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Title	Public prescription drug plan coverage for antiretrovirals and the potential cost to persons living with HIV in Canada: a descriptive study
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Reviewer 1	Sharmistha Mishra
Institution	Department of Medicine, University of Toronto, Toronto, Ont.
General comments (author response in bold)	Abstract 1) Recommend couching the objective a bit more carefully and referring to the 'potential influence' rather than 'impact'. The study methods use hypothetical scenarios and a pauci-modeling type approach rather than an empirical study to measure 'impact'. The methods are appropriate for the research question, but would suggest the authors use more nuanced language around the objectives. **It is correct that we did not conduct an empirical study to measure impact and thus we removed the word "impact" in the sentence describing our objective and used language as suggested by Dr. Mishra. The second sentence of the background section of our abstract now reads "We described the reimbursement policy of all Canadian public drug insurance programs for antiretroviral drugs and illustrated how these policies might influence patients' annual out-of-pocket expenditures"** 2) In the abstract – 'higher income case' is mentioned in the results, but not defined in the methods so was not easy to follow (i.e. please define in methods). **We have added more descriptors of the cases in the methods section of our abstract. The sentence is now "We estimated the annual out-of-pocket costs incurred by individuals living with HIV by applying the cost-sharing rules to two hypothetical cases, a single man and a married woman with a net household income of $39,000 and $80,000, respectively...."** 3) Abstract – interpretation statement. The first sentence is self-prophesizing - ("heterogeneity leading to marked variation") and I would suggest rewording that sentence for clarity – e.g. what aspects of the heterogeneity across provinces led to the marked variation (as demonstrated in the results) – or what are the gaps identified between policies that lead to the variation in out-of-pocket expenses. The last phrase re: "potentially impact the HIV epidemic" is somewhat vague and does not really draw directly from the results, and thus - would remove. **We agree, and have changed the interpretation section in our abstract as follows:** **"There is considerable inter- and intra-jurisdictional heterogeneity in the cost-sharing policies for antiretrovirals across Canada's public drug programs. Policy reforms that either eliminate or set national standards for co-payments, deductibles, or premiums would minimize variation and could reduce the risk of cost-associated non-adherence to HIV therapy."** Introduction: 1. The rationale for why out-of-pocket expenses might influence medication adherence is described but not detailed (e.g. there is one statement with 2 references to the potential for a casual link between out-of-pocket expenses and non-adherence). Recommend reducing the content outlining the objectives (see suggestion below) and providing a stronger rationale up-front with details of the potential casual pathway or association, and – importantly – in whom this matters (.e.g. age-group, etc.). **We agree it is important to understand potential reasons why financial burdens may influence adherence and added more detail on the potential casual pathway.** **"Financial burdens are associated with medication non-adherence. Research indicates that medicine costs sometimes compete with other demands, leading to cost-related non-adherence, which may manifest as foregoing prescribed medications in favour of spending on other priorities or altering a medication's dosing to make a prescription last longer. Accordingly, cost-sharing mechanisms that require large out-of-pocket payments for antiretrovirals may be important to address, particularly for people without drug insurance and those with more limited income. Non-adherence to antiretrovirals can lead to uncontrolled HIV replication and subsequently, to increased risks of disease progression, drug resistance, and HIV transmission. Because viral suppression prevents infection at the individual level, and may be effective in reducing transmission at the population level, affordable and accessible antiretroviral therapy for all should be considered and has been highlighted as fundamental component of a public response to the HIV epidemic.** **(page 2, paragraph 2)** 2. Although the journal is Canadian, the readership may be international. Please include a description of the number of PT in the introduction or early in the methods. **We agree, and have added the following sentence to the Introduction: , "Instead of a single national plan, each of the 10 provinces and 3 territorial governments of Canada manage and deliver health care services for their residents....". (page 2, paragraph 1)** **We have also added this detail in our abstract: "All five federal programs and 6 of 13 provincial and territorial jurisdictions offered universal coverage."** 3. Please rephrase the following sentence for clarity: "...process makes recommendations to 18 participating public plans; final product listing decisions are made by individual jurisdictions, at times resulting in inconsistent coverage across the country8,9, including variations in eligibility criteria and levels of subsidy10." **We decided to omit the description of the drug review process and edited the sentence to: "Each plan decides on eligibility criteria for public drug insurance, level of subsidy, and products listed on the drug formulary. Consequently, Canadians with identical prescriptions may pay substantially different amounts and may rely on private insurance, public funders, out-of-pocket payments, or a combination of these to pay for their medication." (page 2, paragraph 1)** 4. There seem to be several statements that could be read as 'objectives'. E.g. part of the objectives was in the middle of the introduction. Could be collapsed together at the end of the introduction where the rest of the objectives were outlined, and stated as one clear objective. i.e. in Para 2 "Thus, we explored the nature and extent of antiretroviral coverage across Canadian jurisdictions to explore the financial burden that people living with HIV in Canada encounter in trying to obtain their HIV medications. Herein, we investigate variations in coverage for expensive drugs for the treatment of HIV infection." Then in Para 3 "Our primary objective was to describe and compare the reimbursement policy of all Canadian public drug insurance programs

