Article details: 2022-0113
Title: Reasons for not using HIV PrEP and strategies that may facilitate HIV PrEP uptake in Ontario and British Columbia among gay, bisexual and other men who have sex with men
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Reviewer 1: Dr. Pierre-Paul Tellier
Institution: McGill University
General comments (author response in bold)

This is a cross sectional study of gay, bisexual and other men who have sex with men to identify reasons for not using PrEP and strategies that may facilitate its use. The study provides some useful information, but it is limited by its small sample size. The text is succinct but provides us with what is required to understand this study. It is accompanied by several charts that are used to illustrate and summarize the data. Based on the included track change version of the manuscript it is evident that the authors have received feedback, accepted it, and have adjusted the paper accordingly. I would agree with the publication of this manuscript since it provides us with data on the population in two provinces in Canada and will have some impact on clinical work.

The abstract provides us with a good summary of the study and should remain unchanged

1. The introduction presents us with the currently known information on the reasons that affect the uptake of PrEP. I like the way the authors have divided this material into, the individual, interpersonal, community and structural level. The aims or questions that guide this analysis are clearly stated. In stating the aims the GBM acronym is first used. However, it is not explained, and it should be. This could be done by either adding the definition at this point or adding the acronym at the end of the title in parentheses.
Changed as suggested. (Page 3, line 27)

Methods

2. We are first presented with an explanation as to why the authors have chosen to conduct this study in British Columbia and Ontario. They state the similarities and the major difference between the two provinces. Recruitment of participants is explained as well as data gathering and inclusion and exclusion criteria. We are provided with some information on how the survey was generated. However, there is no explanation given on how the list of reasons for not using PrEP and the strategies to improve uptake were generated. This should be clarified to better understand the validity of the questionnaire.
Included in the last two paragraphs is how the data is presented, how the sample size was calculated, ethics approval and where and how the data is stored.
Please see our response to comment #2 from the Editor #1.

Results

The principal findings are presented in the text and the tables provide a complete picture of the information gathered.

Thank you. Please see response to individual comments above.

Discussion

This is based on the results and presents some ways in which to address these issues. The limitations are appropriate and outlined in the last paragraph. They include the fact that the sample size is limited and affects the analysis of the data.
Thank you. Please see response to individual comments above.

Conclusions

These are supported by the results and offer suggestions for further interventions.
Thank you. Please see response to individual comments above.

Tables and appendices

There are several of these which presents all the data gathered in relation to this particular manuscript. This makes the paper more interesting.
Thank you. Please see response to individual comments above.

Reviewer 2: Dr. Affan Shoukat
Institution: Yale University
General comments (author response in bold)

In this manuscript the authors present the results of an observational survey where they studied the barriers to PrEP usage. I find that the science is methodologically sound and add value to current understanding of HIV dynamics and population dynamics. The data in this study can be further used to parametrize models and inform public-health decision-making.
Thank you. Please see response to individual comments below.

1. There are a number of abbreviations used in study that are not defined. For example, the term 'GBM' appears in introduction, which I believe stands for 'gay and bisexual men', though this took me a minute to realize. Similarly, the term 'MSM' is defined on page 9. Please be clear with the terminology.
Changed as suggested. (Page 3, line 27)

2. The phrasing 'We also asked never PrEP users' (page 9, line 17) can be presented more clearly, i.e. 'we also asked non-PrEP users'. Initially, I thought there was a typo and the phrase was really saying 'we also never asked PrEP users...'. This language is repeated again in captions and elsewhere in the manuscript.
We have replaced the term with "(respondents, participants or GBM) who had never used PrEP". Initially, we used the term "never PrEP users" to differentiate them from those who used PrEP in the past but had stopped.

3. I am curious to hear the author's interpretation of the reported p-value have in Table 1? For example, what is the significant of the p-value of the 'age' column?
Thank you for pointing that out. The biostatistical reviewer also provided good advice about limiting the number of statistical tests to reduce the risk of type I error. We have dropped the column with the p values since our main aim is to

describe barriers to PrEP and possible interventions to increase its uptake, rather than to do hypothesis testing.

Reviewer 3: Dr. Joanna Merckx
Institution: McGill University Faculty of Medicine
General comments (author response in bold)

Summary

The manuscript investigated reasons for non-PreP use and surveyed strategies to improve PreP uptake in a gay, bisexual and MSM population in two Canadian provinces with differing medication re-imbursement structures. It provides a mostly descriptive analysis of the binary reported answers of a group of 260 non-prior PreP users. Common reasons for non-uptake that were reported were worries about side effects, insufficient perception of being at risk and costs, among others. Structural improvement of shorter waiting time prior to access to medication was by a majority of participants identified as a potential mechanism to improve uptake.

