Reviewer’s report

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

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Reviewer: Annunziata Faustini

Reviewer’s report:

COMMENTS TO THE AUTHORS
The authors carried out a systematic review to estimate the strength of the association between alcohol and tuberculosis (TB) and to determine if a causal relationship between the two is adequately supported in the scientific literature.

After searching many electronic databases for papers dealing with alcohol or alcoholism and TB, the authors selected 53 papers. They found a three-fold risk increase of TB associated with high-level alcohol exposure (drinking more than 40g of alcohol per day or a diagnosis of alcoholism).

MAJOR COMMENTS

THE AIM OF SYSTEMATIC REVIEW
One of the criteria to evaluate a systematic review is the consistence between the aim of the paper and the inclusion/ exclusion criteria of the original papers. The authors maintained that they wanted to summarize the causal relationship between alcohol abuse and TB incidence or TB death.

Unfortunately they searched the literature for TB prevalence, the occurrence indicator coming from the surveys and the cross-sectional studies, that does not allow estimating a causal relationship with exposure. In fact, it measures contemperaneously chronic diseases, recurrent disease, relapses and even previous disease (as is the case of the 5th study in table 2) whose exposure occurred at different times. The condition the authors added, i.e. that the population samples were patients with alcohol use disorders (AUD), is not enough since the original papers may have estimated the exposure to alcohol with a cross-sectional method and this approach makes the authors (and the readers) unable to assess the timing between exposure and disease, that is a condition for a causal relationship. The correct choice would be to select the papers that longitudinally estimated incident pulmonary TB in cohorts of AUD.

I am afraid that the fact that the authors did not consider the estimates of the association, such as RR or IRR or Odds ratios in the original papers represents another point of weakness in assessing a causal relationship because they did not estimate the strength of the association, which is another essential condition of causality and thus could not report on the heterogeneity between the studies.

A LANGUAGE NOTE: in epidemiologic literature IRR is usually the incidence rate ratio.
METHODS

1. The methodology of the Systematic Review was somewhat limited.
- The authors reported searching 11 electronic databases, but they did not give data about the number of papers they found in each database or how many duplicates they found.
- They did search the archives of “the major epidemiological journals”, however they did not specify which ones nor if the journals searched specialised in TB, such as the International Journal of Tuberculosis and Lung Diseases, or journals that focus on alcohol such as Alcoholism, clinical and experimental research or the Journal of Alcohol Studies, or the WHO documents.
- The authors maintained they did not limit the search to the English language, but neither report which languages were searched for nor the results produced by this effort.
- The authors did not clearly define the inclusion criteria or the exclusion criteria and the process by which they selected the papers is unclear - from reading the initial abstracts and the complete text (215 papers excluded) and the second step up to the final selection of the 53 papers. Moreover, how did they treat the studies listed in table 1 that did not report the exposure definition? I am afraid they could not use them for the pooled estimate in the meta-analysis since this would have required a quantitative assessment of alcohol consumption.
- The possible limits used in the search are not reported.
- The authors have to report the number of papers they excluded according to each criterion; summary tables of the papers excluded have to be prepared as additional documents available on demand.
- There is no mention of any quality rating for the included/excluded papers.
- The authors did not report covariates studied in the searched data, the known confounders of the association between alcohol and TB at least have to be checked. Information on these factors is very important in assessing a causal relationship, as they may represent alternative explanations to the observed association.

2. The methods of the meta-analysis were not reported at all and as results they provided only a pooled estimate - no forest plot to give an idea of heterogeneity, and no funnel plot to indicate publication bias.

I think the only conclusion the authors can reasonably present based on the basis of their results is the general estimate they found between alcohol consumption and TB disease.

**Level of interest:** An article of insufficient interest to warrant publication in a scientific/medical journal

**Quality of written English:** Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I have no competing interest