Author’s response to reviews

Title: Decreased sex ratio following maternal exposure to polychlorinated biphenyls from contaminated Great Lakes sport-caught fish: a retrospective cohort study.

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Dear Drs. Grandjean and Ozonoff,

We are quite pleased that you are satisfied with our responses to the reviewers’ comments and the changes we made to our manuscript (“Decreased sex ratio following maternal exposure to polychlorinated biphenyls from contaminated Great Lakes sport-caught fish: a retrospective cohort study”). Thank you also for your additional comments on our manuscript. We have revised the manuscript in response to these comments as described in the point-by-point responses below, and believe that the quality of the paper has been improved. We are now submitting the revised version.

Thank you for your interest in our manuscript.

Sincerely,

Marc Weisskopf

Point-by-point responses:

1) This is a good point. The bias towards the null we spoke of was in relation to the exclusions of subjects who had donated blood. However, as you point out, there is potential bias as a result of the low response rates for blood donation. We have added text in the discussion of this issue (p. 14, 1st para.).

2) Controlling for parity is an important point. And, in fact, we have controlled for it in our models (see p. 7, last para. and figure 3 legend, Table 5, 6 notes).

3) We do indeed mean brother and not sibling here, but we have not preferentially excluded sons from our analysis. As we discuss on p. 7 (Data Analysis, 1st para.), concerns about the effects of childbirth and breastfeeding on maternal PCB concentration led us to analyze only the most recent child of mothers in our sample to avoid the introduction of a large amount of variability in our exposure measure (note that we did not have this restriction for our analyses of paternal exposure, see also p. 7: Data Analysis, 1st para.). Since only the most recent child of mothers was analyzed it was possible that earlier children could have been either boys or girls. Having an older brother is a predictor of the sex of subsequent children and so should be controlled for. As it turns out, all the most recent children who were not firstborn had at least one older brother, therefore the dichotomous variable of having an older brother was a linear combination of our parity variables, which we were also controlling for. Therefore, controlling for parity effectively controlled for having an older brother as well.
4) This is a very good point. The high sex ratios among the children of our mothers has to do with those children not being all children of the mothers, but only the most recent. In fact, the sex ratio among all children of mothers in our sample is 0.535. We have added text to explain this (p. 10, last para. & p. 11 1st para.).

5) This line was intentionally left out because we analyzed only 1 child per mother (the most recent). It does seem though that it would be good to put it in this table to emphasize that point. We have done this and also split the table into 2 separate tables because the single table was getting too large for one page. In addition, considering this point as well as points # 2 & 3, we thought that changing the wording from "most recent" child to "last" child for those children of mothers whom we analyzed might be more clear about this point of only analyzing one child per mother. Therefore, we have made this alteration throughout the text.

6) We have corrected the references indicated. There are no editors listed for the two books mentioned so we have cleaned up the reference accordingly.