Author’s response to reviews

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

Authors:
Monica Bolton (alan.mould@phonecoop.coop)
Alex Hodkinson (alexander.hodkinson@manchester.ac.uk)
Shivani Boda (shivani.boda@student.manchester.ac.uk)
Alan Mould (alan.mould@phonecoop.coop)
Maria Panagioti (maria.panagioti@manchester.ac.uk)
Sarah Rhodes (Sarah.A.Rhodes@manchester.ac.uk)
Lisa Riste (lisa.riste@manchester.ac.uk)
Harm Van Marwijk (H.VanMarwijk@bsms.ac.uk)

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Dear Dr. Alessandro Recchioni,

Thank you for your email of 23rd November 2018 which outlined the third editorial decision that this revised manuscript is suitable for publication in BMC Medicine with the addition of very minor changes following the responses to the reviewers’ comments.

The main concern raised by the reviewer was about the suitability of the GRADE assessment. In response, we have now removed this from the manuscript.
We believe that these changes have significantly improved our manuscript but we are happy to provide further clarification if necessary. We look forward to hearing from you soon.

Kind regards,

Dr M. Bolton
Dr A. Hodkinson
Dr M. Panagioti

NIHR School for Primary Care Research
Division of Population Health, Health Services Research & Primary Care
University of Manchester

Reviewer 2 (Igho Onakpoya)

- The authors have addressed most of my concerns. However, they still do not properly report correctly report the GRADE. I had suggested in my earlier peer review for the authors to take it out if they lack expertise - this will not decrease the quality of the paper as already presented.

They authors have presented textual analysis for judging the GRADE - this is misleading. Under methodological quality for example, you state "..no reason to downgrade the evidence. Although most of the RCTs were judged unclear risk of bias on several criteria". This is sufficient evidence to downgrade in GRADE.

Response: Thank you for drawing our attention to this. We have now removed the GRADE assessment throughout the manuscript to avoid any confusion.