

Dear Editor,

Thank you very much for the opportunity to revise our manuscript “Outcomes of long-acting injectable antipsychotics use in pregnancy: a literature review”. We have carefully read reviewer’s comments. Herein we provide detailed responses to the reviewer’s comments and explain how we revised our manuscript based on those comments point-by-point:

Reviewer #1:

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Minor revision

**Specific Comments to Authors:**

This review aimed to provide an up-to-date summary of the relevant data on maternal, pregnancy, neonatal, and developmental outcomes from available published cases of LAI antipsychotics use in pregnancy. A literature search was performed in three online databases, A total of 19 publications include 3 case series, 15 case reports, and 1 conference abstract. The result is there were no reported negative long-term developmental outcomes. Further well-designed research is needed to properly evaluate the risks and benefits of LAI antipsychotics use during pregnancy. The title of the article is relatively novel, and the content to be written is also attractive. However, due to the limited amount of literature and the lack of large sample sizes and good experimental designs that can be included in the analysis, the conclusions drawn seem to have little reference value. The suggestion is to expand the search scope, even including clinical studies registered on the website, to better understand the current ongoing research and results.

**Response:** Thank you very much for the time and effort provided to review our manuscript. As currently available published data consists only of case reports and series, according to your suggestion, we expanded our search scope with the search of ClinicalTrials.gov database to identify currently ongoing clinical studies on this topic.

Following sentences were added to the revised manuscript to address this comment:

- Introduction: “We also aimed to identify whether there are ongoing clinical studies assessing LAI antipsychotic use during pregnancy.”
- Methods: “To identify ongoing clinical studies aimed at assessing the use of LAI antipsychotics during pregnancy, we searched the ClinicalTrials.gov database on January 23, 2024. We performed a search by entering previously mentioned LAI antipsychotics in the intervention/treatment search field, and pregnancy in the condition/disease search field.”
- Results: “*Ongoing clinical studies* We identified only one currently recruiting study (“Long-acting Injectable Antipsychotics for Mental Ill-Health in Pregnancy and Postpartum” – NCT05766007) that specifically aims to assess safety and clinical outcomes of LAI antipsychotic use during pregnancy and

postpartum<sup>[50]</sup>. This study also aims to determine the magnitude of changes in pharmacokinetics during pregnancy, assess the extent of fetal exposure at delivery, describe breastmilk pharmacokinetics of selected LAI antipsychotics, the extent of breastfed infant exposure, and the sources of variability in maternal and fetal/breastfed infant LAI antipsychotic exposure<sup>[50]</sup>. The study population includes pregnant and postpartum women aged at least 18 years receiving maintenance doses of LAI antipsychotics (risperidone, paliperidone palmitate, fluphenazine decanoate, flupenthixol decanoate, and zuclopenthixol decanoate)<sup>[50]</sup>. This observational prospective cohort study is being conducted in Nigeria and is sponsored by the University of Liverpool<sup>[50]</sup>. The study started on August 01, 2023 and is estimated to be completed in August 2025<sup>[50]</sup>. The estimated number of participants enrolled is 125<sup>[50]</sup>. We also found three currently recruiting studies that aim to evaluate outcomes of antipsychotic treatment during pregnancy, but these are not restricted to LAI antipsychotic use: “Maternal And Infant Antipsychotic Study” (NCT06049953)<sup>[51]</sup> being conducted in the United States since 2023, “National Pregnancy Registry for Psychiatric Medications” (NCT01246765)<sup>[52]</sup> being conducted in the United States since 2008, and “The National Register of Antipsychotic Medication in Pregnancy” (NCT00686946)<sup>[53]</sup> being conducted in Australia since 2005.”

- Discussion: “Our review identified only one ongoing observational prospective cohort clinical study conducted with the specific aim of assessing the safety and clinical outcomes of LAI antipsychotic use during pregnancy<sup>[50]</sup>. We hope that this study will provide further insights into the risks and benefits of LAI antipsychotic use during pregnancy.”

Furthermore, considering that Table 1 is longer than 2 pages, we have provided it as a supplementary material (Supplementary Table 1) in accordance with the “Guidelines and Requirements for Manuscript Revision: Minireviews”.

The English language polishing in the revised manuscript was performed by a professional English language editing company to ensure that all grammatical, syntactical, formatting, and other related errors are resolved.

The revised/added contents are highlighted with yellow color in the revised manuscript.