

Can verbal autopsies be used on a national scale? Key findings and lessons from the South Africa National Cause-of-Death Validation Study.

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Abstract

Background

The quality of cause of death (COD) statistics in South Africa has room for improvement. It is possible that supplementary use of verbal autopsy (VA) interviews for the deaths that occur outside of health facilities might be useful. This study describes the challenges and successes of collecting a national sample of VA interviews.

Methods

We recruited next of kin who registered deaths in 27 randomly sampled sub-districts across South Africa between September 2017 – April 2018. Trained fieldworkers (84) conducted face-to-face interviews using the WHO2016 verbal autopsy (VA) instrument. A team of physicians (51), trained in medical certification of cause of death and reading VAs, certified the underlying causes of death. Feasibility was assessed considering response rates, participation and quality of data. Cause specific-mortality fractions (CSMF) based on physician reviews and InterVA-5 automated software were compared with 2017 Statistics South Africa (Stats SA) data and assessed for plausibility against burden of disease estimates.

Results

Only 26% of the 36,976 total deaths registered in the sample area were identified during recruitment and 65% of the next of kin agreed to be contacted. A total of 5,375 VA were conducted (overall response rate of 55%) and 83% of physician reviewed VAs were judged to have good quality data for assigning underlying cause of death. Fifty-nine percent of the VAs occurred in the 27 sampled sub-districts, with the remainder ones coming from adjacent areas. Comparing the CSMFs, the physician reviewed VA identified 22.3% HIV/AIDS and InterVA-5 18.5% deaths, in line with burden of disease estimates, while Stats SA identified 4.9% HIV/AIDS deaths.

Conclusions

The study demonstrated feasibility of using VA on a national scale, but immense challenges in identifying and recruiting next of kin highlights the importance of formalising VAs within the country's death notification system.

Background

Reliable, continuous, and timely mortality and cause-of-death (COD) data are essential for improving health and population policies and supporting countries to respond to emerging health threats and epidemics (1, 2). The importance of recording vital events is well recognized, and Civil Registration and Vital Statistics systems (CRVS) that provide continuous data on births, deaths and COD are now seen as a fundamental data source to monitor the Sustainable Development Goals (3). Fifteen of the goals require CRVS data, and 14 of the indicators require cause-specific mortality (3). However, in many low- and middle-income countries low infrastructure and fiscal investments in civil registration systems have resulted in countries having low levels of death registration and limited or no medical certification of COD.

Verbal autopsy (VA) is a method used to collect and analyse COD information based on an interview conducted with the next of kin or close caregiver about the illness and circumstances leading up to death. Although VA is an imperfect tool to determine the COD, it is often the only population-health option in identifying the COD for out-of-

facility deaths (2). It has been suggested that in countries with limited access to health services or medical officers, more extensive use of VA could help fill the information gap (4). In 2017, de Savigny and colleagues (5) presented a detailed system view of how VA can be integrated into CRVS. The Bloomberg Philanthropies Data for Health Initiative conducted a structured mapping exercise to identify and map current system responsibilities and data flow for CRVS systems in 16 countries (6). Both studies revealed the challenges involved with integrating VA into CRVS systems. To-date we are not aware of any country that has fully integrated VA into CRVS.

In 2005, the first international technical standards and guidelines for VA were introduced (7). The 2007 VA standard instrument includes separate questionnaires for three age groups with a defined VA list of causes and corresponding codes from the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) (8). In 2016, questions were added or edited to reach full compatibility with the available automated analysis methods to reduce clinician burden in reviewing questionnaires (9).

South Africa has made great strides in increasing geographic coverage of death registration (10) following integration of the "homeland" areas and the enactment of the Births and Deaths Registration Act of 1992 (11). Deaths must be registered within 72 hours. Recent estimates indicate that completeness for persons above age two years is over 90% (12). Despite these improvements in death registration, there are still concerns about the quality of data relating to the COD. These include a high proportion of deaths with ill-defined causes (13%), with an additional 13% having a COD that is not valid as an underlying cause in 2016, under-reporting and misclassification of HIV deaths and an inaccurate profile of injury deaths (13). The extent of these problems differ at district and national levels (14) and arise from a combination of certifying medical doctors not having access to a full medical history at the time of certification, poor certification practices, and some of the deaths being certificate. Although, South Africa has three health and demographic surveillance sites (15–17) as well as a Child Health and Mortality Prevention Surveillance site (18) that routinely use VA to track COD, there has never been national implementation of VA.

