Author's response to reviews

Title: Household smoking and dental caries in schoolchildren: the Ryukyus Child Health Study

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The Editor

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Title: Household smoking and dental caries in schoolchildren: the Ryukyus Child Health Study
First author: Keiko Tanaka

Dear Sir:

We appreciate your suggestions and the comments of the 4 reviewers regarding the above-referenced manuscript. We have revised the manuscript and are resubmitting it for publication in the *BMC Public Health*.

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

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

We thank you in advance for your consideration.

Sincerely,

Keiko Tanaka, DDS, PhD
Referee 1 (Dr. Scott L. Tomar)

This cross-sectional study examines the association between exposure to environmental tobacco smoke (ETS) and dental caries in a large sample (20,000) of schoolchildren in Japan. It found that household smoking was positively associated with the number of decayed primary or permanent teeth, with evidence of a dose-dependent association. The authors conclude that SHS exposure was independently associated with an increased prevalence of dental caries.

Response:
We appreciate your careful review and helpful comments. Our revisions are described below as well as our response to the comments.

General Comments
This paper is generally well written and the study is based on large, representative sample of schoolchildren aged 6–15 years in 2 cities in Okinawa, Japan.

The major concern with this study is that even extremely small associations achieve “statistical significance” when the sample is very large. The adjusted prevalence ratio estimates are all very modest (1.03–1.11), even if their associated 95% confidence intervals exclude 1.0. The prevalence of decayed and/or filled teeth differs by less than 6 percentage points between those children never exposed to smoking in the house and those currently exposed to 15 or more cigarettes per day. Similarly, the mean number of affected teeth ranged from 4.1 in the never exposed group to 4.5 in the most heavily exposed group, although the p-value of <.0001 suggests a strong dose-response association.

Response:
In the present study, the large sample size contributed to the detection of relatively small associations between household smoking and dental caries in children. We added the sentence to the end of the Discussion: “With regard to testing for statistical significance, the observed significant positive relationships might be ascribed to a Type I error due to the large sample size.” (page 12, lines 7-9 from the bottom of the page in the revised manuscript).
Comment:
One potential explanation for the “significant” associations may be uncontrolled confounding. In particular, smoking appears to be strongly associated with socioeconomic status in Japan [Fukada et al. Socioeconomic pattern of smoking in Japan: income inequality and gender and age differences. Ann Epidemiol. 2005;15(5):365-72]. The only marker for SES in this study was maternal and paternal educational attainment, collapsed into 4 categories each. Virtually all parameter estimates in this study were attenuated when adjusted for potential confounders, and for the “strongest” associations such as ETS and decayed teeth, the degree of attenuation was greater than the remaining degree association. For example, the crude prevalence ratio for current #15 cpd of 1.29 was reduced to 1.11 after controlling for potential confounders. This pattern suggests the crude associations were largely explained by confounding, and residual confounding due to relatively crude measures for confounding variables could account for the remaining modest but statistically significant association.

Response:
In the current study, we used parents’ educational levels in order to control for socioeconomic status. After adjustment for only parents’ educational levels, the prevalence ratios (PRs) were rather reduced. For example, compared with never smoking in the household, the adjusted PRs of decayed teeth for former, current <15 cigarettes smoked in the household/day, and 15+ cigarettes smoked in the household/day were 1.09 (95% confidence interval [CI]: 1.04-1.15), 1.16 (95% CI: 1.12-1.20), and 1.18 (1.13-1.22), respectively. As you suggested, the crude associations are likely to be in part explained by parents’ educational levels. Unfortunately, information on socioeconomic status other than parents’ educational levels was not available in the present study. We added the sentences “However, residual confounding effects could not be ruled out. In particular, information on socioeconomic status was based on only paternal and maternal educational levels. Part of the observed positive relationships between SHSe and dental caries may be ascribed to uncontrolled for confounding effects of socioeconomic status.” (page 11, lines 7-11 in the revised manuscript).

