Author’s response to reviews

Title: Tuberculosis and HIV are the leading causes of adult death in northwest Ethiopia: evidence from verbal autopsy data of Dabat Health and Demographic Surveillance System, 2007-2013

Authors:

Yigzaw Kebede (gkyidzaw@yahoo.com)
Gashaw Bikis (gashawab@gmail.com)
Abebaw Worku (gabebaw2worku@gmail.com)
Tadesse Ayele (tawoke7@gmail.com)
Mezgebu Mengistu (mezgebuy@gmail.com)
Solomon Abebe (solomekonnen@yahoo.com)
Mamo Wubeshet (mamowubeshet@gmail.com)
Temesgen Azmeraw (tazmeraw@gmail.com)
Yihunie Lakew (yihunierh@yahoo.com)
Kassahun Gelaye (alemukass@yahoo.com)

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Author’s response to reviews:

Rebuttal Letter Reviewer #1: General comments

Reviewer Comments Author Responses

Methods

1. Page 4, lines 51-52 - Please clarify what is meant by 'causes of registered deaths'.
We would like to appreciate for your valuable comments, time and concerns to increase the quality of the manuscript.

The word “registered” cancelled in the text. See the details in the documents.

Verbal autopsy interviews conducted as part of longitudinal registration or surveillance activities should be conducted as soon as practically possible after the report of the event is received, but after any culturally prescribed mourning period has passed. When verbal autopsies are to be included in cross-sectional household surveys, recall of more than one year should be done with

2. Page 4 continuing on page 5 - Please provide appropriate reference(s) for verbal autopsy technique.

The appropriate references for VA technique cited as per the comment

3. It is not clear when the VA data were collected. Please clarify if the data presented have been collected since 2007. If these data were collected recently and given that symptoms are documented in VA interviews, please describe how recall bias was accounted for deaths that occurred much prior.

The VA data presented have been collected since 2007

4. Page 5, lines 9-12 and lines 24-42 - Please mention the number of VA interviewers who collected these data, and the number of physicians who were involved in assigning the cause of death.

Eighteen trained VA data collectors and 5 trained field data collectors’ supervisors were involved in the data collection. A total of nine physicians (three pediatrician, three internist, and three gynecologists) were involved in assigning the causes of deaths.

See the details in the text
5. Page 5, lines 24-42 - Please explain why INTERVA was not used to assign cause of death in place of physicians.

In this manuscript we want to identify causes of deaths using trained physicians. We are currently working a manuscript to compare physicians and INTERVA model in assigning specific causes of deaths.

See the details in the text

6. Page 5, lines 56-58 - Please specify what is meant by regular supervision. Were any interview data re-checked by the supervisors?

Five trained supervisors were involved in data collection and did regular supervision by rechecking the collected data by enumerators'. The research team also did regular supervision to re check the progress of data collection and sort out problems that may have been encountered by enumerators. See the details in the text

7. Page 6, lines 15-18 - Please provide details of the logistic regression model. Binary logistic regression model was employed to identify the determinants of EBF. Variables in the bivariable analysis with a P-value of < 0.2 were entered into the multivariable logistic regression analysis to control confounders. Adjusted odds ratio (AOR) with corresponding 95% confidence interval (CI) were estimated to show the strength of association. The model fitness was checked using the Hosmer and Lemeshow goodness of fit test. See the details in the text

Results

8. Please give some description about the total population, proportion of migration, and calculate death rate (overall or for each year as appropriate, by sex and place of residence).

This data was published partly at Ethiopia based journal” ETHIOPIAN JOURNAL OF HEALTH AND BIOMEDICAL SCIENCES. March 2015, vol 7, special issue. ISSN 2070-6898”
9. Table 1 - Is it possible to provide a column for total population, and then the number of deaths?

This data was published partly at Ethiopia based journal” ETIOPIAN JOURNAL OF HEALTH AND BIOMEDICAL SCIENCES. March 2015, vol 7, special issue. ISSN 2070-6898.

10. Table 1 - Please provide explanation of categories as relevant in the footnote Foot note; *IQR: Inter quartile range

11. Page 6, lines 41-58 - Please keep the details here only at the broad cause of death level and delete specific causes. Figure 2 shows variation in the broad distribution in years 2009, 2012 and 2013. Please report 95% confidence limits around the proportions for each year, and indicate if any are significantly different.

Amended as per the recommendation (Figure 2).” See the details

12. Table 4 and related description is more suited under the section on broad causes of death. It is not very clear what the odds ratio indicate. It was aimed to show the trends of the causes of deaths. The comments are very important and table 4 is deleted

13. Figure 2 - Why is pregnancy kept separately here?

Pregnancy was taken as one of broad causes of deaths
14. Figure 3 and the related text does not add anything additional to the data presented. These can be deleted.

The figure 3 is deleted as per the recommendation.

15. Table 2 - The current format of this table does not allow comparative understanding of cause of death by place of residence. Please change the format to show for each cause of death (row) - total deaths, deaths in rural area, and deaths in urban area - for the years considered. Also please report chi-square test values where appropriate.