The South African National Cause-of-Death Validation Project aims to validate the CRVS COD information by collecting VA, medical, and forensic pathology record data on the COD for a national sample of deaths and then compare this with information recorded in the CRVS system. The initial data analysis of the VAs demonstrated the feasibility of setting up a national collection of VA data (19). This paper presents the methodology and findings related to VAs and highlights important issues for countries considering to use VAs within a national initiative.

Methods

The detailed methodology is reported elsewhere (19). We conducted a cross-sectional study that collected data for a fixed-period census of deaths that occurred in a nationally representative sample of health sub-districts in South Africa during parts of 2017 and 2018, using a probability proportional to population size sampling strategy.

In the first phase of data collection funeral practitioners, who serviced the sampled area and were designated by the Department of Home Affairs as official registration agents, were recruited to the study. Since the Protection of Personal Information Act (POPIA) (20) of 2013 precludes Department of Home Affairs or the Department of Health from sharing personal information of the next of kin without their consent, it was necessary to work

through funeral practitioners and Department of Home Affairs officials as intermediaries to obtain consent to participate in the study. They were requested to share information about the study with the family or informant and request permission to be contacted by researchers.

Trained fieldworkers contacted consenting informants and arranged VA interviews at least 3 months after the date of death. In addition, the medical records and forensic pathology records were collected from facilities serving the selected areas. The VAs and records were reviewed by medical doctors trained in medical certification of COD. In the final phase of the study, the underlying COD reported in the CRVS system will be validated against the underlying cause identified through the highest level of evidence collected in the study for each decedent.

Sampling and sample size determination

The study population comprised registered deaths from 1 September 2017 until 13 April 2018. We randomly selected 27 sub-districts from the whole country (Fig. 1) for inclusion of all the registered deaths that occurred over a 3-month period in these areas. Using pseudo stratification three sub-districts were selected from each province according to socio-economic status based on the population size. Due to the true frequency of specific causes of death, the error rate and the extent of clustering that would arise through geographic correlations, sample size determination was not feasible. Instead, scenarios were considered based on the estimated COD profiles, considering the correction factor to be 50%, allowing for a design effect of 2 and a response rate of 85%. It was determined that a sample size of 13,000 deaths would produce a 2–3% precision on the correction factor for HIV/AIDS; 4–5% for cerebrovascular disease; and 7% for diabetes mellitus and interpersonal violence.

Data collection

We modified the WHO 2016 questionnaire to start with the narrative which outlines the events leading up to the death in order to establish rapport during the interview and prevent the respondent repeating the story of events after having provided these details through the questions. Minor changes were made to clarify questions related to maternal deaths and to injuries. We used the Open Data Kit dictionary to set up the questionnaire in KoBotoolBox, an online data collection tool (21) with translations into 8 local languages. A hard copy of the information sheet was given to the respondents to sign and keep. The KoBotoolBox data collection form made provision for digital signatures.

A team of 84 fieldworkers, selected on the basis of having a university degree or a school leaving certificate with adequate fieldwork experience, were trained in conducting VAs. Each fieldworker received a tablet containing the data collection tools and fieldworker manual. The fieldworkers were also trained to capture photographic images of de-identified medical and forensic records (22). During the training, continuous assessments identified issues that required further input for the trainees.

Identification of cause of death

A total of 51 physicians with clinical experience in the South African Public Health Service reviewed the collected information and identified the underlying COD. The physicians were orientated to the VA instrument, how to review completed VA questionnaires and use of the customised data collection tools. In order to standardise COD information, physicians were trained in the principles of ICD-10 medical certification of COD (8) and were given standard operating procedures for record reviews.