for antiretroviral drugs. To illustrate the impact, we used two clinical case studies to estimate the potential annual out-of-pocket expenditures when patients are prescribed HIV medication in each jurisdiction."
We agree, and have stated the study objective once at the end of the second paragraph.

Methods: This is nicely written, but I found it hard to think about who it could be reproducible based on the description of the steps.
1. Page 6, line 16: Please reference the websites searched (or include as an appendix).
As suggested, we have listed the URLs of the websites searched and included as appendix 1.

2. Define 'non-senior'. Page 6, Line 38.
"Senior" in our paper has been defined as 65 years of age or older. (page 3, paragraph 2)

3. How did you decide on the 2 cases study scenarios? It would be helpful to include additional variability such as age and income within the case scenarios based on the sources of heterogeneity identified in the descriptive review. Given the focus on heterogeneity in policies – it would be helpful to know what sources of heterogeneity in policies could have the largest influence in variability in out-of-pocket expenses. Specifically, depending on my characteristics (age, income, etc.) as a person living with HIV – will I experience the least or the most variability in out-of-pocket expenses depending on where I live in Canada? I recognize that the aim was not to be comprehensive (addressed in the limitations section), but I think with a few additional strata, the approach to the 2nd objective could be strengthened and draw directly from the findings from the first objective.
[editorial note: please do not feel that you need to include additional variability to the scenarios.]
We have addressed the selection of the study scenarios in our previous response to the Editors. As suggested by the Editors, we have not included additional variability to the scenarios.

4. Please describe the: age for the two case studies' patients; and the insurance types of the patients' were in the case studies (e.g. were they with and without work-place or private drug coverage/insurance?)
We have provided greater details in our two case studies.
"...we created two clinical scenarios that reflected a typical patient seen in clinical practice that did not have any work-place or private drug insurance and did not belong to groups eligible for publicly funded drug coverage, such as seniors (age ≥65 years), children, and social assistance recipients. The first case study was a single man, age 30, with no dependents and a net annual household income of $39,000. The second case study was a married woman, age 48, with two children and a net annual household income of $80,000." (page 3, paragraph 2)

Results:
1. Statements such as "Several other points merit emphases" are not needed in the results section.
We have removed this statement.

