Author's response to reviews

Title: Low birth weight, preterm birth or small-for-gestational-age are not associated with dental caries in young Japanese children

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The Editor

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Title: Low birth weight, preterm birth or small-for-gestational-age are not associated with dental caries in young Japanese children
First author: Keiko Tanaka

Dear Sir:

Thank you for your email of February 10, 2014. We are pleased that you are interested in our manuscript for possible publication as an Original Article in BMC Oral Health. We appreciate the thoroughness with which the reviewers have considered our manuscript. We have addressed the comments raised by the reviewers and have carefully revised the manuscript.

I am sending the revised manuscript with changes highlighted in red.

Specific revisions and responses to the each reviewer are described below.

We thank you in advance for your consideration.

Yours sincerely,

Keiko Tanaka, DDS, PhD
Reviewer 1 (Dr. Sam Leary)

Major compulsory revisions:
1) The authors need to make clear that the birth weight and gestational age variable are from obstetric records, for example, in the abstract they state “data on birth conditions were obtained using a questionnaire” which made implies they were self-reported and therefore less reliable. The authors also need to provide more justification for the need for their study (e.g. are the published studies smaller? Are they based on less reliable data?)

Response:
We appreciate your careful review and helpful comments.
In order to clarify the data collection methods, we changed the sentence “Data on birth conditions were obtained using a questionnaire.” in the Abstract to “Data on birth conditions were obtained through the transcription by parents or guardians of the information from their maternal and child health handbook, in which the data were recorded by staff at the birth hospital or clinic, to our self-administered questionnaire.” (page 2, lines 6–9 in the revised manuscript)

To clarify the justification of our study, we also added the following sentences to the Background section:

“Investigations regarding the relationship between birth conditions and dental caries have been conducted in Western populations. To date, no epidemiological study has examined such relationships in non-Western populations.” (page 3, pages 16–18 in the revised manuscript)

2) The term “statistically significant” should be avoided; see Sterne JAC, Davey Smith G. Sifting the evidence: what’s wrong with significance tests? BMJ 2001; 322: 226-31. The authors should talk of the strength of statistical evidence instead.

Response:
Thank you for your useful comments. In the revised version, we made the following changes:

The sentences in the results in the Abstract “Preterm birth was marginally significantly associated with a decreased prevalence of dental caries (adjusted prevalence ratio = 0.60, 95% CI: 0.36–1.02, p = 0.06). There were no significant
associations between LBW or SGA and the prevalence of dental caries.” were changed to “Preterm birth tended to be associated with a 40% decreased prevalence of dental caries (adjusted prevalence ratio = 0.60, 95% CI: 0.36–1.02, p = 0.06). There were no associations between LBW or SGA and the prevalence of dental caries.” (page 2, lines 17–20 in the revised manuscript)

The phrase in the Results section “preterm birth was marginally significantly associated with a decreased prevalence of dental caries” was changed to “preterm birth tended to be associated with a 40% decreased prevalence of dental caries” (page 6, line 9 in the revised manuscript)

The sentence in the Results section “There were no significant associations between LBW or SGA and the prevalence of dental caries.” was changed to “There were no associations between LBW or SGA and the prevalence of dental caries.” (page 6, lines 11–12 in the revised manuscript)

The sentence in the beginning of the Discussion section “The present study found that preterm birth was marginally significantly associated with decreased prevalence of dental caries.” was changed to “The present study found that preterm birth tended to be associated with a decreased prevalence of dental caries.” (page 6, lines 15–16 in the revised manuscript).

The word “significant” in the Conclusion section was deleted. (page 9, line 13 in the revised manuscript)

3) The last paragraph of the results section seems to appear out of nowhere; the hypothesis was not pre-specified so therefore the findings need to be treated as exploratory. There is no discussion of the results / comments on whether any of the published studies have looked at this issue.

Response:
We moved the paragraph regarding an interaction between preterm birth and maternal smoking during pregnancy to the Discussion section (page 7, line 2 from the bottom of the page–page 8, line 5 in the revised manuscript). We also added the following sentences to the Discussion section:

“Maternal smoking during pregnancy is the leading cause of LBW and preterm birth. It also might increase the risk of dental caries in children. Our previous
study showed that prenatal smoke exposure was associated with an increased prevalence of dental caries in children [16]. No previous studies have addressed an interaction between preterm birth and prenatal smoking with respect to dental caries.” (page 7, lines 22–26 in the revised manuscript)

The following reference, mentioned in the above passage, was also added.

4) At the end of the conclusions the authors state that further studies are needed – what specifically needs to be studied?

Response:
We changed the last sentence in the Conclusion “Further studies are needed in order to confirm our findings.” to the following: “Further studies, particularly prospective studies, are needed in other populations to confirm that there is indeed no association between birth conditions and dental caries in children.” (page 9, lines 18–20 in the revised manuscript)

Minor essential revisions:
5) In the methods the authors state that out of the 8269 eligible children, 8064 were provided with questionnaires; why weren’t the others given questionnaires?

Response:
When 8,269 children received the physical examination at public health centers, our staff attempted to distribute our questionnaires to all parents or guardians of the children. However, our staff either missed the opportunity to distribute the questionnaire to some of the parents or guardians of the children or the questionnaires were refused. Consequently, we were able to distribute our questionnaire to the parents or guardians of 8,064 children. We added the following sentence to the Methods section:

“The parents or guardians of 205 children declined the receipt of these materials or were failed to be provided with them.” (page 4, lines 8–9 in the revised manuscript)
6) Presumably it was the researchers rather than the parents that classified the children as having dental caries, being low birthweight etc but could the authors please clarify this.

Response:
We changed the sentences “Children were classified as having dental caries if one or more primary teeth had decayed, were missing, or had been filled. LBW was defined as a birth weight less than 2500 g.” to “We classified children as having dental caries if one or more primary teeth had decayed, were missing, or had been filled. We defined LBW as a birth weight of less than 2500 g.” (page 4, line 1 from the bottom of the page–page 5, line 2 in the revised manuscript)

Discretionary revisions
7) As the literature in this area is quite limited it would be worth including papers that have looked at associations between birthweight (across the whole distribution) and dental caries for example “Is there a relationship between birthweight and subsequent growth on the development of dental caries at 5 years of age? A cohort study” by Kay et al.

Response:
Thank you for your suggestion. We added the following sentences, with one reference, to the Discussion section:

“On the other hand, a prospective cohort study in the UK showed that birth weight was positively associated with the risk of dental caries in 985 children aged 61 months: the adjusted OR per 100 g increase was 1.08 (95% CI: 1.03–1.13) [12].” (page 6, lines 25–27 in the revised manuscript)

The following reference, mentioned in the above passage, was also added.

8) Additional confounders such as parity and maternal age at the time of birth have also been included as potential confounders in previous work in this area; are these data available for this study? Also the authors state that gestational age was
removed from models when pre-term birth was assessed, but shouldn’t it have also been removed when SGA was assessed?

Response:
In the present study, information on parity and maternal age at the time of birth were available. When we additionally adjusted for parity and maternal age at the time of birth, associations between birth conditions and dental caries were essentially unaltered: the additionally adjusted PRs for LBW, preterm birth, and SGA age were 0.95 (95% CI: 0.70–1.30), 0.66 (95% CI: 0.40–1.07), and 0.99 (95% CI: 0.71–1.36), respectively. When parity and maternal age at the time of birth were additionally included in the analyses, the study population was slightly reduced (n= 2048) due to missing data. Thus, we decided not to take the parity and maternal age at the time of birth into account in the multivariate models. We did not describe this circumstance in the paper. Moreover, we decided that gestational age should be removed from not only SGA analysis but also LBW analysis. If the LBW analysis was adjusted for gestational age, the results would be of a similar interpretation to those of the SGA analysis. We changed the numbers in the Table 2 to reflect the results of these re-analyses.

9) The low response rate is obviously an issue, but the authors have highlighted this. However, the discussion would flow better of the data provided on the comparison with the population census were first introduced in the results section, and just commented upon in the discussion.

