Reviewer's report

Title: Do pregnant women's socioeconomic status influence the relationship between use of selective serotonin-reuptake inhibitors and the risk of congenital heart defects? - a cohort study

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Reviewer: Edi Vaisbuch

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Summary
This cohort study was designed to verify the association between SSRI use during the first trimester of pregnancy and congenital heart disease and to assess whether the risk differs between various socioeconomic groups. The study used several register data and included more than 72,000 pregnancies in Funen, Denmark. Of the 845 pregnant women exposed to SSRI during the first trimester, 11 had a fetus with CHD [AOR 4.03 (95% CI 1.75-9.26)]. The authors found no association between socioeconomic status and the risk of congenital anomalies among SSRI users.

General comments
This study is well conducted, not easy to performed and well written; however, it is not novel, replicates previous data (probably with a lower power) and its rational is not fully defined. The small number of exposed cases with congenital heart defects weakens this study as it has insufficient statistical power to draw useful conclusions. Thus, the more interesting part of this manuscript comes to be the strengths and limitations section, which is the central part of the discussion section, as the authors had to admit with several limitations that make this manuscript pointless.

Specific comments:
1. The authors used "improved" data from the Danish EUROCAT Register? Improved compare to what? (Discretionary Revision)

2. The rational for assessing the "socioeconomic position" on the risk for congenital anomalies among SSRI users is not clear. As it sounds from the title of the manuscript this was the main objective of the study. The authors state in their discussion that "no other published studies have examined the association between SSRI-use and congenital malformations stratified by socioeconomic groups." This, by its own, is not a good justification to perform this study. Why should the risk be modified according to marital status, level of education or income? Indeed, it is well known that SSRI-users tend to differ in their socioeconomic status from non-users (as it has been found in this study), but once SSRI is used during the first trimester, why should the risk for congenital defects be further modified?
It would make sense for these variables to affect compliance to treatment, and by that to indirectly affect the amount of exposure of the fetus to the drug. However, this was probably not the case in this study as the authors found that "Exposed women had redeemed similar amounts of prescriptions for SSRIs regardless of socioeconomic positions"; thus, why should the risk be different? ((Major Compulsory Revisions).

3. On page 10, it is stated that the "information on exposure The Danish National Prescription Registry and reported SSRI-use from the Danish EUROCAT Register were consistent in only 5 of the 11 exposed cases." - What does it mean? That only 5 fetuses, indeed were exposed to SSRIs during the first trimester of pregnancy? (Minor Essential Revision)

4. The authors state in the abstract, discussion and conclusions that this study could not provide convincing evidence regarding interaction between socioeconomic status and maternal SSRI-use on the risk of severe congenital heart defects. I would delete the word "convincing" as it sounds that there was some interaction but not too strong, but this study did not present any interaction between the two. (Discretionary Revision)

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests