Reviewer's report

Title: Descriptive epidemiology of chronic liver disease in North-Eastern Italy: an analysis of multiple causes of death

Version: 1 Date: 14 August 2013

Reviewer: Ali Mokdad

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Major Compulsory Revisions

My biggest concern with the design of this paper is the vague distinction among the definitions of an underlying cause of death, disease related cause of death, and comorbid disease at the time of death. I do not believe this was made clear or appropriately addressed in the paper. I am not quite familiar with the death certificate of the indicated region in Italy. Generally, however, causes reported besides the underlying cause of death are comorbid conditions not necessarily causal to the death at the time of death. While, exploring these conditions for the purpose of discerning, in this case, the etiology of chronic liver disease (CLD) (hepatitis, alcohol, etc...) is appropriate, assuming all cases that report CLD in the death certificates are CLD-related deaths will lead to bias in the mortality estimates. This was evident in figure 1. In our work on liver cirrhosis mortality, as is generally done, we used the stated underlying cause of death and at times the second documented cause. Other conditions were disregarded in the calculation of mortality estimates. I recommend the following while revising the paper: (i) paying particular attention to the choice of the following words; underlying, related, attributed; (ii) estimate and compare to your current results CLD mortality using the underlying and first reported condition only (using ICD codes in strategy 2).

Minor Essential Revisions

Background

1. Paragraph 1: Report the actual mortality rate for HCC instead of stating “very high”

2. Paragraph 1: Change the semi-colon to a period

Methods

3. Paragraph 1: Last sentence is long and confusing. Revise

4. Paragraph 2: List the ICD codes used in the third strategy

5. Paragraph 5: “Share of total CLD deaths”. I am assuming the share by etiology. The phrase needs revision to make clear to the reader.

Results

6. Paragraph 4: Delete “already” in “already in the 45-54”
7. Paragraph 4: The phrase, “And further increased in subjects #65 years especially among females, reaching levels higher than in males above 75 years” is not clear as phrased now. Needs revision. I am assuming the male to female ratio decreased. I am not clear to what increased since the prior sentence reported a peak at ages 45-54.

8. Paragraph 4: The phrase “Due to limited numbers, in all analyses deaths with multiple etiology are listed both among HCV and alcohol-related CLD” needs revision for grammar and structure.

Table 1

9. I am not clear as to what the category “no etiology” exactly refers to. Is it those cases where neither hepatitis nor alcohol was reported or no causes whatsoever were identified? If the former, I recommend changing the category name to “Other” which includes metabolic diseases, unidentified causes, etc…

Discretionary Revisions

1. Selection of ICD codes for identifying CLD cases remains variable across the literature. The selection code choice is generally dependent on the characteristics of the database at hand, a wider net for databases with major under-reporting and vice-versa. I suggest adding I85 (esophageal varices) and K76.6 (hepatorenal syndrome) to code selection 2 as both are complications related to liver cirrhosis and are fairly specific. K71.7 (Toxic liver disease with fibrosis and cirrhosis of the liver) and K72.1 (Chronic hepatic failure) are also appropriate.

2. I would raise concerns related to K76.0 (Fatty change of the liver) as part of the first 2 selections strategies. This condition is fairly common and generally benign. I recommend estimating the percent contribution of this etiology to the mortality estimate in order to ascertain there is no bias. A similar concern is related to including B15 (Acute hepatitis A) in selection strategy 3.

3. It is important to note that, as per ICD rules, hepatocellular carcinoma (HCC) deaths are not counted toward CLD deaths. While HCC is generally a complication of CLD, reported mortality estimates for CLD exclude HCC deaths. The following comments pertain to the ICD code selection number 3.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

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