Reviewer's report

Title: Risk Factors for Addiction Among Patients Receiving Prescribed Opioids: A Systematic Review Protocol

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Reviewer: Junqiao Chen

Reviewer's report:

Opioid epidemics is a very hot topic in North America. The potential implication of this review, which is "reducing opioid prescribing among opioid-naïve patients at high-risk of developing subsequent addiction", is very interesting and valuable. I can't wait to read the review conclusion.

With that said, however, this protocol has three major areas for improvement. The first area for improvement is the lack of discussion on potential risk factors. There is only one sentence under the subheading "Topic" in this regard. It is not enough to just take a figure from another paper without even minimum discussion on its applicability to your review. If I understand correctly, the figure is just for patient-level risk factors. Then the protocol presents no discussion on provider- and system-level risk factors. It is important to have some discussion on potential risk factors because of two reasons. Firstly, it could help/accelerate the search and screening of articles (and help other researchers to replicate your search and screening). Secondly but most importantly, in order to fulfill your objective to reduce opioid prescribing among opioid-naïve patients at high-risk of developing subsequent addiction, these risk factors have to be observable by providers at the point of prescribing. I can't stress this more as I don't want to you to waste time on finding evidence for some risk factors that can't immediately inform change in practice because they are not easily observable for prescribers at the point of care. Some hypothetical examples would be a fancy genetic testing that is not universally available, or a sensitive personal matter that is not usually shared during a clinical encounter. So I would suggest you to define the scope of risk factors, and only collect evidence for those that are measurable at point of prescribing.

The second area for improvement is the inconsistency in different parts of the protocol. For example, "drug-"/ "medication-" level risk factors are mentioned in some places but not in others. Another example is that in Abstract's Method session, it says you "will perform subgroup analyses for naïve patients". This is not consistent with the title and the Population session in the full text, where opioid-naïve patients are the only/main group for analysis instead of a subgroup. One more example is that in the Objective session, it mentions to synthesize evidence on "prescription (e.g., type of drug, dosage, quantity dispensed, length of exposure) of the initial opioid prescription", which is not in Appendix C Data Collection Form.
The third area for improvement is that there is no enough discussion on how to handle evidence from different study designs. Special caution should be taken when a review is looking at both randomized and non-randomized studies. More discussion is needed on topics like whether data from randomized and non-randomized studies will be analyzed together or separately; what if data from different study types differ significantly; how to handle adjustment and confounders in observation studies, etc. Now the only discussion in this regard is the different tools for Risk of Bias assessment.

Thank you for your work!

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