Reviewer’s report

Title: Serious adverse events reported in placebo randomised controlled trials of oral naltrexone: a systematic review and meta-analysis

Version: 2 Date: 09 Oct 2018

Reviewer: IGHO ONAKPOYA

Reviewer's report:

The authors have adequately addressed most of the concerns raised by Reviewer 3. However, further revisions are required to clarify uncertainties.

That AEs are inconsistently reported is not a strong enough reason to exclude them from the review. Attempts could be made at getting more data from the corresponding authors, manufacturers, etc. Although nausea, sleep disturbance and dizziness are common adverse events does not necessarily indicate that they are all mild in intensity. Since the authors have already specified in their protocol that they were assessing SAEs, it would be helpful to explain upfront at the introduction why the review is focused on SAEs only.

As a side note, the authors report that the studies were of high quality based on the GRADE criteria. However, I am unable to see the GRADE tables. It appears they have mixed up GRADE with ROB. If the authors did not formally conduct the GRADEing of the evidence, they should remove GRADE from the manuscript.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

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Are the conclusions drawn adequately supported by the data shown?
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