Author's response to reviews

Title: Problem drinking as a risk factor for tuberculosis: a propensity score matched analysis of a national survey

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Author's response to reviews: see over
Dear Editor

According to your request regarding the article:

MS: 8661176469687830
Problem drinking as a risk factor for tuberculosis: a propensity score matched analysis of a national survey
Annibale Cois and Rodney Ehrlich

a revised copy of the manuscript has been submitted through the electronic system.

We thank the reviewers for the thoughtful review of our manuscript, and for their helpful comments and critiques. Their suggestions have been incorporated in the revised version of the manuscript as summarized below.

Reviewer 1: Brian G. Williams

1 - Use of the term “multivariable”

We acknowledge the imprecision of the use of the adjective “multivariable” as synonymous of “multivariate”. In the original version of the manuscript this term appears twice with reference to classical regression techniques (“traditional multivariable adjusted modelling”).

In the revised version of the manuscript, both instances of “multivariable adjusted” (p. 6, row 11 and row 18) have been replaced by “multivariate”.

Reviewer 2: Mats Ramstedt

1 - Non-response rate

Household and individual response rate for the survey have been reported in the Methods section, together with a reference for further details, adding the following sentence at the end of the first paragraph of p. 4:

The overall response rate for the SADHS was 71% at individual level, with large differences between urban and rural areas (65% and 82%, respectively), with the main reason of nonresponse being refusal [7].

In the discussion section, the limitation arising from these relatively low response rates have been acknowledged inserting the following sentences (p. 12, at the end of the “Discussion” section):
Finally, even though suboptimal response rates as those observed in the SADHS do not automatically reflect in selection bias, especially in analytical studies [36], we cannot exclude the possibility that differences between respondents and non-respondents drinking behaviour and TB status – untestable with the available data – could have affected our estimates of the association between problem drinking and TB.

The new reference is:


2/3 - Instability of problem drinking and temporal relationship between measurements

We acknowledge the observations and, we modified the fourth paragraph of p.11 as follows:

*The major limitations of this study derive from its cross-sectional design and the consequent use of measures of lifetime prevalence instead of incidence to infer causality. The intrinsic lack of temporal information attached to these measures, together with the unstable nature of problem drinking – characterised by multiple onsets followed by remission periods – did not allow us to establish the relative timing of exposure and outcome.*

Moreover, we revised the section on measurement of problem drinking (p. 4, last paragraph) as follows:

*Problem drinking was assessed using the CAGE questionnaire in its original form with no time constraints, in which questions refer to the subjects’ lifetime experience [10]. The CAGE questionnaire is one of the most frequently used screening tools for alcohol problems both in clinical practice and for research purpose. Its predictive validity in various non-clinical populations is well supported [11, 12], and specifically confirmed in a validation study conducted in South Africa [13]. In accordance with the prevalent literature, an affirmative response to ≥ 2 of the four questions of the CAGE questionnaire was regarded as a proxy for problem drinking. Subjects with any lifetime use of alcohol but less than two affirmative responses were considered as moderate drinkers.*

4 - Alternative reference group

According to the reviewer’s suggestion, we repeated the analyses using, as a control group (1) only non-drinkers or (2) only moderate drinkers.

The results were:

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<th>POR</th>
<th>95% Confidence Interval (normal approximation)</th>
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<tr>
<td>(1)</td>
<td>2.25</td>
<td>(1.59 ; 3.20)</td>
</tr>
<tr>
<td>(2)</td>
<td>1.80</td>
<td>(1.25 ; 2.58)</td>
</tr>
</tbody>
</table>
The results seem to be reasonable. The effect size shows a moderate (not statistically significant) increase when the control group is constituted only by non drinkers, and a moderate decrease (also not significant) when problem drinkers are compared with moderate drinkers alone.

In the new manuscript, the following sentence is added (p. 8, end of the “Problem alcohol use and TB” section):

The repetition of the analyses comparing problem drinkers separately with non drinkers and moderate drinkers produced similar results, with modest differences in the adjusted PORs: 2.25 (95% CI: 1.59 to 3.20) and 1.80 (95% CI: 1.25 to 2.58), respectively.

In addition to the changes above, made as a result of the reviewers’ comments, we have corrected a few typos that we missed in the first versions.

We look forward to your response.

Kind regards

Annibale Cois

Rodney Ehrlich