Reviewer's report

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

Version: 5
Date: 13 February 2015

Reviewer: Alan Stern

Reviewer's report:

Major Compulsory Revisions

The authors have made a few improvements in the previous MS. However, the fundamental problem I identified with the previous version remains - although the authors' test of their model was to predict the concentrations of Hg in the fish the pregnant women had consumed, the model, in fact, does a poor job of predicting the Hg concentration in either tuna or in fish in general. The authors have not really acknowledged this key point, and the MS still reflects the claim that their findings validate the model. The authors hypothesize that, for total fish consumption, this could be due to the women having followed advice and eaten fish low in Hg rather than having eaten according to the market basket-based average. While this could be a factor, it is no more than hypothesis and the authors present no evidence to substantiate this possibility. Rather, the much more likely explanation seems to me to be that dietary recall of fish consumption has limited reliability. Studies that have compared dietary recall of fish consumption (over a much shorter window of recall than the 17 months in this MS) with independent biomarker measurements of fish constituents of fish (Hg or omega-3 fatty acids) have shown, at best, a correlation of 0.3-0.4 (Lucas et al., Public Health Nutr. 2009 Oct;12(10):1783-90; Mozaffarian et al., Hypertension. 2012 Sep;60(3):645-52; Wennberg et al., Am J Clin Nutr. 2011 Jan;93(1):27-36; Vejrup et al., Public Health Nutr. 2014 Sep;17(9):2071-80.). Furthermore, there is good evidence that the variability in blood Hg during pregnancy is not well represented by a single blood sample such as was used in the model in this MS (Tsuchiya et al., Environ Health. 2012 Jun 7;11:37. doi: 10.1186/1476-069X-11-37).

I think that the model per se is interesting and may have better applicability where the timeframe and/or the nature of the recall is different. Given this, I would encourage the authors to consider restructuring this MS as a discussion of the model and its potential applications. However, I cannot recommend publication of this MS in its current form as a demonstration of the validity of the model.

Level of interest: An article whose findings are important to those with closely related research interests
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.