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Commentary

Reply to: Shukla et al., Commentary on: Prenatal exposure to acetaminophen and children's language development at 30 months [1]

We thank Shukla and co-authors for their comments on our recent article.

The commentators' primary concern was that our use of stratified analysis was post-hoc and exploratory. In fact, the primary goal of our analysis, explicitly stated in the last paragraph of the introduction, was to examine sex-specific associations between estimated APAP exposure in weeks 8–13 of pregnancy and language development at 30 months of age. Not only is this aim appropriate, given a body of literature demonstrating sex-differences in associations between prenatal acetaminophen exposure and neurodevelopmental end-points, it is responsive to the NIH requirement that NIH-funded research must examine sex as a biological variable; "NIH expects that sex as a biological variable will be factored into research designs, analyses, and reporting in vertebrate animal and human studies" (NOT-OD-15-102, June 9, 2015). Results of our sex-specific analyses would have been included in our publication, even if they had not shown significant sex differences.

An additional concern of the commentators was that we had not controlled for multiple comparisons. In fact, we examined a single exposure (to APAP, estimated by two different approaches, based on questionnaire data and human biomonitoring) and a single outcome, our sex-specific analyses were few and planned *a priori*. The statistical literature does not support controlling for multiple comparisons in such cases [2].

Finally, the commentators stated that we "binned continuous variables into categories". In fact, this stratification was not one we imposed; the standardized instrument used for language screening at 30 months of age in Sweden asks parents to report the number of words the child uses in these categories (<25, 25–50 or >50).

References

[1] Bornehag C.-G., Reichenberg A, Hallerback MU, Wikstrom S, Koch H, Jonsson B, et al. Prenatal exposure to acetaminophen and children's language development at 30 months. Eur Psychiatry 2018, doi:http://dx.doi.org/10.1016/j.eurpsy.2017.10.007.

[2] Rothman KJ. No adjustments are needed for multiple comparisons. Epidemiology 1990;4:3–6.

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