Importance and originality

The manuscript is mostly descriptive and seems a revision after a first submission. Direct surveyed information from patients is important and the topic is of interest. The manuscript might be well suited for a short communication. The manuscript remains sometimes complex to read with its long sentences. In addition, further qualitative studies seem necessary to improve the knowledge on how to improve uptake, given the questions (and answers) do not provide in depth insight.
We have modified some sections of the manuscript and added sub-headings to improve readability. We also agree with the Reviewer that qualitative studies would be useful to improve knowledge on how to improve PrEP uptake, and note that a qualitative component of the PRIMP project involves in-depth interviews with GBM in both provinces to explore these issues in more detail. We have briefly added a comment to this effect in the Discussion. (Page 9, line 1)

Major comments

1. While a descriptive analysis with provision of proportions and the differences between groups is informative as such, additional details in the analysis can improve the value of this study. For example, it is not known from the results section which answers were often given together or separate. Are some choices mostly affirmative together? In the introduction a detailed categorization within a framework is given (individual level, interpersonal level, structural.), this is missing in the reporting of the results.

We agree with the Reviewer that identifying patterns of responses could be informative. However, we decided to present a direct description of the results instead of analyzing clusters of responses, for which we would need a larger sample size. In addition, we chose to sort the list of barriers and facilitators based on number of responses, rather than following a specific framework, in order to highlight which problems and interventions might be of greatest importance. However, in response to this comment, we have added a comment to the Methods section reinforcing that the list of barriers and mitigation strategies included items

relevant to the individual, interpersonal and structural levels discussed in the introduction. (Page 4, line 29)
We have added information regarding how participants were instructed to answer the questions, in the methods section (Page 4, line 32)

2. Extra assessment: How many would be more covered if Ontario had similar payment structure? Is the proportion nonusers also higher in Ontario compared to BC? How much higher in the sample? Are there other data on at-risk population on PreP by province? These background data are needed to better interpret the differences between the provinces. This is also necessary to evaluate the representativeness of the study population and the generalizability.
This is a relevant point. Although we believe increasing coverage is fundamental to increase PrEP uptake, it is unlikely that increasing coverage will solve the issue of access to PrEP. We have added information on this in the discussion (Page 8, line 17). In addition, we have expanded our discussion to include limitations in terms of generalizability. (Page 9, line 5).

3. Only one province with PreP coverage and one without covered access to PreP have been included in the study. Would including more provinces with different reimbursing schemes not be necessary or other study designs (time-series - diff-in-diff), be necessary to assess the impact of reimbursement of Prep?
In this paper, we reported reasons for not using PrEP and strategies that might influence people's decision to start PrEP, and we found that cost is a big barrier that deserves being highlighted. We agree that including more provinces and using a study design like time-series would be great to examine the effects of policy interventions such as introducing universal coverage on PrEP uptake. However, we our paper was not intended to study the effects of policy interventions; we feel that such questions would best be addressed in future work.

4. More formal subtitles, mostly in the methods section can improve readability of the manuscript.

Changed as suggested.

5. It is not clear by reading the methods section or results how the questions were rated or asked. Were the questions yes/no questions? Addition of the questions is a major improvement. This can however be described in the methods section.
We have added this information in the methods section. (Page 4, line 32)

6. How many missing data were there by question, was this differential by question? Or were there no missing data? More detail on the methods of the questions asked and reporting on missingness can help interpreting the results.
There was missing data. We analyzed and present data for each individual variable (proportions are based on available data for each variable presented). We have added information in the methods section for clarity. (Page 5, line 9)

7. Discussion: Side effects are summed up for the reader, however it is unclear *how* side effects affect the reluctance to take PreP and if they are uberhaubt in agreement with the proven side effects (as discussed in the result section where evidence-based side effects are placed in their context, including the rarity of events). Is it known if the feared side-effects are those discussed by the authors?

Good point. Kidney toxicity is one of the most common concerns. Unfortunately, however, the survey not distinguish which specific side effects people are more concerned about and how that relates to their decision of using or not using PrEP.

8. Including health care providers in providing better information as well as re-informing the true risk of the patient implies that the at-risk participants have come out as MSM towards their provider. Canadian research shows that there is still a large proportion who has not come out to their provider or finds this difficult to discuss. How can this element be included in the strategies or does this influence the findings (are those only among those who came out)?