Anonymised responses to the VA interviews were batched into 40 and independently reviewed by two physician reviewers. Once the batch was completed, quality assurance reviewers checked the submissions and identified cases where reviewers assigned different underlying COD. For these cases, re-review and discussion was necessary to reach consensus.

Physician reviewers also assessed the quality of the clinical information available to identify the COD. They used a subjective score on a scale of 1 (very poor) -5 (excellent) based on the consistency and coherence of clinical information provided in the narratives and the questionnaire responses. In addition, they scored the sufficiency of the information, on a scale of 1 (very poor) -5 (excellent), to make a decision about the underlying COD.

Data processing and analysis

We used IRIS V5.8.1 automated software (23) to code the text from the medical certificates and select the underlying COD in ICD-10. We extended the dictionary of medical terms that was developed for IRIS for the Western Cape local mortality surveillance system (24) by adding terms that were commonly used by physicians. Two researchers trained in ICD-10 coding and a co-principal investigator manually coded records that were rejected by IRIS. In addition to the physician reviewers' assessment of the information, the quality of the physician reviewed COD data was assessed using ANACONDA (25).

The cause-specific mortality fractions (CSMF) based on the VA data reviewed by physicians was compared with that from the COD data reported by Stats SA (26) based on the death notifications. Stats SA code the information written on the medical certificate of cause of death to ICD-10 and use the 2011 Automated Classification of Medical Entities in addition to IRIS to identify the underlying cause of death (26). The COD data from both sources were aggregated to a basic National Burden of Disease (NBD) list aligned with the South African National Burden of Disease (SA NBD) list (27) (shown in Annexure 1) which has been developed to suit the characteristics of the country's disease profile and the quality of routine data.

The CSMF derived from the physician reviewed VAs were compared with those derived from the InterVA-5 algorithm (28) according to the VA list of conditions (9). In this article, the VA results differ slightly from the preliminary findings (19), because some changes were made to the VA data through additional data cleaning, and the InterVA-5 CSMF have been calculated using the three highest likelihoods for each case rather than the single most likely cause (19).

Feasibility and acceptability were broadly assessed by considering response rates during the recruitment and interview phases, the quality of interview data and plausibility of the findings.

Ethical consideration and permissions

Ethical clearance for research involving human participants was obtained from the South African Medical Research Council Ethics Committee, and the Health Research Ethics Committees at provincial health facilities. This project was reviewed in accordance with Centers of Disease Control and Prevention (CDC) human research protection procedures and was determined to be research, but CDC investigators did not interact with human subjects or have access to identifiable data or specimens for research purposes.

Funeral practitioners and Home Affairs officials identified all the deaths that occurred in the sample area within the study period. They recruited the next of kin, documented the contact details of consenting informants, and explained that researchers would contact them to arrange the VA interview (19).

During the fieldworker training the importance of confidentiality was explained. Project staff signed a confidentiality agreement form undertaking to work ethically and ensure confidentiality. Personal information of the decedent was de-identified and a unique study ID allocated (19). The study ID was applied to the individual patient records in multiple formats and anonymised datasets were created.

Results

A total of 353 funeral practitioners and 95 Home Affairs offices were engaged to recruit next of kin (Table 1). During the first 6 weeks we realised that recruitment of next of kin was extremely challenging. The study period was therefore extended to 8.5 months after which 9,730 informants were approached and 65% consented. The study protocol was amended to increase the sample size by including deaths of decedents who died in a health facility or who were referred to forensic pathology services. Neither the next of kin nor their dwelling could be located for 560 decedents (8.9%). Out of the 5,756 located dwellings, there was a high response rate and 85.2% of respondents completed an interview resulting in an overall response rate of 55%. The main reasons for refusing an interview are shown in Table 2.

Table 1 Total number of Funeral Parlours, Department of Home Affairs Offices and next of kin recruited for the South African National Cause of Death Validation Project 2017/18 across the three subdistricts in each province.