The table format is changed as per the valuable comments.

16. Page 7, lines 24-36 - Interpretation of these findings need to better. For example, though meningitis is listed on position 4 for urban areas, its proportion is similar to that in the rural areas where it is listed on position 3. In the year 2007 to 2013, meningitis in urban was 25(7.42%), whereas in rural was 51(6.85). so meningitis was one of the leading causes of deaths for both urban and rural residents.

17. Page 9, lines 4-19 and Table 3 - Please see point 14 above for Table 2. Similar changes can be made and appropriate interpretation written. Table

18. Tables 5 and 6 - The denominator considered is all those who have died and not all the population >15 years of age. If inferences have to be made at population level, then it would be better to consider all the population (dead and alive) for the outcomes of interest. The aim of the manuscript was to communicate the causes of deaths using VA and determine factors associated with specific causes of deaths.
Discussion

19. Currently, this section is only repetition of the study findings and comparison with other countries. If the purpose of these data were to guide possible actions, then none is discussed.

The discussion was based on the key findings of this study. In this study, the broad and specific causes of deaths were identified and interpreted with similar studies done before. This finding would be helpful for developing countries particularly Ethiopia to move on action on the identified causes of deaths.

20. No attempt is made to interpret the findings for the population.

As the findings were not on the population we preferred to discuss on died and causes of deaths using VA.

21. Limitations of VA interviews should also be discussed. As it is indicated that health utilisation is poor in the study population, it would be useful to note how many and what type of disease conditions history were documented in the interviews.

The limitations are addressed in the documents. See the texts.

Rebuttal Letter Reviewer #2: General comments

Reviewer Comments Author Response

1. In the study setting section, a few details of the population coverage and health services (primary health centers; hospitals; doctors; local health staff etc.) available to the HDSS community should be provided. According to Ethiopian Central Statistics Agency, the district had an estimated population of 145,458, resided in 27 rural and 3 urban kebeles (CSA). In the district, four health centers, and 30 health posts provide health care services for the community. HDSS uses longitudinally follow up on well-defined subjects (individuals, households, and
residential units) and all related demographic and health related outcomes within a clearly defined geographic area.

2. VA data collection procedure: Describe some details of the questionnaire - language version used; any local modifications to the INDEPTH version; use of paper forms or electronic data collection platform; educational qualifications of VA interviewers The VA data presented have been collected since 2007. Verbal autopsy is a method used to ascertain the cause of a death based on an interview with next of kin or other caregivers. The VA questionnaire prepared by World Health Organization (WHO) and INDEPTH (International Network of field sites with continuous Demographic Evaluation of Populations and Their Health in developing countries) was used

A paper form platform questionnaire was adapted and translated into Amharic, the national language of Ethiopia. The cause of death, or the sequence of causes that led to death, are assigned based on the data collected by a questionnaire and any other available information. Eighteen diploma graduated and trained and resident full-time enumerators visited the household every month for events and reported all deaths to Dabat HDSS database. VA interviews were carried out after 45 days of the date of death in respect of the local mourning time. VA was conducted using a standardize World Health Organization (WHO) questionnaire endorsed by international Network for Demographic Evaluation of Populations

3. Data quality management - more details on training programs for physician reviewers and evaluation of physician training; whether physician certification was according to multiple causes followed by ICD rules for the underlying cause; or based on physicians directly adjudicating and mentioning only the underlying cause A total of nine trained physicians (three pediatrician, three internist, and three gynecologists) were involved in assigning the causes of deaths. International Classification of Diseases (ICD-10) was used to classify main, underlying and contributing causes of death following independent assessment of the completed questionnaires by two or three physicians

4. Broad causes of death: it is not clear for which period the data presented on lines 2-4 of this paragraph refer to. Also, the percentage for NCDS (13.22%) in this sentence appears to be
wrong. Of the total deaths, between 2007 and 2013, communicable diseases (47.97%); non-communicable diseases (34.8%); and external causes (10.44%) were the main causes of deaths in the study area. In 2009 and 2010, communicable diseases were the major broad cause of deaths followed by non-communicable diseases, and external cause of deaths. In this study, the proportion of NCDs increased out of total deaths from 2007 to 2013. Pregnancy related causes of death were high in the year 2007.

5. Broad causes of death (contd). The results presented on lines 4-9 of this paragraph needs to be substantiated, in terms of some reasoning for the variations causes across different years. Is there some specific trend? Could these variations be an artefact of the low numbers of deaths (small numbers?) Or, could they be a result of variations in VA procedures. A couple of essential details here; followed if necessary, by more details in the discussion would help explain the variations. Though deaths from NCDs increased, deaths varied from year to year during the study period. The variations may result in VA procedures.

