Author’s response to reviews

Title: An Umbrella Review of the Literature on the Effectiveness of Psychological Interventions for Pain Reduction

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The Editor of BMC Psychology

Dear Editor,

We are submitting a revised version of our manuscript "An Umbrella Review of the Literature on the Effectiveness of Psychological Interventions for Pain Reduction" (PSYO-D-17-00051) which we would like to be considered for publication in BMC Psychology. An item by item response to the editors’ and reviewers’ comments is attached below.

Thank you for considering our submission and we look forward to your reply.

Sincerely,
Response to the reviewers

Editor Comments:

Dear authors,

In addition to the reviewer's comments, I also have the following comments on your manuscript that I would ask you to consider in your revised version.

Major revisions:

- Please follow one of the edited guidelines for the methodology and report of umbrella reviews, such as the one described in Aromataris E1, Fernandez R, Godfrey CM, Holly C, Khalil H, Tungpunkom P, Summarizing systematic reviews: methodological development, conduct and reporting of an umbrella review approach. Int J Evid Based Healthc. 2015 Sep;13(3):132-40. doi: 10.1097/XEB.0000000000000055. Please explain in your response to the reviewers how you have included this methodology and these guidelines in your revised version. As suggested in these guidelines, use a flowchart as described in the PRISMA guidelines and use standardized tools for research synthesis quality criteria such as AMSTAR or ROBIS. It is a necessary requirement that you use one of the published guidelines to report your umbrella review.

We thank the editor about this suggestion. We have now amended our manuscript to better reflect that it is consistent with published umbrella review guidelines, such as the one suggested by the editor that is now referenced in the paper. We have also now cited the following paper: Ioannidis JP: Integration of evidence from multiple meta-analyses: a primer on umbrella reviews, treatment networks and multiple treatments meta-analyses. CMAJ 2009, 181(8):488-493. We present below a list of points describing how our umbrella review complies with the published guidelines:
• The objectives of our umbrella review are clearly stated in the last paragraph of the introduction.

• In “Literature Search and Data Extraction” in the methods section, we clearly provide our search and inclusion and exclusion criteria.

• In the results section, we provide a flowchart consistent with the PRISMA reporting guidelines.

• In the first paragraph of the results and now in table 1, we provide a short summarization/description of the included meta-analysis papers.

• According to the umbrella review guidelines, we have now included a methodological quality assessment of the included meta-analyses using the AMSTAR quality assessment tool (Table S6).

• We extensively describe the findings of this umbrella review across the results section.

• We provide a summary of the evidence along with a strength of the evidence categorization on table 2 and table S5.

- Make sure that you explain all the abbreviations that you use in your text (for instance SMD).

We have now provided an explanation for all used abbreviations.

Sam Norton, Phd (Reviewer 1):

This paper provides a comprehensive overview of the evidence for psychological interventions for chronic pain. It is well written and provides a detailed but also clear description throughout
that makes a large contribution to understanding the literature. I have only relatively minor comments:

1. At the end of the introduction an umbrella review is introduced. The articles 21-25 cited are all themselves umbrella reviews where it would be more useful for unfamiliar readers to provide reference to a paper describing the methodology for umbrella reviews. I don't know the literature on methodology for umbrella reviews well but perhaps Grant & Booth (2009). Health Info Libr J, 26(2):91-108 would be appropriate

We thank the reviewer for his comments. We have now included two references introducing the umbrella review concept and/or methodology (Ioannidis JP: Integration of evidence from multiple meta-analyses: a primer on umbrella reviews, treatment networks and multiple treatments meta-analyses. CMAJ 2009, 181(8):488-493.; Aromataris E, Fernandez R, Godfrey CM, Holly C, Khalil H, Tungpunkom P: Summarizing systematic reviews: methodological development, conduct and reporting of an umbrella review approach. Int J Evid Based Healthc 2015, 13(3):132-140.). However, since the scope of our umbrella review is broader than what is described in these articles, as we have included quantitative analysis of the included M-As and an assessment of evidence strength, we opted to also keep our initial references to other relevant umbrella reviews.

