Author’s response to reviews

Title: Antidepressants during pregnancy and risk of autism spectrum disorder and attention deficit hyperactivity disorder: systematic review of observational studies and methodological considerations

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Version: 1 Date: 06 Dec 2017

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BMED-D-17-01616: Antidepressants during pregnancy and risk of autism spectrum disorder and attention deficit hyperactivity disorder: systematic review of observational studies and methodological considerations

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Reviewer reports:

Reviewer #1: The authors have been thorough in their response to reviews. The manuscript is substantially strengthened with these changes. I have no additional comments.

RESPONSE: Thank you.

Reviewer #2: The manuscript has improved considerably and will be an important addition to the literature. I only have one more comment that should be addressed. Please provide specific results of the investigation for publication bias and state the methods used in the Methods section.
RESPONSE: Thank you for highlighting this to us. We have now added the following information to the methods section:

“Publication bias was assessed by testing for funnel-plot asymmetry using the Egger test for studies reporting results of the classical reference group with ASD and ADHD.” (Line 231)

We have now added the following information to the results section:

“No evidence of publication bias was detected when testing for funnel-plot asymmetry using the Egger test for either ASD (p-value=0.433) or ADHD (p-value = 0.901).” (Line 364)

Editor: In addition to the reviewers’ comments, please also add the following information:

- List of abbreviations
- Authors’ contributions section

RESPONSE: These sections have now been added (Line 63 and Line 529 respectively).

Additionally, small number of included studies reported estimates for both SSRI exposure and any antidepressant exposure and we noted minor inconsistency in the use of these two different estimates for the meta-analysis (table 4). We have now included the following statement in the methods section:

“When estimates for SSRI exposure and any antidepressant exposure were each reported within the same study, the effect estimate for SSRI exposure was preferentially used because it is the most widely used group of antidepressants, with sensitivity analysis performed using estimates for any antidepressant exposure.” (Line 229)

We also provide the same results substituting the effect estimates for any antidepressant exposure as a sensitivity analysis with very similar results and included them as an additional supplementary table (new supplementary table 5). This does not lead to a material change in the results of the manuscript and provides additional transparency. We hope this is acceptable.