

07-Feb-2024

BMJ-2023-078084.R1

The efficacy of psilocybin for the treatment of depressive symptoms: a systematic review and meta-analysis

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Yours sincerely,

Tiago Villanueva
Associate Editor
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In your response, please provide, point by point, your replies to the comments made by the reviewers, explaining how and where you have dealt with them in the paper.

Reviewer: 1

Recommendation:

Comments:

I appreciate the authors' responses to the initial round of reviewer and editor comments. My only remaining suggestion is to encourage the authors to clearly report in the manuscript any deviations from their preregistration, even minor ones. In my view, this upholds the spirit of preregistration. This could, of course, be done in supplemental materials.

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Recommendation:

Comments:

The authors present a systematic review and meta-analysis of the use of psilocybin for treating depression. I have some comments mainly on the presentation.

1. The paper is well-written, but it is still far too long. I recommend shortening the Results and Discussion by around 50%. This can be done by shifting a lot of material to the Supplement, by writing more concisely, and by omitting detail that is less pertinent.
2. The searches were updated on 10/08/2023 – it would be worth extending them.
3. Page 6. To clarify, is psychedelic micro dosing acceptable as control, but not as psilocybin treatment? It would be better to list all the inclusions then all the exclusions, rather than mixing them. Perhaps give them in separate paragraphs.
4. Outcomes measured within 3 hours of dosing were excluded - what was the shortest interval between dosing and outcome that was included?
5. With the data collection and extraction, it's conventional to name the researchers involved (usually by their initials). This would highlight the fact that one of them was not an author, which is unusual.
6. I am not familiar with Hedge's g. If it is equivalent to the SMD then perhaps call it that instead. The Greek term used for it in the Results is nowhere defined, which adds to its impenetrability.

7. On page 12 line 16 it should be 875 not 857, to match Figure 1.
8. Table 1. There is a mix of dots and commas in the numbers. I suggest you give % Female as whole percentages and omit the corresponding numbers (as they can be back-calculated).
9. The Results on pages 16-19 are detailed descriptions of each study. It would be better to summarise them by putting the results in a table, then drawing out the main features in the text. Consider putting the descriptions of each trial in a supplementary table. Similar comments apply to the RoB and heterogeneity Results too.
10. For all the numbers presented, be aware of the size of the corresponding SE and adjust the precision accordingly, e.g. one decimal place for Hedge's g ; RRs to one decimal place if the CI is wide, e.g. RR=2.02, 95%CI: 1.33 to 3.07, P-values to one significant digit, and PIs either as whole numbers or to one decimal place. Do see my guidelines at <https://adc.bmj.com/content/100/7/608>.
11. As an example see Table 3 – the prediction intervals are all very wide and also very similar. The text says PI 95%CI is -1.720 to 5.034 - this would be much better as -1.7 to 5.0 or even -2 to 5.
12. Many of the figure titles include this phrase: "Forest plot for the overall change in depression scores pre- and post-treatment". It needs rewording as it is unclear – the change is from pre- to post-treatment.
13. 16 figures in the main text is too many. I suggest including just figures 1, 2 and 4 in the main text, and putting the others in the supplement. Similarly I would put Tables 3-5 in the supplement.
14. The Discussion should not repeat numbers from the Results, e.g. page 32: "Meta-analyses of response and remission rates showed that treatment response was approximately two times greater (RR=2.02, 95%CI: 1.33 to 3.07) with psilocybin, and the likelihood of remission was nearly three times greater (RR=2.71, 95%CI: 1.75 to 4.20)." The aim is to put the numbers in the Results, then provide an overview of them in the Discussion.

Tim Cole

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