Comment:
Consistent with that explanation, the present study found an association between ETS and decayed teeth, but not filled teeth. %D/DMFT is used as a measure of unmet treatment needs, and generally is higher for population with reduced access or utilization of dental care and is also strongly associated with SES. In the present study, %D/DMFT for those never exposed to SHS was 1.4/4.1 = 34%, while for those most heavily exposed it was 1.8/4.5 = 40%. At least some of the difference in prevalence of decayed teeth may have been due to SES factors unrelated to ETS exposure.

Response:
I agree with your statement that access to or utilization of dental care might explain the positive association between household smoking and dental caries in children. We changed the sentence “In the current study, we found no association between household smoking and FT, which is indeed not only an indicator of caries experience, but also a reflection of access to restorative care that may not be related to exposure to ETS.” to the following: “In the current study, we found a positive association between SHSe and DT, but not FT, which is indeed not only an indicator of caries experience, but also a reflection of access to or utilization of restorative care that may not be related to SHSe.” (page 10, lines 5-8 from bottom of the page in the revised manuscript).

Comment:
There have been a few other cross-sectional studies that similarly reported modest degrees of association between ETS exposure and dental caries, so this study adds to that limited body of literature. However, the preponderance of evidence finds no association between active smoking and dental caries (see, e.g., the 2004 U.S. Surgeon General’s Report on the Health Consequence of Smoking). It seems counterintuitive that ETS would increase the risk for dental caries but active smoking does not.

Response:
According to the 2004 U.S. Surgeon General’s Report on the Health Consequence of Smoking, epidemiological evidence on the association between smoking and dental caries was not sufficient to infer a causal relationship. Furthermore, many of the published studies did not control for potential confounding factors, such as socioeconomic factors, diet habits, and oral health behaviors. The 2004 U.S. Surgeon
General’s Report was based on a search for English language publications from 1965-2000. In the last decade, epidemiological studies on the association between smoking, including passive smoking, and dental caries are increasing. Available literature is fairly consistent in suggesting that smokers may experience slightly more decayed, missing, or filled coronal tooth surfaces. Several biological mechanisms, such as changes in bacterial ecology, the availability of saliva in the mouth, and alterations in immune responses, appear to be responsible for the increased risks of dental caries among smokers. In addition, smokers may have different lifestyle habits that further modify their oral health. However, no clear conclusion has been reached. Further research that controls for potential confounding factors on the smoking-dental caries relationship is necessary to draw a conclusion regarding whether active and passive smoking increase the likelihood of dental caries. Regarding this circumstance, we did not add any further information in the manuscript.

Specific comments
1. p5. It is unclear how accurate these measures of household smoking might be. For elementary school students, the parents complete the questionnaire, and presumably could give reasonable answers on the number of cigarettes they smoke per day and age at which they started. But junior high school students completed at least some of these questionnaires themselves; is there evidence that children 12–15 can provide accurate answers to those questions? In addition, it is not clear whether the number of cigarettes per day refers to the number actually smoked in the household (as is suggested in e footnote to Table 2) or the total number smoked per day by one or more smokers who live in the household (as is suggested in the description of the questionnaire). If it is the latter, many of those cigarettes may actually be smoked outside of the household. Exactly what were the questions asked concerning smoking?

Response:
As you indicated, a pattern of replies might differ between the parents and the children themselves. We added the sentences “In addition, responders differed between elementary schools and junior high schools. Parents of elementary school children completed our questionnaires whereas with junior high school students the questionnaires were completed by either the students themselves with or without parental help or by their parents. This could have driven the results.” to the Discussion
The following is the translated question about household smoking used in our present study.

