Author's response to reviews

Title: Are psychosocial stressors associated with the relationship of alcohol consumption and all-cause mortality? Findings from the MONICA/KORA Augsburg Cohort Study, 1984-2002

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Author's response to reviews: see over
To the  
Editors of *BMC Public Health*

Neuherberg, 15/01/2014

Dear Sir/Madam,

Please find enclosed our revised manuscript entitled “Are psychosocial stressors associated with the relationship of alcohol consumption and all-cause mortality? Findings from the MONICA/KORA Augsburg Cohort Study, 1984-2002” carried out within the framework of a large, population-based cohort study in southern Germany.

We appreciate the very constructive review of our manuscript. We have carefully studied and considered the comments of the reviewer and revised the manuscript based on these comments. Moreover, we edited the manuscript regarding formatting points and include now subtitles also in the results and discussion part. We feel that these modifications have considerably improved our manuscript. Please find our point-by-point response to the concerns and comments of the reviewer below in italic letters.

Again, all authors have read and approved the revised final manuscript. The results of this paper have not been published elsewhere nor are they under consideration at any other journal. We would be very pleased if our manuscript could be considered for publication in *BMC Public Health*.

Looking forward to hearing from you.

Yours sincerely

Prof. Karl-Heinz Ladwig,

Neuherberg, Germany

Reviewer’s report:

This paper uses the MONICA/KORA, a large prospective cohort study to examine potential confounding as an explanation for the J or U-shaped curve seen with alcohol use and mortality. Specifically, this paper addresses an important issue of the potential confounding of psychosocial stressors in the relationship between alcohol and mortality. This is an important study addressing an existing research gap.

*We appreciate the very positive overall appraisement of our manuscript by the reviewer and would like to thank for the careful reading and constructive comments.*

**Major Compulsory Revisions:**

**Results:**
The inclusion of Table 1 showing abstainers are more unhealthy/sicker seems like a separate issue from the main question of this paper (are psychosocial stressors confounding the relationship of alcohol and mortality?). Particularly because these individuals are not even included in the main analysis, I would suggest taking this table out and just discuss who was excluded in the text of the methods.

After careful consideration, we agree with the reviewer that Table 1 is not really necessary. Therefore, we omit it and focus now on the study population of the main analyses (n=11,282). We removed the paragraph describing the former Table 1 to the methods part under the revised subtitle “Study population”. In the Abstract, we changed the number of the study population to 11,282 participants.

Discussion

1. Second paragraph discussing the separation of lifetime abstainers and ex-drinkers is unclear. It needs to be clearer on stating which group showed a protective association. Authors should also discuss other possible differences between former drinkers and abstainers that they were not able to account for such as potentially previous problematic drinking among former drinkers.

We revised the second paragraph to address the differences of lifetime abstainers and ex-drinkers regarding their mortality risks clearer. A meta-analysis conducted by Gmel et al (EJE 2003) revealed that ex-drinkers had a higher mortality risk compared to lifetime abstainers which was found especially for men; for females, this effect was less pronounced.

We agree with the reviewer that a hint regarding other possible differences between former drinkers and abstainers due to those factors which could not be taken into account should be discussed. Regarding previous problematic drinking patterns among former drinkers, similar risks for negative health conditions were shown for former heavy drinkers among former drinkers compared to current heavy drinkers (Lown et al., Subst Use Misuse 2003). However, in our study, we were not able for accounting previous problematic drinking patterns in former drinkers or other possible differences between former drinkers and abstainers.

2. In the strengths and limitations, authors should discuss the limitation of measuring alcohol for only a single week and the limitation of applying a single weekday of drinking to all weekdays.

We discussed the limitation of measuring alcohol for only a single weekday/weekend by including the following sentences to the limitations part:

“In addition, we couldn’t perform a multiple measurement of alcohol intake but only a single week and only a single day/weekend measurement. Therefore, only volume could have been analyzed but not also specific drinking patterns such as heavy drinking episodes.”

Our measurement using a 7-day recall method was validated against a 7-day diet record method in a subsample previously and revealed sufficient validity. A sentence addressing this validation is included in the methods part now.

3. The paragraph beginning with “despite of simultaneous consideration...” is unclear. It begins by discussing that there may still be uncontrolled confounding but I do not understand the meaning of
the following sentences and how they relate to this issue, as this analysis controlled for smoking and some socioeconomic variables.

*The reviewer is right; therefore, we revised and rewrote the paragraphs concerning potential mechanism completely and excluded unclear sentences to be more consistent.*

4. The short paragraph discussing potential biological mechanisms should be expanded.

*See answer to point 3.*

5. The authors mention that binge drinking specifically may be harmful, but this was not measured in this study so is that a limitation of the study?

*Yes, it is. In the limitations we mentioned that we could not adjust for drinking patterns so this could be seen as a limitation. Binge drinking was not assessed in the MONICA/KORA study and could unfortunately not be analysed.*

**Figures/Tables**

1. Authors do not discuss Figure 1, except for in the methods to say that it uses different drinking categories. It is not mentioned in the results. What is the significance of this figure?

