Reviewer’s report

Title: Using verbal autopsy to assess the proportion of HIV-associated deaths in the ART period in rural Uganda: a prospective cohort study, 2006-2008

Version: 1  Date: 31 March 2011

Reviewer: Melissa Marx

Reviewer’s report:


Stated objectives:
1) To evaluate the usefulness of verbal autopsy among adults after the introduction of ART in 2004 in identifying HIV-associated deaths and ART-related deaths.
2) To compare the proportions of HIV-associated deaths before and after ART introduction

Stated methods:
1) VA interviews for deaths identified through existing yearly censes
2) HIV-associated determined by combining verbal autopsy interview with existing annual serosurvey data.
3) Two clinicians coded the death, focusing on whether they were HIV-associated and/or ART-related.
4) Data were summarized and the magnitude of HIV-associated deaths was compared pre- to post-ART.
5) Inter-observer agreement was calculated.

Conclusions:
Substantial reductions in HIV-associated mortality were observed.

Reviewer’s overall comments:
This was an interesting paper describing the change in HIV-associated mortality before vs. after “universal” access to ART. It is one of the first analyses of its kind on the subject. The analysis is strengthened by its use of an established cohort and verbal autopsy methods.

Specific comments:
Strengths:
Connection of verbal autopsy to an existing and active cohort.
Use of the same instrument in the 1990s and 2006-8.
Short lag time between identification of deaths and interviews.
Weaknesses:

Major Compulsory Revisions
1) “HIV-associated” is not clearly defined in the manuscript. It is also not clear how cohort reports of HIV status were integrated with proxy-report at verbal autopsy interview, or even whether relatives had the opportunity to indicate whether the decedent was known to be HIV+ before death.

2) There are no sample sizes given for the cohort or the verbal autopsy interviews. Without n’s and confidence intervals on estimates, it is very difficult to interpret the data.

Minor Essential Revisions

Methods:
1) The population of Uganda and the area under study needs to be given.

2) It is unclear whether community-based recorders record deaths for the whole country or just the study areas, and whether these data are collected during the yearly censes or separately.

3) Please describe verbal autopsy instrument in more detail. How does it compare to the World Health Organization’s recommended questionnaire?

4) Specify what the physicians who reviewed the Verbal autopsy questionnaires were experienced in. Medicine? Verbal autopsy coding? HIV?

5) How did reviewing physicians determine whether deaths were ART and HIV-associated? What guidance/definitions were they given?

6) In identifying deaths in people who had been HIV-positive, was the serosurvey data, verbal autopsy interview data, or some other source used? How were the data integrated?

Results:

7) In order to make sense of the numbers of deaths, and HIV-associated deaths, we need denominators. How many people were identified in censes in the study area? You could also calculate rates with denominators if you chose to do so.

8) Were decedents’ relatives asked his/her HIV-status at death? Clarify this in the text.

9) Specify the gold-standard used to calculate the specificity and PPV of HIV-associated.

10) You say HIV-related is 25.8% at one point and 26.0% the next. Is there some difference in the figures? Please be consistent with significant figures and/or explain the difference in these two numbers.

11) Please reiterate the methods for the original data collection period, including the contents of the questionnaire and methods of data collection.

Discussion:

12) How is reliability assessed? Relative to what? I don’t see any data to convince me it’s reliable.
13) When discussing the limitations – “However, this recorded cause of death was non-selective and could not have affected the estimated HIV attributable mortality fraction…” do you mean the interviewer could have noted the COD was related to HIV, biasing the coder? Whether yes or no, this needs to be clarified in text. Please also define “non-selective”?

14) I suggest adding that the two-month interval likely minimized any difficulty participants had recalling the circumstances of their loved ones deaths.

15) Please explain how HIV-status and cause of death from verbal autopsy were used in determined HIV-associated status, and if not, why not?

Conclusions:

16) It is not clear how/on what basis it was determined by these data that verbal autopsy had good performance? Please clarify or remove.

Tables:

17) Table 1) I would suggest acknowledging that sample size (of deaths) was low and so uncertainty high in your tables.

18) Table 2). This wasn’t discussed much if any in the text, I would suggest adding a sentence or two about it there.

19) Another strength from your tables is that your cohort gives you HIV-status in addition to your verbal autopsy interview. However, the cohort may have slightly out-of-date information for the deceased. I think this point should be discussed.

20) Generally how VA report data were used in defining HIV and ART-associated deaths needs to be revised in the next version.

When assessing the work, I have considered the following points:

1. Is the question posed by the authors new and well defined?
   Yes, the question is new (whether HIV-mortality has changed in the period between the original and current data collection points). It is defined well in the abstract and objective sentences in the background section.

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?
   The paper’s main weakness lies here, in the description of the methods. HIV-associated mortality and ART-associated mortality are not well-defined. Particularly unclear is how the VA interview contributed to ascertaining HIV-associated nature of cause of death. The paper suggests that the cohort data are used exclusively for this, but the table and some text seem to allude to use of the VA data as well. This needs to be clarified in the text.

3. Are the data sound and well controlled?
   The data appears to have been carefully collected. The analyses are crude, which is probably alright/appropriate for a cause of death/SAVVY analysis.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
Yes.

5. Are the discussion and conclusions well balanced and adequately supported by the data?

The aspects of the discussion that focus on changes in HIV-associated mortality are supported by the data. I can’t find data in the paper to support the assertion that the data were reliable and/or had “good performance”.

6. Do the title and abstract accurately convey what has been found?

The title wording could be improved, but a case could be made that it conveys the study that was conducted. I would probably have focused on the comparison of HIV-associated deaths in the two periods. The abstract is acceptable.

7. Is the writing acceptable?

Yes

**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