Have (Has) you (your child) ever lived with a smoker?
1. Never
2. In the past
   You (your child) lived with a person or persons who smoked a total (   ) years from the age of (   ) years to (   ) years.
   How many cigarettes a day did the person or persons smoke when you (your child) were (was) at home? Please fill in the number of the total cigarettes when two or more people were smoking cigarettes at home.
   (   ) cigarettes a day
3. At present
   You (your child) live (lives) with a person or persons who smoked a total (   ) years from (   ) years of age.
   How many cigarettes a day does the person or persons smoke when you (your child) stay (stays) at home? Please fill in the number of total cigarettes when two or more people are smoking cigarettes at home.
   (   ) cigarettes a day

2. p. 5. How was pack-years of smoking handled in the analysis if it was greater that the child’s age?

Response:
Because the term “pack-years of smoking” was not appropriate, we changed the term to “pack-years of passive smoking” in the text and tables.

3. p. 6. If 42% of children were exposed to ETS in the household and half were not, who were the other 8%?

Response:
The sentence “Among participants, 9.1% were from households with former smokers. " was added to the Results (page 7, lines 10-11 in the revised manuscript).

4. p. 8. The discussion section cites two studies on the association between active smoking and salivary factors or bacterial counts, but does not mention that most epidemiologic studies found no association between active smoking and caries.

We added 3 references and the following statement to the Discussion: “On the other hand, epidemiological studies on the association between active smoking and dental caries showed inconsistent results. Some studies suggested that smoking was positively associated with dental caries [18, 19], while another study reported no association between smoking and dental caries [20]. Many of the published studies showing no association between smoking and dental caries did not control for potential confounders, such as socioeconomic status, diet, and oral health behaviors. Therefore, it is possible that the observed associations were influenced by confounding factors. “ (page 10, lines 2-9 in the revised manuscript).
Referee 2 (Dr. Melbourne Hovell)

Purpose and significance. This study offers a remarkably large sample of Japanese children as participants of a study if dental carries and their relationship to Second Hand Smoke exposure (SHSe). As such this study offers findings for an Asian culture and for dental health uniquely that suggests that tobacco smoke exposure may have an etiological role in the development of carries. This adds to the cumulative evidence of the likely harm due to tobacco smoke and more importantly due to SHSe. As such the study offers a remarkably large epidemiological study of considerable significance for dental health and also contributes to the wide range of biological systems that appear to be damaged by tobacco smoke, including passive exposure.

Methods. This study employed a cross-sectional design to test hypotheses about SHSe and dental carries. The sampling procedures and size are major strengths of the study offering sufficient power to detect relatively small effects in children but effects that may have life-long impact on their dental health that might have been avoided had the children been protected from SHSe. Since children exposed as children are very likely to be exposed for much of their life, the cumulative exposure and the risks for premature morbidity and mortality are likely to be arithmetically greater than estimated by this study, making the estimates observed conservative.

Measures. In general, this study offers reasonable measures of reported SHSe and dental carries, based on the observation of a clinical dentist. The only concerns raised about measures pertain to possible refinements in the quality assurance or fidelity of some of these measures. First, the measures of dental carries might be strengthened if a subsample of the children’s findings for carries could be compared to dental chart records or even a second dental examination by another dentist. These types of checks would provide evidence of reliability if not validity. While the dental examinations offer considerable face validity, absent X-ray confirmation there may be an under-estimate of carries and it is not clear how this might alter the association with SHSe. Use of dental charts also might offer the opportunity to confirm number of carries in a subset of children for whom X-ray information is the dental chart. If this sort of reliability check is possible, I suggest it be considered for a nominal subset of the children selected at random.
Response:
Thank you very much for your very comprehensive comments and recognition of the role that passive smoking might play in dental health. We hope that our results will shed some light on this situation. We also appreciate your useful suggestions regarding the reliability of the outcome measurement. In the current study, we secondarily used school records of dental examinations as an outcome variable. Therefore, unfortunately, we were not able to check the reliability of information on dental caries, such as making comparisons with dental chart records or a second dental examination. This is one of the weaknesses of our cross-sectional study. We think that a statement regarding the reliability and bias of the outcome measure, such as intra- and interexaminer consistency and absence of X-ray examination, had been given in the Discussion as follows: “Data on dental caries taken from school records are likely to avoid information bias. The school dentists were given detailed criteria for the examination, but calibration was not performed among school dentists. Therefore, it was unknown if intra- and interexaminer consistency was established. Additionally, radiographs were not taken. Oral examinations without radiographic information are likely to underestimate the prevalence of dental caries, especially interproximal caries [26, 27].” (page 11, lines 11-16 in the revised manuscript).

