

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Do smoking habits differ between women and men in contemporary Western populations? Evidence from half a million people in the United Kingdom Biobank study
<b>AUTHORS</b>	Woodward, Mark; Peters, Sanne; Huxley, Rachel

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Paolo Boffetta Icahn School of Medicine at Mount Sinai, New York NY USA
<b>REVIEW RETURNED</b>	05-Jun-2014

<b>GENERAL COMMENTS</b>	<p>1. This is a straightforward analysis of smoking habits by gender, birth cohort and SES in the UK Biobank. It largely confirms what has been observed in other populations.</p> <p>2. The higher relative risk for several tobacco-related diseases in women compared to men can be explained by a lower incidence among non-smoking women compared to non-smoking men, possibly because of exposure to other risk factors (e.g., occupational lung carcinogens). In general, this analysis is not adequate to address the supposed increased susceptibility of women compared to men, and these sections of the manuscript are highly speculative.</p> <p>3. It would be of interest to analyze simultaneously the differences in smoking habits between men and women according to birth cohort and SES. This can be done to some extent by comparing the subsequent e-Tables, but it is not clear why the authors did not fit a multivariable model including terms for both determinants (and their possible interactions).</p> <p>4. The cross-sectional nature of the investigation complicates the analysis of some of the time-related variables. In particular, the comparison of age at quitting across birth cohorts might be problematic because of right truncation (i.e., younger birth cohorts would have less opportunity to quit at old age compared to older birth cohorts).</p>
-------------------------	---

<b>REVIEWER</b>	Ane Johannessen Centre for Clinical Research, Haukeland University Hospital, Bergen, Norway
<b>REVIEW RETURNED</b>	08-Oct-2014

<b>GENERAL COMMENTS</b>	The paper "Do smoking habits differ between women and men in contemporary Western populations? Evidence from half a million
-------------------------	---

	<p>people in the United Kingdom Biobank study" describes smoking habits in men and women across time. It concludes that gender differences have decreased over time, and that even past differences cannot explain the increased susceptibility to smoking-induced diseases in women compared to men. The findings are not all that novel, we know that men used to smoke more than women and that women and men are now more equal with regard to smoking habits. We also know that women seem more susceptible to damages of smoking than men, and after this paper we still do not know why. Clinical implications are very limited: the paper is purely descriptive with regard to smoking habits and has no clinical outcomes. Even if the paper is very well written and has a major strength in its huge study population, the lack of novelty and clinical implications as well as serious shortcomings with regard to population representativeness unfortunately prevents it from being recommended for publication in its present context, in my opinion.</p> <p>Major comments:</p> <ol style="list-style-type: none"> <li>1. The study population is absolutely not representative despite its enormous size. In the UK population 19% of women and 20% of men are smokers. In the UK Biobank study, however, only 7% women and 9% men were smokers. This is stated but not discussed in the manuscript. The authors should discuss thoroughly the very low proportion of smoker in the Biobank study, what consequences may this have for the estimates? How can the authors assume that gender differences in smoking habits are representative for the general population when the smoking prevalence is not? Also, page 5: Women smoked on average 16 cigarettes per day while men smoked on average 20 cigarettes per day, while the 2010 smoking statistics in England estimated that men smoked 13 cigarettes per day and women 12 cigarettes per day. This is indeed a large discrepancy for both men and women, and should be emphasized in the discussion on representativity.</li> <li>2. Pack years as an exposure variable would be very valuable in a study such as this. It takes into account both duration of smoking and amount smoked and might add important extra information from a gender perspective.</li> </ol> <p>Minor comments:</p> <ol style="list-style-type: none"> <li>1. It says in the abstract (main outcome measures paragraph) that the birth cohorts covered in this study range from 1935 to 1970. However, it says in the results part of the abstract that the youngest are born 1965-1969. And then, in the introduction of the paper itself, it says that "we examined the current and past smoking habits of women and men born 1935-1975..." Which is it, 1970, 1969 or 1975? Please correct where necessary.</li> <li>2. Also results for occasional smokers should be presented; I would expect this to be quite a large group with perhaps large gender differences across time. If possible, the authors should keep this group as a separate group in the analyses.</li> <li>3. Page 8: What thus study adds: "Smoking habits in UK Biobank participants are less hazardous than in the overall UK population but they are more deleterious in men than women (as in the general UK population)." I fail to see how the present manuscript leads up to this conclusion? As far as I can see, there is a lower proportion of smokers in the Biobank study, but the smokers (both men and women) smoke much more cigarettes per day than in the general population.</li> </ol>
--	---

## VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name Paolo Boffetta

Institution and Country Icahn School of Medicine at Mount Sinai, New York NY USA

Please state any competing interests or state 'None declared': None declared.

1. This is a straightforward analysis of smoking habits by gender, birth cohort and SES in the UK Biobank. It largely confirms what has been observed in other populations.

2. The higher relative risk for several tobacco-related diseases in women compared to men can be explained by a lower incidence among non-smoking women compared to non-smoking men, possibly because of exposure to other risk factors (e.g., occupational lung carcinogens). In general, this analysis is not adequate to address the supposed increased susceptibility of women compared to men, and these sections of the manuscript are highly speculative.

Thank you for these comments. We agree with that further analyses will be required to determine whether the relative risk of tobacco-induced diseases is different between men and women, and if confirmed, which factors are responsible for such differential. We have mentioned this in the manuscript.

