Author's response to reviews

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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Author's response to reviews: see over
Authors’ response to Review

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Topic: Alcohol consumption in relation to maternal deaths from induced-abortions in Ghana

Authors: Benedict O Asamoah, Anette Agardh

The Reproductive Health Editorial Team

Dear Sirs,

Thank you very much for your response to our submitted article. The comments from the reviewers and the editor were of such nature that we decided to make a very substantial revision of the focus of the study and therefore the analysis. We have addressed all the comments raised by the two reviewers and revised the manuscript accordingly. We have attached two versions of the revised manuscript, one with tracked changes and another without tracked changes. We have also included point by point response to the concerns raised by both reviewers. We trust that you find this version much improved and acceptable for publication.

Kind regards

Benedict Oppong Asamoah on behalf of all co-authors

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Reviewer 1

Comment 1: The authors for this paper may want to review the theory and redo the analysis regarding direct obstetric deaths accordingly. For instance, I am not certain there is a theoretical basis for the link between the use of contraceptives prior to pregnancy and maternal death due to obstructed labor etc.

Response: The theory on which this paper was based has been revised. The analysis has been redone with the focus on alcohol consumption and deaths from induced abortion.

Comment 2: Similarly, regarding the association between alcohol consumption and direct causes of maternal death, the authors may want to employ the ‘frequency of alcohol consumption’ rather than ‘Yes’ or ‘No’ (the latter presupposes that drinking ‘rarely’ is the same as drinking alcohol ‘daily’). Additionally, one needs to take into consideration whether or not the deceased stopped drinking and the duration of cessation prior to death. In the survey questionnaire, Q704 further inquired “Did (NAME) stop drinking before death?” and Q705 “How long before death did (NAME) stop drinking?”
Response: The new analysis includes four alcohol consumption variables, three of which have been used in the logistic regression analysis. 1) consumer of alcohol (at any time in the past or present); 2) consumer of alcohol within 12 months of death 3) frequency of alcohol consumption ((a) frequent consumer: consumed alcohol daily or weekly, (b) occasional consumer: consumed alcohol once in a while, or (c) abstainer: never consumed alcohol); and 4) history of alcohol consumption (less than one year, or one or more years). The variable consumer of alcohol within 12 months of death was generated from responses to the questions “Did (NAME) stop drinking before death?” and “How long before death did (NAME) stop drinking?”

Comment 3: The authors may want to redo the analysis focusing on abortion deaths as the dependent variable and leave out causes such as obstruct labor which may not be influenced by use of contraceptives prior to the index pregnancy. Nevertheless, in chapter 5 of the 2007 Ghana Maternal Health Survey report is a detailed analysis of abortion vs socio-economic characteristics (including quintile analysis), use of contraceptives, health seeking behavior, etc


Response: The analysis has been redone as stated above. We have now narrowed our paper to focus on induced abortion deaths as our dependent variable and alcohol consumption as the independent variable. We have also analyzed the possible factors lying behind the alcohol consumption patterns. It is true that the Ghana Maternal Health Survey report presents the percentage distribution of induced abortion by background characteristics. However, What they present in chapter 5 of the report about induced abortion, is the responses from the general
Women`s Questionnaire and does not include any information on alcohol consumption. Also, this information includes only survivors of previous induced abortion and does not include any information of the background characteristics of those who died from induced abortion. Information on deaths from induced abortion and alcohol consumption was collected through the Verbal Autopsy Questionnaire and that is what we have analyzed.

**Reviewer 2**

**Comment 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 behavioral 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.

**Response:** The analysis has been redone and the focus has been narrowed to deaths from induced abortion and alcohol consumption. The conceptual framework has been revised accordingly. Unwanted pregnancy and contraceptive use variables have been removed from the analysis. Maternal age, marital status, rural-urban residence status and educational level were deemed as possible factors lying behind the alcohol consumption patterns and were therefore adjusted for in a stepwise manner. These factors were not included in the same regression analysis since they would lead to over-adjustment and falsely underestimate the impact of alcohol. However, the sample was too small for investigating effect modifications.

**Comment 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.

Response: We have included a flow chart that illustrates the sample selection process (see figure
1). Our study is a type of case control study design where the cases are maternal deaths from
induced abortion and all the other maternal deaths served as the controls to which the cases were
compared. These types of controls have limitations which have been discussed in the manuscript.
However, we find that in this current study, using controls that are more homogeneous to the
case group besides the outcome under investigation (deaths from induced abortion) makes them
comparable in terms of the exposure under investigation (alcohol consumption). Also, with a
prevalence of 13.7%, deaths from induced abortion could be considered a rare outcome and thus
makes this design suitable to use. Moreover, the ratio of controls to cases is approximately 6:1
and this gives the study enough statistical power to detect possible associations between the
exposure and outcome variables.
**Comment 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).

**Response:** Please see response to comment 1.

**Comment 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?
Response: The analysis has been revised and as mentioned above, the focus of the paper has been narrowed to deaths from induced abortion and alcohol consumption. The new analysis includes four alcohol consumption variables, three of which have been used in the logistic regression analysis. 1) consumer of alcohol (at any time in the past or present); 2) consumer of alcohol within 12 months of death 3) frequency of alcohol consumption ((a) frequent consumer: consumed alcohol daily or weekly, (b) occasional consumer: consumed alcohol once in a while, or (c) abstainer: never consumed alcohol); and 4) history of alcohol consumption (less than one year, or one or more years). The variable consumer of alcohol within 12months of death was generated from responses to the questions “Did (NAME) stop drinking before death?” and “How long before death did (NAME) stop drinking?”

Comment 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.
**Response:** The potential effect of the non-response to the verbal autopsy in phase II of the survey has been discussed in the manuscript.

**Comment 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.

**Response:** The analysis and all the Tables have been redone. Tables 3 and 4 have been removed.

**Comment 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.

**Response:** The discussion has been revised according to the revised analysis and conceptual framework.
Comment 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?).

Response: The abstract has been revised accordingly.

Comment 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 summarizing risk factors for maternal mortality could be reduced).

Response: The introduction has been revised.

Comment 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.

Response: The Tables have been modified accordingly. Tables 1, 2 and 3 in the previous version of the manuscript have been removed.

Comment 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?
**Response:** All the Tables have been revised and new simplified Tables that are easy to read have been presented.