Comment:
The variables employed included age and other factors that may be presumed to be count variables, if not continuous. However, most variables were converted to ordinal measures without clear rationale for doing so. If these measures were highly skewed and could not be adjusted to a normal distribution, the authors should explain this and how the final ordinal measure offered a more reliable measure than would be true as a count or continuous variable. This issue is of some concern due to the loss of precision and power true for continuous variables that are reduced to ordinal or dichotomous variables. This issue pertains to both independent and Dependent variables.

Response:
When we analyzed our data using pack-years of passive smoking, age, and daily sugar intake as a continuous variable in the multivariate model, the log-binomial model failed to converge. In this case, Poisson regression capability with the robust variance would likely to be used. However, compared with log-binomial maximum likelihood
estimators, the Poisson estimates are not fully efficient. Therefore, we decided to put those independent variables in the multivariate models as ordinal variables. In the current study, we used a log-binomial regression model in order to estimate the prevalence ratio for household smoking in relation to dental caries. With regard to a dependent variable, a binary variable is used to estimate a relative risk such as prevalence ratio and odds ratio.

Comment:
Results and discussion. The results are overall quite clear. However, in the context of a modest proportion of youth who did not participate, and in the context of education and other factors likely associated with failure to participate, the authors should explore the likelihood of under-estimates of carries (for their prevalence results) or at least add discussion of this issue. The loss of children at higher risk for carries and SHSe also raises an concern that the results may under-estimate the strength of the association reported. Thus, this too should be discussed.

Response:
We added the sentence “The loss of children who were at higher risk for caries and who had parents with a lower educational level might lead to underestimation of the strength of the association between household smoking and dental caries.” to the Discussion (page 12, lines 14-17 in the revised manuscript).

Comment:
The Discussion section should make clear that there is now sufficient evidence and biological plausibility for concern that SHSe may contribute to carries in children. They authors also should outline follow on studies that might confirm these findings in the context of methodological improvements in the research design and fidelity.

Response:
Recently, research on the association between secondhand smoke exposure and dental caries in children are growing. To our knowledge, 9 epidemiological studies addressed the relationship between passive smoking and dental caries. The available literature is
fairly consistent in suggesting that passive smoking may contribute to the experience of more decayed teeth. However, evidence based on the above-mentioned 9 studies is insufficient. We have not yet had convincing evidence on such a relationship. Moreover, there are no cohort studies that infer a causal relationship. We added the sentence “Although the biological and behavioral plausibility for an etiological relationship between SHSe and dental caries is likely to be high, epidemiological evidence is still insufficient.” to the Conclusion section (page 12 lines 1-3 from the bottom of the page in the revised manuscript).

Comment:
Larger issues for Discussion. Following traditionally conservative research culture, cross sectional and other non-experimental studies always are reported in tempered language and conclusions are restricted in scope and scale. However, this can be a risk to a special form of Type II error. The current results add to a growing list of biological and behavioral risks to children and/or adults with exposure to SHS. Thus, the biological and behavioral plausibility for an etiological relationship is quite high. In this context, the authors are encouraged to discuss the importance for dentists to be involved in routinely screening youth for SHSe and counseling avoidance for older children and counseling parents to establish no smoking bans in their home. Formal controlled trials of dental counseling of this nature might also be recommended as one of the strongest and quickest means of showing a “causal” relationship between SHSe and dental caries by demonstrating a protective effect when prevented. Thus, while all of the normal limitations of cross-sectional designs should be acknowledged, this study should also offer direction in the follow on science that might confirm causal relationships while also testing services to prevent the likely effects of SHSe.