Province	Offices		Informant			Next of kin	
	Funeral Parlour	Department of Home Affairs	Approached	Consented	Response rate	Interviewed	Overall response rate
Eastern Cape	70	11	1,108	695	63%	575	52%
Free State	51	11	968	733	76%	656	68%
Gauteng	45	13	1,552	626	40%	463	30%
KwaZulu- Natal	30	11	1,578	1,026	65%	884	56%
Limpopo	20	10	611	483	79%	377	62%
Mpumalanga	53	12	896	737	82%	610	68%
Northern Cape	28	6	907	545	60%	506	56%
North West	44	11	1,846	1,293	70%	1,102	60%
Western Cape	12	10	264	220	83%	202	77%
South Africa	353	95	9,730	6,358	65%	5,375	55%

Table 2

Response category and reason for refusal to participate in verbal autopsy interview (N =	
5,756), South African National Cause of Death Validation Project 2017/18.	

Re	sponse category and reason for refusal	Number	%
Dw	elling located	5,756	100.0%
Vei	bal autopsy conducted	5,375	93.4%
Refused verbal autopsy			6.6%
Rea	ason for refusal		
1	Too emotional about the death of their loved one to take part	182	3.2%
2	No interest in taking part in such a study	101	1.8%
3	Refused, either telephonically or face-to-face	47	0.8%
4	Respondent suspicious of all surveys	25	0.4%
5	Respondent cited a lack of time	15	0.3%
6	Information regarding the next of kin/informant incorrect	6	0.1%
7	Respondent indicated concern about legality of study	5	0.1%

After completion of data collection, it was established that 36,976 deaths were registered during the study period and the VAs accounted for 15% of the target sample sub-districts. The geographic location where the interviews were conducted was often outside the sampled sub-districts, as the example of KwaZulu-Natal province in Fig. 2 shows. The proportion of VAs falling within the boundaries of the designated sampled sub-district varied by subdistrict. For instance, Jozini sub-district had a very good response rate with the majority of addresses falling within the target area. In contrast, the southern sub-district of Richmond had as many VAs falling outside of the designated area as those which fell within the designated area.

The majority of VAs were conducted within the recommended time interval since the death occurred (83.0%), with a median time between death and the VA interview of 9.2 months. However, a small proportion (0.2%) were conducted less than 3 months since the death occurred, and 16.7% were conducted more than 12 months since the death occurred (median interval of 13.6 months).

Table 3 shows an assessment of the quality of VA information. The information was subjectively assessed on a scale of 0 = (poor) to 5 = (excellent) based on the clinical consistency of information in the narrative and the questionnaire responses, as well as the sufficiency of the VA information for purposes of certification of COD. The physicians scored the majority (81.6%) of the VAs as good quality (score 3-5) while less than 13.2% of the records were assessed as poor-quality information (Table 3). About 66% of VAs had sufficient information to assign the underlying COD (score 3-5). Out of the

5,086 cases with complete information on both criteria, 61.3% had exactly the same score for quality and sufficiency. The kappa statistic was 0.45 (95% confidence interval (CI): 0.44–0.46), indicating a moderate level of agreement between the two dimensions.

Table 3

Physicians' assessment of quality and sufficiency of information from verbal autopsy (N = 5,375
for the South African National Cause of Death Validation Project 2017/18.

Score	What was the quality of information?	How sufficient was the information?
	%	%
1 (very poor)	1.9	10.5
2 (poor)	11.3	18.5
3 (good)	45.3	37.6
4 (very good)	31.7	21.9
5 (excellent)	4.6	6.2
Missing	5.1	5.3
Total	100.0	100.0

The two independent physician reviewers selected the same underlying cause of death in 56.9% of the VAs, while consensus was reached after initial disagreement for 31.7% and 10.0% required a panel decision to reach consensus, the remaining 1.3% were flagged for review by a maternal mortality specialist to exclude maternal deaths. In 68% of the deaths the cause of death was coded to a usable code. Overall, 8.7% of the underlying COD were coded to ill-defined signs and symptoms, and 16.6% of the causes were considered to have insufficient specification within an ICD chapter.

