

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Health programs and services addressing the prevention and management of infectious diseases in people who inject drugs in Canada: a systematic integrative review
AUTHORS	Bouzanis, Katrina; Joshi, Siddharth; Lokker, Cynthia; Pavalagantharajah, Sureka; Qiu, Yun; Sidhu, Hargun; Mbuagbaw, Lawrence; Qutob, Majdi; Henedi, Alia; Mitchell, Levine; Lennox, Robin; Tarride, Jean-Eric; Kalina, Dale; Alvarez, Elizabeth

VERSION 1 – REVIEW

REVIEWER	O'Keefe, Daniel Burnet Institute
REVIEW RETURNED	28-Jan-2021

GENERAL COMMENTS	<p>I commend the authors on the work that has gone into their paper so far - it is definitely a lot of effort. And whilst I understand the authors intent with the paper, I have to admit being quite conflicted with it. There is admitted value in organising recommendations for Canadian policy and practice following an extensive review of the available scientific literature.</p> <p>Conversely, I don't believe the authors have actually addressed the stated purpose of the work, as given in the introduction: "The purpose of this study is to describe key features of health programs and services in Canada relating to the prevention and management of infectious diseases in PWID, with the hope of informing policy, practice and future research".</p> <p>Rather than being a description of the "key features of health programs and services in Canada", the paper is instead a description of the reviewed papers - generally being information of little significance.</p> <p>As an example, the results section regarding SIFs describes the number of papers focusing on HIV or HCV, whether cost-effectiveness analysis was performed, and some of the study outcomes in the reviewed papers. The section does not describe the number, variety or distribution of SIFs operating in Canada (which has the highest number of SIFs of any country), whether SIFs are actually cost-effective, or how they impact the outcomes of interest. This example is generally consistent with the other results sections of the paper.</p>
-------------------------	---

	<p>The information contained in Table 2 is the paper's key significance - and elaborating on this information should be a priority for the authors, because currently, the reader has little foundation on which to base these recommendations (the "implications for policy" section runs for less than one page, compared to approximately ten pages of other results). As a reader, I would find the information in Table 2 far more digestible if it was first supported by a specific write-up per intervention - including the level of implementation (coverage, distribution, effectiveness, etc) and outcomes for Canadian PWID.</p> <p>In the introduction, the authors state that "The scope of health care services and programs across Canada that aim to prevent and treat infectious diseases in PWID remains unclear". However, I have difficulty seeing how this paper brings clarity to the scope of Canadian service provision.</p> <p>To amend this issue, I suggest some amendments:</p> <ol style="list-style-type: none"> 1) Restate the papers objective or broaden your literature search. Because the authors have focused on reviewing scientific literature, you are constrained by what has been published (as said in the limitations). This means you are not giving a clear indication of the level and type of service provision in Canada, but rather what has been published. Therefore - in essence, if it's not published, it hasn't happen - which is obviously not correct. 2) Overhaul the results section. As a reader, I'm not interested in how many papers explored cost-effectiveness of a particular outcome, but the results of that cost-effectiveness. 3) Give far more space to the write-up of the policy implications. Without Table 2, this discussion constitutes approximately 3 pages in the results and discussion sections. <p>Because the reviewed papers were too heterogenous to perform a meta-analysis, the authors are not constrained by a statistical method, and could apply a narrative review methodology. This I feel would be of far greater value to the audience.</p> <p>The authors clearly have the right intentions with the paper, but I don't think the correct approach. I feel that bringing more depth to the review will result in quite an interesting and valuable paper.</p>
--	--

REVIEWER	Springer, Sandra Yale School of Medicine, Internal medicine
REVIEW RETURNED	02-Jun-2021

GENERAL COMMENTS	<p>This is a Systematic review of health programs and services addressing the prevention and management of infectious diseases in PWID in Canada.</p> <p>Eligible articles were those that were published between 2008-2019 that addressed Injection or IDU and health programs or services related to prevention or management of infectious diseases in Canada . They identified 835 articles and 97 of which were included in this systematic review. Overall it is an important</p>
-------------------------	---

subject matter and requires more in depth review as the authors intended. The work that went in to this is tremendous but I would suggest more directed careful organization of the data organized in tables per subsection or at least referencing the studies where points are made to better synthesize the data is needed to strengthen the paper and might want to organize by what the authors found.. where were the major gaps ? what would be the recommendations for future research/ policy changes etc? For instance the U.S. National Academy of Sciences, Engineering and Medicine (NASEM) released in January 2020 a guideline after a study in the U.S. to evaluate programs that did integrated Infectious disease and opioid use disorder prevention and treatment services and made recommendations on overcoming barriers to successful integration of addiction and infectious disease prevention and treatments. Perhaps something can come of this review ?