Response:
Thank you for your thorough consideration of the issues raised in our manuscript. As we mentioned above, evidence on the association between passive smoking and dental caries is insufficient to infer a causal relationship, although the biological and behavioral plausibility for an etiological relationship is likely to be quite high. It is too early to make any conclusion about the relationship between passive smoking and dental caries right now. Therefore, in this report, we cannot infer clinical implications and recommendations based on our results. We think that the issues that we addressed in
the Conclusion section provided direction for future research.

Comments:
Minor issues. The term ETS is reportedly a product of the Tobacco Industry to move the attribution from cigarettes to a more general environmental source of smoke exposure and thereby protect the Industry. Many of the investigators involved in SHSe have adopted second hand smoke exposure (SHSe) as the preferential name. I recommend that be done for this paper too.

Response:
Thank you for your suggestion. As suggested, we changed the term “environmental tobacco smoke (ETS) exposure” to “secondhand smoke exposure (SHSe)” in the text.

Comments:
While the rate or smoking among young children is likely quite low, the study should attempt to identify smokers and eliminate them from the analysis or discuss why this is not possible.

Response:
We added the sentence “When sensitivity analysis excluded these active smokers, the results were not changed, however (data not shown).” to the Discussion (page 12, lines 5-6 in the revised manuscript).

Comment:
While region of residence was one of the control variables it is not clear how this coincides with city. Since two cities were employed it should be made clear how these were similar or different and then how the control for region of residence controls for city influences. This could be conceptualized as a cluster effect for which control for cluster effects would be important. However, this is not likely to provide a big influence given the likely similarity between city populations.

Response:
In the present study, we controlled for the region of residence because the characteristic
of these cities differed. Naha city is the largest city in Okinawa Prefecture, whereas Nago city is rural. The population densities of Naha and Nago city are about 8,000 and 290 persons/km$^2$, respectively. We added information on the population density to the Methods (page 5, lines 4-6 in the revised manuscript).

About clustering effects, we decided to control within schools, but not cities. We recalculated prevalence ratios by taking into consideration clustering within schools using via the PROC GENMOD procedure. This did not change our results. We added the sentence “We took into consideration clustering within schools via the PROC GENMOD procedure.” to Materials and Methods (page 6, lines 3-4 from the bottom of the page in the revised manuscript).

**Comment:**
Regardless of how city may have been included in the current analyses, it might strengthen the results to replicate findings within each city independently. If patterns are the same, even if the power to detect significance is compromised especially in the smaller population from one city, this might offer an internal test of generalizability.

**Response:**
The table below shows prevalence ratios for dental caries in relation to smoking in the household in the separate analysis according to cities. We added the sentences “When we analyzed study subjects separately according to city, the results for Naha city were similar to those in the overall analysis. Likewise, the results for Nago city were similar to those in the overall analysis. “ to the Discussion (page 12, lines 17-19 in the revised manuscript). Details of the results were not shown in the manuscript.

<table>
<thead>
<tr>
<th></th>
<th>Naha city (n = 17,163)</th>
<th>Nago city (n = 3540)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted PR$^1$ (95% CI)</td>
<td>Adjusted PR$^1$ (95% CI)</td>
</tr>
<tr>
<td><strong>Decayed and/or filled teeth</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking in household</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Former</td>
<td>1.02 (0.99, 1.04)</td>
<td>1.06 (1.01, 1.10)</td>
</tr>
<tr>
<td>Current $&lt;15^2$</td>
<td>1.03 (1.01, 1.05)</td>
<td>1.06 (1.03, 1.10)</td>
</tr>
<tr>
<td>Current $\geq15^2$</td>
<td>1.04 (1.02, 1.06)</td>
<td>1.07 (1.04, 1.11)</td>
</tr>
<tr>
<td></td>
<td>Pack-years of passive smoking in household</td>
<td></td>
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<tr>
<td>----------------</td>
<td>------------------------------------------</td>
<td>----------------</td>
</tr>
<tr>
<td></td>
<td>None</td>
<td>1.00</td>
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<tr>
<td></td>
<td>0.1-2.9</td>
<td>1.03 (1.01, 1.05)</td>
</tr>
<tr>
<td></td>
<td>3.0-6.9</td>
<td>1.02 (1.00,1.05)</td>
</tr>
<tr>
<td></td>
<td>≥7.0</td>
<td>1.04 (1.02, 1.06)</td>
</tr>
<tr>
<td>P for trend</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**Decayed teeth**

