Reviewer's report

Title: Treatment outcomes in patients with opioid use disorder initiated by prescription: A systematic review protocol

Version: 0 Date: 04 Jul 2017

Reviewer: Stephanie Lake

Reviewer's report:

The proposed systematic review and meta-analysis addresses a critical and highly relevant research question during our current opioid crisis. As more individuals are becoming dependent on opioids through the use of prescription opioids, and the patient population of those requiring opioid substitution therapy is quickly changing, this review will be a useful resource for clinicians and researchers working to understand the shifting needs of opioid-dependent patients. Aside from a few minor issues and suggestions, this manuscript seems well-suited for publication in the journal.

Introduction/Rationale:

-Page 4, line 96: ("illicit opioids use is associated with an increased risk of infection…").

--> This part of the statement seems quite broad, as infection could mean many things.

-The authors state on Page 5, line 124 that "variability in treatment outcomes may be partially explained by the way in which an individual is first introduced to opioids".

--> The paragraph that directly follows describes demographic shifts in the OST patient population as the underlying explanation for this variability. This paragraph alludes to inherent differences between OST patient populations who were first exposed to opioids via prescription vs. not, rather than the initial opioid itself. I don't think this is a problem, but it might require a bit of clarification (e.g., "variability in tx outcomes may be partially explained by a shifting OST patient population resulting from changes to the way in which an individual is first introduced to opioids").

-Page 5, line 135-138: "Some studies show that this cohort of patients have better treatment response in comparison to people who obtained opioids illicitly [20], while other studies demonstrate that the introduction to opioids through a prescription increases the likelihood to misuse opioids and other illicit substances [21]".

--> As the first sentence in this paragraph (line 133-134) would indicate, these two statements are meant to demonstrate conflicting findings between studies with respect to OST treatment response among prescription and illicit opioids users, but they address two research questions
that aren't directly comparable. The first statement describes OST treatment response between patients who began opioid use through a prescription to those who began opioid use through illicit opioids; the second statement describes initiation into opioid use via prescription opioids, but doesn't examine OST response. The second statement also alludes to a measure of risk for prescription opioid vs. illicit opioid, but the supporting study [21] is an exploratory qualitative study with descriptive statistics.

Methods

- How will the authors address patients who initiated opioid use through a prescription but are now using prescription and non-prescription opioids or non-prescription only?

- Will this review include individuals who began their opioid use via non-medical use of prescription opioids (e.g., obtaining prescription opioid from a friend or parent's prescription)?

- The "outcomes and prioritization" section seems like it would fit better immediately following the "eligibility criteria" section.

Table 1 (search strategy)

- Perhaps I am misunderstanding, but it seems that MEDLINE search line 19 should be "9 and 18" rather than "9 and 15" ("9 and 15" already appeared on line 16)

- Unless I am again misunderstanding, CINAHL search lines 13, 14, and 15 are off. Each of these lines contains that line. For example, line 13 says "12 AND 13", but if this were actually imputed into the search, it would yield a search error. It looks like line 10 has not been included in the final search, and I suspect the correct line 13 was supposed to be "10 AND 12", and was accidentally omitted, so line 14 was labeled 13, line 15 was labeled 14, and so on.
Level of interest
Please indicate how interesting you found the manuscript:

An article whose findings are important to those with closely related research interests

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal