Peer-Review comments and author responses

Reviewer 1

1. Introduction

-**Comment:** "The aim of the systematic review and meta-analysis is to evaluate the effectiveness of non-pharmacological interventions, specifically mindfulness interventions…". In fact, authors only evaluated mindfulness interventions, as shown in Figures 4 and
1. Please clarify.

Response: We have revised the aim to clarify that our review specifically evaluates mindfulness interventions via mHealth applications instead of "non-pharmacological"

2. Methods

-**Comment:** An Embase search would have been important to include studies that may have not been included in the Pubmed dataset. I suggest this issue should be included as one of the limitations of the present work.
I am also missing a reference for the Rob-2 tool. I suggest using the following: Sterne JA, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomized trials. *BMJ, 2019;366*:I4898.

Response: We have addressed this issue by stating the limitations of including only 2 databases in the meta-analysis: Pubmed and Cochrane. The RoB 2 tool reference has been added as suggested.

-**Comment:** "Overall, the risk of bias assessment reveals that while two studies are methodologically sound with a low risk of bias, the majority of the included studies (five out of seven) present significant concerns."
his issue is very relevant for the interpretation of results. Authors must be cautious with the conclusions of this meta-analysis, as there were methodological flaws for most studies, thus potentially introducing bias to the results. Please consider conducting a sensitivity analysis excluding poor quality studies, to see how results could change.

Response: As suggested, we have performed sensitivity analysis including only the studies without high risk of bias domains according to RoB2 (Zhang 2023 and Sun 2021). Description of the analysis was added at the end of section 3.8 Meta-analysis, direction and significance of effect were consistent with the main analysis.

3. Results

-**Comment:** It is interesting that authors reported a significant effect of mindfulness interventions, measured with EPDS score, with a p-value of 0.04. In general, we recommend not to dichotomize the p-value to significant/non-significant, because under this metric, a p-value of <0.0001 could be equally interpreted as statistically significant when compared with a p-value of 0.04. I would suggest changing the wording to "borderline evidence" when it comes to the interpretation of a p-value of 0.04. Additionally, in the conclusion I would emphasize that although the intervention might prevent depressive symptoms, the persistence of the effect through the postpartum period is unclear.

Response: We thank you for this insightful comment. We agree that the interpretation of p- values should be nuanced and not only based on a significance threshold. We have revised the manuscript to use more precise language, such as "strong evidence" when appropriate. In the case of the p-value of 0.04, we have rephrased the interpretation to "suggestive evidence," acknowledging the limitations of statistical significance.

-**Comment:** Please consider rounding figures to 1 decimal throughout the manuscript. For instance, 5.00% to 26.52% is equally informative as 5% to 25.5%. I would suggest spelling out the abbreviation US. While the abbreviation is very obvious for any American reader, this journal is read by many others outside the United States. In addition, the US could stand for ultrasound in the medical literature.

Response: Thank you for this suggestion, we agree that rounding to 1 decimal will help make our manuscript more readable without losing any information. Accordingly, all figures have been rounded. Likewise, the abbreviation "US" was spelled out instead to avoid any confusion.

-**Comment:** Please consider changing the wording" …our results demonstrated…" to "our results suggested…" Please include a paragraph referring to the strengths and limitations of this study. I would emphasize here that no definite conclusions can be drawn from this work, given that the confidence intervals were wide, and further research is needed.

Response: Thank you for your suggestions. We have revised the discussion section to clarify the tentative nature of our findings by rephrasing "our results demonstrated" to "our results suggested.". Additionally, we have added a paragraph outlining the strengths and limitations of our study, including the wide confidence intervals and the need for further research to confirm these findings. This adjustment provides a more balanced perspective on the study's implications and acknowledges the preliminary nature of our conclusions.

4. Discussion

-**Comment:** Regarding the paragraphs:
a. "However, the literature inconsistently reports the effects of these treatments on depression. A 2022 meta-analysis by Zhou et al. and a 2022 study by Tsai et al. showed conflicting evidence on the effect of mHealth interventions on EPDS scores. Zhou et al. reported a decrease in EPDS scores with mHealth interventions, while Tsai and colleagues found that mHealth apps did not improve perinatal depression.
b. Recent studies have assessed the acceptability of mobile health apps. Their findings showed effectiveness in monitoring mood symptoms and EPDS scores, although there is limited evidence regarding the evaluation of the onset of PPD using EPDS (Miura et al., 2023)."
These paragraphs could fit well in the discussion session, where authors can contrast their results with previous literature. Also, this could help shortening the introduction section, which seems a bit long.