*Figure 1 was included in the manuscript aimed to give an impression about the mortality in different categories of alcohol consumption. Due to low case numbers and rather similar mortality risks, the three higher alcohol consumption categories (40-59.9, 60.0-79.9, ≥ 80 g/day) were combined to one category and used for the main analyses displayed in the results and discussed in the discussion part. We revised the sentence in the methods part regarding Figure 1 to clarify the aim of the figure.*

**Minor Essential Revisions:**

**Introduction:**

1. Author does a good job of explaining that there is a relationship between both psychosocial stressors and alcohol and psychosocial stressors and mortality, but more discussion of the potential mechanism of this would be helpful in the introduction. The paragraph on internal/external psychosocial stressors and health is unclear.

*We appreciate the positive comment of the reviewer. The paragraph concerning potential mechanism as well as the paragraph concerning internal/external psychosocial stressors and health were revised and rewritten.*

2. Some awkward phrasing throughout paper. For example, pg. 3 “…relationship between alcohol consumption and mortality is accomplished by psychosocial factors.” Pg. 4: “moderate alcohol consumption as typical element…”

*We revised the whole manuscript carefully and hope to omit such phrasing now.*

3. As gender differences are looked at throughout the paper it would be nice to have some background on sex differences in the alcohol/mortality relationships in the introduction and what the authors hypothesize for males and females.
We added a sentence concerning sex differences in the risk pattern of alcohol consumption in the introduction part. The rationale for performing the analyses separately for men and women was based on the differences in alcohol consumption concerning distribution and adverse effects on health conditions as shown in previous studies. Moreover, it is very common to analyse mortality risks separately for men and women as the impact of risk factors as causes of death are assumed to be different between men and women.

Methods:

1. Delete “a number of “ in study group section

The expression was deleted.

2. Authors should bold or italicize variables or separate them by paragraph to make it easier to see at a glance of the text what variables were included.

We agree with the reviewer and decided to use new clauses for each variable which improved readability.

3. Authors should include a citation for the ‘person-years method used to estimate crude incidence rates.

A reference for the person-years method is now included.

4. Author states that the proportional hazards assumption was assessed but not whether it was met. Please clarify this.

The reviewer is right. The PH assumptions were met which is added to the appropriate sentence now.

5. Change “goodness of the explanation” to goodness of fit

We changed this expression.

6. Authors should clarify why all possible interactions of alcohol with psychosocial covariates were tested.

The rationale of the interaction analyses was to assess whether the relation of alcohol consumption and mortality was modified by any of the psychosocial stressors. We thought before it might be possible that the protective effect of moderate alcohol consumption could be found only in specific subgroups and vanished in other subgroups. This was the case for living alone as shown and discussed in the manuscript: Please see our answer to point 2 of discussion below.

Results:

1. Why was the abstainer group chosen as a reference? It seems like it would be useful to have the moderate group as the reference in order to see if there is an increased risk for heavy drinkers compared to moderate drinkers.
We thought carefully about using the moderate group as reference group but decided to keep the abstainer group as reference group as most studies. This enables an easier comparison with the findings of other studies.

Discussion

1. Authors should discuss the advantage/disadvantage of including only a healthy population at baseline and the impact on external validity by doing this.

We decided to include only a healthy population at baseline to avoid the “sick quitter bias” which might lead to decreased external validity. In the first paragraph of the discussion part, two sentences addressing this issue were added.

2. There was a counter intuitive finding that among men, moderate drinkers living alone had a reduced risk of mortality compared to moderate drinkers not living alone. I would be interested to see a brief discussion of potential reasons for this finding.

We agree with the reviewer that a brief discussion here would be interesting. However, the sentence in the discussion was misleading as the reference was “no alcohol consumption” (as stated in the results part) and not “moderate drinkers not living alone” (as stated in the discussion part). We revised this paragraph which is now written as follows:

“In our data, we found that the effect of alcohol consumptions on all-cause mortality was modified by living alone or not alone in men: Whereas men living alone had a significantly reduced mortality risk compared to the group stating no alcohol consumption, no significant differences in mortality risk were found for the three alcohol consumption groups in men living not alone. Therefore, alcohol consumption had no effect on mortality in men living not alone. One explanation for this finding might be that men living not alone had already a reduced mortality risk compared to men living alone and therefore, there was no space for a significant decreased mortality risk by moderate alcohol consumption (however, a tendency of risk reduction was found with HR 0.85).”

3. Also, the finding that there were no differences in depression and other psychological distress was interesting given that many others have found differences. Authors should explain why they think they did not find this in their study.

After careful thinking, we have no clear explanation for the lack of significant differences in depression and other psychological distress in our study as opposed to other studies. It might be possible, that the use of different instruments/measurements contributed to these inconsistencies. We added a sentence addressing this issue.