2. Given the scope of an umbrella review it is clearly a challenge to fully describe all the results in clear and succinct way. The results section does a good job at this but it is hard to understand which types of intervention have been applied across different conditions. A table or figure here summarising the primary studies would be helpful as it is not possible to get this info from the table due to repeated studies in some reviews.

Gathering and describing in a concise way all the primary studies included in 150 meta-analyses included in 38 publications would not be feasible. Instead we chose to create a new and detailed table (Table 1) providing a summary of the 38 included meta-analysis papers in order to better describe the included meta-analyses.
3. In the results section concerning excess statistical significance, some comment is need to aid interpretation of the meaning of the excess positive studies. What are the implications particularly where there was or not evidence for small study effects

This information has been added in the methods: “An excess of statistical significant findings in a meta-analysis may imply the presence of selective reporting bias, as many underpowered studies with statistically significant results may be identified in the field.”

Also, this information has been added in the results: “An excess of significant findings in a meta-analysis coupled with an indication of small study effects based on Egger’s p-value can provide further evidence for the presence of selective reporting biases in the field. Only two meta-analyses presented indication for both excess significance and small study effects bias.”

4. In the results grading the evidence section please restate the criteria used and the elements not met to increase clarity around how decisions were made. I realise this is given in detail in the methods but currently it is unclear and the reader has to manually go through the table to determine which criteria were missed.

This information has been added in the grading of evidence section of the results. It now reads: “None of the examined associations could claim either strong (random effects $P < 10^{-6}$, > 1,000 participants, statistically significant largest study, the $I^2 < 50\%$, the 95% prediction intervals were excluding the null value, and no indication of small study or excess significance bias) or highly suggestive (random effects $P < 10^{-6}$, > 1,000 participants, statistically significant largest study) or highly suggestive evidence.” … “None of these meta-analyses could reach the higher categories of evidence for a combination of reasons. Only 2 out of 12 meta-analyses had $P < 10^{-6}$, the largest study was not significant in 7 out of 12, prediction intervals included almost always the null value (8 out of 12) and there was potential for small study effects (3 out of 12) and excess significance bias (4 out of 12).”

5. I'm not clear on the purpose of the sensitivity analysis for grading. An analysis that lowers the bar required for certain criteria finding that more associations cross the bar is hardly informative

Although what the reviewer notes is correct about our sensitivity analysis, one must consider the setting under which these criteria are applied. As it can be seen from our results, despite the large number of trials in the field, the vast majority of the primary trials include a very small number of participants. The median number of participants across the 150 meta-analyses was 250 and the
75th percentile was 531 participants. However, as the majority of these trials are randomized experiments one may expect to see valid estimates even with a lower sample size. We chose to present the sensitivity analysis of lowering the threshold for the number of participants in a meta-analysis as a method of checking the robustness of our evidence grading approach, which was in general supported.

6. Related to the above, it would be useful to comment in the discussion about what may push the grading up to highly suggestive - e.g. are any areas where a single large study that if it were statistically significant would raise the grading (presuming no change to heterogeneity)?

This information has been added in the grading of evidence section of the results: “None of these meta-analyses could reach the higher categories of evidence for a combination of reasons. Only 2 out of 12 meta-analyses had P<10^-6, the largest study was not significant in 7 out of 12, prediction intervals included almost always the null value (8 out of 12) and there was potential for small study effects (3 out of 12) and excess significance bias (4 out of 12).”

7. The discussion needs to emphasise what is still unknown. Are there areas of chronic pain research where the efficacy of specific types of intervention under researched? Also, for a pain researchers it would be useful of there was a clear summary indicating where the authors think the priority for further research lies

We have already included several sentences in the Discussion as a guide for future research in this area, and we have now amended those sentences to better address the reviewer’s comment, as shown below.

