Author's response to reviews

Title: Effects of Exposure to Polychlorinated Biphenyls (PCBs) and Chlorinated Pesticides on Serum Lipids in Residents of Anniston, Alabama

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Author's response to reviews: see over
Dear Philippe:

Thank you for the reviews on our manuscript, “Effects of exposure to polychlorinated biphenyls (PCBs) and chlorinated pesticides on serum lipids in residents of Anniston, Alabama.” We appreciate the very helpful comments of Mary Turyk and Monica Lind, and have extensively revised the manuscript.

A major issue raised by both reviewers concerned the long theoretical section on the issues of multicollinearity. We agree that inclusion of this section in the Discussion was distracting, but this is an essential part of this body of work. We suspect that in the long term this analysis will have a longer lasting impact than the experimental section, as it is applicable to research done by many others as well as by our group. We have removed this section from the main text, and included a revised version of it as an Appendix. I hope that this is not inappropriate for Environmental Health.

Let me address first our responses to the comments by Mary Turyk. Her first comment concerned other medications beside those specific for lowering serum lipids might alter serum lipids. This is certainly a valid consideration, and we have acknowledged that in two places in the text. In fact we did do preliminary attempt to exclude individuals on some of these medications other than lipid-lowering drugs, but the problem is that by doing so we drastically reduced our population number and lost power. So I hope that it is satisfactory that we have discussed other medications as a factor beyond our control.

Mary’s other concern was our use of categorizing smoking as 100 or more cigarettes over a lifetime. We do have current smoking values, and have found that using current smoking did not give any different results. We have clearly stated this in the revised version. We chose to present the 100 or more cigarettes over the lifetime because we felt that that measure might better reflect the influence of smoking on serum lipids, but we have made clear that there was no significant difference if we used current smoking rates.

With regard to her discretionary comments, we have added the Warner reference, and expanded the discussion of the biological significance of the various congener groups. This will be a continuing interest for my group, as we certainly don’t understand it all very well at present.

Monica Lind was a bit more critical, but we have accepted most but not all of her suggestions. We have much more clearly stated our hypothesis. We have drastically shortened the discussion, but do not accept her suggestion to delete the theoretical statistics section (as discussed above) and send it to a more statistical journal. Its primary value is to the experimental data presented in this manuscript, and it could not stand alone without reference to the experimental data. But by moving it to an Appendix it does not disrupt the flow of the experimental part of the manuscript, but can still directly reference the experimental results. We very much do not agree with her suggestion to delete the Model 2 data throughout the manuscript. The major contribution of this study comes from use of the Model 2 data, although it is certainly appropriate to detail at length, as we have, the possible dangers from uncritical use of over-adjustment.
We have expanded on the use of POPs levels normalized for lipid concentrations, and reviewed the evidence from several sources that indicate that this approach is prone to bias. It is much more complicated when investigating changes in lipid levels in relation to POPs levels, since the POPs are in the lipids, and we have discussed this and the issue of reverse causality. We cannot totally rule out reverse causality, as noted in the discussion, but it is an unlikely explanation for our observations since the different lipid components are changed so differently and by different POPs.

We have clarified the issue of multiple testing, and this is central to the problem of multicollinearity. The references have been checked and reviewed. The discussion has been totally rewritten, much shortened and more focused. We have improved the grammar throughout, and corrected the format to be appropriate for Environmental Health.

One additional issue beyond responses to the referees: We have three tables to the main text listed as “Additional files” as well as the Appendix which has one table and three figures. Are the “Additional files” appropriate, or since the journal is electronic would it be better to incorporate them just as three more tables to the manuscript? They contain important data, but the data is not central to the main experimental issue.

Thank you for your consideration. I hope that you will find our manuscript acceptable for publication in Environmental Health. Very best regards.

Yours sincerely,

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