Reviewer’s report

Title: Opioid substitution therapy trials exclude the common addiction patient: a systematic review and analysis of eligibility criteria

Version: 1 Date: 4 May 2015

Reviewer: Sarah Larney

Reviewer’s report:

This paper presents findings of a systematic review of eligibility criteria for clinical trials of opioid substitution therapies, and a. considers the extent to which participants included in clinical trials are representative of the opioid dependent population, and b. considers how trial evidence is incorporated into clinical guidelines. The paper addresses important clinical issues of generalisability of clinical trial evidence, and how we interpret evidence in providing care to a vulnerable population with a high degree of comorbidity.

Major revisions:

Could the authors please provide some detail about what the risk of bias assessment adds to this particular review? I can see the importance of a risk of bias assessment in interpreting results of trials and a review of trials (and the importance of risk of bias assessment in preparing clinical guidelines), but this is a review of inclusion/exclusion criteria and I am having trouble seeing how the risk of bias assessment adds to our understanding of this.

I have some concerns about the choice of guidelines used in relation to the third study objective (to assess how guidelines incorporate evidence from trials). What is the justification for choosing these guidelines in particular? For the UK, the authors are referring to guidelines for opioid detoxification rather than maintenance treatment. It may be more appropriate to use the NICE Technology Appraisal Guidance 114 “Methadone and buprenorphine for the management of opioid dependence” http://www.nice.org.uk/guidance/ta114 – these are the guidelines for maintenance pharmacotherapies.

It may also be useful to apply the analysis to the WHO clinical guidelines for opioid pharmacotherapies, as these are internationally relevant guidelines that were written with the intention of informing national/regional guidelines: http://www.who.int/substance_abuse/publications/opioid_dependence_guidelines.pdf.

The authors make the important point in the discussion of the need for implementation trials, suggesting that these are uncommon in OST trials. Do the authors have any recommendations for increasing the number of implementation trials that are undertaken, and what eligibility criteria should be applied?

The PRISMA checklist says that the limitations of the study can be found on page 16 of the manuscript, but I’m not sure that I agree. The discussion should include an explicit limitations section – including limitations of reviewed studies (data limitations), and limitations of the current study.
Minor essential revisions:
Table 1: I don’t see how the notes are linked to the data in the table (i.e. what data do the asterisks refer to?)
Methods, fourth paragraph: Was the search string “opioid dependence, opioid addiction, and opioid substitution treatment”, or were these terms searched separately? A combined string such as that would restrict results; I am assuming the authors actually searched the terms separately – if so, this should be made clearer.

Discretionary revisions:
Some minor typographical errors throughout e.g. Introduction, second paragraph: should be a comma between methadone and buprenorphine in the third sentence; methods, second paragraph: substation should be substitution. A thorough proof reading is suggested.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests