Evaluating the performance of the InterVA Model for determining AIDS mortality in the Adult Population of Addis Ababa.

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Abstract

Background Verbal Autopsy (VA) is a method for determining the cause of death based on an interview with next of a kin or other caregivers and is a useful tool in areas where routine death registration is unsatisfactory. Most commonly, causes of death are assigned by physicians who review completed VA questionnaires. This is time consuming and expensive and has led to several initiatives for attributing causes of death using expert algorithms such as the InterVA model. We evaluate the performance of the InterVA model using gold standard, which is based on hospital diagnosis and HIV serostatus of the deceased.

Methods Surveillance of hospital admissions and outpatient visits from the TB/HIV clinic was initiated in Zewditu Memorial Hospital. The records obtained from the hospital were used to define the gold standard of TB/AIDS deaths. A VA interview was conducted for those died in and out of the hospital. The InterVA model is used to interpret the VA interviews to arrive at probable causes of death.

Results A total of 193 VA's were conducted provided that their gold standard is known. The probabilistic model assigned the likely causes of death for all the records with a certainty value of 81%. The proportion of AIDS death determined by the gold standard is 56% while that of the InterVA is 54.4%. Both the InterVA and the gold standard gave identical results of AIDS and Non-AIDS death in 81.3% of the cases. Classifying all deaths as AIDS and non-AIDS, the sensitivity value is 0.86 and specificity is 0.73. The sensitivity and specificity values of TB/AIDS death are 0.92 and 0.78, respectively.

Conclusion Verbal Autopsy is potentially an important way in which population levels and trends of AIDS specific mortality can be examined. The analysis of VA based on probabilistic model produces promising results when compared to the gold standard to estimate adult AIDS mortality. The InterVA model can be applied to guide priority health interventions activities in low-income countries.

Key Words Verbal Autopsy, InterVA, Mortality, Validation, Cause Specific Mortality Fraction, HIV/AIDS, TB/AIDS.

Introduction

In developed countries, data on cause-specific mortality are readily available from vital registration. Estimation of cause of death is difficult as the coverage of vital registration and reliability on death certificate are generally low in developing countries[1]. One of the reasons is the difficulty of obtaining population based data on causes of adult deaths[2].

The demand for accurate data on levels and trends in cause specific mortality is escalating. Mortality statistics are important advocacy tools in the area of Anti Retroviral Therapy (ART) for documenting AIDS mortality[3, 4]. AIDS mortality in the population is useful to assess the effectiveness of ART scale-up as well as programmes to treat opportunistic infections[5]. Verbal Autopsy (VA) is an alternative gadget to estimate AIDS mortality[6]. It is a method of finding out the cause of death based on an interview with next of a kin or other caregivers[7]. VA is increasingly being used to monitor the distribution of death by cause in places where medical certification of cause of death is rare. They are valuable for health managers to establish baseline data on causes of death in the population[8].

Interpretation of VA has largely relied on either expert assessment of the VA interviews by physicians, or other application of predetermined algorithms, often based on a decision-tree approach[9]. Expert assessment has been shown to be a reliable tool for VA interpretation[10, 11] but, legitimate concerns remain as to standardization between different experts, the risk of having change of experts over time, and the sheer volume of work involved in assessing large number of VA's[11]. Algorithms have the potential to address all of these concerns but raise others such as reliability, and the difficulty of considering parallel possibilities with different clinical diagnosis. The InterVA model is one of those algorithms and shown in many cases to be relatively effective[11, 12]. It processes inputs from the VA data and lists up to three likely causes of death[13]. It has already been evaluated on a preliminary basis in Vietnam[12] and Ethiopia[6].

The objective of this paper is two fold: first, to estimate the Cause Specific Mortality Fraction (CSMF) of HIV/AIDS; second to validate the performance of the InterVA model against hospital records taken as gold standard. Most validation studies were against physician review due to the lack of hospital statistics. Hospital validation studies are the only feasible way to validate a VA questionnaire[7].