6. Specific causes/Major causes: Again, the text merely repeats what is stated in the tables. Some interpretation of the trends or variations (or similarities) across time or between urban and rural areas needs to be mentioned. In regard to meningitis, more details on the age-sex distribution would be helpful. Were meningitis deaths concentrated in any specific age/sex group? Of the total death during the period of the study, 3.6% of deaths were female due to meningitis, and 3.3% of whom were males. In the year between, 2007 and 2010, 31(5.5%) died of meningitis were females and, 15(2.7%) were males. In the year between 2011 and 2013, males, 21(4%) died of meningitis and 9(1.7%) females. Of the total death due to meningitis in the year between 2007 and 2013, 122(11.3%) died. Of these, 76(67.9%) were in the year between 2011 and 2013, 46(41.0%) were in the year between 2007 and 2010. Of these, 33(29.5%) were 65 and above old age groups, followed by the age group between 15 and 34, 24(21.4)

7. Table 2: Provide total numbers of deaths at the bottom of each column. Percentages need only one decimal place. Check formatting of brackets The table is amended as per the comments. See table 2 in the document.
8. Similar to comment 6 above; more interpretation is required of the data presented in regard to climactic zones and deaths among women. Formatting and details in Table 3 should conform to recommendations made above for Table 2.

Of the total deaths, 776(67.1%) lived in highlands. Of these, 388(46.6%) were women.

The table is amended as per the comments. See table 3 in the document.

9. The results of the Chi squared test presented for trends in communicable and non-communicable diseases in Table 4 are not clear. Which differences are statistically significant? Table 4 presents odds ratios, but not marked for any statistical significance; nor displayed with 95% CI, to infer statistical significance. This should be rectified. We accepted the valuable comments and deleted the table in the manuscript.

10. Factors associated with specific causes of death. In general, Table 5 needs a major revision.

   a. The abbreviations COR and AOR need to be expanded; I assume they mean 'Crude odds ratio' and 'adjusted Odds ratio' but these need to be spelt out.

   b. It would be easier to consistently interpret in all instances 'excess' risks of mortality in all the associations, rather than the use of 'reduced' risk in some instances and excess risk in others. For example; reduced risk of non-communicable disease mortality in rural areas could be alternatively (and more meaningfully) presented as 'excess' risk of NCD mortality in urban areas. Reduced risks are generally discussed in regard to the effect of specific clinical or public health interventions; in terms of a 'protective' effect. It is suggested to redo the table presenting and highlighting the findings in terms of 'excess' risks of mortality.

   c. In particular, for external causes; you could use the OR for ages above 50 years as the base; and compute the ORs for the younger age groups as 'excess' risks. This will convey a more meaningful epidemiological interpretation of the data, for planning interventions. Also, in the text of the results section, some information on the proportionate composition of external causes (road accidents/falls/occupational injuries etc) could be presented. Table 3 presents some of the
specific external causes, but the presented data in the table accounts for only 41 of the 124 total deaths from external causes, something appears to be missing.

d. Statistical significance is to be highlighted & discussed only for 'Adjusted Odds ratios'; and not crude odds ratio.

e. Statistical significance of association of Education with any of the mortality outcomes should be removed; since they are not consistent either across all the outcomes; or with common knowledge of the associations between education and health outcomes. In all probability, the observed statistical significance in some instances are an artefact of small numbers.

Corrected as per the valuable comments. See the table and text in the document.

11. Discussion: The article compares findings from this study with at least two other HDSS sites in Ethiopia. It would be interesting to see a pooled analysis of data across these three (or potentially any additional) HDSS sites in Ethiopia; in an attempt to get an understanding of broader national mortality patterns. While such an analysis is beyond the scope of this article; the discussion should raise the potential as well as the need for such analysis, and suggest mechanisms, and potential benefits from the same. The potential as well as the need for such analysis, and suggest mechanisms, and potential benefits from the same.

12. Towards the end, the authors mention challenges in regard to physicians agreeing on the probable cause of death. If data are available, the authors could present the percentage of cases with agreement between two; percentage referred to the third and subsequent agreement with either of the first two; and finally, the percentage remaining undetermined due to disagreement across all three reviewers. This will give a better understanding of the nature of the challenge. As we could provide frequent training for physicians, we minimized the disagreement between two physicians, particularly the third physician reduced the disagreement occurred between two.
13. The discussion could also clarify whether the VA questionnaire included a 'free text' section for the interviewer to record an open narrative provided by the respondent about the terminal illness and events. If such a section was present in the questionnaire, the authors could also seek and provide opinion from physician reviewers as to the general value of such a section in formulating a diagnosis of the probable cause of death, in addition to the information from structured questions. The valuable comment is address in the discussion section. See the text

14. Finally, the discussion could also highlight any immediate clinical interventions or public health measures that could directly be informed or implemented, as guided by the findings from this study. Finally, the discussion could also highlight any immediate clinical interventions or public health measures that could directly be informed or implemented, as guided by the findings from this study.

15. The article needs to be carefully checked for spellings; typos, and occasional grammatical errors. The spellings, typos, and grammatical errors thoroughly revised and edited