Author's response to reviews

Title: Swedish snuff and incidence of cardiovascular disease. A population-based cohort study

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Author's response to reviews: see over
Dear Editor

Thank you very much for your response. We have been working further after the guidance of the two, very qualified reviewers who I am well acquainted with from the literature. First I will mention that professors Göran Berglund and Gunnar Engström names were removed from the paper authors list since they mentioned that he had not contributed to the development.

I would like to express my gratefulness to the revivers who both with useful comments have been improving this work. I regret and agree that there were many unnecessary faults in the manuscript.

Here follows our answers to each reviewers report:

Dear professor Lee. Thank for you useful comments and also for the attached manuscript. It was not possible to tract changes, but I read carefully. I have followed the instructions.

1. The numbers are presented in the revised manuscript on p. 4, paragraph 2, line 3 -4

2. Thank you for the advice and the references. They were very useful and we have inserted these references in the revised manuscript

3. As suggested all relative risk is now presented with two decimal in table 2.

4. Daily cigarette consumption in the Malmö Diet Cancer study was assessed by the question “How many cigarettes do you smoke per day? This information is now in the revised manuscript presented on page 4, paragraph 4, line 3, and the results as grams per day in table 1.)

5. This section on occupational level has been re-written in the revised manuscript. This has unfortunately extended the paragraph but hopefully makes it more understandable (p 6, paragraph 3)

6. Most studies from the Malmö Diet and Cancer study on stroke has used the STROMA (Stroke in Malmö) registry. The information on STROMA, validity and ascertainment of cases has previously been presented (see reference 17, Zia et al. Stroke 2007; 38: 2681-5). In accordance with these previous studies all incident stroke in the present study were assessed in a similar way.

7. Results presented in Table 1 were changed after suggestion to % (n). As in previous studies from this cohort on occupation have we furthermore decided to present occupational level in four groups (ref.22)

8. Thank you for the suggestion to examine mean cigarette consumption among snuff user it contributes to the work. Snuff reduced significantly cigarettes smoked among both men and
women, most among women and the result is now presented in Table 1 in the revised manuscript.

9. Thank you for the attached revised suggestions. We have worked further with the language. Hopefully you will find that it has been improved.

10. The numbers of incident MI and stroke have been corrected in the revised manuscript. The correct numbers should be 4 and 2 (see p 10, paragraph 1, line 1-2).

11. Thank you for the advice and the references. They were very useful and have improved the work considerable. Most of them are now included in the reference list. We will just mention that at the beginning of the discussion we referred to tobacco smoking health hazard therefore not all the articles were used.

12. This section has been re-written and reference 24 in the previously manuscript has been as suggested omitted.

13. We are sorry for the incorrect citation of reference 28. This has been corrected in the revised manuscript.

14. See answer to point 12.

15. We have checked for errors and poor wording and tried to correct all errors in the revised manuscript.

16. The reference list in the revised manuscript has been checked and corrected for possible errors.

Dear professor Ram Sing,

We have tried to revise our manuscript according to your queries and comments.

The consumption of snuff has now been dichotomised into three group low, medium and high.

1) We do agree that the participation rate in the Malmö Diet and Cancer study in only 40% and that snuff use among non-participants could possibly be associated with an increased incidence of CVD. We have tried to address this possibility by comparing the prevalence of smoking habits among corresponding age groups of Malmö citizens who participated 1994 in a health survey based on a mailed questionnaire (see reference 16 in the revised manuscript). The participation rate in that study was almost 80%, and non-participation was associated with lower prevalence of smoking, however higher rate of all-cause mortality. The prevalence rate of smoking in our present study (39.9%) is rather similar to that found in the health survey (37.5%) in similar age groups. This indicates that the estimated prevalence of snuff users in our present study should not be underestimated. This information has been added on page xx in the revised manuscript.
2) The consumption of snuff packages was assessed by the question: “How many packages of snuff do you use every week?” (pp 6) The range among snuff users was 1-24 packages per week. This information has been inserted in the revised manuscript on page 9.

3) We do not agree with the reviewer about this matter. Our main objective has been to present further contribution to the scientific discussion on possible health effects on incident CVD (in terms of MI and stroke). Although this study is based on 27,000 middle-aged subjects and almost 900 CVD events we found no statistically significant increase risk for incident CVD in snuff users, however, it should be stressed that analysis was based on few female snuff users and numbers of events. Thus, we do claim and conclude that snuff is harmless. As discussed on page xx it is opinion that all health effect should be reported. Snuff use has evidently negative health effects when it comes to development of cancer and should not be recommended as a substitute for smoking.

4) As suggested we have also assessed tobacco chewing in the revised manuscript (see page x in the methods section for definition). We have furthermore calculated the relative risk for MI in tobacco chewing men. Although based on small numbers and wide confidence interval we found that the point estimate of RR for incident MI (1.5; 0.5-4.5, p=0.512) was higher than for snuff users. No similar analysis was performed in women due to small number of users and events. These results have been included in the revised manuscript on page 12.

Best regards

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