Author's response to reviews

Title: Validating physician review and probabilistic modelling (InterVA) approaches to verbal autopsy interpretation using hospital causes of adult deaths

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Version: 3 Date: 3 June 2011

Author's response to reviews: see over
Dear Dr Muller,

Re: Our submission “Validating physician review and probabilistic modelling (InterVA) approaches to verbal autopsy interpretation using hospital causes of adult death.”

Many thanks for allowing us the opportunity to present a revised version of our manuscript. We hope we have been able to address them all to your satisfaction in this re-submission.

We respond as follows:

Reviewer 1

Reviewer comment:
(2) “The sample size and limited categories of causes of death are not sufficient to support the conclusions regarding utility of the InterVA method. There is no information on several important causes of adult deaths; such as site specific cancers, chronic obstructive pulmonary disease, major subdivisions of cardiovascular disease - e.g. ischaemic heart disease/stroke; or other conditions such as liver cirrhosis; renal failure; or pneumonia”.

Response:
Our study would certainly have been more definitive with a larger sample size and acknowledged this as a limitation of our study in the manuscript. Nevertheless, the overall picture of CSMF for the major causes of death in our study population was similarly determined by both methods. Although there are other important causes of adult deaths, our study had 2 cases of cancer (1 cancer of the cervix and 1 leukaemia), 1 case of chronic obstructive pulmonary disease (asthma), 1 case of ischaemic heart disease/stroke (stroke cases were due to other underlying causes such hypertension), 1 case of liver cirrhosis (alcoholic liver disease), 1 case of renal failure and 2 cases of pneumonia. These frequencies were so low that a massive
study would be required to meaningfully investigate the performance of the different models for these conditions or sub-divisions thereof. While we acknowledge that this would be a valuable aim of future and larger studies this was not possible under the power and budgetary constraints implicit in this pilot single site study. In this regard we have made changes to the text in the discussion.

Reviewer comment:
(2) “.. the methods used do not produce directly comparable data; since the HCOD and physician review yield underlying causes of death (presumably based on the ICD principles, although not stated as such in the article); while the InterVA yields only the likelihood of one or more causes based on probability, without taking into consideration any causal relationship (or absence thereof) between the multiple causes of death”.

Response:
We apologise for lack of clarity regarding this point. The PR and HCOD are based on the ICD 10 guidelines, which we have made more clear in our revised manuscript.

In this study, the interVA model assigned most of the cases 118 (81%) to a single cause and 20 (14%) cases to two causes, of which 8 cases agreed with either HCOD or PR. The model is based on certainty and hence, the effect of causal relationship is difficult to address in our context. Thus conceptual classification that reflect the real public health issues are as appropriate as the International Classification of Diseases (ICD-10) coding. We have revised the manuscript in this context

Reviewer comment:
(3) “The inferences derived from the apparent similarity in cause-specific fractions observed from the different methods are misleading. These similarities seem fortuitous; when you take the misclassification patterns into account. Additional files 3 and 4 indicate that physician review demonstrates higher validity and markedly less misclassification than InterVA, at the individual level.”

Response:
We agree with the reviewer that the physician review performed better than the interVA at an individual level, however, as the reviewer will appreciate, the purpose of VA is to describe the underlying cause of death structure at the population rather than at the individual level. In this regard we have made the following changes to the text:

It appears that the misclassification by the model gives a different picture regarding deaths due to HIV and tuberculosis. However, if one considers that tuberculosis and HIV share many clinical features or when they occur as a co-infection, a TB/HIV category will show a similar pattern to that derived from the HCOD and PR. Similarly it was observed that for meningitis both the PR and the model misclassified many of the cases to the ambiguous “Others” category. The physician review performed better than the model at an individual level; however, both arrived at broad agreement in identifying cause of death at population level.
Reviewer comment:
(4) “The kappa scores also suggest much higher accuracy for the physician review (0.52) as compared to the InterVA (0.32).”

Response:
We agree with this statement and believe that we have presented the data in a very open and honest way in the submitted paper. This comment is addressed in the changes we have made above.

Conclusion
We appreciate the editorial comments and hope you will find the revised version acceptable for publication in Population Health Metrics Journal. We look forward to your positive response.

With kind regards,

Yours sincerely

Dr. Evasius Bauni.