Author’s response to reviews

Title: Efficacy of vitamin D supplementation in depression in adults: a systematic review protocol

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Author’s response to reviews: see over
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Dr. Lehana Thabane
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Dear Dr. Susanne Hempel,

Re: Manuscript - MS: 1861504715975824 - Efficacy of vitamin D supplementation in depression in adults: a systematic review protocol

Thank you for your email dated May 28, 2013 with the reviewers’ comments on our paper. We thank you again for the opportunity to submit a revised version of the above paper. The comments were very helpful. Please find attached the revised version of the manuscript. In this cover letter we have provided a point-by-point response to the concerns raised in the review. All new changes have been highlighted in blue in the revised version of the manuscript. We hope we have adequately addressed all the comments, and that the paper is now in an acceptable form. We look forward to hearing from you.

Sincerely,

Lehana Thabane, PhD
Professor, Clinical Epidemiology and Biostatistics, McMaster University

**Major revision**

1. The data collection and analysis section outlines that observational studies will be integrated in a Bayesian analysis but the inclusion criteria are limited to RCTs. The selection of observational studies should also be determined in the protocol.

Response: Thanks you for raising the issue. We have specified the inclusion of eligible
observational studies in our statistical analysis section (Page 7, the first Paragraph, the second sentence): observational studies investigating relationship between vitamin D measurements as a risk factor and depression as the outcome of interest in adults, will be eligible for pooled analysis as prior distributions to conduct Bayesian meta-analysis.

2. The inclusion or exclusion of cross-over RCTs should be specified in the protocol given the topic.
Response: As suggested, we added the exclusion of cross-over RCTs to clarify the type of included trials (Page 4, Paragraph 4, the last sentence).

3. The protocol should specify how "at risk of depression" will be operationalized in the review.
Response: Thank you for the suggestion to define ‘at risk of depression’. Based on our research question and population, we specified the risk factors of depression in adults (Page 4, Paragraph 5, the second sentence) as: having a family history, obesity for adults, postpartum period for women, perimenopause for women in midlife, bereavement, sleep disturbance, disability, prior depression and female gender for the elderly.

4. The funding source and the role of the funder should be specified.
Response: We had no funding to support this study, and it was clarified at the end of the manuscript (Page 10, the first Paragraph).

Minor revision
1. I would suggest to use the PICOTS framework to outline the inclusion criteria.
Response: Thank you for the suggestion. The PICOTS format was presented in the ‘Aims’ (Page 4, Paragraph 3) and ‘Criteria for considering studies for this review’ (Page 4-5). Specifically, in the criteria, ‘Type of participants’ explained Population (Page 4, Paragraph 5), and ‘Type of interventions’ defined Intervention and Time (Page 5, Paragraph 2), while ‘Comparison’ interpreted Comparison (Page 5, Paragraph 3) and ‘Type of outcome measures’ defined Outcome (Page 5, Paragraph 4-5).
2. The inclusion criteria should outline whether studies given other vitamin supplements in addition to vitamin D are excluded or included.

Response: As suggested, we revised the inclusion criteria for intervention to exclude other types of vitamin supplementations (Page 5, Paragraph 2, the third sentence).

3. The dimensions that will be used to assess the strength of evidence could be explained in more detail.

Response: We thank you for the positive comments on the strength of this study. More detail of the strength was supplied in Discussion (Page 9, Paragraph 3, sentence 2-3).

4. The assessment of publication bias should not be limited to visual inspection of the funnel plot.

Response: Thank you for the advice. We added Begg’s and Egger’s tests along with the funnel plot description (Page 8, Paragraph 5).

Discretionary revision

1. It would be helpful for the reader to have more information about which intervention-specific details will be abstracted such as the type of vitamin D supplement used, including the chemical form, brand (if commercial), or ascertainment of purity.

Response: Thank you for the advice on adding some details on vitamin D. We provided more information on vitamin D in the Background (Page 3, Paragraph 3, the 2-5th sentences).

2. In terms of participants, data on baseline serum vitamin D levels and the assay method, interim and final vitamin D serum levels, washout periods for antidepressants and other supplements are most likely important variables.

Response: Thank you for the suggestion on data extraction. We added these variables to be extracted and updated our data extraction form accordingly (Page 6, Paragraph 5).