Author's response to reviews

Title: Number of teeth and myocardial infarction and stroke among elderly never smokers

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Dear Björn Olsen, the JNRBM Editorial Team

Please find attached our revised manuscript entitled “Number of teeth and myocardial infarction and stroke among elderly never smokers”. Thank you for the constructive comments on our manuscript. Answers to the referees’ comments are provided here. Main changes have been bolded and some linguistic and stylistic changes have been made. Crude PPR for myocardial infarction and stroke has been added in Table 3 and in Table 2 some corrections has been made.

We hope that our article will now be acceptable for Your journal JNRBM.

For reviewer 1

In material and methods, first chapter, the sentence describing the sampling strategy has been rephrased as: “The study population was a random sample from a census register consisting of ...”. The restriction to never smokers was the reason why this subpopulation consisted of only 392 subjects. This aspect has been added into Methods section and Discussion section.

Confounding has been more thoroughly discussed. Also survival bias as an explanation and its implication has been discussed. To our experience confounding in the association between oral diseases and CVD causes normally positive (artificial) association, which association can be eliminated totally or partially by controlling for confounders. Thus, based on this we do not consider that a lack of any significant association is a sign of confounding. Also controlling for confounders (by restrictions and multivariate modelling) is fairly profound, compared to many of studies in this field.
Discussion

1) In discussion in the first chapter the sentence “On the condition that these extrapolations are true, one possible underlying biological mechanism is that a large number of teeth predispose subjects to dental or periodontal infection, which through different mechanisms may lead to accelerated atheroma formation” has been omitted as suggested.

2) In the second paragraph in discussion the sentence “In order to reduce confounding...” has been changed as suggested.

3) In the second paragraph in discussion the sentence “However, despite profound adjustment and restrictions, the possibility that some residual confounding existed cannot be excluded...” has been changed as suggested.

4) Discussion includes now also other possible causes of tooth loss.

5) The term ‘validity’ has omitted in connection with the extent to which tooth loss reflects oral diseases.

6) In Conclusion the last sentence “However, based on the restrictions of the data, it must be underlined that the results of this study do not exclude the possibility that a causal association between tooth loss and cardiovascular diseases exist.” has been omitted as suggested. The text of the conclusion has been made clearer as suggested.
7) Language revision has been made.

8) The fact that the same geriatrician made both oral (partial) and clinical examination meant that geriatrician was possible aware about disease history of the subject when performing oral (partial) examinations. We do not know whether this has any affect on results, but the fact that the aim of this paper did not originally belonged to the aims of this study project, means bias in registration is difficult to imagine. These aspects have been added in the Discussion section.

9) Smoking among women was fairly uncommon in these age-groups. Due to different smoking habits between men and women, there were more women in this subpopulation. Due to this unequal gender distribution, we have tested whether there were any interaction between explanatory variables and gender. It must be remembered that we can generalise (external validity) only to respective population, i.e. non-smokers 75 years old or more. These aspects are now discussed more thoroughly.

10) We have expanded the discussion about survival bias and it significance.

11) Unfortunately, there was an error in the variable category in table 1. Instead of ‘low education’ there should be ‘high education’. Furthermore, we have commented the possibility of residual confounding related to socioeconomic or behavioural factors.

12) We had added crude estimates in table 3. In addition, we have explained the rationality of covariate selection in the method section. Despite existence of different methods in covariate selection, we prefer to select covariates based on the previous
knowledge and based on their association with outcome variable and different distribution between categories of explanatory variables. Based on these criteria we did not use glucose level or total cholesterol in the final model.

13) They are based on the estimates from Table 3. Despite these figures show positive association between number of teeth and history of MI and stroke we do not want emphasise this finding, because estimates are subject to uncertainty.

14) This study is a secondary analyses of the larger epidemiological study. The starting point for that study was that sample size of 700 was enough to represent the population. It means that about every fifth of that population was sampled. We are not aware of sample size calculation, made possibly for other purposes. In the discussion section we had mentioned that this study was a secondary analysis of the study, originally planned for other purposes.

For reviewer 2

We consider that there could be a survival bias, which may affect the results. Such bias cannot be eliminated in this kind of cross-sectional study. This means the follow-up studies are needed in order assess causality between tooth loss and CVD. This aspect has been added in the Discussion section.

Unfortunately no registration of periodontal status was made. We have omitted the term ‘oral clinical examination’ in the manuscript. We have explained oral examination to be a part of clinical health examination. Also more details about oral examination have been
added. This has been taken into account in the Abstract, in Material and Methods section and in the Discussion.

Unfortunately, we have no registration of CRP or periodontal microbiology. We have omitted in large extent speculations about possible role of periodontitis.

The title has been changed as suggested “Number of teeth and myocardial infarction and stroke among elderly never smokers” as well as the short title has been changed as suggested “Number of teeth and cardiovascular diseases”.

In the Abstract the sentence “Oral infections may be aetiological factors in atherosclerotic vascular diseases.” has been omitted and the text has been rephrased as suggested.