Reviewer's report

**Title:** Alcohol consumption, alcohol use disorders and incidence and disease course of tuberculosis (TB) - is there a causal connection?

**Version:** 2  **Date:** 29 March 2009

**Reviewer:** Fredrik Spak

**Reviewer's report:**

Major Compulsory revisions:

In this meta-analysis paper articles scrutinized are based on various concepts of alcohol abuse or similar. That appears to inevitable. But is casts some questions that also pertains to pathway 2 (social). What I refer to is that sometimes the alcohol "exposure" label is "alcoholism" sometimes, eg. Hemila 1999, abuse, which in fact sometimes, as with Hemilas paper, actually is consumption. There ought to be considerable diffences concerning the social marginalization in the drinking group vs fullfledged diagnosed "alcoholics", and thus, probably, the social marginalization theory has a different application under these different "labels" of alcohol abuse conditions. Some of these studies using alcohol consumption as the alcohol label also are quite large as compared to the others. I suggest that you provide details on if using the alcohol concepts of drinking as compared to diagnosis, makes a difference in the relationship between alcohol and TB.

It is probably correctly pointed out in the paper that the social marginalization explanation is important. Maybe even more than the paper suggests, as the number of "alcohol" persons ending up in a hospital for TB treatment only constitute a minority of all "alcoholics". So for many alcoholics this is probably not a of a larger importance, so for whom is it important? I think this could be better explained.

2. It is not clear how many subjects were men and women. Is some cases this info is probably not possible to provide. But in some it may be. It may well be that the association between alcohol(ism) and TB is different in the sexes. As a small part of that relationship there is the definition of alcohol abuse as being an alcohol exposure above a certain limit (eg 30 g/day) which of course means different risk exposures for women and men.

I think this subject should be discussed. Maybe even there are so few women in the studies that the relationship between alc. and TB is not so certain?

3. Aim:

I believe this could be made clearer, by referring to the double scope of providing a review of the possible causality between alcohol and TB, and providing a meta-analysis that establishes this relationship (but that does not explain it).
Often this would be published as two separate papers. As the present choice of publication does not restrict this way of presenting the data, that may not be a problem. But the procedure could be clearer. There is a short introduction that actually does not provide information of previous attempts and reviews on presenting explanations of the relationship between alcohol(ism) and TB. Instead that information is presented as a result following a very short presentation of the meta-analysis finding under the result section. However, this presentation is not based on the meta-analysis. It is not even clear what type of reading of the literature this lengthy section is based on as the authors under Methods only describe the literature search that was conducted for the meta-analysis.

And as the paper appears to consist of three different parts, as I read it, 1. meta-analysis and results, 2. review of possible causal pathways, 2a. alcohol and immunology 2b. social marginalization, the reader may wish to know if the review for the two latter parts were done as thoroughly as the one proceeding the meta-analysis.

Also, in spite that length is not a problem under this publication method, I thought the section on immunological mechanisms was to lengthy. Many readers will not be very enlightened by that anyway, as many will not understand. However, I thought that the parts where the (possible) impact of alcohol on immunology was mentioned, were interesting.

Minor essential revisions

Conclusions in the abstract:

the text that heavy alcohol consumption use or alcohol use disorders constitute risk factors etc, is debatable. It can be read as that AUD as well as heavy consumption are risk factors or that those entities combined are risk factors. Have you run the analyses to prove the first of these interpretations?.

Methods:

under the list of key words neither incidence or harmful use or hazardous use was included, why not?

In the tables the notion Pulmonary TB etc is used. Could you please provide en explanation of what those terms indicate clinically relevant information (for a layman), especially concerning the severity of TB.

Results:

Maybe the authors have considered where the presentation of data, apart from the meta-analysis, should be presented: under introduction, results or discussion. There actually is a lot of discussion under the result section. If it shall remain under this heading I think you could clarify that there are two types of results: A metanalysis B Your understanding of the literature, including extensive work og f the group of authors.

Dose response relationship
Here I come back to the exposure levels and if they relate to men or both sexes. Reference 17 (Campbell) is rather old so that may well be men. In that case that should be made clear.

Under Reversability:

The first sentence lacks a reference

Under Interruption of treatment

To what extent is such treatment available in poorer countries or areas? Could be interesting if you are able to provide some information on that.

Discussion:

Rather short. More like Summary. This is probably because the result section contains the main bulk of the discussion.

I think this should be made explicitly clear to the reader, but also that you take a step back and consider the limitations of your own work, eg. concerning the relations between AUD and TB vs what you here call alcohol use and TB, and as to the limitations of your discussions on the causal mechanisms.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests