Author’s response to reviews

Title: Short-term versus long-term psychotherapy for adult psychiatric disorders: a protocol for a systematic review with meta-analysis and Trial Sequential Analysis

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Author’s response to reviews:

Response to Reviewer 1:

Reviewer comment #1:

This meta-analysis will include various mental conditions, and the primary efficacy outcome, "symptom severity" combines widely divergent measures of depression, social anxiety, post-traumatic stress disorder, (perhaps) suicidality, eating disorders... across very different conditions. This highly heterogeneous mix will confound the clinical relevance of the findings. In addition, one might be more interested about function as an outcome than solely using symptoms. As it appear in the current version, quality of life is listed as the 3rd outcome. It should be the first one in my opinion, especially of one is interested in long term outcomes. Of course you might argue that this outcome will be poorly studied/reported. However, if there is no evidence on this outcome in the literature, it is of great concern and it reduces the importance of the findings.

Response #1:

We very much appreciate this comment, and we agree. We have therefore changed the order of primary outcomes, so that quality of life is now the first primary outcome and symptom severity is the third primary outcome. Please refer to the manuscript page 8 under the heading “primary outcomes”. We have also changed this in the PROSPERO database.
Further, we agree that pooling all symptom scales for all disorders will not be feasible. We plan to analyze the symptom outcome separately for each disorder. We have now specified this in the protocol, please see page 8 under the heading “Primary outcomes”

Reviewer comment #2:

I missed a clear definition of what are short term and long term therapies. A protocol is intended to make the research reproducible. I'm not sure that it will be the case with such fuzziness. You suggest that you will use the author definition but this might again confound the findings of the meta-analysis: i.e. for a 3 months VS 6 months, short term could be 6 months and for a 6 months vs 12 months, short term could be 6 months... Can you reconsider and/or explain this choice in details in the method section? It makes strong assumptions on the dose-response relationship. In addition, it is not clear to understand how you will handle short term therapies and long term therapies with the same number of sessions (a difference in term of frequency).

Response #2:

We agree that using trialists definitions of short and long potentially introduces problems with heterogeneity. However, we believe that our choice of methodology from a pragmatic point of view is the best solution there is. First, trialists often report poorly and often do not themselves use thresholds and important data might be excluded from our review if we demand exact definitions of lengths; and what do the reviewer suggest we do if the lengths of interventions differ between participants? Based on our experience, using arbitrary thresholds may lead to exclusion of important data. Second, we do not expect to include many trials in this systematic review. Hence, relying on trialists definitions of short versus long may increase the number of trials being eligible for inclusion. These issues have now been clarified in our revised manuscript (see Discussion).

It is correct, that we will include trials with the same dose (sessions) but with different frequencies, e.g. 12 sessions delivered over 6 weeks compared to 12 sessions delivered over 12 weeks. We have now specified this in the method section, please see page 8 under the heading “Types of interventions”. To handle this, we have planned a subgroup analysis titled: “Trials above and below the mean difference in intervention lengths”. Please see page 14 under the heading “Subgroup analyses”.
Reviewer comment #3:

I would like to suggest that sometimes (and possibly in this case) it is better to perform a systematic review without a meta-analysis.

Response #3: We strongly agree. Systematic reviewers should always only consider meta-analysing data based on a thorough assessment of heterogeneity. We have now highlighted this. Please see the revised manuscript, page 13, 14 and 16.

Reviewer comment #4:

In the last part of the introduction you refer to non inferiority. You must be clear a priori about this and explain what possible magnitude of differences you will consider as non inferior. This is important to pre-specify this.

Response #4: We have now deleted the term non-inferiority in the introduction, as we will not perform any non-inferiority analyses in the meta-analysis. We apologize for the confusion, and we thank you for noticing.

Reviewer comment #5

Minor suggestions:

• Please also consider to have a look at Pim Cuijpers' database (http://www.evidencebasedpsychotherapies.org/index.php?id=25);

Thank you, we have now added this. Please see the revised manuscript, page 9 under the heading “Searching other resources”.

• Please give the search strings for all electronic searches.

We have now uploaded the search strings for all electronic databases as a supplementary material. Due to our lack of access at the moment, the search string for PsychInfo will be given at review stage.

• You are saying that you have performed preliminary searches and identified a few studies comparing long VS short term psychotherapy for one or more specific disorder.
Could you indicate what kind of searches you have already performed? Please add information in the web appendix.

We knew two RCTs comparing short-term and long-term psychotherapy in advance. Hence, we have not performed any preliminary systematic searches for previous trials when writing the protocol. We apologize for this confusion. We have, however, performed a preliminary search for previous systematic reviews. We have now specified this in the introduction section under the heading “Why is it important to do this review”.

- Could you present in a table the studies that you have identified at this point? Please add this information in the main paper.

Again, we apologize for the confusion. We knew two RCTs in advance, and we did a preliminary search in the Cochrane Register of Systematic Reviews for previous reviews. We identified one review, which was empty. Thus, we do not find it necessary to present a table with only one review.

- Can you confirm that you have done systematic searches of previous meta-analyses already addressing this question (overlapping meta-analyses on the same topic)? If yes, please indicate this.

Yes. See previous response.

- By the way, these preliminary searches are not reported in the PROSPERO database (status = not started). Please edit.

We have now specified that this preliminary search for previous systematic reviews (which is far from sufficient) was conducted when writing the protocol. This has now been edited in the PROSPERO database. Thank you very much for noticing.

Response to Reviewer 2:

Reviewer comment #1:

The introduction appears a bit verbose, I don't think using a paragraph for each disorder is necessary. Readers will be aware of what these disorders entail. The description of the
psychotherapies might also be reduced. For instance, the historical information is not necessary, again readers will be informed.

Response #1: We have discussed this point of view, however we have decided to keep it for the interested reader. But we do agree that the introduction is quite long, so we have deleted some superfluous sentences. Please see the revised manuscript, in which all deletions are highlighted with the “track changes”-function. We hope that the editor can accept keeping the description of each disorder.

Reviewer comment #2

Instead the introduction could benefit from a discussion of previous meta-analyses of psychodynamic/psychoanalytic therapy. These issues are very briefly touched, but would benefit from being expanded, particularly in lieu of the extensive part describing the disorders. For instance, I was surprised this landmark meta-analysis was not even mentioned: https://www.ncbi.nlm.nih.gov/pubmed/22227111

Response #2: The suggested meta-analysis has now been added. Please see page 5.

Reviewer comment #3: Did I understand correctly that all therapies that define themselves as psychoanalytic or psychodynamic be included?

Response #3: Yes, this is correct. We have now specified this, please see page 5.

Reviewer comment #4: Will interpersonal therapy be considered in any category?

Response #4: Yes, interpersonal therapy will also be considered. This has now been added to the introduction.

Reviewer comment #5: The paragraph about pharmacological treatment (p.7, l.12-16) is superfluous. Are the authors using pharmacological treatment in any way?

Response #5: We agree, we have now deleted this paragraph from the introduction. We are not including pharmacological trials in our systematic review, but we will extract available data, if trialists report allowing pharmacological treatment as co-intervention in their psychotherapy trials.
Reviewer comment #6: Regarding treatment duration, the authors will just extract total duration, as well as number of sessions. Maybe a measure of treatment intensity might be useful (e.g., sessions per week, or time between sessions), some of the short-term therapies might be more intensive and this might be a confound.

Response #6: We agree, we have now added “session lengths (in minutes)” and “number of sessions per week” to the data collection part of the methods section. Please see page 10 under the headings “short-term psychotherapy” and “long-term psychotherapy”.

Reviewer comment #7: Instead of using overall risk of bias for subgroup analysis, given that I doubt many studies (if any) will have low overall risk of bias, the authors might consider using just one RoB domain for this analysis, for instance allocation concealment, shown to be the most strongly related to effect sizes in meta-epidemiological analysis, or incomplete outcome data, where in general all studies can be rated.

For blinding, many studies will use self-report measures. Following the RoB 2.0 tool that the authors are following, these should get high risk of bias. But again this might be the majority of studies and it might mean that few studies overall will have low RoB.

Response #7: While we appreciate the comment, we do not agree with Reviewer 2 on this issue. We follow the Cochrane Handbook for Systematic Reviews of Interventions, in which it is recommended to do subgroup analyses for overall RoB scores. Hence, we do not believe, that this should be revised. Doing subgroup analyses on specific RoB domains will result in a large number of subgroup analyses, which will increase the number of type 1 error. Further, several meta-epidemiological studies have clearly shown that several other bias risk domains bias trial results, and therefore we do not believe that there is a basis for only selecting e.g. allocation concealment or incomplete outcome data.

Reviewer comment #8: For the actual meta-analysis, I would like the authors to consider including a data sharing statement and, if feasible, to share their data and code.

Response #8: We will publish all data including code in the supplementary material of the actual meta-analysis. This has now been stated in the protocol as well, please see page 17 under the heading: “Availability of supporting data”.