Response:
Thank you for your suggestions. As you indicated, in order to more easily follow our results, it may be better for the comparison of study population with the population census to be provided in an earlier portion of the paper. However, we feel that it is more suitable that the descriptions of the comparison with population census and the generalizability of our results be provided in the Discussion section rather than in the Results section. Although the comparison with the population census is an important consideration when interpreting our findings, it is not, strictly speaking, a result generated from our study. We therefore believe that the Results section would be better served if it simply provided results that were free of any interpretation.

10) It has been suggested that the earlier eruption of deciduous teeth in babies that are larger at birth may offer one explanation for a possibly higher risk of caries in the deciduous teeth of babies of higher birthweight; it is unlikely that the authors
have the available data to be able to look at this in their study, but the issue should mentioned in the discussion.

Response:
Regarding descriptions about the explanation of the potential mechanisms underlying our observed associations, we added the following sentences, with one reference, to the Discussion section:

“Another possible explanation is that the delayed tooth eruption in children born preterm might contribute to a decreased risk of dental caries. In a retrospective study in Turkey, compared with children at >37 weeks of gestational age, children at ≤37 weeks of gestational age demonstrated a significant delayed eruption of the first primary tooth [15].” (page 7, lines 17–21 in the revised manuscript)

The following reference, mentioned in the above passage, was also added.
Reviewer 2 (Dr. Jonathan Broadbent)

Major Compulsory Revisions:
1. In results, clarify the meaning of “mean number of dental caries” – was this teeth or surfaces? It isn’t stated. Presumably the value of 0.70 among the entire study population, please clarify this. This would mean that since ~80% of the sample had no caries, the mean among the remaining 20% would be 3.5, which suggests a very skewed dataset with a lot of zero values. The distribution of dental caries is not reported and this would be important information to have available to the reader. This also has implications to the analysis – the investigation of the prevalence of dental caries may be too simplistic, it may well be the premature-born children who have greater severity of dental caries (rather than just a greater risk of having any). Other methodological approaches may be more appropriate for this purpose.

Response:
Thank you for your careful review. In order to clarify the distribution of dental caries, we modified the beginning of the Results section as follows:

The sentences “Of the 2,055 children, 426 (20.7%) had dental caries. The mean number of dental caries was 0.70.” were changed to “Of the 2,055 children, 426 (20.7%) had experienced dental caries and 1,629 (79.3%) were caries free. The mean number of teeth with dental caries for all subjects and for subjects who had experienced caries was 0.70 and 3.4, respectively.” (page 5, lines 25–27 in the revised manuscript)

Certainly, an association between birth conditions and the severity of dental caries is very interesting. However, our study population is too small to assess such associations. In the present study, the number of cases with LBW, preterm birth, and SGA were 31, 12, and 28, respectively. Thus we chose to focus on whether the birth conditions affected dental caries in children. Because our outcome is not rare, we computed the crude and adjusted PRs by using the SAS PROC GENMOD and the log-binomial regression model. In our previous studies using the data set of the Fukuoka Child Health Study, we used the same statistical methods (J Epidemiol. 2012; 22:72-7; J Dent. 2010; 38: 579-83; J Pediatr. 2009; 155: 410-5). We believe that the statistical methods used in our study are appropriate. We did not add comments to the text regarding this information.
2. The authors refer to research that has identified greater rates of hypoplastic enamel defects in the teeth among premature-born babies, while others have also pointed to an increased risk of MIH for those that are born late. MIH is the type of defect that increases risk of dental caries.

Response:
Thank you for your suggestion. We added the following sentence to the Conclusions section:

“Although the present study did not find an association between birth conditions and dental caries in the primary dentition, it is possible that such an association may exist in the permanent dentition.” (page 9, lines 15–17 in the revised manuscript)

3. Smoking is more associated with periodontal disease than dental caries, and a systematic review of the literature by these same authors concluded that the association of dental caries and second-hand smoke is very tenuous. Since smoking during pregnancy is an important predictor of pre-term birth and small-for-dates, the authors should consider interaction between birth-related factors and smoking upon dental caries.