Smoking in household

|                | Never                                   | 1.00           | 1.00                                     |
|                | Former                                  | 1.09 (1.03, 1.16) | 1.06 (0.97, 1.15) |
|                | Current <15 ²                            | 1.16 (1.11, 1.21) | 1.08 (1.01, 1.16) |
|                | Current ≥15 ²                            | 1.16 (1.11, 1.21) | 1.08 (1.01, 1.16) |
| P for trend    | <0.0001                                  | 0.003                                      |

Pack-years of passive smoking in household

|                | None                                     | 1.00           | 1.00                                     |
|                | 0.1-2.9                                  | 1.09 (1.04, 1.14) | 1.06 (0.98, 1.14) |
|                | 3.0-6.9                                  | 1.17 (1.12, 1.22) | 1.15 (1.08, 1.23) |
|                | ≥7.0                                     | 1.16 (1.11, 1.21) | 1.11 (1.03, 1.19) |
| P for trend    | <0.0001                                  | 0.002                                      |

**Filled teeth**

Smoking in household

|                | Never                                   | 1.00           | 1.00                                     |
|                | Former                                  | 1.01 (0.97, 1.05) | 0.98 (0.91, 1.07) |
|                | Current <15 ²                            | 1.01 (0.98, 1.03) | 1.03 (0.98, 1.09) |
|                | Current ≥15 ²                            | 1.01 (0.98, 1.04) | 1.02 (0.96, 1.09) |
| P for trend    | 0.49                                     | 0.28                                      |

Pack-years of passive smoking in household

|                | None                                     | 1.00           | 1.00                                     |
|                | 0.1-2.9                                  | 1.04 (1.01, 1.07) | 1.02 (0.96, 1.09) |
|                | 3.0-6.9                                  | 0.99 (0.96, 1.02) | 1.01 (0.95, 1.07) |
|                | ≥7.0                                     | 1.00 (0.97, 1.03) | 1.03 (0.97, 1.09) |
| P for trend    | 0.79                                     | <0.37                                    |

1 Adjustment for sex, age, toothbrushing frequency, use of fluoride, sugar intake, and paternal and maternal educational level.
Number of cigarettes smoked in the household per day.
Referee 3 (Dr. Othman Shibly)

Comment:
This paper “Household smoking and dental caries in schoolchildren: the Ryukyus Child Health Study.” Is very important paper at it might be of interest to the readers of this Journal

1) The abstract is little bit week on the result section. I think it should include some data that give the reader quick information on how harmful smoking compared to non-smokers household. The results only state significant difference without any data showing the magnitude of differences.

Response:
As suggested, we inserted adjusted prevalence ratios and 95% confidence intervals to the Abstract.

Comment:
2) Another point the authors classified toothbrushing frequency into 2 (1 or less and _2 times per day).
I believe that should be distinction between people who brush once a day and those who do not brush at all. Putting them together as the authors did may influence the outcome.

Response:
We classified toothbrushing frequency into 4 (<1, 1, 2, and >2 times/day) categories and reanalyzed prevalence ratios. We corrected the corresponding figures in the Tables.

Comment:
3) Authors used terms such as “approximal caries”. They meant interproximal caries. I think they should re edit the paper from English perspective

Response:
The term “approximal cares” was changed to “interproximal caries” (page 11, line 16 in the revised manuscript).
Comment:
Discretionary Revisions
Authors adjusted confounding factors such as diet, intake of sugars, sex, etc. I think data will be more meaningful had they showed the data before adjusting especially that related to sugar intake and caries.

Response:
We newly tabulated the results of unadjusted analyses for selected covariates in Table 2. We also added comments regarding the unadjusted analysis in the Results (page 7, lines 13-19 in the revised manuscript).
Referee 4 (Dr. Olalekan A Ayo-Yusuf)

General comment:
This cross-sectional study demonstrated a positive association between household smoking and dental caries prevalence among a population of Japanese schoolchildren. The strength of the study includes the use of a large sample size and adjustment for known caries risk factors. This is a generally well-written paper, but there are some concerns that needs to be addressed to improve the paper:

Minor essential revisions
Abstract
1. To attend to minor grammatical/typo errors in the abstract.

Response:
The present manuscript has been carefully reviewed by an experienced medical editor whose first language is English and who is specialized in the editing of papers written by physicians and scientists whose native language is not English.

Introduction
2. I do not think the authors have accurately reflected the findings in reference [7] by suggesting association between household smoking and dental caries was not shown in a previous study in Japan. That study results states ‘no statistically significant relationship was observed between household smoking and caries experience. However, smoking in the household was independently associated with an increased prevalence of decayed teeth.

Response:
We changed the sentence “On the other hand, a positive association between smoking in the household and dental caries in Japanese children aged 1 to 14 years was no shown [7].” to the following: “Smoking in the household was shown to be associated with a higher prevalence of untreated decayed teeth, but not caries experience (decayed and/or filled teeth) in a cross-sectional study among Japanese children aged 1 to 14 years [7].” (Background, page 4, lines 14-17 in the revised manuscript).
Comment:
3. Given that other cross-sectional studies have demonstrated the relationship between household smoking and caries, in order to motivate the reader upfront, it is important for the authors to more clearly provide strong support of superiority of current study over others previous studies.

Response:
We changed the last sentence in Background to the following: “Therefore, we examined the potential association between household smoking and dental caries using the data set of the Ryukyus Child Health Study (RYUCHS), which involved a large sample size and collected information on important factors in relation to dental caries and smoking, and school records of dental examinations.” (page 4, lines 5-8 from bottom of the page in the revised manuscript).

Major compulsory revisions
4. Although the authors have correctly used PR for effect estimation since the outcome was common (caries rate), but of major concern is that the large number children examined were nested in schools, thus there is a potential for Type I error that may result from considerable intra-cluster (school level) correlation. Given that this could significantly change the study results, could the authors clarify if this cluster sampling was accounted for in their analysis? If so this should be more clearly indicated in the analytical plan. From the error estimates displayed for mean number of teeth affected and a considerably small excess risk between those exposed and those not exposed, it will be important to address this concern in order to refute that the results are not likely subject to type I error.

Response:
As you suggested, we recalculated prevalence ratios by taking into consideration clustering within schools using via the PROC GENMOD procedure. This did not change our results. We added the sentence “We took into consideration clustering within schools via the PROC GENMOD procedure.” to Materials and Methods (page 6, lines 3-4 from bottom of the page in the revised manuscript).
Comment:
5. Could the author confirm, if the quantity/intensity of cigarette smoking measured are those smoked exclusively in the household or those smoked generally as reported by the parents or the children themselves (in the case of the older children)? Could this explain the fact that there was little or no exposure dose-response effect demonstrated with regards quantity smoked?

Response:
Unfortunately, we were not able to ascertain whether responders to the questions regarding household smoking were the parents or the children themselves. Accuracy of the replies might differ according to whether parents or children completed the questionnaire. We added the sentences “In addition, responders differed between elementary schools and junior high schools. Parents of elementary school children completed our questionnaires whereas with junior high school students the questionnaires were completed by either the students themselves with or without parental help or by their parents. This could have driven the results.” to the Discussion (from page 11, line 2 from the bottom of the page to page 12, line 2 in the revised manuscript).

