Reviewer’s report

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

Version: 2 Date: 27 Sep 2019

Reviewer: Ferrán Catalá-López

Reviewer's report:

Thank you for re-submitting a revised version of your study protocol.

Overall, this appears to be a protocol for an interesting review. There are certain areas where additional clarity may be necessary to improve the transparency of the study protocol. My comments are mainly requests for details and clarification.

Before formal acceptance of your manuscript, please, consider the following minor comments.

Abstract.

p.2. Methods. Lines 47 and 48. Authors' state: "Potential studies will be identified through electronic databases (PubMed/MEDLINE, EMBASE, Psychlit/PsychINFO and Web of Science) up until December 2018". Please, update the database coverage, or consider the inclusion of "from inception onwards". For example: "Potential studies will be identified through searches in the following electronic databases: PubMed/MEDLINE, EMBASE, PsycINFO, and Web of Science (from inception onwards".

p. 2 Methods. Line 47. "PsychINFO" should be "PsycINFO".

p.2 Methods. Please, delete subsections: "Study selection:" (line 48), "Data extraction:" (line 52), "Risk of bias assessment:" (line 55), "Statistical analysis:" (line 57).

p.2 Methods. 48-52, Authors' state: "Study selection: The focus will be on published or unpublished observational studies reporting telomere length in persons with substance use disorder compared with a control group. Non-human studies or other study designs such as reviews, case-only, family-based and/or population-based studies with only health participants will be excluded, as well as those focused solely on nicotine addiction". Please, be more explicit about study designs ("observational studies: case-control, cohort?"), patient population (e.g. adult patients with substance use disorder), etc…

Similarly, please list all outcome(s) for which data will be sought, including prioritization of main and additional outcomes. For example: "The primary outcome will be [please, include]. Secondary outcomes will be [please, include].
p. 2 Discussion. Where: "To our knowledge, this meta-analysis will be the first systematic review and meta-analysis to assess (...)", should be "This systematic review will assess the association (...). Please, revise.

Methods

p.6 line 126. Where: "The study protocol was designed according to (...)", should be: "The study protocol was reported according to (...)". To clarify, PRISMA-P is a reporting guideline (no a methodological/conducting guideline). Please, revise through the text.

p.6 line 131-133. Where: "Studies will be identified through PubMed/MEDLINE, EMBASE, Psychlit/PsychINFO and Web of Science databases (Web of Knowledge up until December 2018 using the following search terms for SUDs: "drug, substance, addiction, alcohol*, heroin, cocaine, opioid, methamphetamine, morphine" and for telomeres: Telomeres, telomerase, and telo*" (see Additional file 2)." should be: "We will search PubMed/MEDLINE, EMBASE, PsycINFO, and Web of Science (from inception onwards) using the following search terms for SUDs: (...) (see a draft search in Additional file 2)."

p.7 lines 143-156. Please, delete and revise this subsection as follows (and as appropriate):

Eligibility criteria

Studies will be selected according to the following criteria: study design, participants, comparator and outcome(s) of interest.

Study design: We will include observational studies (e.g. cohort, case-control, cross-sectional studies) reporting telomere length in persons with SUDs compared with a control group (e.g. without SUDs). We will exclude studies in animals, experimental studies, reviews, case reports, case series, studies conducted in healthy populations and/or families.

Participants: We will include adult people with SUD (regardless of age or sex) assessed by clinical interviews or established standard diagnostic instruments including, but not limited to, the Structured Clinical Interview for DSM-IV (SCID), Computerized National Institute of Mental Health Diagnostic Interview Schedule (CDISIV), Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria, or Composite International Diagnostic Interview (CIDI). We will exclude participants with nicotine addiction.

Comparator (or control group): [please, define/clarify. For example, if appropriate: "The comparator group will be based on subjects with no history of SUDs (e.g., the general population, the community, unexposed outpatient, or hospital-based controls").

Outcome(s): [Please, list and define study outcomes e.g. "telomere length"?]

p.7 line 157. "DATA EXTRACTION (SELECTION AND CODING)", should be renamed: "Selection and data collection".
Discussion
p.13 line 283. Please, delete subheading: "Ethics and disseminations"

p.13 line 286. Please, delete subheading: "Amendments"

p.13. Please, discuss potential limitations at study (outcome) level, and at review level you anticipate.

Level of interest
Please indicate how interesting you found the manuscript:

An article whose findings are important to those with closely related research interests

Quality of written English
Please indicate the quality of language in the manuscript:

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