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)	Evaluating Comparative Effectiveness of Psychosocial Interventions for Persons Receiving Opioid Agonist Therapy for Opioid Use Disorder: Protocol for a Systematic Review
AUTHORS	Rice, Danielle; Hutton, Brian; Poulin, Patricia; Sproule, Beth; Wolfe, Dianna; Moher, David; Thavorn, Kednapa; Garber, Gary; Taha, Sheena; Porath, Amy; Willows, Melanie; Esmaeilisaraji, Leila; Yazdi, Fatemeh; Shea, Beverley; Skidmore, Becky; Corace, Kimberly

VERSION 1 – REVIEW

REVIEWER	Sonia Hines Evidence in Practice Unit (EPU), Mater Health. Australia
REVIEW RETURNED	08-May-2018

GENERAL COMMENTS	Overall this is an excellent protocol on an important topic. The only improvement I would suggest is to define the primary outcome of opioid use with more clarity.

REVIEWER	Silvia Minozzi Department of Epidemiology, Lazio Regional health Service, Rome, Italy
REVIEW RETURNED	02-Jun-2018

| GENERAL COMMENTS | Background
1. The background starts stating that North America is facing with an opioid crisis, and then the authors provide prevalence data for Canada and US. It is not clear to me why authors state that the problem of opioid abuse concerns North America only and provide prevalence data only for Canada and US. It is true that the problem of abuse and dependence from prescribed opioids is higher in North America compared to European countries; nevertheless I think that a comprehensive systematic review comparing different psychological treatments should be seen under an international perspective; I suggest to add prevalence data also for the other developed and developing countries, keeping an international perspective
2. I also suggest to add a paragraph with some considerations (and prevalence data) about the distinction between dependence from prescribed opioid and from street heroin (illicit); to my understanding, the review aims to include both types of participants, who are different population indeed, mainly for psychosocial variables ,age, etc.
Methods
3. Authors could explain why they will prefer the Bayesian approach over the frequentist approach
4. Authors stated that "We will consider additional analyses to address study deficiencies found in RoB assessments by excluding |
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	low quality studies"; given that the Cochrae RoB tool does not provide an overall rating for risk of bias, authors should state how they will operationalize the definition of "low quality studies", i.e. on the basis of which domains with high risk of bias

VERSION 1 – AUTHOR RESPONSE

Reviewer Comments

Reviewer: 1

Overall this is an excellent protocol on an important topic. The only improvement I would suggest is to define the primary outcome of opioid use with more clarity.

We thank the reviewer for the enthusiasm for this work and the recommendation. We have expanded upon the opiate outcome of interest to further clarify the measurement type (Pg. 9, Lines, 20-21). Specifically, this portion of the text now reads as: "The co-primary outcomes of interest will be treatment retention and opioid use (including abstinence from opioids and opioid use based on urinalysis results)."

Reviewer: 2

Background

The background starts stating that North America is facing with an opioid crisis, and then the authors provide prevalence data for Canada and US. It is not clear to me why authors state that the problem of opioid abuse concerns North America only and provide prevalence data only for Canada and US. It is true that the problem of abuse and dependence from prescribed opioids is higher in North America compared to European countries; nevertheless I think that a comprehensive systematic review comparing different psychological treatments should be seen under an international perspective; I suggest to add prevalence data also for the other developed and developing countries, keeping an international perspective. I also suggest to add a paragraph with some considerations (and prevalence data) about the distinction between dependence from prescribed opioid and from street heroin (illicit); to my understanding, the review aims to include both types of participants, who are different population indeed, mainly for psychosocial variables ,age, etc.

We thank the reviewer for this suggestion. We have broadened our abstract and introduction to include an international perspective. Specifically, we have incorporated prevalence data and international guidelines (Pg. 5, Lines 13-21), now stating: "In Europe, heroin use continues to account for the majority (approximately 80%) of new opioid-related treatment.[8] There has also been a dramatic rise in illicit drugs being contaminated with fentanyl in both North America and Europe. In 2016, there was a 281% increase in the number of deaths attributable to fentanyl within Canada as compared to the preceding year.[5, 6] These alarming trends have prompted recent international, national, and provincial level actions including the development of the 2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain, and Canadian, American, World Health Organization, and European guidelines for opioid use disorder [3, 7], and the encouragement of prescribing cautiously and in smaller quantities to decrease misuse and dependence.[8]"

We have also added international prevalence data for prescription and illicit use of opioids (Pg. 5, Lines 7-9), which reads as: "In Europe, 84% of drug-related deaths in 2015 were related to opioid use, with heroin (often in combination with other drugs) contributing to more than half of drug-related

deaths.[6] Problematic opioid use is also prevalent in Asia, which accounts for approximately two thirds of all opiate users.[7]"

Methods
Authors could explain why they will prefer the Bayesian approach over the frequentist approach

We have selected the Bayesian approach based on the teams past experience and expertise using this method, as our team members were trained and have employed this approach in a variety of past publications. We have no reason to believe that selecting the Bayesian approach will result in substantive differences as compared to if the frequentist approach were used (Sadeghirad et al., 2017).

Authors stated that "We will consider additional analyses to address study deficiencies found in RoB assessments by excluding low quality studies"; given that the Cochrae RoB tool does not provide an overall rating for risk of bias, authors should state how they will operationalize the definition of "low quality studies", i.e. on the basis of which domains with high risk of bias

We appreciate this comment and have considered the best way to approach the risk of bias within studies given the lack of an overall rating. Rather than try to select a cut-off we have decided to consider risk of bias for each outcome and remove the potential sensitivity analysis. Instead, we will consider risk of bias providing a detailed listing of all assessments, by providing a summary description of key study limitations, and will use these assessments when contextualizing the findings for each outcome. We have removed the original statement and have added the revised approach to Pg. 12, Lines 13-15, which now reads as "Results from RoB appraisals will be summarized in the review and reported in full on an item-by-item basis in an appendix. They will also be considered when contextualizing the results for each outcome."

References
Sadeghirad B, Brignardello-Petersen R, Johnston BC, Guyatt GH, Beyene J. Comparing Bayesian and Frequentist Approaches for network meta-analysis: An empirical study. Global Evidence Summit, 2017;18515.