Reviewer's report

Title: Persistent organic pollutants and non-alcoholic fatty liver disease in morbidly obese patients: a Cohort Study

Version: 2

Date: 1 September 2015

Reviewer: Dania Valvi

Reviewer's report:

MS: 1241189702166327
Persistent organic pollutants and non-alcoholic fatty liver disease in morbidly obese patients: a Cohort Study
Panu Rantakokko, Ville Männistö, Riikka Airaksinen, Jani Koponen, Matti Viluksela, Hannu Kiviranta and Jussi Pihlajamäki

Environmental Health

Reviewer’s reply to the Editor and the Authors:

The authors’ effort to reply to my comments and questions is much appreciated. The authors have successfully addressed the issues raised. However, I consider that there is one more issue related to the new data presented that is worthy to be raised. This refers to the conclusions of the comparison between the multivariate-adjusted estimates (reported in the original version) and the estimates adjusted only for age (added in the revised version). The editor and the authors may wish to consider the two minor essential revisions listed below prior to manuscript's acceptance for publication:

1. Lines 246-247 “Associations for b-HCH and PCB-118 in the models adjusted only for age were similar to those in the fully adjusted model and are shown in the supplementary information (Table S1).”

Effect estimates in the two models are indeed very similar for b-HCH, however, it can be argued that this is not the case for PCB-118. Adjustment for additional covariates in the PCB-118 model seems to increase the precision of the effect estimates (as shown by the narrower 95% CI in the fully adjusted model compared to the model adjusted only for age) increasing the magnitude of most of the associations shown. For example, the associations between PCB118 and diagnosis or grade of steatosis become significant only after the inclusion in the models of additional covariates (Tables 3 and S1). This is somewhat unexpected because the inclusion of additional covariates in the models commonly tends to decrease the precision of effect estimates (i.e. the 95% CI become wider) especially when the sample size is small. My suggestion is to notify these differences for the PCB-118 associations in the text and further, briefly explain, perhaps later in the discussion, what is a possible explanation for the increased precision of estimates in the multivariate-adjusted model. My assumption is that this is due to the inclusion of the BMI covariate in the models; however, if BMI were a confounder, related to both the exposure and the outcome, then I would
expect the inclusion of BMI in the models to influence the effect estimates but not to influence that much the precision of effect estimates (or to decrease, but not to increase, the precision).

2. Lines 251-253 and Tables 4 and S2: As the authors also clarify in the text, associations of PFASs become significant after inclusion of additional covariates in the models. Similar to my comment above, the precision of effect estimates is largely improved in the multivariate adjusted model. For example, for PFNA the ORs (95% CI) for the outcome categories change from 0.96 (0.23, 3.97) and 0.15 (0.01, 2.16) into 0.29 (0.05, 1.61) and 0.02 (<0.01; 0.66), respectively. This is surprising and some explanation to justify the changes in the precision of estimates is required for the readers.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

nothing to declare.