“Our results come in discordance with the generally strong belief in the literature that psychological therapies are universally effective on a variety of pain conditions [76-78]. However, this belief is mainly established based on a limited number of small primary studies, and future larger studies are warranted.”
“A combination of different forms of biases might still be affecting the results. One such is the selective reporting of “positive” versus “negative” findings. In various areas of clinical investigation “negative” findings are of “limited impact” and, therefore, remain often unpublished. Statistical significance testing should not be used in the future as a criterion for publication. Moreover, one cannot exclude the possibility of questionable research practices, such as selective reporting of study methods and results, p-value fishing, or deciding to collect more or stop collecting data only after looking whether the results are statistically significant, which have been shown to constitute common research practices [15, 79-81].”

“Nevertheless, the selection of valid outcome measures for pain and pain-related disability is of great importance due to its close relationship to treatment efficacy replication. Moreover, in pain-related clinical trials, there is generally a lack of standardization both in the pain-related outcome measurement and in pain-related outcome reporting, hampering efforts to synthesize evidence [82]. Even, for the pain reduction assessment per se, there are a number of parameters that can contribute to the observed heterogeneity and/or affect the level of bias operating in the field; statistical versus clinical significance and the usual lack of minimal important difference metrics, daily home data collection challenges, questionnaire and scale structure variations, length of follow-up and appropriateness thereof. The validity and feasibility of objective pain measurements are all attributes of the study design that affect the validity of the evidence base and jeopardize its translational potential.”

“In conclusion, the present findings support that the effectiveness of psychological treatments for pain management is overstated and the supporting empirical evidence is weak. The present findings combined with the fact that psychological intervention trials are still at an early research stage and fall short compared to drug trials [87] underline the necessity for larger and better-conducted RCTs [85] Future research should further focus on building networks involving all stakeholder groups to achieve consensus and develop guidance on best practices for assessing and reporting pain outcomes. The use of standardized definitions and protocols for exposures, outcomes, and statistical analyses may diminish the threat of biases and improve the reliability of this important literature.”

Josef Jenewein (Reviewer 2):

Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, Review
Submission ID: PSYO-D-17-00051

Title: An Umbrella Review of the Literature on the Effectiveness of Psychological Interventions for Pain Reduction

This is an interesting paper investigating the effectiveness of psychological interventions for pain reduction using an umbrella review approach.

In this umbrella review 38 publications were identified, investigating 150 associations between several psychological interventions and 29 different types of pain and including 856 individual studies. Of the 141 associations based on only randomized controlled trials, none presented strong or highly suggestive evidence according to the authors' criteria.

Strengths of this paper include an important topic of both clinical and research interest; careful attention to measurement-related and statistical issues; and on the whole, the paper is clearly written including a nicely described statistical analysis section and discussion.

I have only some minor points to address:

1. Methods: literature search and and data extraction: the authors report that they selected papers in the first step by reviewing the titles of the papers. I am not sure if one can decide whether or not a paper reports a meta analysis by only reading the title.

   We thank the reviewer for the positive comments. As we describe in detail in the methods section: “Two investigators (GM and ER) examined independently the titles, abstracts and full texts of the shortlisted meta-analyses to decide on eligibility. Discrepancies were resolved by consensus and with discussion with a third investigator (KKT).” Many meta-analyses or systematic reviews do reflect their study design in their titles, which is also suggested as good practice by published guidelines for study reporting. If the study design (e.g., meta-analysis) of a publication was not clear in the title, we reviewed sequentially the abstract and the full-text to find this information before making a decision on the eligibility of the publication.
2. There are some typos, for example, p 6, line 27: the abbreviation of standardized mean difference is SMD, not MD

All typographical errors have now been corrected.

3. The methods section including the criteria for classification should be reviewed by a statistician who is familiar with those topics.

We are happy for our methods to be reviewed by a statistician. We have included transparently and in detail descriptions of the methods we used, many of which are standard in the meta-analysis literature. We have also cited herein several other published umbrella reviews that we have conducted in several research fields.