RESPONSE TO LETTER

Response to Concerns on "Inadequate Evidence for Acupuncture as an Alternative or Adjunct to Antidepressants/Psychotherapy for Postpartum Depression: A Bayesian Systematic Review and Network Meta-Analysis" [Response to Letter]

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Dear editor

Thank you for bringing the *Letter to the Editor* regarding our publication, "Inadequate Evidence for Acupuncture as an Alternative or Adjunct to Antidepressants/Psychotherapy for Postpartum Depression: A Bayesian Systematic Review and Network Meta-Analysis",[1] to our attention. We appreciate the opportunity to address the comments and concerns raised by Xilong Yang et al and value their engagement with our work.

Below, we provide our response to the points raised in the letter.

On Heterogeneity Introduced by the Use of Different Antidepressants in the Control Group

The letter notes that our review "did not thoroughly examine the heterogeneity introduced by the use of different antidepressants in the control groups of the included RCTs."

We appreciate this observation and would like to clarify the rationale for our approach. Due to the stringent inclusion and exclusion criteria, only 13 RCTs were included in the review. Among these, eight trials used antidepressants as controls, involving five different antidepressants: Fluoxetine, Escitalopram, Sertraline, Venlafaxine, and Maprotiline. This information is explicitly outlined in the results section of our paper.

In meta-analysis, it is conventional practice to combine studies with homogeneous characteristics, and to conduct subgroup analyses or meta-regressions only when there are sufficient studies to support meaningful conclusions. The *Cochrane Handbook for Systematic Reviews of Interventions* (Version 6.5; updated August 2024)[2] clearly states in Chapter "10.11.5.1 Ensure that there are adequate studies to justify subgroup analyses and meta-regressions", that "It is very unlikely that an investigation of heterogeneity will produce useful findings unless there is a substantial number of studies". Specifically, the handbook recommends at least 10 studies for each characteristic being modeled. Given the small number of homogeneous

studies in our analysis, subgroup analysis or meta-regression to assess heterogeneity related to different antidepressants was not feasible. Moreover, such an analysis, even if attempted, would likely have produced inconclusive results.

In our paper, we explicitly state:

> First, certain outcomes, notably SDS and SAS, had a very limited number of included RCTs (<3), precluding meta-synthesis and comprehensive analysis. This dearth of RCTs also hindered subgroup and sensitivity analyses aimed at detecting sources of heterogeneity in these outcomes.

This shows we were fully aware of this limitation.

On Varying Severity of Postpartum Depression (PPD) at Enrollment

The letter also raises an important point regarding the varying baseline severity of PPD across the included RCTs and its potential impact. We acknowledge this as a valid concern and one that we also highlighted in our paper.

In the "Interpretation of Findings" section, we noted:

> …in the reviewed RCTs, the baseline severity of depression among patients varied considerably, which impedes determining the efficacy of acupuncture for different levels of PPD. Hence, it is recommended that future trials standardize the severity of depression among recruited participants to ensure more consistent and comparable results. Such a design would also help to more clearly delineate the specific applicability of acupuncture in PPD patients.

This underscores our awareness of the issue and its implications for interpreting our findings.

It is worth noting that this limitation stems primarily from the design of the original RCTs rather than from our review. While all included studies recruited patients who met PPD diagnostic criteria, some did not specify clear inclusion criteria for the severity of depression. Among those that did, different measurement tools (EPDS, HAM-D, SDS) and cut-off scores were used, introducing considerable heterogeneity. Given only 13 RCTs were included, any analysis based on these covariates would have small sample sizes, which would be insufficient for meaningful subgroup analysis. Additionally, since all studies were RCTs, the random heterogeneity in baseline scores likely had minimal impact on the results, except for adding minor error variance. Nevertheless, we agree that future systematic reviews/ meta-analyses on this topic, if supported by a larger pool of high-quality RCTs, should investigate this issue more thoroughly.

On the Quality of the Included RCTs

Finally, the letter raises concerns about the inadequate quality of the included RCTs. We fully agree that this is a critical issue, one which we have carefully addressed in our paper. In the quality assessment section, we noted the methodological limitations of the included studies, which is precisely why we concluded that the current evidence is insufficient to strongly recommend acupuncture for PPD. Despite some positive findings in the meta-analysis, we emphasized the need for more high-quality and rigorously designed RCTs before drawing definitive conclusions.

Conclusion

We are grateful for the thoughtful feedback provided by the letter's authors. Their insights highlight important areas for further exploration and underscore the complexities of systematic reviews in emerging fields such as this. While we stand by the validity of our conclusions based on the methods and data presented, we deeply value the opportunity to clarify these points and engage in this important academic dialogue.

We remain committed to fostering constructive discussions and advancing research in this area. Thank you once again for the opportunity to address these concerns.

Abbreviations

EPDS, Edinburgh Postnatal Depression Scale; HAM-D, Hamilton Depression Rating Scale; PPD, Postpartum Depression; RCTs, Randomized Controlled Trials; SAS, Zung's Self-Rating Anxiety Scale; SDS, Zung's Self-Rating Depression Scale.

Disclosure

The authors report no conflicts of interest in this communication.

References

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