Study Area and Population

The population size of Addis Ababa is approximately 2.7 million with a sex ratio of 0.93 in 1999[14]. The first AIDS cases were diagnosed in 1986[15]. The main source for HIV surveillance trend data in Ethiopia is the antenatal clinic (ANC) based HIV sentinel surveillance system, which was established in 1989[16]. In 2005, HIV/AIDS prevalence in the country is 1.4% with urban and rural values 5.5% and 0.7%, respectively. For Addis Ababa the prevalence is 4.7%, with great disparity between men (3%) and women (6%)[17].

Methods

Data

In this paper, we used the data from the medical diagnoses as well as the results of VA that were carried out from hospital and burial records. The burial surveillance was initiated in February 2001 at 70 cemeteries registering approximately 20,000 deaths in a year. Basic characteristics of the deceased such as age, sex, lay diagnosis of causes of death, address, etc. were collected at the time of burial ceremony from the person who accomplishes the funeral[18].

Zewditu Memorial Hospital is a government medical facility in Addis Ababa and was one of the few hospitals with a Voluntary Counseling and Testing (VCT) center of sufficient capacity to accommodate our study. Surveillance of hospital admissions and outpatient was initiated in the Zewditu Memorial Hospital in May 2003 and continued for nine months. Initially, the surveillance covered the TB/HIV clinic (TB, ambulatory patients only), the medical emergency (ER), the internal medicine (IM), gynaecology (GY) and paediatric wards (PE). For each patient a ward nurse collected basic background characteristics such as age, sex, marital status, education, religion, diagnosis of admission and discharge diagnosis - if available- addresses for Addis Ababa residents.

After few patients were identified, a ward nurse contacted the coordinator of the VCT unit who assigned a VCT nurse to a pre-test counseling and ask for written consent of the patient or his/her guardian. Patients were approached for an HIV test. A VA interview was administered for those that died in the hospital. For those that died outside of the hospital, the records of the burial surveillance and the hospital record were matched and a VA interview was administered by taking the burial surveillance as a sampling frame.

Gold Standard

Detailed medical records and clinical evidence of patients treated at the hospital were reviewed to establish the cause of death in the gold standard. AIDS death is defined based on the underlying cause of death and HIV test result. Individuals who were HIV positive at a baseline survey based on antibody testing and was not reported to have suffered major injury from motor vehicle accident, injury that was self inflicted (suicide) or deliberately inflicted by another person (homicide) in the two weeks prior to death are defined to have died of AIDS in the gold standard. For females, direct obstetric deaths-defined as death shortly before delivery, with excessive bleeding and/ or severe headaches or death during child birth were classified as non-AIDS[19]. TB/AIDS death is defined as an accumulation of tuberculosis related deaths on AIDS death.

InterVA

One hundred ninety three VA's were conducted with information on the cause of death, hospital service utilization, socio-economic background characteristics, and care-giving. The information from the VA were double entered using a Microsoft Access database program which were further transformed in to STATA to generate the input variables for the algorithm.

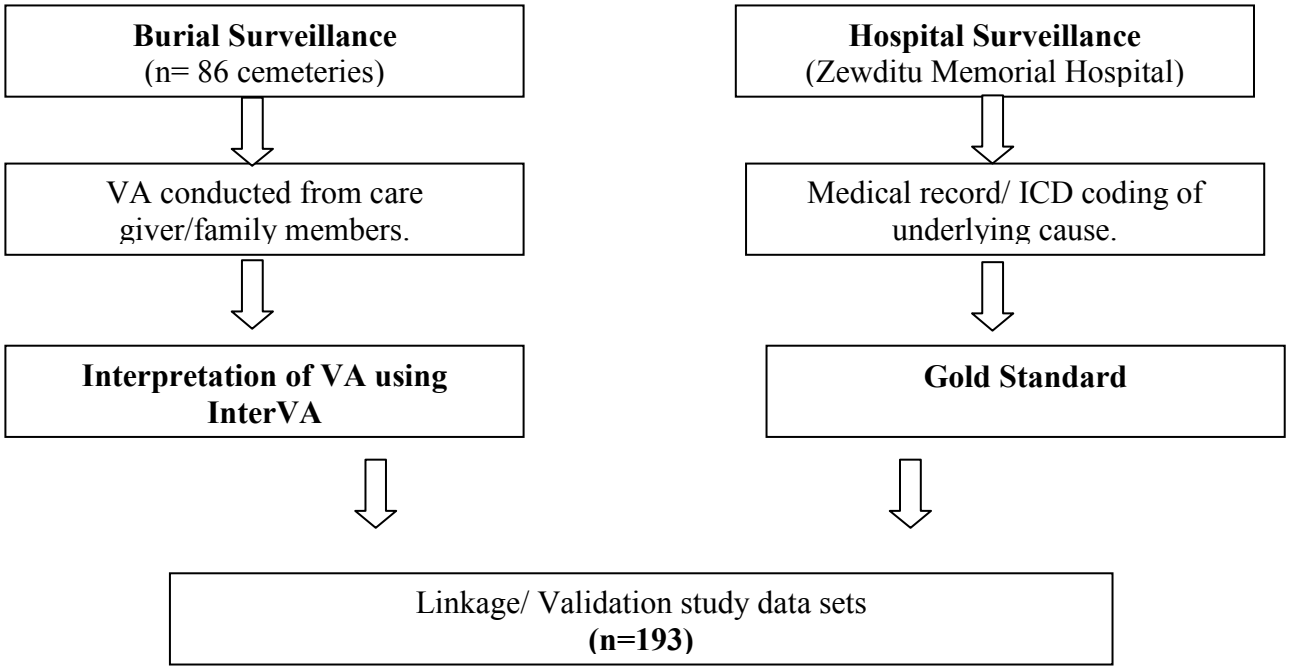
InterVA accepts a range of "indicators" relating to a particular death, processes them in a mathematical model based on Baye's theorem, and produces likely cause (s) of death with their associated probabilities. "Indicators" is the blanket term used by the InterVA to describe the whole range of information about the circumstances of death, including basic background characteristics, details of illness (signs and symptoms) leading to death, previous medical history, etc. The prevalence of Malaria and HIV/AIDS, entered as low and high respectively, are basic epidemiological parameters for the model as their prevalence varies from place to place. When the program has worked through all indicators, it presents its findings as probable cause (s) of death. Up to three likely causes as primary cause and co-causes may be given for a particular case, with its own likelihood. "Certainty", the average of the three likelihood causes, measures of the confidence with which the model has reached its conclusion[20].

Validation Study

Likely causes of death produced by the model will be compared with causes previously determined using hospital records as gold standard. Merging Tuberculosis and HIV/AIDS is quite reasonable due to their similarity of clinical symptoms for the calculation of sensitivity and specificity. The absolute deviation in CSMF of the model from the true value is also

computed to look the pattern by age. Figure 1 shows the data collection process and the study protocol.

Fig 1. Flow chart showing the study protocol and data collection.



Results

The sex ratio of the study population is 0.95. Age reporting of burial surveillance, hospital surveillance and the VA indicates a similar pattern with an average age of 40.3, 38.2 and 40.2 years, respectively. 88% of the observations are on the age interval 15-59. Thirty four percent of the deceased were single, 45% married and 21% are either divorced or widowed. Of those who were approached for counseling, 82.4% of the respondents had tested for HIV with a prevalence of 63.5%.