Response:
Regarding an interaction of prenatal smoking and preterm birth on the risk of dental caries, we believe that this issue has already been mentioned in the Results section in the original manuscript (page 6, lines 7-14 in the original manuscript). In the revised manuscript, we moved these descriptions about the interaction to the Discussion section (page 7 line 27–page 8, line 5 in the revised manuscript), and added the following sentences, with one reference, to the Discussion section:

“Maternal smoking during pregnancy is the leading cause of LBW and preterm birth. It also might increase the risk of dental caries in children. Our previous study showed that prenatal smoke exposure was associated with an increased prevalence of dental caries in children [16]. No previous studies have addressed an interaction between preterm birth and prenatal smoking with respect to dental caries.” (page 7, lines 22–26 in the revised manuscript)

The following reference, mentioned in the above passage, was also added.

4. Dental caries is relatively low in Japan, and there may be unique cultural and social factors in Japan that may affect the generalizability of results of this study to other countries. The authors already comment on the issue of lack of representativeness of the sample in the Japanese context, but I believe a comment on generalizability in the international context (or lack thereof) is needed in the discussion and perhaps the abstract also. Considering this, another important question is why the authors have chose to publish in an international journal rather than a Japanese language journal – it may actually have more impact in Japan rather that overseas (this is a decision for the authors themselves to consider, however).

Response:
Previous studies on the association between birth conditions and dental caries in children have been conducted in Western populations. This is the first study to investigate such association in non-Western populations. To date, studies on the association between birth conditions and dental caries are very limited and the results are inconsistent. Furthermore, it is difficult to compare findings between studies because the definitions of outcome, study populations, study designs, assessment methods, and confounding factors are different across such studies. As is true for these previous studies, it is difficult to generalize our findings to other populations because various factors, such as cultural and social factors and the prevalence of outcome, are different across populations. Regarding this issue, we made the following modifications:

The sentence “Further study is needed in other populations to confirm the generalizability of these findings.” was added to the Abstract (page 2, lines 22–23 in the revised manuscript)

The sentences “Investigations regarding the relationship between birth conditions and dental caries have been conducted in Western populations. To date, no epidemiological study has examined such relationships in non-Western populations.” were added to the Background section (page 3, lines 16–18 in the revised manuscript)

The sentence “However, it should be noted that the above mentioned studies used different definitions of outcome, study population, assessment methods,
and confounding factors, thus limiting the feasibility of inter-study comparisons.” was added to the Discussion section (page 7, lines 2–5 in the revised manuscript)

The sentence “Further, it is difficult to generalize our findings to other populations because various factors, such as cultural and social factors and the prevalence of outcome, are different across populations.” was added to the Discussion section (page 8, line 2 from the bottom of the page–page 9, line 1 in the revised manuscript)

The sentence in the Conclusions in the original manuscript “LBW has been increasing in Japan.” was deleted (page 8, lines 21–22 in the original manuscript).

The sentence in the Conclusions in the original manuscript “Further studies are needed in order to confirm our findings.” was changed to “Further studies, particularly prospective studies, are needed in other populations to confirm that there is indeed no association between birth conditions and dental caries in children.” (page 9, lines 18–20 in the revised manuscript)

5. Table 1 is not very informative, as it is a Table with only one data column. Comparison of demographic and dental characteristics by birth-related factors would be advantageous.

Response:
In the present study, there are three variables regarding birth conditions: LBW, preterm birth, and SGA. Therefore, a presentation of the comparisons of the characteristics of the study population according to birth conditions is likely to be complex and confusing. Generally, in the epidemiological study, the characteristics of the study population are presented for the whole sample. We therefore believe that the original format of Table 1 is appropriate.

Minor Essential Revisions
1. A surprisingly large number of children were exposed to second-hand smoke at home, but on reading other literature I see that a large proportion of Japanese are smokers. It would be informative to add a reference to explain this to the reader.
Response:
As you indicated, the smoking rate is relatively high in Japan. According to the National Health and Nutrition Survey in Japan, 2006, the proportions of smoking in men and women aged 30–39 years were 53.3% and 16.4%, respectively, although smoking habits at home are unknown. Thus, the percentage of exposure to household smoking shown in the present study seems to be reasonable. The present study investigated the association between the birth conditions and dental caries. We merely used household smoking exposure as one of confounding factors in the multivariate models. We think that a discussion on smoking is beyond the scope of our present study. We therefore did not add any comments to the text regarding this information.