Author's response to reviews

Title: Early menopause: Association with tobacco smoking, coffee consumption and other lifestyle factors - a cross-sectional study

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Author's response to reviews: see over
Dear Editor of BMC Public Health

The authors thank you again for your interest in our manuscript entitled “Early Menopause: Association with tobacco smoking, coffee consumption and other lifestyle factors—a cross-sectional study”. Please find enclosed our revised manuscript: We have revised the manuscript according to your recommendations, and do also provide you with a more detailed commentary where we address our responses to your concerns.

The changes are specified and commented below.

The tables have changed number. Table 4 (stimulants) in the previous version is now number 2. Table 2 (exposure to tobacco smoke) and 3 (passive smoking) are now 3 and 4 respectively.

Referee 1:
1) Conclusion lacks comment of total exposure of smoking and the role of education. It is left unclear how are these correlated: are highest educated the least exposed to smoking? I guess this is true, but it would be good to add this interrelationship to results section.

Answer: We have now added the following paragraph at page 9:
At the same time the women with the highest level of education are the ones the least exposed to smoking. Among the ones with more than 12 years of education, the percentage of never smokers is 54.0 % and the percentage of current smokers is 16.9 %. These same percentages among the women with less than 8 years of education are respectively 40.8 % and 33.1 %.

2) 2123 women were included to the study, but how large proportion of them had early menopause during age 40-44 years?

Answer: The proportion of women who had early menopause is 9.6 % (203 women). This is now added at page 9.

3) From Table 1 it seems that 2119 out of all respondents (99%) had early menopause by marital status, which is quite unprobable. Please check the table headline and/or analyses.

Answer: The number N is the total number of participants who have answered for example “married” on the question about marital status. The number N therefore includes both those who had early, normal and late menopause. All in all the number adds up in 2119 for this particular category, and not 2123, because four of the participants have not answered the question. The same goes for the other categories. The percentage in the other column shows the proportion that had early menopause. We have now changed it so that the percentage is presented first, followed by the total number N. We have also added “total number that answered” in the headline in stead of only “total number”. Hopefully this makes it a bit clearer.

4) In discussion the use of HRT is suggested to overestimate the age of menopause. If HRT is started before menopause, there is no clear menopausal age estimated if HRT is not cessated. Thus it could be both under- and overestimation- confounding anyhow.

Answer: This may be true. We have changed the term ”overestimate” to ”not correctly estimate”.

5) Page 9 states that 'more than four cups of coffee a week showed an association...' This may be rather 'a day'?

Answer: This is correct. It has been changed.
6) Please delete horizontal lines from the tables.
Answer: It is stated in Instructions for authors that “Columns and rows of data should be made visibly distinct by ensuring the borders of each cell display as black lines”. This has therefore not been changed.

Referee 2:
1) In Table 1 results for each variable must be presented adjusted by the other variables which have been shown to be related with the end point, the early menopause in raw analyses: marital status, educational level, social participation, self reported health, or coffee consumption.
Answer: We have performed these analyses, but they did not change the results much. We have now added the following paragraph at page 9: \textit{Adjustment in relevant analyses for marital status, educational level, social participation, self reported health and coffee consumption changed the point estimates by 0.1-0.2, but the significance levels were not much affected. (It was affected only for one out of three levels of education – 11-12 years).}

2 Tables 2, 3 and 4, authors must explore the relationship between all variables showed in Table 1 and smoking variables, coffee, and alcohol. All variables related both with early menopause (Table 1) and smoking must be included as covariates in the analyses for Tables 2 and 3. The same procedure applies for coffee and alcohol (Table 4).
Answer: This has been done and is thoroughly commented on in the result section and in the discussion (page 15).

3) Why are the results for smoking and early menopause repeated in Table 4, when they are also presented in Table 2?
Answer: This was done to include smoking in the “general overview” of the population (table 1), smoking (table 3) and stimulants (table 2) – for the totality of each table – but we have changed it, and the data are now presented in table 2 only.

4) There is a lack of data on physical activity and its relationship with early menopause.
Answer: Data on physical activity are now presented.

5) Discussion page 13) the response rate is very low, and the representativity of the sample is highly compromised, not only “some bias is expected”, and of course the selective participation could affect the data obtained. The second paragraph must be re-written in this way.
Answer: We agree that the response rate is low, but the study of self-selection shows that there is not a serious or large selection bias that concerns our study. We have added this paragraph to explain better why this, according to us, is so: \textit{There is no evidence or indication of connection between survey participation and menopausal age, so that self-selection for participation had probably little or no impact on the associations we found. Moreover, it has been shown that less educated persons were less likely to participate in the Oslo Health Study than were higher educated, but further that this had probably little impact even on prevalence data for risk factors such as smoking [19].}

We have also changed from ”some selection bias is expected” to simply ”selection bias is expected”.
6) Objectives are not clearly defined. They must be shortened for Abstract purposes.
Answer: The objectives are now presented as follows: The objective of this study is to investigate the association between early menopause and active and passive smoking including a possible dose–response relationship with active smoking and early menopause. One further main aim of this study is to investigate the association between early menopause and coffee and alcohol consumption.

In the abstract we have shortened the objectives:
The objective was primarily to investigate the association between early menopause and current, past active and passive smoking. A second aim was to investigate the association between coffee and alcohol consumption and early menopause.

7) Put the quotation et al. after the name of a first author.
Answer: This has been done.

8) Was the questionnaire used for recording alcohol and coffee consumption a validated questionnaire? If so, please put the citation. If no, this must be included as a limitation of the study.
Answer: This is now commented on at page 12. The new paragraph is: In the Tromsø Heart Study the relative validity of the question on coffee consumption per day was compared with a dietary history survey two years later and the answers agreed well for coffee as well as other food items used every day in easily recorded unites [21]. Also, the reproducibility of the Tromsø survey questionnaire was studied by comparing it with a new questionnaire assessment one year later, and the concordance of coffee consumption was 67 % for exact agreement and 99 % for agreement within one category (Rho=0.65). In the same study the concordance of alcohol consumption (beer, wine and spirit were recorded separately) was 66-76 % for exact agreement and 96-100 % for agreement within one category [22]. The references have been included.

9) Why participants were not asked for natural or surgical menopause? Privacy reasons?
Answer: The main reason why it was not asked for natural or surgical menopause was that the survey contained a lot of questions. Those who formulated the questions were from many fields of science/epidemiology, not only gynaecology, thus they may not have appreciated the importance of the surgical menopause issue. Many questions had to be eliminated and unfortunately this was the case for the question about natural or surgical menopause.

10) There is no data concerning percentage of passive smokers.
Answer: A definition of passive smokers is added on page 6. The percentage of passive smokers is added on page 9.

11) Discussion. Page 15 last paragraph. The link among education, genetics, and intrauterine life is highly speculative.
Answer: This paragraph is left as it was as we consider genetically influenced factors such as intelligence to be important selection factors for higher education. This may be the case particularly in countries (like Norway) with free public schools and universities.

Thank you for your attention!
On behalf of all co-authors who have read and approved the changes

Thea Falkenberg Mikkelsen