

## **Reviewer's report**

**Title:** A cohort study of the association between secondary sex ratio and parental exposure to polybrominated biphenyl (PBB) and polychlorinated biphenyl (PCB)

**Version:** 1 **Date:** 13 March 2009

**Reviewer:** Marc Weisskopf

### **Reviewer's report:**

Comments on Terrell et al. "A cohort study of secondary sex ratio and parental exposure to polybrominated biphenyl (PBB) and polychlorinated biphenyl (PCB)."

This paper examines the association between parental serum PBB and PCB concentrations and the sex ratio of their children in a cohort of parents exposed to PBB from a food contamination incident in Michigan. It addresses an important question in a unique exposure setting. There are a few issues, though, which may affect the overall interpretation, that I see as needing to be addressed.

Major compulsory revisions:

1) Tables 2 & 3

a. The number of fathers in the lowest paternal exposure group seems too small to maintain that as a separate category. Instead I think it would be preferable to divide the fathers in half at the median.

b. The numbers suggest to me, not an increase in SSR with increasing paternal exposure (seen marginally), but a possible decrease in SSR that is confounded by maternal levels. It does not seem that models were run that simultaneously adjust for maternal and paternal exposure levels (among those children where both parents' levels are known). (An interaction between them could be tested, but it doesn't look to me like it's there.)

c. These same comments apply to the PCB analyses.

2) Better description of the cohort. Items that are mentioned without any detail include:

a. How many individual fathers and mothers were there? Overall and in the different subsets that go into the different analyses?

b. What is the distribution of timing between births and blood collection?

c. PBB/PCB adjustments are made based on models that include information on breastfeeding, but how/when was this breastfeeding information collected? What is its distribution.

d. Need to be clearer in tables what the n's refer to (children I assume).

e. In the results it's stated that 116 children had no maternal PBB measurement

and were excluded. Is it just coincidence that also 116 children are reported in the discussion (this should come earlier, at least in results section) to have been born before the mother's blood was drawn for PBB analysis?

3) It seems that even in models with only maternal exposures, only children born 1975-1988 are included. Why not all 1,392 born 1975-2005?

4) It seems odd that father's PBB levels are not extrapolated to the time of birth of the children while the mothers' levels are. While there may not be an exact model, the PBB exposure was close to a point source and presumably at the very least a simple time decay should be considered. If not, I think there should be stronger justification for why not.

Minor essential revisions

5) What was the covariance structure of the GEE model?

6) What was correlation between PCBs and PBBs?

7) In 2nd paragraph of "Association with sex ratio" in results, it should be made clear for the reported OR what the reference group was and what the overall categories were.

Discretionary revisions

8) Last sentence of page 11: I don't see how a continuous PCB exposure necessarily means that it will be lower than a one-year PBB exposure. Isn't the relevant point how high that PBB exposure was?

9) Despite the skewing in the contaminant levels, it would be of interest to know what happens if they are modeled continuously (possibly log transformed).

10) I'm still a little unclear on how the breastfeeding data was handled, but since it and childbirth in general might introduce changes in PBB/PCB levels that are hard to quantify, it would be interesting to run sensitivity analyses restricted to the first child after a mother's PBB/PCB concentrations were determined.

**Level of interest:** An article of importance in its field

**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.