2. Please clarify this sentence (Page 8, Line 45-46): "In addition, the government of Quebec would have collected a greater annual income-based premium compared to the man". Also, the sentence implies that the reason for the difference is gender here – is that correctly inferred?
Quebec is the only jurisdiction that requires a mandatory premium to be paid by all residents without private drug insurance. The amount is income dependent and the phrase "compared to the man" was meant to refer to the first scenario. To provide clarity and the reason for the difference, we have changed the sentence to: "Our second hypothetical case, a married woman with about twice the annual household income of the first case, received her medications at no cost in the same six regions, incurred the same expense if she lived in Nova Scotia, the Yukon, and Quebec (although would have had to pay a greater premium when she filed her higher household tax return) and paid $2720 to $7993 (17% to over 50% of the antiretroviral cost) if she lived in one of the remaining regions (Figure 1 and 2, appendix 3). (page 5, paragraph 4)

3. Please provide more details to understand these results when looking at the figure (Figure 1) – it took several attempts at reading to try to understand. Also, the statement re: "inversely proportional" is really drawn from the description of the policies rather than the calculations since only 2 scenarios examined. "Public reimbursement of drug costs was inversely proportional to household income in Manitoba, Newfoundland and Labrador, Ontario, and Saskatchewan but was independent of income in Nova Scotia, Quebec, and the Yukon (Figure 2)."
We appreciate the feedback from Dr. Mishra in trying to understand our results in relation to the figure. We believe the confusion may be that we were not clear when describing the results displayed in Figure 1, that both intra- and inter-provincial/territorial variances were evident.
We have removed the statement "public reimbursement of drug costs was inversely proportional to household income..." and changed the results section to simply read "Our first hypothetical case of a single man with an annual income of $39,000 had no out-of-pocket expenses if he lived in ... but had an annual prescription cost that varied from $45 to $1866 if he resided elsewhere (Figure 1, appendix 3). Our second hypothetical case, a married woman with about twice the annual household income of the first case, received her medications at no cost in the same six regions, incurred the same expense if she lived in Nova Scotia and the Yukon, and paid $2720 to $7993 (17% to over 50% of the antiretroviral cost) if she lived in one of the remaining regions (Figure 1 and 2, appendix 3)
We have tried to provide more detailed analyses in the interpretation section (page 6, paragraph 2) regarding the relationship of income and out-of-pocket costs.
". Our main finding was that there is considerable variability across public drug insurance programs for these high-cost drugs, such that an individual may incur hundreds or thousands of dollars of additional costs based solely on location. Our descriptive review identified this disparity was most striking for high income earners without private drug insurance. For these individuals, out-of-pocket expenses would be zero in six regions and could be up to 100% of the antiretroviral cost in jurisdictions with no maximum annual contribution, namely Saskatchewan, Manitoba, Ontario, and Newfoundland and Labrador. While the principle of progressivity - that high income earners should contribute a greater proportion of their income to shared expenditures - is often cited as a criterion for fairness, our cases illustrated that this philosophy is not universally adopted across the country. In our scenarios, the lower income male paid a greater proportion of his income for antiretrovirals than the woman with a higher income in Nova Scotia, Quebec and the Yukon (Figure 3).

4. Please clarify or rephrase/rewrite the following sentence: Thus, based on her location, she incurred no out-of-pocket expenses to obtain her antiretrovirals or paid over 50% of the antiretroviral costs (Figure 3)."