Response: We appreciate this advice, we addressed these paragraphs in the discussion section as suggested.

5. -**Comment:** The formal definition of mindfulness could vary, and therefore it would be difficult to reach consensus as to whether a given intervention is considered a form of mindfulness or not. In addition, the distinction between mindfulness and cognitive

behavioral therapy seems not clear. I suggest including this issue as one of the limitations in the discussion section.

One of the reasons why some patients did not complete follow-up throughout the pregnancy would be precisely because they were depressed, thus potentially leading to informative censoring and selection bias. This should be included in the discussion section.

Response: We have included the limitation regarding the variability in defining mindfulness interventions in the discussion section, noting that the lack of a formal definition and the overlap with cognitive behavioral therapy may lead to challenges in reaching consensus. Additionally the discussion now notes the concern for possible informative censoring and selection bias, as some participants who were depressed may not have completed follow- up.

5.Conclusions

-**Comment:** This section reads like an extension of the discussion section, rather than a conclusion statement. In general, the conclusion section should be limited to three or four sentences. Furthermore, some of the statements made in the conclusion section were already included in the discussion section. The study should be concluded with a very concise and strong message in this section.

Response: Thank you for your feedback on the conclusion section. We have revised it to make it more concise and focused, following your recommendation. The conclusion was shortened, summarizing the core findings and implications with a strong, clear message. Elements that overlapped with the discussion section were removed to avoid redundancy, aligning the conclusion more closely with the purpose of providing a final, impactful statement on the study's relevance. We appreciate the guidance on improving the clarity and precision of this section.

6. Graphs

-**Comment:**
Figure 1: Please consider increasing the font of the text. Also, I would suggest changing the word "wrong" to "different"
Figure 3 doesn't provide much more information, as compared to **Figure 2.** Is it necessary to include Figure 3 here?
Figures 4 and **5** should be self-explanatory. Please provide a brief description of abbreviations used (e.g., EPDS, CI, df, IV). Also, please briefly interpret the results in one or two sentences.

Response: We have updated figure 1 replacing the word "wrong" for "different" and slightly increasing font size. Figure 3 has been removed, as we agree on its redundancy upon revision.
Regarding figures 4 and 5, abbreviations have been added as footnotes for clarity. These figures are already briefly interpreted in two sentences in section 3.8 Meta-analsyis as follows
Results presented in figure 4 are described in the second and third sentence of the second paragraph:
"The summarized mean difference was -1.93 with a 95% confidence interval of -3.78 to -
0.08. Additionally, the test for overall effect showed a significant effect (Z = 2.04, P= 0.04)
[sentence 1]. *However, significant heterogeneity was detected (P<0.01), suggesting inconsistent effects in magnitude and/or direction.* ***[sentence 2]"***
Results presented in figure 5 are described in the third and fourth sentence of the third paragraph:
"There was no statistical difference between the two groups, the summarized mean difference was
-2.63 with a 95% confidence interval of -6.13 to 0.86 and non-significant test for overall effect (P

= 0.14) [sentence 1]. Similarly to the analysis of post-intervention scores, significant heterogeneity was detected (P<0.01), suggesting inconsistent effects in magnitude and/or direction [sentence 2]"

We believe the sentences preceding the descriptions of the results are necessary to provide context and more specific details about the analysis parameters that might be of interest to readers. The implications of these findings are explored in the discussion.

Reviewer 2:

1. Abstract:

-**Comment:** The length is adequate and it is well written. When reading, it might be a little confusing if you considered only the pregnant period, or the postpartum, or both, please clarify. Maybe you can refer to the period as perinatal. Conclusion might also be confusing, as the study shows the intervention could reduce depressive symptoms rather than prevent depression from scratch.

Response: We have clarified the study period by using the term 'perinatal period,' which includes both pregnancy and the postpartum period. Additionally, we revised the conclusion to state that the interventions reduce depressive symptoms rather than prevent depression.

2. Introduction:

-**Comment:** The introduction is clear, easy to read and the flow of information adequate. Length could be reduced, as for example paragraph 1 and 2 refer to the relevance of the condition. The gap is clearly stated. Some aspects to consider:
- why did you decide to include both pregnancy and postpartum period? It is clear why the topic is relevant, but not why did you included the 2 periods.
- what is the standard treatment?

*Response: Both periods were included as most trials of mindfulness intervention start during pregnancy, recognizing that the risk of depression starts before delivery and targeting its causes. This is reflected in the third paragraph, reading " In recent years, mindfulness-based interventions **during pregnancy** have been suggested to improve mental health and pregnancy outcomes. Mindfulness is observing the present moment without judgment, often achieved through meditation (APA Dictionary of Psychology, n.d.). It can help in **understanding the causes of maternal depression, providing targeted training based on these causes**"*

-**Comment:** Regarding standard treatment, there is no current guideline-recommended treatment for perinatal depression previous to its diagnosis (the patients included in the reviewed studies were at risk but not diagnosed with perinatal depression). Treatment received by control arms in the reviewed studies are described in the last paragraph of section *3.3 Characteristics of interventions*, and consisted mostly of only usual perinatal care or educational modules. Line 3 of 2nd paragraph: please cite properly

Response: Thank you for pointing this out. We have corrected the citation in line 3 of 2nd paragraph which now reads "(Goodman, 2009)".

-**Comment:** Line 1 of paragraph 3 please briefly explain the EPDS scale. As a reader, I would like to know which cut off value did you use and why different values would be

important to mention in the introduction.

Response: We have revised line 1 of paragraph 3 to include a brief explanation of the Edinburgh Postnatal Depression Scale (EPDS). We describe the EPDS as a widely used screening tool for detecting postnatal depression symptoms, typically scored from 0 to 30. Additionally, we specify the cutoff value used in our study and mention that different cutoff values are often applied across studies, which could affect the interpretation of prevalence rates and diagnostic accuracy.

-**Comment:** Last line of paragraph 4: please cite only with the last name of the author.

Response: Thank you for pointing this out. We have corrected the citation to contain only the last name of the author. It now reads "(Green et al., 2022)"

-**Comment:** Paragraph 8: in the aim of the paper, I would change "improve PPD" for "improve perinatal depression" to avoid confusion.

Response: Thank you for the suggestion. Although the number of paragraphs in our introduction has been modified, as suggested, to enhance clarity and better align with the study's aim we have changed references to "improve PPD" to "improve perinatal depression symptoms" where the aims of our study are mentioned (like the fifth or final paragraph of the introduction and the first paragraph of the conclusion).

2. **Methods**:

-**Comment:** Detailed and clear. It's well written.
Some aspects to consider:
   a. What was the time frame of the articles included in the search?
   b. Any language in particular for the search? Please clarify.
   c. Did you consider studies with women previously using mindfulness interventions before the pregnancy?
   d. Section 2.2: in the search strategy you used a broad approach. But you didn´t include m-health as an intervention option, or depressive symptoms as an outcome option. Are you concerned about missing some studies?.
   e. Primary and secondary outcomes are not specified. Please clarify.

Response: Thank you! All points were addressed.
   a. The articles included in the systematic review range from 2018 to 2023. Although this is described in 3.1 Identification and selection of studies reading "The earliest study began in July 2018, and the most recent in November 2023", we have included this information along with other characteristics in table 1 Study characteristics to improve clarity about the general characteristics of the included studies.Regarding the rest of the articles encountered during the search, no time filters were utilized in the search strategy and the timeframe for the search is described in 2.3 Search strategy and data extraction and 3.1 Identification and selection of studies.
   b. Only articles published in English were included without any additional filters applied. Accordingly, 2.3 Search strategy and data extraction section states "No database filters were used, and only the articles available in English were selected"
   c. Previous use of mindfulness interventions was neither an inclusion or exclusion criteria for this review. Some of the included studies however, in particular most of those included in the meta-analysis (Sun 2021 ; Leng 2023; Zhang 2023) explicitly excluded women with

previous or current mindfulness practices.

d. *We acknowledge that we left out the keyword m-health in our search strategy, and addressed the issue in section 4. Discussion as a limitation.*
   Regarding "depressive symptoms" as an outcome option, we were not concerned about missing articles since mentions of "depression symptoms" were already captured by the inclusion of the keyword "depression".

e. *Although not explicitly identified where mentioned in the introduction (last paragraph), the primary and secondary outcomes are summarized and clearly stated in Material and Methods, section 2.2 Primary and secondary outcomes.*

3. Results:

-**Comment:**This section is detailed and clear. All major aspects of analysis are mentioned , following a reasonable flow of information. Some aspects to consider:

   a. Figure 1: please clarify when the screen was made by title and abstract, and when by full text reading.
   b. Section 3.4: first and second sentence refer to secondary outcomes and not the primary (EPDS scale).
   c. Section 3.5, line 5: what does mindfulness refer to? It seems an intervention and not an outcome, please clarify.
   d. Section 3.7: please consider moving before section 3.6, as it is related, or splitting the effects to primary and secondary outcomes sections.

