Author's response to reviews

Title: Prenatal Mercury Exposure, Autism, and Developmental Delay, Using Pharmacokinetic Combination of Newborn Blood Concentrations and Questionnaire Data: A Case Control Study

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We thank the reviewer for the additional comments. While the model certainly has limitations, which are articulated in the discussion, the methods of using either (1) biomarkers alone or (2) self-reported dietary questionnaire data alone also have major limitations. In our study, we are primarily interested in measuring mercury exposure from seafood exposure over the gestational period. A single blood biomarker cannot be reliably extrapolated to mercury exposure over the entire course of pregnancy, and using questionnaire data alone is also questionable due to potential inaccuracies in the self-reported seafood consumption rates, lack of data on specific species of seafood consumed by the mothers in our study, and reliance on external information regarding the mercury concentration of various seafood species. This paper provides an alternative approach that combines the information from both sources (biomarkers and questionnaire data) in an attempt to ameliorate some of the reliability issues that arise when using either of the data sources alone.

We agree with the reviewer that dietary recall of past fish consumption undoubtedly introduces error to the mercury concentration estimates. The reviewer expressed concern that our estimated seafood mercury concentration of 42 ppb is roughly half of the 90 ppb estimated by Groth et al. for the U.S. population. As pointed out before, this comparison may not be appropriate given that mothers are advised to consume species of fish with lower concentration of mercury and would be expected to eat species of fish that, on average, are lower in mercury. Unfortunately, as the reviewer pointed out, we were not able to substantiate whether mothers tended to eat species lower in mercury because the dietary questionnaire did not ask about specific species of fish within each general category. However, the discussion does not suggest that we evaluated whether mothers avoided seafood with high mercury levels; we only offer this as a plausible reason why we could expect to observe mothers eating seafood with low mercury concentrations. To highlight the limitation resulting from the self-reported seafood consumption, we have added a sentence to the conclusion sentence clearly describing that the seafood mercury concentration estimates can be prone to error resulting from imperfect recall. We have also added the following line to the discussion section: "Future studies using pharmacokinetic calibration could employ Bayesian techniques (Shin et al., 2014) to account for uncertainties in self-reported exposure behaviors, rather than treating them as fixed covariates as we have done here."

Overall we agree with the reviewer that this method can still be prone to error resulting from imperfect dietary recall, but that using both sources of data while incorporating various pharmacokinetic parameters should lead to estimates of mercury exposure over time that are more reliable than estimates that could be made using either of the sources alone.