Abstract:

Results section: Could they state the number of the articles that addressed testing and management of HIV and HCV and the other prevention and treatment strategies identified. It is not clear in the abstract the number of articles or exactly what were the key findings?

Introduction ...

Page 5, "against medical advice (AMA)..." tends not to be used any longer as stigmatizing and rather use 'unplanned discharge ' or 'self discharge'.

Results:

Please use person first language including in table 1 " HCV positive / HIV positive/ prisoners- should be ' persons without HIV , with HIV, persons in prison etc...'

It seems like the first part of the results section is just a list .. is there a better way to synthesize this data .. maybe a table that addresses the study included then with columns going across that have the different attributes like type of study, population, jurisdiction, number, infection , health care system etc , type of healthcare provided/ to understand the different research done?

Under Health programs and services- could you group these in tables? For the second paragraph under this section of testing, prevention with antivirals for HIV or HCV ... the references should be given for each section ... starting with 'many studies address the provision of antiviral treatment and testing n=27, 27%) " then list the references that you are referring to for these 27 studies or refer to table to put them in to compare them ...

Term antivirals used. , ART used for antiretroviral treatment for HIV but I don't think spelled out unless done earlier.. ART and HAART typically are the same ... unless you think they mean different things? you could use one term.

	<p>It is hard to understand what is meant by these results.. they just seem to be listed</p> <p>Would be better to characterize the studies in tables and what they evaluated, how they evaluated the different outcomes ...</p> <p>It is also hard to understand what the authors are referring to “The post-exposure prophylaxis intervention was community based...” what are they referring to? Next sentence “ similarly point of are testing and seek and treat initiatives included...” are they discussing the two studies referenced...? It is not clear The last “ TasP involves the delivery of ART as a method of HIV prevention... “ . So what exactly are they discussing ? one study or description of what TasP is? In fact this is more of a definition then should be introduction and what it means.. U=U campaign etc that suppression of HIV means cannot transmit to those with HIV if partake in condomless sexual intercourse or share IDU equipment etc...</p> <p>HCV .. the articles are not referenced in the text. as well as other subsections.. SSPs, peer counseling etc.</p> <p>Same for the other sections like Supervised injection facilities & Opioid agonist therapy etc..... need references when discussing each section e.g.“ a number of studies n=12) and would highly suggest a separate table of studies for each section to denote what was studied etc so the reader can evaluate the studies faster and denote the sections ... and then provide references next to each statement... so “ seven studies focused on methadone MMT” (list the superscript citations for the studies).... Same for heroin assisted treatment and so on / as well as for the other sections in the results section.</p> <p>Of note, We now refer to opioid treatment as medication treatment for opioid use disorder (MOUD).</p> <p>Discussion:</p> <p>Typically the first sentence states what you found.. this just says you found 97 articles included in the study.. Typically you make your main point here so would restructure.</p> <p>Overall it is needs more work to identify the common themes, gaps in the literature and recommendations for future research. It was hard to really identify what studies did what and a way to make sense of the literature.</p>
--	---

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Daniel O’Keefe, Burnet Institute

Response: Thank you for this criticism. In response to the above two comments, the stated purpose of the work has been re-worded in the introduction and throughout the text in order to better characterize the

content of the paper and more accurately describe the goals of the paper. This revision has also been addressed in a below comment, where we have provided greater detail on the changes made to address these criticisms.

As an example, the results section regarding SIFs describes the number of papers focusing on HIV or HCV, whether cost-effectiveness analysis was performed, and some of the study outcomes in the reviewed papers. The section does not describe the number, variety or distribution of SIFs operating in Canada (which has the highest number of SIFs of any country), whether SIFs are actually cost-effective, or how they impact the outcomes of interest. This example is generally consistent with the other results sections of the paper.

Response: Thank you for the above comments. Due to constraining word limits, description of the number, variety and distribution of SIFs operating in Canada was omitted. This description has now been included in the text. Similar information has also been included in the other results sections.

As was noted in these comments, we were unable to determine overall cost-effectiveness of SIFs due to the heterogeneity in study methodologies and as each included study has used different methodologies, modelling techniques and focussed their research question on different outcomes. To address the above comments, we have added a description of the effectiveness of the interventions, as described by the authors. We also hope that you may now refer to Supplementary Table 1, which provides a summary of the results of each included study.

A summary of implications for policy, practice and future research has been described for each health program or service identified. This description now provides details on how each study impacts the outcomes of interest of this paper, which is to inform policy, practice and future research, and reflects the information which is summarized in Table 2.

The information contained in Table 2 is the paper's key significance - and elaborating on this information should be a priority for the authors, because currently, the reader has little foundation on which to base these recommendations (the "implications for policy" section runs for less than one page, compared to approximately ten pages of other results). As a reader, I would find the information in Table 2 far more digestible if it was first supported by a specific write-up per intervention - including the level of implementation (coverage, distribution, effectiveness, etc) and outcomes for Canadian PWID.

Response: Thank you for your comment and, indeed, the information in Table 2 is of critical importance to the paper's findings. As per these comments, a specific write-up per intervention has been added to support the information in Table 2.

In the introduction, the authors state that "The scope of health care services and programs across Canada that aim to prevent and treat infectious diseases in PWID remains unclear". However, I have difficulty seeing how this paper brings clarity to the scope of Canadian service provision.

To amend this issue, I suggest some amendments:

1) Restate the papers objective or broaden your literature search. Because the authors have focused on reviewing scientific literature, you are constrained by what has been published (as said in the limitations). This means you are not giving a clear indication of the level and type of service provision in Canada, but rather what has been published. Therefore - in essence, if it's not published, it hasn't happen - which is obviously not correct.

Response (1): Thank you for your comment. You are correct that there are likely many programs which have not been captured due to a lack of formal reporting on them, in either peer-reviewed or grey literature. The literature search of this study does include grey literature, however, as you may have noted, not many articles of this type were found in our searching, which is an interesting finding in and of

itself. Given these findings, it may be unlikely that broadening the literature search would result in a clearer indication of the level and type of service provision in Canada, as publications (either grey or peer-reviewed) on these health programs and services appear not to exist. In alignment with your comment, this paper is perhaps better characterized as a description of the available literature on health programs and services to treat infectious diseases in PWID in Canada. In an effort to clarify the goals and content of the paper, the paper's objectives have been re-worded. The text now states "The purpose of this study is to describe literature available on health programs and services in Canada relating to the prevention and management of infectious diseases in PWID, with the hope of informing policy, practice and future research". We feel that this description now more aptly describes the objectives and results of the paper.

2) Overhaul the results section. As a reader, I'm not interested in how many papers explored cost-effectiveness of a particular outcome, but the results of that cost-effectiveness.

3) Give far more space to the write-up of the policy implications. Without Table 2, this discussion constitutes approximately 3 pages in the results and discussion sections.

Response (2/3): Implications for policy and practice have been added for each health program/service described, and the effectiveness of programs and services (e.g. the cost-effectiveness of SIFs) has been added in as many cases as possible.

Because the reviewed papers were too heterogenous to perform a meta-analysis, the authors are not constrained by a statistical method, and could apply a narrative review methodology. This I feel would be of far greater value to the audience.

Response: Thank you for this comment. A narrative review methodology would provide great value to the field and audience. An integrative systematic review was a first step in collecting and understanding the diversity of published and grey literature available on this topic. Applying a narrative review methodology is next step now that there is a greater understanding of the breadth and methodologies on this topic.

The authors clearly have the right intentions with the paper, but I don't think the correct approach. I feel that bringing more depth to the review will result in quite an interesting and valuable paper.

Response: We hope that in providing a specific write-up per intervention which elaborates on the findings in Table 2 and provides greater space on the policy implications identified, and describing the effectiveness of the interventions, we have brought greater depth to this review.

