Reviewer's report

Title: The association of telomere length with substance use disorders: systematic review and meta-analysis protocol

Version: 0 Date: 20 May 2019

Reviewer: Yen-Fu Chen

Reviewer's report:

This protocol describes the methods for a planned systematic review to examine the association between telomere length and substance use disorders. The rationale for conducting this review is well explained. The protocol is well structured and clearly written, and conforms to PRISMA-P guidelines. My comments are mainly related to clarification of the rationale for some of the chosen methods and the implementation of the chosen risk of bias assessment tool.

Major comment

Newcastle-Ottawa Scale will be used to assess the risk of bias of included studies. The two items under "Comparability" requires reviewers to assess whether the most important confounding factor(s) were adjusted for. It is currently unclear in the protocol whether unadjusted or adjusted mean differences in telomere length will be used, and whether any (and if so, which) confounding factors would be considered to be most important when assessing comparability between the groups with and without substance use disorders.

Minor comments

Page 9, lines 188-194: presumably the effect size index being computed here is what commonly known as Hedge's g, and the correction factor is introduced to mitigate bias associated with the measure when sample sizes are small? (If so) you may wish to explain these to general readers who are less familiar with these statistics/formulae.

Page 9, line 205: please explain the reason for using the method proposed by Hartung and Knapp - presumably due to potential/expected departure from normality for the distribution of effect sizes?

Page 10, line 218 (and also in the abstract): would 'subgroup analyses and meta-regression' be a more accurate term here (for exploring the sources of heterogeneity) than 'sensitivity analyses', which are mainly conducted to examine the robustness of findings under various assumptions/methodological choices?

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