Response: Thank you!

a. *In figure 1, "Studies screened" refers to those reviewed only by title and abstract while "Assessed for eligibility" refers to those reviewed by full-text reading. For clarification, a footnote has been added to the figure. Additionally, section 2.3 Search strategy and data extraction describes the steps at which abstract or full text review were performed with their corresponding dates, reading:*
   *"Initially, 28 researchers **screened** the studies based on their **titles and abstracts** on April 5th, 2024 . The **full-text** was assessed for eligibility criteria based on predefined inclusion and exclusion criteria and was completed on May 8th, 2024"*

b. *Thank you for pointing this out. The primary outcome was EPDS scores, accordingly the first sentence of section 3.4 reads "All authors measured EPDS as part of their primary outcomes to quantify depressive symptoms…". Secondary outcomes are separately described in 3.5 Secondary outcomes.*

c. *Text has been corrected. Mindfulness is the intervention, the text now reads "Impact of mindfulness on…"*

d. *Thank you for the suggestion, we agree the order as recommended is clearer and adjusted accordingly.*

4. Discussion:

-**Comment:** The topics raised in this section are solid, with good justification. Limitations of the manuscript are properly mentioned. Did you consider younger than 27 year old women could also be at higher risk of perinatal depressive symptoms? How about the variability in the implementation of the intervention among studies? Conclusion is concise and clear too, showing good understanding of the analysis made. I would consider changing the word "prevent" (keep from happening) for "reduce", as it might be confusing.

Response: Thank you for the great discussion points, we edited the discussion to include mentions of the variability of the interventions (as a limitation for analysis) and changed the word "prevent" for "reduce" to avoid confusion as suggested.

Regarding women younger than 27 years old, many such participants were included in the reviewed trials. Section 3.2 Characteristics of intervention includes "The mean age of participants varied across studies, ranging from 27 to 32.7 years" referring to the range of absolute ages of the participants but the ranges of the average age across studies. These averages were accompanied by standard deviations from 3 to 5 years, encompassing the most common ages for childbirth (including younger than 27).

We agree however that the effectiveness of these interventions in the youngest age groups could be interesting to further explore in future studies.

Reviewer 3

1. **Introduction**
   -**Comment:** While the topic and its relevance of interest to the reader and the clinical field, its reporting structure was not necessarily engaging. Specific points that were rather distracting. For instance:
   - There was an overemphasis on diagnostic tools, particularly cut-off values, sensitivity and specificity
   - Redundancy in respect to mHealth
   - Wide range of epidemiological values were often described without serving a clear purpose e.g. authors started off with describing prevalence variations then its impact on maternal mortality then the increasing prevalence. While data is interesting, readers could benefit more from data that is directly relevant to the study, and presented in a concise, coherent fashion that supports the authors arguments

Response: Thank you for the suggestion, we agree there is room for improvement in the introduction. The description of the cut-off value used in our study was kept in the manuscript as it was requested by one of the other reviewers. However, the text has been modified with a clearer and more coherent writing style. The information on sensitivity and specificity were synthesized to improve engagement and the explanation about mHealth was synthesized so that it is more

straightforward and not redundant.

2. **Methods**
    -**Comment:** In the eligibility criteria were patient who are taking meds for depressive symptoms included?