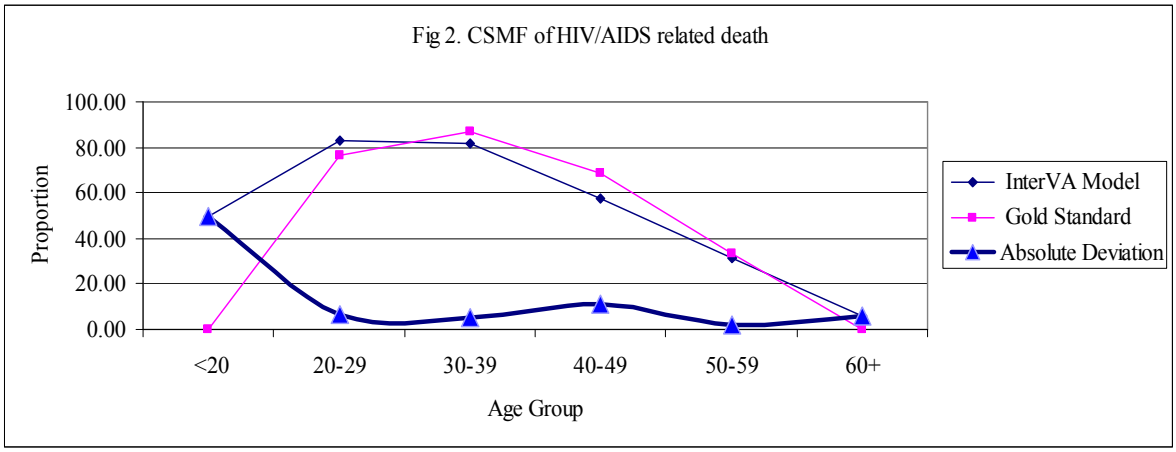
The InterVA model assigned causes of death with a certainty value of 81% and a standard deviation of 21. The model diagnosed HIV/AIDS as a major cause of death (54.4%). Twenty-eight observations had a second likely cause of death with a mean likely ratio of 40% and standard deviation of 8. None of the observations had a third likely ratio. 89% causes of death determined by the InterVA have a certainty value of greater than 50 (Table 1).

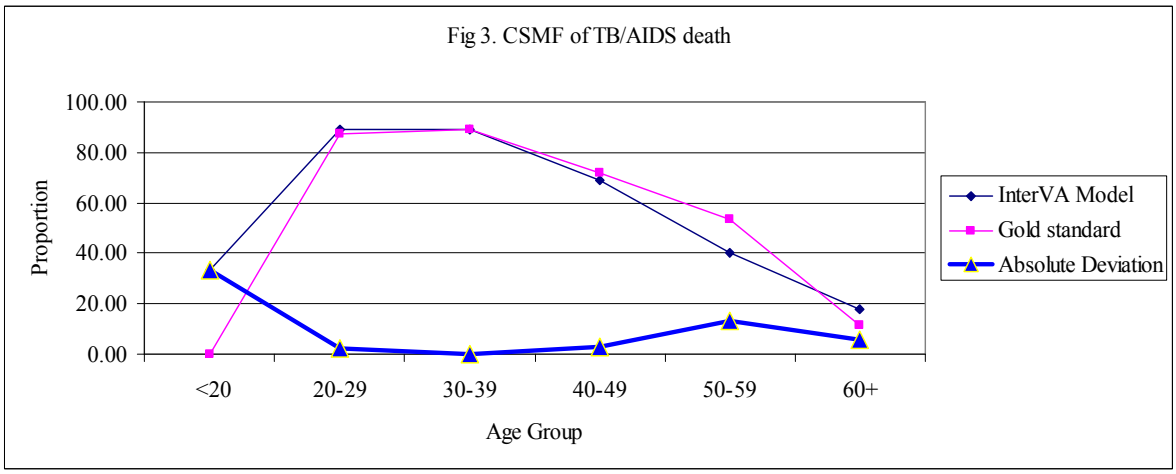
Table 1. The distribution of the likely cause of death assigned by the InterVA model.					
		n	%	Mean Likelihood of Cause of Death	Standard Deviation
Most Likely Cause of Death		193	100.0	81.7	19.5
	HIV/AIDS related death	105	54.4	85.8	16.8
	Liver disease	30	15.5	83.4	20.2
	Tuberculosis (pulmonary)	28	14.5	80.8	16.0
	Others	30	15.5	65.7	23.2
Second Likely Cause of Death		28	100.0	39.7	7.8
	HIV/AIDS related death	12	42.9	41.0	5.3
	Liver disease	4	14.3	33.0	4.1
	Tuberculosis (pulmonary)	6	21.4	42.7	9.8
	Others	6	21.4	38.5	10.3
Certainty				80.7	20.9

In the gold standard 56% of the records had been identified as AIDS, 30.6% as non-AIDS death. Similarly, 66.8% and 23.3% were identified as TB/AIDS and non-TB/AIDS death, respectively. Nearly 10% of the records were not classified as Tuberculosis or AIDS death due to lack of adequate information (Table 2).