Figure 3 shows the leading causes of death from the physician reviews compared with vital statistics using the SA NBD list (27). A slightly higher proportion of the VAs (15.7%) were coded to ill-defined natural causes as compared to 13.3% of deaths in the Stats SA data. However, the ranking and proportions of the specified causes differed considerably. The VA identified 22.3% HIV/AIDS and 6.9% TB deaths whereas, in Stats SA data the HIV/AIDS and TB deaths accounted for 4.9% and 6.7% respectively (Fig. 3). According to WHO ICD-10 coding guidelines, TB deaths with co-morbid HIV are allocated HIV/AIDS as underlying cause while TB deaths without co-morbid HIV are coded to TB as underlying cause-of death. Compared with the SA NBD study,(29) albeit 5 years earlier, the VA profile appears more realistic than the Stats SA data which are known to have extensive misattribution of HIV as a cause of death (30).

An additional feature of the VA data has been the use of 4-digit ICD-10 codes. This makes it possible to identify the deaths due to HIV that resulted in TB (B20.0) which cannot be differentiated in the Stats SA data using 3-digit ICD-10 codes. Almost half (49.3%) of the HIV/AIDS deaths (604/1 224) had associated tuberculosis, while 61.3% of the TB deaths had underlying HIV (604/984). These are important metrics for monitoring HIV and TB programmes.

From Fig. 3, we also observe that the ranking of leading causes of non-communicable diseases differ

from Stats SA. The Stats SA data ranks diabetes highest followed by stroke and hypertensive heart

disease whereas it is the opposite for the VA data. The VA identified a slightly higher proportion of deaths from external causes than Stats SA (12.8% vs 11.2%).

Figure 4 shows different profiles of injury deaths. Homicide accounted for 30.8% of the VA deaths and only 13.8% of Stats SA causes. This appears to be related to the high proportion of ill-defined unintentional deaths (33.6%) in the Stats SA data shown in Fig. 4. The ranking of the external causes of death based on the physician reviewed VAs aligns more closely with the SA NBD study (29) and the 2017 Injury Mortality Survey (31) which rank homicide highest, followed by transport and then suicide.

CSMF derived by InterVA-5 and ranked to the top 15 causes from the VA list are compared with those from the physician coded VA in Fig. 5. Although there is considerable similarity in the selection of the underlying COD, physicians assigned more cases to indeterminate underlying COD than the InterVA-5 tool, and there are some notable differences in the CSMF. Physicians identified lower proportions of acute cardiac disease and digestive neoplasms, and higher proportions of HIV/AIDS related deaths, other unspecified non-communicable diseases and other unspecified neoplasms compared with InterVA.

Discussion

The study demonstrates that collecting COD data on a national scale using VA is achievable and provided good quality COD information. The participation rate of next of kin was good once they had been identified and located and 93.4% completed an interview. The physician reviewers found good quality COD information was provided in 83% of the VAs. Of the identified COD, only 8.7% were coded to ill-defined natural causes and 68% were assigned a specific and valid underlying cause of death. The remaining 16.6% were assigned an underlying cause of death without sufficient specification. Although the sample cannot be considered nationally representative, when compared with SA NBD estimates,(29) the VAs provided a more realistic proportion of HIV/AIDS deaths and better information related to external causes of death than COD data from CRVS system. Improved information related to injuries was obtained from the additional information provided by the narratives compared to Stats SA data. The use of experienced interviewers was beneficial as it resulted in a very low refusal rate.

Recruitment of next of kin through funeral parlours and Home Affairs offices was only partially successful because accessing next of kin in the context of the POPIA (20) is challenging and should VA be implemented nationally, a routine mechanism to facilitate the identification of deaths that occur outside of health facilities and making contact with the next of kin will need to be regulated.

The use of both physician review and an automated computerized model to ascertain probable COD provided similar results. However, physician review is time consuming and costly. Variability in the identification of the underlying COD between physician reviewers, further necessitates a review panel. Although automated computerized models such as InterVA are cheaper, faster, more consistent, and can be considered for routine coding of high volumes of VAs, quality assurance processes will still be important. Byass et al (32) compared physician coded VA with InterVA-4 assigned COD from some African and Asian countries and found strong concordance between physician coded VA and InterVA-4 assigned COD, however, they could not prove which approach provided the true cause of death (32).

Whilst the VA narrative is not used by the algorithms to assign a COD, clinicians found this information critical in determining the COD. In addition, the narrative provided an opportunity for the interviewer to establish a rapport with the respondent, thus we feel strongly that the narrative be conducted at the beginning of the interview.

Limitations

In this study, the COD patterns presented cannot be assumed to be nationally representative because of the low sample realisation (55%) of VAs achieved. However, the sample does have national coverage, and the results are largely consistent with the national burden of disease profile. The potential bias due to poor sample realization is not expected to have a major impact on the estimation of correction factors, which was the main objective of the project, however the extent and nature of potential biases remain unknown.

Strengths

Quality of the information collected by the interviewers indicates the success of the training conducted by experienced researchers from Health and Demographic Surveillance Sites and a local research organization. All the VA interviews were assessed by two independent physicians trained in medical certification of COD and how to interpret a VA. A systematic quality assurance process insured standardized interpretation of the VAs. The use of KoBoTool and other digital platforms enabled real-time monitoring of the fieldwork and the review of VAs. **Conclusions**

Despite challenges in recruiting the next of kin, our study has demonstrated the feasibility and community acceptability of conducting VAs to ascertain improved COD information. VA could be used at a national scale providing the recruitment of next of kin can be institutionalized into the routine processes for registration of death. It is expected that the use of VA will contribute information particularly for the deaths that occur outside health facilities. We recommend that specific questions in the 2016 WHO VA be clarified to make it easier for interviewers. Re-organizing narratives to be conducted at the beginning of the interview worked well as a way of engaging the respondent and orientating the fieldworker.

Abbreviations

VA Verbal autopsy **CSMF** Cause specific-mortality fractions Stats SA Statistics South Africa Stats COD Cause-of-death CRVS Civil Registration and Vital Statistics systems ICD-10 International Statistical Classification of Diseases and Related Health Problems CHAMPS Child Health and Mortality Prevention Surveillance POPIA Personal Information Act ODK Open Data Kit SA NBD South African National Burden of Disease

CDC Centers of Disease Control and Prevention UCOD Underlying cause-of death

Declarations

Ethics approval and consent to participate

The South African National Cause of Death Validation study was approved by the South African Medical Research Council Human Research Ethics (SAMRC) committee (EC004-2/2017). All methods were carried out in accordance with relevant guidelines and regulations as stated by the SAMRC, and according to the ethical guidelines and principles of the Department of Health: Ethics in Health Research: Principles, Processes and Structures (2015), as well as the Declaration of Helsinki (2013). The SAMRC Ethics Committee is registered as an institutional review board (IRB) with the Office for Human Research Protections (OHRP) of the United States of America Department of Health and Human Services, IRB organisation identifier: IRB00001569. The Medical Research Council's unique Assurance Number is FWA00002753, and the unique Organisation Number is IORG0001163 as well as OLAWA5726-01. In addition, further local ethics requirements, were adhered to, i.e., the Health Research Ethics Committees at provincial level for all nine provinces, as well as the district-level requirements for participating health facilities. The protocol was also reviewed in accordance with the Centers for Disease Control and Prevention (CDC) human research protection procedures. CDC investigators did not interact with human subjects, neither have access to identifiable data or specimens for research purposes, as required by the CDC. All the participants provided written informed consent to participate. Details on how informed consent was obtained have already been published (19).

Consent for publication

"Written informed consent to participate in the study and for publication of aggregate data were obtained from the next of kin of the deceased in most cases. In the remainder of cases written informed consent was obtained from an informant knowledgeable about the circumstances of death before they responded to the interview."

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

D.B., J.J. and P.G. conceived and designed the study. D.B., P.G., M.M., N.N., O.A., C.K., T.G. prepared data for analysis. M.M., N.N., B.N. and D.B. conducted the literature review and drafted the manuscript. D.B., P.G., M.M., N.N., O.A., C.K., T.G. and Z.N. interrogated and interpreted results. All authors critically reviewed the manuscript for important intellectual content and all authors approved the final version before submission.