Response: Patients on current treatment for depressive symptoms were excluded in all reviewed studies. This was part of the eligibility criteria for studies to be in the review as stated in section 2.1 Eligibility criteria which on its last sentences reads as follows:

> *"Studies were excluded that included patients with previous mental health symptoms and were on medical treatment for depression or presented health problems prior to the current pregnancy, as well as studies that included patients with history of substance abuse or addiction."*

3. **Results**
    -**Comment:** While authors started off with clear descriptions of study identification and selection, the reporting of characteristics was rather distracting. Remaining parts of the results may improve from a clearer structure.
    Instead of reporting "some studies included over 100 subjects, while others had fewer than 100 subjects", please report descriptively e.g. Among the 7 included clinical trials, the number of participants ranged from x - x, with a median/mean xxx (IQR: xx) (SD: xx)
    Report age as median (IQR) or mean (SD) based on data distribution
    - Ethnic/race group reporting can follow the same reporting method, however, as frequencies. Eg. Among the 7 included trials, x(%) reported xxx. Of these, then add an account of race/ethnic group aggregated data e.g. White or Caucasian (xx%)
    - "Most women included were either married or living with their partner" => please provide data no(%)
    - Why "less than" when reporting small proportion not cohabitating with a partner (<8% in all studies.). Please report accurate values where present.
    - Same same reporting structure i.e. descriptive reporting, for the remaining of 3.2. Characteristics of included studies, 3.3. Characteristics of intervention, Outcomes, and rest of results.
    - You may use a table to describe findings of each study separately but keep text reporting concise with relevant values.

Response: Thank you for the suggestion, we agree the presentation of results have room for improvement in clarity and consistency. The section has been edited to included only critical information and use specific measures when appropriate.
We also agree a table would make the information more accessible for readers. Accordingly, a table describing the basic characteristics of each included study was inserted (table 1).

4. **Discussion**
    -**Comment:** Please use discussion to interpret findings. Also compare your findings with previous research and provide small conclusions.

Response: Thank you for the suggestion. Discussion has been edited and now focuses on interpretation of the findings, its comparison to previous research and impact for future studies.

Reviewer 4:

1. **Methods:**

   -**Comment:** I would rephrase the first sentence as follows: "The eligibility criteria established for the studies are: (Liu et al., 2022) pregnant patients from 18 to 45 years of age, with completed…"
   - I would change in the fourth sentence "uploaded TO Covidence…".

Response: Thank you for the suggestions, we agree they would improve the clarity of the text. Proper changes were made to the wording.

2. **Results:**

   -**Comment:** Characteristics of included studies: In the third paragraph, first sentence, I would delete where it says "…enhancing the reliability of this analysis across different obstetric profiles". I would develop this concept further on in the discussion/conclusions.
   - Characteristics of intervention: In the third paragraph, I would unify the expressed numbers either in numbers or written in letters for more clarity.

Response: Thank you for the suggestion. Characteristics of included studies have been edited, the sentence in question has been removed and references to the variety of profiles has been added to the discussion instead.
We agree unifying the way numbers are expressed would improve clarity. Accordingly, the numbers in characteristics of intervention have been all changed to be expressed in letters.

3. **Discussion:**

   -**Comment:** In the third paragraph, third sentence, when you refer to T1 to T5 and if they are statistically significant or not, even though they are detailed in table 6.2, they are unclear for the reader at this point, because they are measured at different time points in each trial, and there are no statistical values in the mentioned table. Therefore, I suggest rephrasing this last sentence to avoid confusion. The same happens in the fifth paragraph, second sentence when you refer to T4.

Response: Thank you for the suggestion. The paragraph has been edited for clarity and now reads:
   "The mindfulness interventions generally show a favorable effect on pregnancy and PPD symptoms. The effectiveness of the interventions varies across different time points, with some studies showing stronger effects than others, contributing to the

overall heterogeneity, as suggested by this meta-analysis. Prior to the intervention, the baseline levels of depressive symptoms are comparable between the two groups."

4. **Acknowledgements:**
   -**Comment:** I don't know if it is empty for some reason, but if there is no one to thank for, I would advise deleting this header.

Response: Thank you for bringing this to our attention. The section was empty by mistake.

5. **Appendices:**

   Comment: EDPS Scale score screening - Detailed timelines
      a. In the T4 row of the article by Leng LL et al, China, 2023, you should delete the "r" where it says "6th week".
      b. In the T2 row of the article by Sun Y et al. 2021, China, you should add an "s" where it says "4 weeks after group allocation".

Response: Corrections were made: 'r' removed in T4 for Leng LL et al., and 's' added in T2 for Sun Y et al.

6. **References:**

   -**Comment:** In the first one: "APA Dictionary of Psychology. (s/f)", you should change the text from Spanish to English.

Response: Thank you for pointing this out. We have changed the text from Spanish to English.