Reviewer: 2

Dr. Sandra Springer, Yale School of Medicine

Response: Thank you for comments and valued criticism. As per your comment, and referenced in the comments below, Supplementary Table 1 contains organization of the data by health program/service. Our sincerest apologies as we now realize this table was illegible upon your first review. Additionally, in the results, a section per health program/service has been added which describes the major gaps, recommendations for future research, policy and practice as identified by the authors of the included studies. We have additionally restructured the discussion in order to highlight recommendations for policy, practice and research derived from the findings of this review. We thank you for pointing out the resource from the U.S. National Academy of Sciences, Engineering and Medicine (NASEM), as it was quite useful in providing greater background to our work and developing recommendations for the discussion. Of course, it would not be included in this paper, as we have only focused on the Canadian context.

Abstract:

Results section: Could they state the number of the articles that addressed testing and management of HIV and HCV and the other prevention and treatment strategies identified. It is not clear in the abstract the number of articles or exactly what were the key findings?

Response: Thank you for this comment. The results section of the abstract has now been updated to state all prevention strategies and treatments identified and the number of articles identified per each strategy. This section has also been edited in order to better represent this paper's key findings.

Introduction ...

Page 5, "against medical advice (AMA)..." tends not to be used any longer as stigmatizing and rather use 'unplanned discharge' or 'self discharge'.

Response: Thank you for raising this concern. The text has been updated to reflect the more appropriate term 'self discharge'.

Results:

Please use person first language including in table 1 " HCV positive / HIV positive/ prisoners- should be ' persons without HIV , with HIV, persons in prison etc...'

Response: Thank you for your comment. This language has been changed in Table 1 and throughout the manuscript to use person first language.

It seems like the first part of the results section is just a list .. is there a better way to synthesize this data .. maybe a table that addresses the study included then with columns going across that have the different attributes like type of study, population, jurisdiction, number, infection , health care system etc , type of healthcare provided/ to understand the different research done?

Response: Thank you for this comment. We now realize that you were unable to read Supplementary Table 1 due to an error in formatting. Exactly as you have suggested, this table includes the study, population, jurisdiction, infection(s) addressed, healthcare setting, type of healthcare provided and main findings, organized by health program/service. I would also draw the reviewers attention to Table 1 in the text which summarizes the "characteristics of included studies" section of the results. We have also removed some of the text in the "Characteristics of included studies" section of the results in order to cut back on words, reduce redundancy between the text of the results and information included in Table 1 and better synthesize this data.

Under Health programs and services- could you group these in tables? For the second paragraph under this section of testing, prevention with antivirals for HIV or HCV ... the references should be given for each section ... starting with 'many studies address the provision of antiviral treatment and testing n=27, 27%)' then list the references that you are referring to for these 27 studies or refer to table to put them in to compare them ...

Response: Thank you for this comment. Please see Supplementary Table 1, which includes health programs and services grouped in tables. All references have been provided for these sections.

Term antivirals used. , ART used for antiretroviral treatment for HIV but I don't think spelled out unless done earlier.. ART and HAART typically are the same ... unless you think they mean different things? you could use one term.

Response: Thank you for this comment. The text has been updated to indicate that these terms are synonymous, yet both terms are found in the literature.

It is hard to understand what is meant by these results.. they just seem to be listed
Would be better to characterize the studies in tables and what they evaluated, how they evaluated the different outcomes ...

Response: Thank you for this comment. Please see Supplementary Table 1 for a detailed description of all studied, included what they evaluated and how they evaluated the different outcomes. I'll note that it would be helpful to include tables characterizing the studies in the main text, however even a simplified table is too large, or exceeds the recommended number of in-text tables, therefore a detailed table of all studies organized by health program/service is provided as a supplementary table (Supplementary Table 1).

It is also hard to understand what the authors are referring to "The post-exposure prophylaxis intervention was community based..." what are they referring to?

Next sentence " similarly point of are testing and seek and treat initiatives included..." are they discussing the two studies referenced...? It is not clear

The last " TasP involves the delivery of ART as a method of HIV prevention..." . So what exactly are they discussing ? one study or description of what TasP is? In fact this is more of a definition then should be introduction and what it means.. U=U campaign etc that suppression of HIV means cannot transmit to those with HIV if partake in condomless sexual intercourse or share IDU equipment etc...

