Author's response to reviews

Title: Urinary bisphenol A and pubertal development in Chinese school-aged girls: a cross-sectional study

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Version: 2 Date: 04 Jul 2017

Author’s response to reviews:

Dear Editor,

Thank you and the reviewers very much for the comments and suggestions. We have revised the manuscript based on your comments and our responses are outlined below:

Reviewer #1: Lines 133-134: The authors make it clear that these variables are self-reported, so the additional "through self-report" may not be needed. The authors may want to add additional information in the methods section particularly addressing how these variables (and other variables in Table 1) were defined.

Response: We thank the reviewer for the suggestion. We have added information on the definition of variables in the method section under the subtitle of “In-person data collection”.

Lines 162-163: It's still a bit unclear why the authors chose to look at associations with B5/PH5?

Response: We apologize for the confusion. In this paper we want to examine the effect of BPA on the profile of pubertal development, which means that not only puberty onset, but also the progression of puberty was our endpoints of interest.
To make this clearer, we have revised the last paragraph of introduction as follows:

“In the present study, we examined the profile of pubertal development in relation to BPA exposure among school-aged girls using menarche and Tanner stages, through which puberty onset and progression were evaluated”.

And we added the following sentences under the subtitle of “statistical analysis” in the method section:

“We examined associations between BPA exposure and different milestones (present or absent) representing the onset of pubertal development, as indicated by breast development stage 2 and above (B2+) and pubic hair stage 2 and above (PH2+), mid-puberty, as indicated by menarche, and late puberty, as indicated by breast development stage 5 (B5) and pubic hair stage 2 (PH5)”.

In the introduction the authors note that associations were assessed with pubarche, thelarche, and menarche. So technically PH2+ and B2+ represents onset of pubarche and menarche? The authors may want to clarify what B5/PH5 represents, why early/late transition to this stage is important, and why early/late transition to onset of pubarche/thelarche would be different than early/late transition to completion of tanner stage 5.

Response: As mentioned above, we tried to examine the effect of BPA on the whole profile of pubertal development, including the onset and progression of puberty. We used PH2+ to represent pubarche, B2+ to represent thelarche. And B5/PH5 was used to represent the late stage of puberty development. Since an earlier pubertal onset may not necessarily be followed by an earlier puberty development due to the compensatory delay (see Ref 20 in the manuscript), we included both earlier and later events of pubertal development to examine the full picture of BPA’s effect. We have added a sentence about this intent in the Method section under statistical analysis.

Lines 169-178: unclear why this entire paragraph was removed? I think the authors may wish to at least keep "the longer since menarche, the less indicative of the current exposure to BPA for the exposure at menarche", as this may be an important reason for sub-setting the different ages.

Response: We thank the reviewer’s suggestion. The paragraph was restored.

Lines 240-245: I would be cautious with over-interpreting the results from different subsets of girls. I would also recommend re-wording the sentence in lines 241-243 as it appears strongly similar to the sentence from Karapanou et al. 2010.

Response: The sentences have been reworded.

Table 1. It may be helpful to include the actual median BPA concentration levels in this table.

Response: The actual median BPA concentration levels were added in Table 1.

Tables 4,5. Unclear what happened to girls aged 12? Should the ages be 9-13 and 14-18?
Response: For each indexed puberty event, we perform the analysis among those at ages with variation on the examined events. At age 12, all girls had reached breast stage 2 (regardless of their BPA level), thus they would have not been useful for us to examine the impact of BPA at B2+. We also excluded girls at 12 in the PH2+ analysis for consistency in the puberty onset analysis.

Similarly, since no girls have reached pubic hair stage 5 at age 12, so girls at age 12 was not included in the analysis of BPA and tanner stage 5.

Reviewer #2: The article can be accepted

Editor:

1. Provide a more complete rationale for dichotomizing the exposure at the median.

Response: We thank the reviewer for the effort that has been made to the manuscript. Since the available evidence didn’t provide any biological relevant cut-points, we used the median of detected BPA as the cut point to examine the effect of BPA for those with relative higher BPA level vs. those with lower one. While any cutoff would have been acceptable at this exploratory stage of the emerging research, a cutoff at the median is conventional and usually the first step in examination of such an association. We have added information on rationale for dichotomizing the exposure at the median in the statistical analysis section.

2. Be sure to use your own words when describing the results of other studies.

Response: We thank the reviewer for the suggestion. We have re-worded several sentences in the Discussion section which described results from other studies.

We hope that the manuscript has been revised in a manner that will make it suitable for publication.

Thank you!

Yours sincerely,

Wei Yuan