Thank you for that observation. We agree that coming out to one's provider is an important upstream determinant of whether PrEP services may be accessed. 27% reported not feeling comfortable discussing their sexual health with their provider (data not shown), indicating that there is plenty of room for improvement. Indeed, people who don't feel comfortable disclosing their sexual health (including sexual identity) face bigger barriers. We have included in the discussion that providers should acknowledge the diversity of sexual behaviors and sexual identity of their patients. (Page 8, line 31)

9. Table 1:

*it is not necessary to report p-values in the table 1, this is not informative; even less so is starring its statistical significance.

We agree. We have deleted the column with p values from the tables.

*Is there information regarding the eligibility for provincial medication re-imbursement among immigrants? (insurance structures are provided in table 1 - however, how do factual numbers compare to the eligibility criteria by province?)

Immigrants are a very diverse group including naturalized citizens, permanent residents, students, refugees, refugee claimants and temporary workers. Their eligibility for medication re-imbursement depends whether they have private insurance through employment/school or if they belong to eligible groups for full coverage such as those younger than 25 or older than 65 in Ontario, or other programs. (See page 3, line 40)

In our sample, 214 (82%) were Canadian citizens, 19 (7.3%) were permanent residents, 1 was a refugee claimant, 14 (5.4%) were temporary workers, 5 were students, 8 were "other".

This is the distribution of medication insurance based on immigration status for the entire sample (not included in the paper).

Type of medication coverage	Citizens	Permanent residents	Refugee claimants	Temporary workers	Students	Other	Total
Private	126	10	0	9	4	4	153
IFHP-refugees	0	0	1	0	0	0	1
NIHB-indigenous	5	0	0	0	0	0	5

BC Fair pharmacare	1	0	0	0	0	0	1
Ontario Drug Benefit	17	3	0	0	0	0	20
Out of pocket	56	6	0	4	1	4	71
Other	1	0	0	0	0	0	1
Prefers not to answer	6	0	0	1	0	0	7
Total	212*	19	1	14	5	8	259

*2 did not provide information.

In BC, eligibility for publicly funded PrEP is consistent with the Canadian PrEP guidelines.

10. the context is missing on how this sample compares to the MSM community in both provinces, regarding baseline characteristics. In which sense is this a selected population? (Compare to other running Canadian cohorts, who used different sampling methods).
Compared to national surveys of GBM like Sex Now, our sample is ethnically more diverse, with more years of formal education, more often with a history of STIs. This is expected, since our sample comes from large urban centers and participants were recruited primarily from primary care settings.
We have added information in the discussion addressing this. (Page 9, line 6)

11. A prior diagnosis of an STI and prior PEP use is conditional on access to health care and being able to pay for those tests and treatment. How does this affect the selection of the study population? Which way will this bias the results?
We have now addressed this point in the Limitations section of the discussion (Page 9, line 13). We believe that including a study population with less access to care, would have resulted in a higher proportion of people citing barriers such as cost.

Minor comments

12. The difference in re-imbursement structures between the 2 chosen provinces is important, can this be included in the abstract as background?
Thank you for this suggestion. We have included more information about this in the methods section, as a context of the study setting. (Page 3, line 40)

13. Which cities have been included in the two provinces? Can this be added to the supplement.
The cities (Toronto, Ottawa, Hamilton, Vancouver and Victoria) are mentioned in the methods section). (Page 3, line 36)

14. Did the authors of the survey also ask the participants for non-included barriers and facilitators? i.e. additional open question? If not, why not.

An "other" option was included. For barriers, examples are included at the end of table 3. That was not the case for facilitators, because we anticipated a high variation of responses, most of which would likely be relevant to the individual respondents and not applicable to many other portions of the GBM population.

15. Will the results be reported back to the participants of the survey? Will the data be made available in lay terms to the included community?

We did not seek permission from our Research Ethics Board to contact study participants with the results of the study. However, we routinely conduct a variety of knowledge translation activities as part of the PRIMP project to inform the community of our results. We hold regular meetings with the community advisory board (CAB) to share updates and results of the study. We have also presented key findings from the PRIMP study at regular meetings of relevant community networks including the Gay Men's Sexual Health Alliance (Ontario) and HIM (BC). Finally, we are planning lay summaries of the work for broader dissemination on our study website. Since we believe the Reviewer is asking this question for informational purposes only, we have not made modifications to the manuscript in response to the question.