Comment:
6. Other than just stating in a footnote, it will also be useful to display the full models for caries prediction so as to support the validity of the study findings, as some of the factors measured are known indicators of caries. This is also particularly important since the instrument used for deriving sugar consumption had not been routinely used in caries research. At minimum, a table showing the bivariate relationship between these potential confounding variables and caries rates in this population should be displayed.

Response:
We newly tabulated the results of unadjusted analyses for selected covariates in Table 2. We also added comments regarding the unadjusted analysis in the Results (page 7, lines 13-19 in the revised manuscript).
Discretionary revisions
Discussion
7. Could the authors provide an opinion on why other studies have found no association between active smoking and caries (presumably in adult permanent teeth) and yet this study showed an association between ETS and caries in permanent teeth of children?

Response:
We added the following sentences with references: “On the other hand, epidemiological studies on the association between active smoking and dental caries showed inconsistent results. Some studies suggested that smoking was positively associated with dental caries [18, 19], while another study reported no association between smoking and dental caries [20]. Many of the published studies showing no association between smoking and dental caries did not control for potential confounders, such as socioeconomic status, diet, and oral health behaviors. Therefore, it is possible that the observed associations were influenced by confounding factors.” to the Discussion (page 10, lines 2-9 in the revised manuscript).
Associate Editor comments:
Reviewers 1 and 4 raise substantial and significant questions about the analytic approach and therefore the validity of the findings. The authors should pay particular attention to these concerns in preparing any revision. The authors should also consider mechanistic questions such as the consistent lack of association between active smoking and dental caries when proposing the link between secondhand exposure and caries.

Response:

Analytic approach
As reviewer 4 suggested, we recalculated prevalence ratios by taking into consideration clustering within schools using via the PROC GENMOD procedure. This did not change our results. We added the sentence “We took into consideration clustering within schools via the PROC GENMOD procedure.” to Materials and Methods.

In the current study, we used parents’ educational levels in order to control for socioeconomic status. After adjustment for only parents’ educational levels, the prevalence ratios were rather reduced. As reviewer 1 suggested, the crude associations are likely to be in part explained by parents’ educational levels. Unfortunately, information on socioeconomic status other than parents’ educational levels was not available in the present study. We added the sentences “However, residual confounding effects could not be ruled out. In particular, information on socioeconomic status was based on only paternal and maternal educational levels. Part of the observed positive relationships between SHSe and dental caries may be ascribed to uncontrolled for confounding effects of socioeconomic status.” (page 11, lines 7-11 in the revised manuscript). As reviewers 1 and 4 indicated, a pattern of replies might differ between the parents and the children themselves. We added the sentences “In addition, responders differed between elementary schools and junior high schools. Parents of elementary school children completed our questionnaires whereas with junior high school students the questionnaires were completed by either the students themselves with or without parental help or by their parents. This could have driven the results.” to the Discussion.

Consideration about an association between smoking and dental caries
According to the 2004 U.S. Surgeon General’s Report on the Health Consequence of Smoking, epidemiological evidence on the association between smoking and dental
caries was not sufficient to infer a causal relationship. Furthermore, many of the published studies did not control for potential confounding factors, such as socioeconomic factors, diet habits, and oral health behaviors. The 2004 U.S. Surgeon General’s Report was based on a search for English language publications from 1965-2000. In the last decade, epidemiological studies on the association between smoking, including passive smoking, and dental caries are increasing. Available literature is fairly consistent in suggesting that smokers may experience slightly more decayed, missing, or filled coronal tooth surfaces. Several biological mechanisms, such as changes in bacterial ecology, the availability of saliva in the mouth, and alterations in immune responses, appear to be responsible for the increased risks of dental caries among smokers. In addition, smokers may have different lifestyle habits that further modify their oral health. However, no clear conclusion has been reached. Further research that controls for potential confounding factors on the smoking-dental caries relationship is necessary to draw a conclusion regarding whether active and passive smoking increase the likelihood of dental caries. Regarding this circumstance, we did not add any further information in the manuscript.