Reviewer's report

Title: Alcohol consumption, unwanted pregnancies, and contraceptive use in relation to direct causes of maternal mortality among different socio-demographic groups in Ghana

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Reviewer: Lisa Hurt

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This paper reports on an analysis of the association between three exposures (alcohol consumption, unwanted pregnancies, contraceptive use) and six specific direct causes of maternal deaths. They also examine which other risk factors are associated with the three main exposures. The dataset used is accessible to all by application through the DHS website, and the methods of data collection in the survey were sound. There is little published information on the association between alcohol consumption, unwanted pregnancies, contraceptive use and specific causes of maternal deaths and this paper could add to the literature in this field, but several methodological considerations need to be addressed before the paper is suitable for publication.

Major compulsory revisions

1. It is not clear what their second analysis (on the association of other risk factors with alcohol consumption, unwanted pregnancies, and contraceptive use) adds, or whether they have examined the data in the most appropriate manner to draw conclusions about the various subpopulations in the analysis.

They state that their hypothesis was that “the likelihood of exposure to these behavioural factors differs for women from various socio-demographic subpopulations”. This is potentially interesting but this information is only useful to policy makers on maternal health if it is discussed in tandem with their original multivariate analysis. That is:

a) Whether the associations between alcohol consumption, unwanted pregnancies and contraceptive use and mortality are independent of the other risk factors (that is, the associations seen are not just because of confounding by the other risk factors)

b) Whether the associations between the risk factors and mortality are independent of alcohol consumption, unwanted pregnancies and contraceptive use (that is, the associations between the risk factors and mortality are not just because of confounding by the main exposure variables)

c) Whether there is an interaction between alcohol consumption, unwanted pregnancies and contraceptive use and the risk factors, in terms of their effect on mortality (although the sample size to look at this in this study is probably too small).
To this end, it would really help if the authors presented and discussed their conceptual framework of how they feel these variables inter-relate with each other to influence mortality, whether some of the risk factors might be on the causal pathway for the main exposures (or vice versa), and so present a more coherent analysis plan.

2. This is a proportionate mortality study, in that the population studied includes all maternal deaths and the odds of dying from a specific cause given a specific exposure are calculated. They have used deaths from the specific direct causes of death as “cases” and I presume all other maternal deaths as “controls” although their methods for selecting which deaths to include need more explanation (for example, are the other five direct causes of death included in the controls when one specific cause is being examined, and why did they not use non-maternal deaths in women of reproductive age as their controls?). To clarify the sample selection, the authors should also include a flow diagram (as they have presented in a previous paper from this dataset).

One of the limitations of using this method is that it is assumed that the control causes of death are unrelated to the exposure status and this might lead to biased estimates (Smith and Kliewer, Epidemiology 1995; 6(1): 55-60). Methods have been suggested to improve estimates, but these are beyond my expertise and I would recommend that a statistician’s opinion of the statistical methods used in this paper is sought.

3. The way in which variables were selected for the multivariate models is also not described. For example, there seems to be missing data for some variables for some causes (education in particular) and it is not clear how these were dealt with (for example, those cases were dropped or the variables were dropped). The authors also state that their logistic regression models included “interaction terms” but do not specify what these are, or whether these were necessary and determined a priori (as they might have made the models complex and unstable, especially given the small sample size).

4. There could be some additional definition of the alcohol use and contraception variables. There are four different measures of alcohol consumption but only the most basic one (ever consumed alcohol) is used in the multivariate model. Contraceptive use is also a dichotomous variable and it is not clear whether this refers to current or past use. The authors should discuss why they chose to define these variables in this way, and the relevance of their definitions to the findings. For example, it seems strange that a woman who never used family planning was far less likely to have died from abortion-related causes – is it possible that this is an artefact of the way that the data were defined rather than a “true” effect?

5. An important problem with the data (which the authors do not discuss) is that the verbal autopsy data is incomplete. Only 4203 of 5931 deaths, or 70% of all deaths, had a verbal autopsy completed and, of those completed, it is possible that some maternal deaths were not coded as such (because the family did not
report or did not know about the pregnancy). This is not surprising (the limitations of verbal autopsies are well-known), but it does mean that the sample included might be a biased sample (because the data may be missing because relatives of women who consumed alcohol, or had unwanted pregnancies, may be less likely to agree to a verbal autopsy or to provide less accurate information). The authors need to consider and discuss how this might affect their conclusions.

6. In addition, the data presented in tables 3 and 4 are very limited, because there are no data available on a denominator in this study (that is, pregnancies). As such, it is not appropriate to draw conclusions on the percentage of deaths from specific causes by socio-demographic variables. For example, maternal mortality is known to be higher in women under the age of 20 years or women aged 40+ than in women aged 20-39 years, but this pattern only becomes apparent when accounting for the fact that there are fewer pregnancies in the younger or older age groups. Thus, it is not appropriate to state for example, as on page 13, that deaths from abortion “was highest among women aged 20 to 25”: the number of abortion-related deaths was highest in this group because this was the group with most pregnancies. This should be clarified when discussing all the percentage distributions in the paper.

7. The discussion could be improved by some restructuring however: currently each association is discussed individually whereas the effects of alcohol, for example, could be summarised and discussed in one or two paragraphs; the discussion of limitations of the methods and data used could be expanded, on the other hand, as this information is needed to assist the reader to interpret the data presented.

8. The title of the paper is appropriate. The abstract does not currently include information on the study design, selection of “cases” and “controls”, and does not give details of the statistical methods used (for example, was there adjustment in the logistic regression models for potential confounders?).

9. The introduction could be shortened considerably (for example, the detailed data on global patterns and trends in maternal mortality are not needed and the studies summarising risk factors for maternal mortality could be reduced).

10. The paper also contains extraneous information that could be omitted. For example, table 1 contains the maternal mortality ratios for the 20 countries with the highest and lowest MMRs in the world. These data could be summarised in one sentence in the introduction. Table 2 shows population characteristics for Ghana which could be summarised in a few sentences. Estimates of cause-specific mortality by age and region from the survey (as presented in table 3) have already been published in the main report of the survey.

11. The remaining tables are cumbersome to read as they stretch over several pages, and the crude and adjusted data for each association are not shown together. I wonder whether smaller individual tables for each specific cause, with the crude and adjusted data for each variable shown together, would be easier to read?
Level of interest: An article of importance in its field

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

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests.