Reviewer's report

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

Version: 4 Date: 5 January 2015

Reviewer: Alexander Tsertsvadze

Reviewer's report:

Study selection
- The following sentence on page 7 belongs to ‘search strategy’ section: “Reference lists of relevant reviews will be searched for additional trials.”
- Will not the authors run into the risk of selection bias if both screening levels will be done by a single reviewer? Will not the second reviewer screen or at least cross-check the included and excluded studies?
- Will the authors document the study flow and reasons for exclusions at full text screen level? If yes, will they use the PRISMA flow chart?
- How will the reviewers reconcile any emerging conflicts/disagreements regarding inclusion/exclusion of any given record?

Risk of bias assessment
- I would suggest to move the explanatory paragraphs for each domain of risk of bias found on pages 8-10 (those in red font) from the manuscript to an appendix
- The paragraph on publication bias should be moved to the end of ‘Data synthesis and analysis section’ (after subgroup analysis subsection)
- I suggest to delete the following sentence on page 10: “However, when we draw conclusions, we will remember that no or only few trials with low risk of bias existed. Hence, the chance to know the ‘true’ intervention effect is low or absent.”

Data synthesis and analysis
- On page 11, the authors state the following: “We will pool data from the experimental groups and compare to the control group.” Would not the greater effects (if present) in higher intensity groups be diluted by simply pooling the exercise intensity/dose arms? Although the authors address this issue in the ‘Subgroup analysis’ sub-section, they may need to make this provision here too (page 11), something in this fashion: “the pooling would be considered only if there is an assumption that these exercise intensity groups have similar effects”
- On page 11, the authors explain that they would address the missing data for a particular binary outcome (lack of remission) using the standard imputation method and sensitivity analysis. Please, reword the following sentence to make this clear: “Regarding the outcome of lack of remission, we will include trials with incomplete or missing data in sensitivity analyses by imputing them according to
the following scenarios.” Something like in this line: “…In case of missing data for the ‘lack of remission’ outcome, we will use the imputation technique such and such….and sensitivity analysis to check the effect estimate across different scenarios…”

• Please, place the above-mentioned information/paragraph (on imputation and scenarios for lack of remission) only after the paragraphs on primary outcomes (sequential analysis and Bayes factor) found on page 12 (flip the order in the text).

• Will the authors mention anything on how they will handle missing data for their primary outcome (i.e., depressive symptoms measured on a continuous scale)?

Declaration of competing interests:

None.