Table 2. The distribution of respondents by sex and causes of death classified in the gold standard.							
Cause of Death		Female		Male		Total	
		n	%	n	%	n	%
AIDS Death	Yes	54	54.6	54	57.5	108	56.0
	No	28	28.3	31	33.0	59	30.6
TB/AIDS Death	Yes	63	63.6	66	70.2	129	66.8
	No	23	23.2	22	23.4	45	23.3

Both the InterVA and the gold standard gave identical results of AIDS and non-AIDS death in 81.3% of the records. Merging TB and AIDS the two models give similar diagnosis in 88% of the cases. There is a similarity between the CSMF of the model and the true values in diagnosing HIV/AIDS as a cause of death by age having an average absolute deviation of 3 from the true value. The average absolute deviation in CSMF of the two models for TB/AIDS death is 0.58 (Fig. 2 & Fig. 3).





Classifying all deaths as AIDS and non-AIDS, the sensitivity value is 0.86 and the specificity is 0.73. On the second classification of deaths as TB/AIDS and non- TB/AIDS, the sensitivity and specificity values elevate to 0.92 and 0.78, respectively (Table 3).

Table 3. Validation of deaths due to selected causes.

	Sensitivity	Specificity	PPV	NPV
AIDS Death	0.86	0.73	0.84	0.76
	(0.78,0.92)*	(0.60,0.84)*	(0.76,0.91)*	(0.63,0.86)*
TB/AIDS Death	0.92	0.78	0.92	0.78
	(0.85,0.96)*	(0.63,0.89)*	(0.85,0.96)*	(0.63,0.89)*

* 95% Confidence Interval

Discussion

Different validation studies for the VA method have been done for deaths in children[21-24] and adults [9, 11] suggesting that the VA method is an important tool for diagnosing causes of death,

predominantly in developing countries. Studies in Tanzania[25] and in Ethiopia[6, 26] have shown the robustness of the VA method in identifying cause of death using lay interviews.

There are many factors that influence the validity of a VA tool-not just those inherent in the tool or affected by prevalence of diseases and causes of death, but also issues with the operational process of collecting and coding VA data[27]. The absence of some variables in the VA questionnaire is one factor challenging the accuracy of the InterVA model to be more realistic with that of the gold standard. The model did not employ open-ended questions which are more relevant in a society with poor knowledge of symptoms of certain disease and more local terms may be used in this case. Misclassification of causes of deaths have a profound effect on the reported estimate of CSMF[8, 28]. Nine percent of the observations were classified as HIV/AIDS death provided that their true serostatus is negative and it may be due to weak report of caregiver or culture specific factors such as stigma and discrimination, which ultimately affect the performance of the model. The relatively small sample size of the study also contributes to underestimating the sensitivity and specificity values. Another limitation of our study is that the performance of the VA has been assessed in subjects who were treated at hospital. The VA may perform differently to those subjects who were not treated at hospital, though clearly there will be no reliable gold standard outside the hospital setting.

The use of VA for assessing causes of death in a population is relatively a new phenomenon. Verbal Autopsy is potentially an alternative technique to examine the population levels and trends of TB/AIDS mortality. The analysis of VA based on probabilistic model produces promising results primarily for those settings where physician review is not feasible or too costly. InterVA is most suitable for determining Cause Specific Mortality Fractions and can be applied to guide priority health interventions activities in countries where vital registration is either weak or non-existent.

Acknowledgement

The Addis Ababa Mortality Surveillance Project (AAMSP) received support from the community health department of the Addis Ababa University and the Ethio-Netherlands AIDS research project (ENARP) and AIDS foundation of Amsterdam, the Netherlands. Religious leaders and the Addis Ababa Labor and Social Affairs Bureau supported the study and facilitated our access to the burial sites. The Ministry of Health, the Addis Ababa Administration Health Bureau and the hospital administrations supported the surveillance of hospital deaths. We would also like to thank the study participants, the data collectors and supervisors for their partaking and accountable data collection.

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