	We have removed this statement and replaced it with "Our second hypothetical case, a married woman with about twice the annual household income of the first case, received her medications at no cost in the same six regions, incurred the same expense if she lived in Nova Scotia, the Yukon, and Quebec (although would have had to pay a greater premium when she filed her higher household tax return) and paid $2720 to $7993 (17% to over 50% of the antiretroviral cost) if she lived in one of the remaining regions (Figure 1 and 2, appendix 3). (page 5, paragraph 4) Interpretation: 1. In general, it would be good to specify which conclusions are drawn from which aspects of the analyses. For example with statements such as "This disparity was most striking for high income earners without private drug insurance whose out-of-pocket expenses were zero in six regions and up to 100% of the antiretroviral cost in Newfoundland and Labrador."... it seems evident that the conclusion was drawn from the descriptive work, but I then expected to find its corollary in the case-based scenarios. So some additional clarity perhaps with statements such as ..."our descriptive review identified that...." and "our case-based scenario demonstrated that..." might help the reader. **We agree, and have added these phrases throughout the first section of our interpretation section:** **"Our descriptive review identified this disparity was most striking for high income earners" (page 6, paragraph 2)** **... our case studies illustrated that this principle is not universally adopted...(page 6, paragraph 2)** **...our review also found a considerable range of program complexity in terms of eligibility...(page 6, paragraph 2)** 2. Please state where (which countries) in: "Our finding of heterogeneity with Canada's public drug programs is consistent with others;..." **We apologize for this confusion and can understand how "others" may have been interpreted as "other countries". We have reworded the statement to "Our finding of heterogeneity with Canada's public drug programs is consistent with prior work" (page 6, paragraph 3)** 3. This is a very important point. Please go into further detail (e.g. around subsidies – which ones, and are there ways to address that?)..." the main differences in coverage were due to variations in the amount of individual subsidies. Our results suggest that while establishing antiretroviral prescribing programs and formulary listings are necessary conditions for access to coverage, they are insufficient to ensure universal equitable access to antiretrovirals." **We agree, and have provided additional details regarding the difference in subsidies and tried to make more explicit examples of solutions to address the disparities. Our analysis did not allow examination of which policy is most prohibitive but does present options for reform.** **"...the main differences in coverage were due to variations in the amount of individual subsidies based on criteria. In six jurisdictions, antiretrovirals are fully covered with an HIV diagnosis being the only requirement for eligibility; in the remaining regions, income and age primarily determined the subsidy received. Our results suggest that while establishing antiretroviral prescribing programs and formulary listings are necessary conditions for access to coverage, they are insufficient to ensure universal equitable access to antiretrovirals. (page 7, paragraph 1)** **Examples of policy options that could address these inequities in eligibility criteria and value of subsidies include a comprehensive pharmacare program or explicit national standards for listing and reimbursing drugs for all age and income groups" (page 7, paragraph 2)**
Reviewer 2	Hug Soudeyns
Institution	Unité d'immunopathologie virale, Centre de recherche du CHU Sainte-Justine, Montréal, Que.
General comments (author response in bold)	Comments to the Author CMAJOpen-2018-0058; Yoong et al. Please also consider the following specific comments: 1. Page 5, third paragraph. References no. 19 and no. 22 are not cited in the text (also see Page 13). **With reorganization and revisions to our text, we have correspondingly changed the citations and their order.** 2. Page 6, third paragraph. Could the authors explain why those two precise clinical scenarios were selected? Also see Page 8, third paragraph. **We have addressed this comment in our response to the Editors (Editorial comment #6).** 3. Page 7, 2 lines from the bottom. How do the authors define « seniors »? **Seniors have now been defined in our manuscript as 65 years or older (page 3, paragraph 2)** 4. Page 10, line 13. « ...national pharmacare... ». One element that is not mentioned in the paper is that in Canada, healthcare is under provincial jurisdiction as derived from the Constitution Act, 1867 (« ...exclusive provincial responsibility for the direct delivery of most medical services... ». This might not be immediately obvious for CMAJ readers who are not of Canadian origin, Canadian residents or Canadian nationals. **We agree, and have added the following to our Introduction:** **"Instead of a single national plan, each of Canada's 10 provinces and 3 territorial governments of Canada manage and deliver health care services for their residents, including medication coverage (several federal plans insure specific populations)." (page 2, paragraph 1)**
Reviewer 3	Kednapa Thavorn
Institution	Clinical Epidemiology Program, Ottawa Health Research Institute, Ottawa, Ont.
General comments (author response in bold)	Major comments 1. Why did the authors focus on the websites of public plans? The details of drug reimbursement policy shown in the websites might by varied across the plans, how did the authors ensure that the information shown on the website is sufficient and up-to-date? Under the methods section, the authors indicated that extracted data were validated by a pharmacist in each jurisdiction. How was the pharmacist identified? It would be great to describe how these pharmacists were identified and chosen. Did the pharmacist work at a designated pharmacy to dispense ARVs for people living with HIV? **Government websites were used to gather data as Canada's standards are such that policies be transparent and available to the public. However, we appreciate that information on websites may not be comprehensive and details may have been missed and we have added this as a limitation. To ensure the information was valid and up-to-date, we asked a local pharmacist to review the data gathered from the website for accuracy. Many of these pharmacists were invited to be a resource for our work because they belong to a national network of pharmacists**