3. It would be of interest to analyze simultaneously the differences in smoking habits between men and women according to birth cohort and SES. This can be done to some extent by comparing the subsequent e-Tables, but it is not clear why the authors did not fit a multivariable model including terms for both determinants (and their possible interactions).

Thank you for this suggestion. The results from the requested analyses are presented in eTable9. We also added supplementary figures on sex ratios or differences, whichever was appropriate, in smoking habits by birth cohort and SES.

4. The cross-sectional nature of the investigation complicates the analysis of some of the time-related variables. In particular, the comparison of age at quitting across birth cohorts might be problematic because of right truncation (i.e., younger birth cohorts would have less opportunity to quit at old age compared to older birth cohorts).

Thank you for this comment. Right truncation of the data will indeed have affected our estimates, especially those that require information on smoking cessation; the proportion of individuals that will ultimately stop smoking but haven't done so already is likely to be larger in the younger birth cohorts than in the older birth cohorts. Comparison of these estimates between birth cohorts is therefore difficult. The impact of right truncation on women and men from the same birth cohort, however, is likely to be similar. The differences in smoking habits between men and women from the same birth cohort are therefore likely to be valid. We have now reported this in the discussion section of the manuscript.

Reviewer: 2

Reviewer Name Ane Johannessen

Institution and Country Centre for Clinical Research,

Haukeland University Hospital,

Bergen, Norway

Please state any competing interests or state 'None declared': None declared.

The paper "Do smoking habits differ between women and men in contemporary Western populations? Evidence from half a million people in the United Kingdom Biobank study" describes smoking habits in men and women across time. It concludes that gender differences have decreased over time, and that even past differences cannot explain the increased susceptibility to smoking-induced diseases in women compared to men. The findings are not all that novel, we know that men used to smoke more than women and that women and men are now more equal with regard to smoking habits. We also know that women seem more susceptible to damages of smoking than men, and after this paper we

still do not know why. Clinical implications are very limited: the paper is purely descriptive with regard to smoking habits and has no clinical outcomes. Even if the paper is very well written and has a major strength in its huge study population, the lack of novelty and clinical implications as well as serious shortcomings with regard to population representativeness unfortunately prevents it from being recommended for publication in its present context, in my opinion.

Major comments:

1. The study population is absolutely not representative despite its enormous size. In the UK population 19% of women and 20% of men are smokers. In the UK Biobank study, however, only 7% women and 9% men were smokers. This is stated but not discussed in the manuscript. The authors should discuss thoroughly the very low proportion of smoker in the Biobank study, what consequences may this have for the estimates? How can the authors assume that gender differences in smoking habits are representative for the general population when the smoking prevalence is not? Also, page 5: Women smoked on average 16 cigarettes per day while men smoked on average 20 cigarettes per day, while the 2010 smoking statistics in England estimated that men smoked 13 cigarettes per day and women 12 cigarettes per day. This is indeed a large discrepancy for both men and women, and should be emphasized in the discussion on representativity.

We thank the reviewer for this comment. Smoking habits of the UK Biobank participants are indeed not representative for those in the UK population. This non-representativeness, however, is likely to have affected men and women to the same extent. Hence, while the absolute estimates on smoking habits should be interpreted with caution, the differences between men and women will likely remain valid. We have discussed this, with appropriate caution, in the revised version of the manuscript.

2. Pack years as an exposure variable would be very valuable in a study such as this. It takes into account both duration of smoking and amount smoked and might add important extra information from a gender perspective.

Thank you for this suggestion. We have added pack years of smoking as exposure variable to our principal analyses and reported the findings in the revised version of the manuscript.

Minor comments:

1. It says in the abstract (main outcome measures paragraph) that the birth cohorts covered in this study range from 1935 to 1970. However, it says in the results part of the abstract that the youngest are born 1965-1969. And then, in the introduction of the paper itself, it says that "we examined the current and past smoking habits of women and men born 1935-1975..." Which is it, 1970, 1969 or 1975? Please correct where necessary.

Thank you. We have corrected this in the revised version of the manuscript.

2. Also results for occasional smokers should be presented; I would expect this to be quite a large group with perhaps large gender differences across time. If possible, the authors should keep this group as a separate group in the analyses.

Thank you for this suggestion. The revised manuscript includes the prevalence rates of previous and current occasional smoking. Data on age at smoking initiation and smoking cessation, and the amount of cigarettes smoked were not available for current or past occasional smokers.

3. Page 8: What this study adds: "Smoking habits in UK Biobank participants are less hazardous than in the overall UK population but they are more deleterious in men than women (as in the general UK population)." I fail to see how the present manuscript leads up to this conclusion? As far as I can see, there is a lower proportion of smokers in the Biobank study, but the smokers (both men and women) smoke much more cigarettes per day than in the general population.

Thank you. We have rephrased this sentence as it was meant to highlight that the smoking rates are lower in the UK Biobank than in the UK population.

## VERSION 2 – REVIEW

<b>REVIEWER</b>	Ane Johannessen Centre for Clinical Research, Haukeland University Hospital, Bergen, Norway.
<b>REVIEW RETURNED</b>	11-Nov-2014

<b>GENERAL COMMENTS</b>	I have read with much interest the revised version of this manuscript, and it has been substantially improved since the original submission. I have no further suggestions for changes.
-------------------------	---

<b>REVIEWER</b>	Paolo Boffetta Icahn School of Medicine at Mount Sinai - New York NY
<b>REVIEW RETURNED</b>	24-Nov-2014

<b>GENERAL COMMENTS</b>	The authors have adequately addressed my comments.
-------------------------	--