Reviewer's report

Title: Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis

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Reviewer: Colin Mathers

Reviewer's report:

This paper reports in somewhat more detail and for a broader time period, the estimates of liver cirrhosis mortality in 187 countries from 1980 to 2010 prepared for the GBD 2010 study published in the Lancet in December 2012. Much of the methods are general to the GBD estimates for cause-specific mortality and not described in any detail here, rather references to GBD-related methods papers are given. Readers will be somewhat frustrated by this, as the GBD methods papers themselves are complex and in many cases do not give complete details of methods or data. For example, this paper references Naghavi et al (2010) on methods for redistributing so-called “garbage codes” for underlying cause of death. That paper in fact only gives selected examples of redistribution algorithms.

It is probably reasonable to rely on cross-citation for much of the general methods, particularly given the length and complexity of already existing GBD methods documentation. However, the methodology specific to liver cirrhosis estimates should be fully explained in this paper.

There are three main areas where I feel that the liver cirrhosis methods need more explanation here, and that the paper should be substantially revised to address these.

Major compulsory revisions

1. Case definition of liver cirrhosis

There is a very brief description of the ICD codes which are mapped to liver cirrhosis, including codes for chronic viral hepatitis, hepatitis NOS, toxic liver disease with cirrhosis, portal hypertension.

The ICD concept of underlying cause is not mentioned, rather the authors say they included “deaths related to liver cirrhosis”. The paper later discusses the role of hepatitis B and C and alcohol in causing liver cirrhosis. Readers who are not familiar with the distinctions between underlying cause and intermediate cause or antecedent risk exposures may find this brief description of the case definition raises more questions than answers. Readers unfamiliar with the limitations and quality issues in ICD-coded data for underlying cause of death may also wonder why deaths are not being classified directly to hepatitis or alcoholic liver cirrhosis in the analysis (ICD codes for these exist).
I think I understand the rationale for the approach taken by the authors with a broad definition and a focus on total deaths with liver cirrhosis as underlying cause (whether itself caused by viral infection or alcohol consumption), but many readers may not. The authors should expand this section to provide a clear explanation of and justification for the approach used.

2. Use of verbal autopsy data

Again, the information on availability and quality of verbal autopsy data in the following paragraph and Table 2 is too brief. The authors do note the lack of useable death registration data for many populations and the reliance on verbal autopsy data, but they provide only global figures for the number of studies in the main paper. Table 2 should be expanded to give a regional summary of the detailed information in the Annex table. This should be by the GBD regions of the numbers of country-years of VR and VA data used. The proportions of national vs subnational VA data should also be shown. It is mentioned in passing in the discussion that physician-certified VA accurately assigned liver cirrhosis as cause of death in only 40% of cases. The available validation data for liver cirrhosis should be discussed in a little more detail in the methods section, and whether this was taken into account in the modelling (false positives, false negatives etc). By “physician-certified VA” do the authors mean “physician-assigned” cause of death, or death certification in which the VA instrument was used to assist in filling out the death certificate. Were all the VA data used, of this type or was there also VA data coded with statistical methods (in which case, what are the comparable quality indices). The implications of VA diagnosis limitations on the results needs to be discussed in a little more detail in the discussion.

3. Population-attributable fractions for liver cirrhosis

The discussion is almost entirely devoted to explaining variations in liver cirrhosis mortality over time and place in terms of the relative importance of viral infections and alcohol consumption. The global attributable fractions are mentioned in the second paragraph with a reference back to the general GBD results. These results need to be given here along with details of how they were derived.

There is a very brief explanation that the authors estimated country-year specific population attributable fractions for Hep B and C and alcohol consumption. However, no results for these fractions are given in the main paper. Annex Table 6 should be brought into the main paper, or a summarized version of it – possibly with a high-level trend graph.

No information on the methods used for the PAF calculations is given in the paper, and no references to other methods publications. The references given appear to be to primary information for the PAF calculation and the authors simply state they did the analysis in three steps without explaining what they did.

This section needs to be significantly expanded to describe the data and methods used in more detail.
Minor compulsory revisions

4. Second last para of “Model development” says that Annex Table 4 includes out-of-sample predictive metrics and coefficient weights. The table does not currently include these. They should be added.

5. The following two subheadings appear to have references in the headings [2] and [24,28]. This needs to be corrected.

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