Author’s response to reviews

Title: The effect of CBT and its modifications for relapse prevention in major depressive disorder: A systematic review and meta-analysis

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Author’s response to reviews:

Dear Editors and Reviewers:

Thank you for your letter of August 14, 2017 and for suggestions concerning our manuscript. We apologize for getting back to you so late because these insightful comments made us modify our manuscript in many places which spent a lot of time. We quite appreciate your favorite consideration and constructive comments. Those comments were all valuable and very helpful for revising and improving our paper. Now we have revised the paper point-by-point exactly according to those comments of editors and reviewers.

1. To Editor:

1) Comment 1: Editor suggested to include a completed PRISMA checklist as an additional file.

Response: We added a completed PRISMA checklist as an additional file.

2) Comment 2: Editor suggested to add details of the search strategy as an additional file.

Response: We added a detailed systematic search strategy as the supplementary appendix 1.

2. To Shadi Beshai (Reviewer 1):
1) Comment 1: The current analysis and presentation did not show superiority over the relevant reviews by Beshai et al., 2011 and Bockting et al., 2015. The conclusions drawn were relatively mundane. The conclusion of a moderating influence of number of prior episodes on MBCT effect was reached even within the trials themselves. Authors should dedicate some space to discuss rationale, or what is new about their meta-analysis that is not offered in previous reviews.

Response: Thank you for your review and pointing these limitations out. Based on your suggestion, we added the discussion about its superiority over these two reviews on Discussion section, line 51, page 10 and the rationale of the moderating influence of MBCT on Background section, line 2, page 4 (marked in red in revised paper).

2) Comment 2: The way the review is currently organized is not easy to follow. Authors did not need to distinguish "CBT" from "CT" and separate TAU from PLA. Reviewer thought that the organization of the results section and corresponding HR plots in the figures needed to be much more simplified for ease of understanding.

Response: Thank you for these constructive suggestions. Based on your excellent comments, we have made extensive modification on the organization of result section, in which the analyses of number of prior episodes were excluded from other sections of meta-analyses. We quite agreed with your comments. Therefore, in the revised manuscript, we did not distinguished these two psychotherapies and control groups. We considered CT as CBT. Relevant method section, result section and corresponding HR plots were amended. These modifications were displayed in method section, line 10, page 6 (marked in red in revised paper) and among all the result section.

3) Comment 3: Some of the conclusions reached in the present review were inappropriate. For example, the authors say "unfortunately, compared to m-ADM, MBCT failed to show a significant relapse prevention effect".

Response: We were very sorry for our inappropriate writing these kinds of inappropriate conclusions. Relevant and similar statements were deleted among revised manuscript in Result and Conclusion section.

4) Comment 4: The writing throughout is not very clear and the manuscript in its present form has several grammatical errors and awkwardly worded sentences.

Response: Thank you very much for your read and review. In terms of grammar errors and awkwardly worded sentences as indicated by reviewer, we tried our best to revise many grammatical errors and awkwardly worded sentences in the manuscript. We hope these revision can make our paper more acceptable.

5) Comment 5: Reviewer thought more space should be dedicated to forwarding the theory.
Response: Thank you for your suggestion. Based on this suggestion, we added several theories of moderating effect of MBCT and the mechanism of CBT and MBCT in Background section, line 49, page 3 (marked in red in revised paper).

3. To Reinhold Kilian (Reviewer 2):

Comment: Reviewer suggested to display a visual interpretation of the funnel plot because the total number of trials were 16.

Response: Thank you for your review and favorable comment. We admitted that examining publication bias was very important and really wanted to examine it by using funnel plots. The total number of trials actually were 16 and more than 10. But these 16 studies could not be included in one separate comparison. One funnel plot could only be made from one separate comparison. Among the displayed separate comparisons, any one of the separate comparison did not covered 10 or more than 10 trials and the largest number of included studies was 9 (CBT and its modifications VS Control). Therefore, we still did not identified publication bias through visual inspection of funnel plots.

4. To Lena Jelinek (Reviewer 3):

1) Comment 1: The differentiation of systematic review and meta-analysis does not consistently reappear in the rest of the paper and it is unclear what is "review" and what "meta-analysis". As one example, there is only one subtitle in the results section on "meta-analytic results" and none for the systematic review.

Response: Thank you for this constructive and helpful comment. We actually neglected to review and describe other included studies which excluded from our meta-analysis in more places. Therefore we added the description of these two studies in Results section, line 41, page 6. Besides, one of the reason for why you pointed this out might be the unclear purpose we stated at the start of this report. Therefore, we modified the statement of the purpose of this study which we thought was more clear and appropriate in Background section, line 43, page 4 (marked in red in revised paper). We included these two studies which were excluded from meta-analysis, because one purpose of this review was to describe relevant research in this topic and these two studies met our selection criteria. Although they were excluded from quantitative meta-analysis, the results of them were still of significant reference in this field.

2) Comment 2: Introduction: While CBT is described in some detail in the introduction, MBCT is not introduced. Reviewer recommended to also describe MBCT in the introduction (e.g., use the sentences now in the discussion section).
Response: Thank you for your helpful suggestion. We were very sorry for our negligence of the description MBCT in introduction section. We have made correction according to the reviewer’s comments which displayed in Introduction section, line50, page3(marked in red in revised paper).

3) Comment 3: Methods: The methodology is not clear. • What were the "strict diagnostic criteria" mentioned in the selection criteria? • What search term/keywords were used? • What was the theoretical basis for comparing subjects with >= 3 previous episodes (could also be included in the introduction). • Was the study preregistered? • Was inter-rater reliability calculated?

Response: Thank you for your critical comments. Based on your advices, we have carefully revised our Methods as follows: • For diagnostic criteria, we added the strict diagnostic criteria in Method section, line 58, page4(marked in red in revised paper); • For the search term/keywords, we added a detailed systematic search strategy as the supplementary appendix 1; • We added the rationale of the moderating influence of MBCT on Background section, line2, page4(marked in red in revised paper); • For the pre-registration, we actually did not registered this review before starting. This was a limitation for our study as stated in the Discussion section, line7, page12(marked in red in revised paper). • For inter-rater reliability, we did not calculated it. Because the score of inter-rater reliability for the procedure of our study could not be calculated. In order to ensure reliability of the results of two investigators, we added a third investigator to carefully check and coordinate the disagreements.

4) Comment 4: It is not clear which of the studies included had relapse as a primary and which as a secondary outcome measure. This information should be included and discussed, also in light of a publication bias.

Response: Thank you for your constructive suggestion. We were sorry for our negligence of reporting this important information. We added this information in Result section, line 7, page7(marked in red in revised paper). Because the only study which reported relapse as a secondary outcome measure was excluded from our meta-analysis and others all reported relapse as primary outcome measure, we thought it did not brought about publication bias.

6) Comment 5: Results: It is not clear why 33 of the 53 initially retrieved articles were excluded. This information should be added to figure 1.

Response: We were sorry for negligence of this and added the reasons in figure 1.

7) Comment 6: The authors claim to have used funnel plots to test for publication bias. I recommend including them in the manuscript.

Response: We admitted that examining publication bias was very important and really wanted to examine it by using funnel plots. But in light of the insufficient number of studies, we did not
identified publication bias. Even if we examined publication bias through funnel plots, the results were unreliable owing to the insufficient statistical power. The reason of reviewer pointing this out might because we did not clearly explained this. Therefore, we added this explanation in Result section, line 23, page 10 (marked in red in revised paper).

8) Comment 7: The forest plots were hard to follow, e.g., legend/title is missing; Sample sizes of studies are missing; If CIs are reported, there is no need in additional z-statistics in my opinion; Subgroup analysis if there is only one study do not make sense to me; Not all headings are precise and do not match the subtitles of the manuscript (e.g. "all", "3 or 3 more previous episodes"); The figure is full of statistical values, which are repetitive to the manuscript. You may want to reduce the detail of statistical values either in the text or in the figure; Some studies are included twice (e.g. Bondolfi, 2010 and Godfrin, 2010); Subgroups should be formed in a way that the exact same study results are not included in more than one subgroup.

Response: Thank you for your pointing this out. Based on your suggestion, we added the revised legend/title in the end of the manuscript and sample sizes of studies in the revised forest plots. For CIs and z-statistics, we quite agreed with your viewpoint, but both of them were generated by statistical software of Review Manager 5 and we failed to delete any one of them. For the subgroup analysis, we have modified each separate meta-analysis among the result section. In the revised results, subgroup analysis if there was only one study was deleted and same study results were not included in more than one subgroup. For several redundant statistical values, we deleted some details of statistical values in the revised manuscript or figure. We hope these modifications will meet with your requirement.

9) Comment 8: The discussion includes detailed comparisons within different therapeutic approaches. Those detailed qualitatively analysis may be better integrated in the results section.

Response: Thank you for your critical comments. Based on your advices, we have moved the detailed comparisons within different therapeutic approaches to Result section, line 10, page 7 (marked in red in revised paper).

10) Comment 9: Reader think the manuscript should be checked by a native speaker (e.g. for the correct use of tenses). Moreover, consistency could be improved (e.g., regarding statistical values, sometimes it is written "95% CI: 0.37-0.86" and at other points "95% CI, 0.87-1.39" to give just one example) and many of the mistakes do not need a native speaker (e.g., opening or closing parenthesis, spaces, a major typo right at the beginning of results sections - "16 trials were depicted" it should be 18).

Response: Thank you for your suggestion and consideration. Based on your advices, we have tried our best to modify the manuscript in either text errors or other obvious errors. For the typo right at the beginning of results sections which you pointed out, the writing of 16 trials was
correct. As displayed in the beginning of results sections, we included 20 eligible articles which represented 16 trials, because some trials were reported in more than one article (at different follow-up periods). 18 represented the number of articles which included in our meta-analysis. Table 1 displayed the characteristics of all included trials. Therefore, the number was 16.

We tried our best to improve the manuscript and make some other modifications in the manuscript. These changes will not influence the content and framework of the paper.

I hope this will make it more acceptable for publication. If you have any questions, please contact us without hesitate. Thanks very much for your kind work and consideration on publication of our paper. On behalf of my co-authors, we would like to express our great appreciation to editors and reviewers.

Sincerely yours,

Zuojie Zhang on behalf of the authors.