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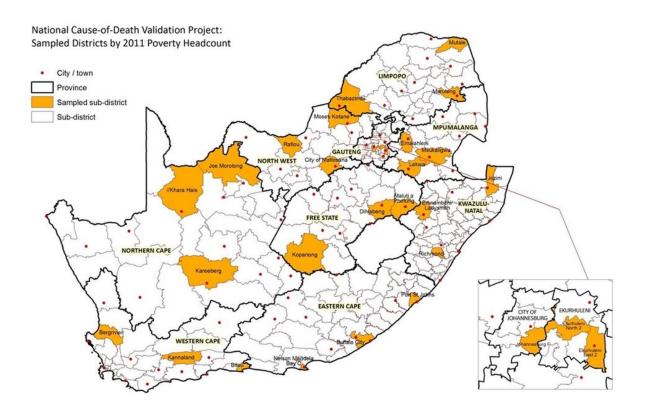
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Figures



Map of selected health sub-districts and provincial boundaries, South African National Cause of Death Validation Project 2017/18.

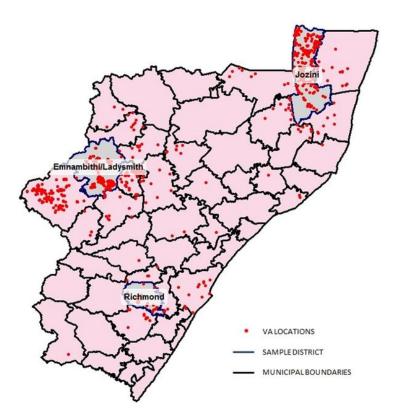


Figure 2

Map of KwaZulu Natal showing selected health sub-districts and the address of verbal autopsy interviews conducted for South African National Cause of Death Validation Project 2017/18

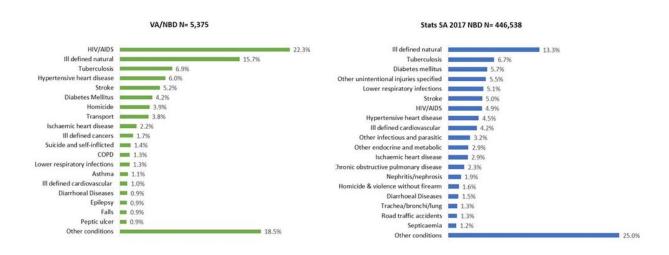


Figure 3

Leading causes of death based on 2017 Stats SA data compared with physician reviewed Verbal Autopsy data aggregated to National Burden of Disease list.

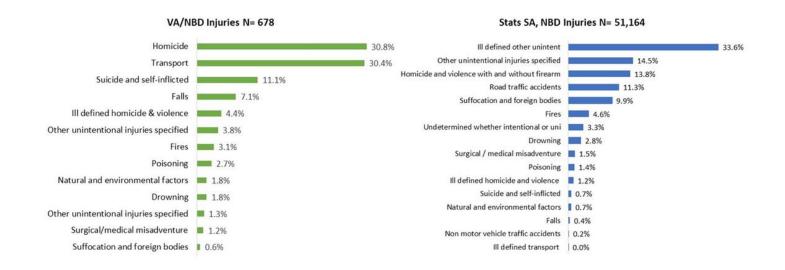


Figure 4

Leading injury-related causes of death Stats SA, 2017 and physician reviewed Verbal Autopsy data aggregated to National Burden of Disease list.

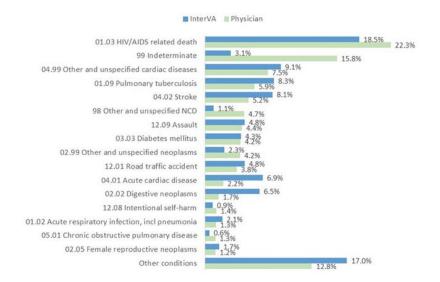


Figure 5

Comparison of verbal autopsy cause-specific mortality fractions based on physician reviews with InterVA-5 for the South African National Cause of Death Validation Project 2017/18.

Supplementary Files

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• Annexure1.docx