" Response: We believe that this comment is similar in nature to Comment #5 by Reviewer #1 – specifically the validity of triage level as a marker of severity – and that our response to that comment also addresses this point. We have therefore not made further changes to the manuscript regarding this point, but would do so if the Editors disagree. Comment #6: " (Minor point) In the Results section, it seems unnecessary or inappropriate to define 95% confidence intervals for what are, in fact, population parameters (not sample statistics)." Response: We agree, and have removed the confidence intervals.
Reviewer 3	Tim Ramsay
Institution	OHRI, Clinical Epidemiology
General comments and author response	Comment #1: " This is a well-conducted ICES-based study of emergency room use by HIV patients compared to non-HIV patients in Ontario. The authors have gone to great lengths to control for confounding factors that differ between HIV and non-HIV patients that might spuriously affect the apparent rate of emergency room visits. Although some residual confounding is inevitable in any observational study of this nature, I cannot think of anything that could have been done differently with this data to better control for confounding in the analysis of the primary outcome: overall emergency room visits." Response: We thank the reviewer for this comment. Comment #2: " I do, however, have some level of unease with the way the rest of the results are presented; not all results appear to have been adjusted for the important confounders. This is particularly important for this study, as the results appear to clearly demonstrate that there is a great deal of confounding in the unadjusted rate ratios. In particular, based on the raw data, the rate ratio for HIV versus non-HIV emerg visits (67.3 versus 31.2 per 100 person-years) would appear to be 2.16 whereas after adjusting for things like socio-economic status and baseline health status it drops to 1.58. Given this substantial degree of confounding, all results should be similarly adjusted. Unfortunately, with the exception of hospital admission after emerg visits, the other outcomes are presented unadjusted. I strongly suggest that all the results for ambulatory care sensitive conditions (Table 3) should be adjusted for the same confounders used to adjust for the primary outcome."

	Response: We agree with the reviewer and attempted to generate adjusted estimates for each ambulatory care sensitive condition. However, the models would not converge. Instead, we have provided the adjusted rate of all ambulatory care sensitive conditions combined in the Results section (page 11). Comment #3: " Apart from this relatively minor revision, I think this manuscript is well-written and represents an important addition to the literature." Response: We thank the reviewer for this comment. We hope that we have addressed all of the concerns, and that the manuscript is now suitable for publication. On behalf of my colleagues, I would like to thank you for your continued interest in our manuscript. Please do not hesitate to contact us if you have any questions or comments