	who provide HIV care and are representatives of their region. **On page 3, paragraph 1 we included the statement: "To validate the data, we asked a pharmacist in each jurisdiction with expertise in providing HIV care or familiarity with the respective antiretroviral reimbursement plans and systems required to secure drug coverage for individual patients to review the information for accuracy (with the exception of the federal programs and Nunavut where we did not have an email address of a representative pharmacist).** 2. Please provide the justification why two clinical scenarios were chosen to present. The contexts provided by the authors may not be sufficient to explain the variation in the out of pocket cost and catastrophic health care expenditure because the cost may depend on many factors such as age, the presence of comorbidity, and access to an employer sponsored insurance. **We have addressed this comment in our response to the Editors (Editorial comment #6).** 3. The authors calculated prescription cost based on the Ontario Drug Benefit Formulary price. Although this approach could reduce variation in medication prices negotiated by each drug plan, it may limit the implication of the study findings to other jurisdictions. It would be great to perform scenario analyses by applying prescription costs obtained from other jurisdictions. **It is true that medication prices may differ in other jurisdictions and using a higher or lower drug cost may have resulted in smaller or greater variation; however, we believe the implications would be minimal as several programs only use income to determine a deductible or the policy is such that there is a maximum out-of-pocket expense. For example, even if we used a lower drug price, the out-of-pocket payment in British Columbia would still be zero, the expense in Ontario would still be ~4% of the household net income, and the resident of the Yukon would still only pay $250 annually. This is regardless of drug price. However, we appreciate the possible variation and have included it in our limitations.** **"Although we solely used the listed drug price from the Ontario drug benefit formulary for our out-of-pocket expenditure comparison and other jurisdictions may have negotiated higher or lower medication prices resulting in different out-of-pocket costs, the actual price would have no implication for patients in jurisdictions which only used income-based deductibles (e.g. Manitoba, Ontario, and Saskatchewan) or capped out-of-pocket payments (e.g. Quebec, Yukon)." (page 8, paragraph 1)** 4. On Page 8, the authors reported that "…there were interprovincial differences in antiretroviral prescribing and dispensing, with five jurisdictions placing restrictions on the prescriber authorizing the regimen and five assigning designated pharmacies to dispense these therapies.". Please list the name of those jurisdictions. **We thank the reviewer for asking us to review the jurisdictions with restrictions as we noted that we made an error in our summation.** **The statement now reads "there were interprovincial differences in antiretroviral prescribing and dispensing, with seven jurisdictions (Alberta, British Columbia, New Brunswick, Nova Scotia, Ontario, Saskatchewan, and the Yukon) and Correctional Service Canada placing restrictions on the prescriber authorizing the regimen, and five provinces (Alberta, British Columbia, New Brunswick, Nova Scotia, Prince Edward Island) and Correctional Service Canada assigning designated pharmacies to dispense these therapies." (page 5, paragraph 3)** Minor comments • The title is misleading. It would be great to revise to reflect that this study was based on a review of public drug plan websites and two case studies. **We have agreed with the editor that our research is best described as a descriptive study, thus the title has been changed to "Public prescription drug plan coverage for antiretrovirals and the potential cost to persons living with HIV in Canada: a descriptive study".** • Under the method section describing the annual out-of-pocket expenditure, please highlight that the authors only included drug ingredient cost but excluded mark-up and dispensing fees. **In our methods section under the subheading of calculation of cost we have the statement "We calculated prescription costs using the amount reimbursed by Ontario's Ministry of Health and Long-Term Care to pharmacies, as listed on the Ontario Drug Benefit formulary in December 2017. We therefore assumed that prices were similar across jurisdictions and that any effect of negotiated prices discounts were minimal and excluded mark-ups and professional's fees." (page 4, paragraph 1)**