Response: The above comments were all in reference to a description of individual studies and the characteristics of the health services delivered in the study. This section has been re-written to provide more clarity and each reference study has been cited after each statement to clarify that these are individual studies.

HCV .. the articles are not referenced in the text. as well as other subsections.. SSPs, peer counseling etc.

Response: References have been added in each section of the results including the sections on HCV, SSPs, peer counselling.

Same for the other sections like Supervised injection facilities & Opioid agonist therapy etc..... need references when discussing each section e.g. " a number of studies n=12) and would highly suggest a separate table of studies for each section to denote what was studied etc so the reader can evaluate the studies faster and denote the sections ... and then provide references next to each statement... so " seven studies focused on methadone MMT" (list the superscript citations for the studies).... Same for heroin assisted treatment and so on / as well as for the other sections in the results section.

Response: References have been added to each section of the results and next to each statement to denote what was studied.

Of note, We now refer to opioid treatment as medication treatment for opioid use disorder (MOUD).

Response: The text has been updated using the term 'medication treatment for opioid use disorder (MOUD)' in place of other terms such as opioid agonist therapy.

Discussion:

Typically the first sentence states what you found.. this just says you found 97 articles included in the study.. Typically you make your main point here so would restructure.

Response: Thank you for this feedback. The first part of the discussion has been restructured in order to highlight main points of the study.

Overall it is needs more work to identify the common themes, gaps in the literature and recommendations for future research. It was hard to really identify what studies did what and a way to make sense of the literature.

Response: We hope that by adding a specific write-up per interventions on implications for policy and practice, recommendations for future research and identified gaps in the literature, we have more rigorously described the literature. Additionally, we have added references throughout each section of the results and provided a legible version of Supplementary Table 1, which describes each included study in detail, organized by health program/service. We hope that this change makes it easier to identify what studies did and helps makes sense of the literature.

VERSION 2 – REVIEW

REVIEWER	O'Keefe, Daniel Burnet Institute
REVIEW RETURNED	04-Aug-2021

GENERAL COMMENTS	The paper has been improved immeasurably by the author's amendments - I commend them again on what is a considerable amount of work.
-------------------------	--

REVIEWER	Springer, Sandra Yale School of Medicine, Internal medicine
REVIEW RETURNED	02-Aug-2021

GENERAL COMMENTS	The authors should be commended on their careful editing and attention to the concerns by the editor and reviewers. Overall i think it is much better, I would say the only minor revisions would be that the authors of this paper should put their thoughts about what the results showed in the discussion section not in the results section. The results is what you as authors identified - the conclusions from the results though should be presented in organized fashion in the discussion section following the order in the results. The other minor point is still that first sentence and first paragraph of the discussion, that is the main point of your paper. In the first sentence of the discussion it just lists everything and I think you have a grammar issue as it seems like a run-on sentence. I would suggest to improve this paper further you really work on that first sentence and first paragraph of the discussion and use the discussion (conclusions) to tell the readers what you make of your review of the literature on this subject.
-------------------------	---

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
Dr. Daniel O'Keefe, Burnet Institute

Response: Thank you very much for this comment and the prior feedback which helped to improve this work.

Reviewer: 2
Dr. Sandra Springer, Yale School of Medicine

Response: Thank you very much for this comment. In response to this comment, we would like to clarify that the implications for policy and practice highlighted in the results section of the paper are those identified by the authors of the articles included in the review. It was unclear that these have been collected from the reviewed literature and do not reflect our comments on the literature. To clarify this, we have added the following sentence in the results "Implications for policy, practice and further research as identified by the authors of the included articles are described for each health program or service." (p.11)

The other minor point is still that first sentence and first paragraph of the discussion, that is the main point of your paper. In the first sentence of the discussion it just lists everything and I think you have a grammar issue as it seems like a run-on sentence. I would suggest to improve this paper further you really work on that first sentence and first paragraph of the discussion and use the discussion (conclusions) to tell the readers what you make of your review of the literature on this subject.

Response: Thank you for highlighting the issues in the first sentence of the discussion. This sentence was poorly written and has now been re-written for clarity and to better state the main findings of the paper. Additionally, the conclusions section of the paper has been amended to better describe the review of the literature.