Reviewer's report

Title: Exercise for patients with depression: a protocol for a systematic review with meta-analysis and trial sequential analysis

Version: 1  Date: 16 September 2014

Reviewer: Alexander Tsertsvadze

Reviewer's report:

Abstract – Methods/design
• Authors need to clarify the research question more explicitly but briefly in PICO format. Namely, a reader needs to know what specific benefits and harms (e.g., outcomes such as severity of depression, compliance to antidepressants, etc...) of exercise will be assessed in patients with depression. What will be the intervention of interest, exercise alone or in combination/add-on with an antidepressant or psychotherapy? What will be comparator interventions, antidepressant alone (without exercise), psychotherapy, placebo, or no intervention?

Background – Objectives
• Same as above, please formulate your objectives/research question using PICO framework

Methods – Eligibility criteria
• Please, delete the first paragraph (e.g., definition of RCT, blinding, etc...) and organize your study eligibility criteria by a) inclusion criteria and b) exclusion criteria. In inclusion criteria, please specify your criteria as bullets by study design (RCTs), language of publication (any language), type of publication (abstract vs. full text), and PICO elements (population, interventions of interest, comparator intervention, outcomes).
• The inclusion criteria needs to be followed by your list of exclusion criteria preferable using PICO framework by specifying which interventions, populations, outcomes and study designs will be excluded.
• Will the authors try to distinguish harms due to medical treatments and exercise?
• Please, move ‘subgroup analysis’ subsection to ‘Data synthesis and analysis’ section on page 8. Rename ‘statistical analysis’ to ‘Data synthesis and analysis’ section.
• Move the following sentence from ‘outcomes’ subsection (“We expect some trials to have several intervention groups. We will pool data from the experimental groups and compare to the control group”) to ‘Data synthesis and analysis’ section.
Methods – Search strategy and study selection
• Will the authors search for grey/unpublished literature? If so, please state this and which databases and other sources will be searched.
• Will there be any language restriction applied to the searches?
• Will there be any date restriction applied to the searches? What periods will be searched in major databases?
• Search methods and screening articles (study selection) are merged in one section; will the authors separate them and create a new separate section ‘Study selection’ right after ‘Search strategy’ section?
• In “study selection’ section, will the authors describe two levels of screening? i.e., screening of all identified abstracts/titles and then full text papers of all potentially relevant records passing the title/abstract screening level.
• Will the authors use the pre-defined piloted screening form?
• How many reviewers will screen? How the conflicts will be resolved?
• Will the authors present PRISMA study flow chart with reasons and numbers for exclusions at the end of ‘Search strategy’ section?

Methods – Data extraction
• Please, add more specifics, what type of data will be extracted for study (e.g., design, sample size, study author, year of publication, etc...), population (e.g., age, sex, etc...), interventions (type of exercise, dose and duration of exercise, dose/duration of antidepressant medications, etc... ), outcomes (e.g., depression mean scores, adverse events, rate of compliance, success rate, etc...).
• Will the authors specify what data will be extracted for study quality/risk of bias (ROB) assessment? Will it be methods of randomization, concealment allocation, or any other ROB domain?
• Description of ROB is too long. Please describe briefly what instrument will be used and what major ROB domains will be addressed using such instrument. Indicate which outcomes will be assessed for ROB and what will be the ratings (e.g., low, high, etc...)
• Please create a new separate section ‘Risk of bias assessment’; it should be separate from data extraction section.

Methods – Data synthesis and analysis
• Please rename ‘Statistical analysis’ to ‘Data synthesis and analysis’ section.
• Explain how evidence will be synthesized qualitatively? Will there be any comparison groups? Should the studies comparing exercise alone to antidepressants be analyzed together with studies comparing exercise as add-on to antidepressant vs. antidepressant alone? Will the evidence synthesis be organized by outcome for each comparison?
• In which cases the authors will consider meta-analyzing the studies? Please list these conditions precluding the meta-analysis (e.g., presence of clinical
heterogeneity in populations, interventions, and outcomes; study design)
• The authors stated that they will use SMD; will they use MD (change from baseline or difference between end points) using original score units by any chance? Its interpretation is more straightforward than that of SMD.
• The authors stated that would use subgroup analysis to explore the sources of heterogeneity; will they also explore the robustness of pooled estimates via sensitivity analysis across ROB domains, sample size, or intention to treat analysis?
• Please inform if there are any a priori selected factors which will be explored for their influence on effect estimates of exercise.
• Will the authors state anything about how they will assess publication bias?
• Are the authors planning to assess an overall quality of evidence (‘strength of evidence’) for their primary outcome (i.e., association between childhood socioeconomic status and LTPI) using the GRADE system?

Discussion
• Will the authors highlight strengths/limitations in identified evidence (e.g., amount, validity, applicability, etc…)?
• Will the authors highlight strengths/limitations of their review (any limitations in the review methods)?
• Will the authors compare their findings with those from other systematic reviews that explored the same or similar question?
• Will the authors highlight future research and policy implications of this review?