Needle autopsies highlight challenges in defining HIV-positive TB deaths using verbal autopsy

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Introduction

- Cause of death data are crucial to guide public health policy
- Verbal autopsy (VA) widely used, but has been validated against mostly suboptimal gold standards
- Full post-mortem the best way to determine cause of death, though needle autopsy (NA) is more acceptable to relatives and can provide high quality information
- In HIV+ individuals, differentiating between deaths due to tuberculosis (TB) and advanced HIV is difficult, but important to guide interventions to reduce mortality
- This ongoing cross-sectional study, nested within the TB Fast Track trial in South Africa, compared causes of death assigned by VA and NA in adults with advanced HIV

Methods

- Adult participants with CD4 count ≤150 cells/μL; not taking TB treatment or antiretroviral therapy
- Consent for NA was obtained from participants at enrolment or families after death

- **NA**: biopsies of liver, spleen, and lungs; aspiration of CSF; and broncheo-alveolar lavage
- Laboratory tests: histology; GeneXpert MTB/RIF; and MGIT, bacterial, and fungal cultures
- Preliminary NA causes of death assigned by investigators using demographic and NA data

- **VA** within one year of death by lay-workers using 2012 WHO tool
- VA causes of death assigned by InterVA-4 and SmartVA (using health care experience and narrative data)

- **Comparison**: causes of death categorised as 'TB', 'AIDS/HIV-related (not TB)', or 'Other'
- Cohen's kappa coefficient used to measure inter-rater agreement

Results

- Of 20 decedents with needle autopsy (NA) and verbal autopsy (VA) data, 12/20 (60%) were female, with median:
  - Age at death 37.8 (Interquartile range [IQR] 31-44) years
  - CD4 count at enrolment 31 (IQR 14-56) cells/μL
  - Time from enrolment to death 45 (IQR 20-103) days
  - Time from death to NA 4.5 (IQR 3-7) days
  - Time from death to VA 106.5 (IQR 60-178) days
- Causes of death assigned by NA and VA (as interpreted by InterVA-4 and SmartVA) were often different (Table 1)
- Agreement between NA and the two VA methods was no better than chance (Table 2: Cohen's kappa is a measure of inter-rater agreement, where 0=no agreement and 1=complete agreement)

Table 1: Causes of death assigned by needle autopsy and by verbal autopsy as interpreted by InterVA-4 and SmartVA

Patient	Cause of death assigned by		
	Needle autopsy (preliminary)	InterVA-4	SmartVA*
1	Tuberculosis	AIDS/HIV-related (not TB)	AIDS
2	AIDS/HIV-related (not TB)	Tuberculosis	AIDS
3	Tuberculosis	AIDS/HIV-related (not TB)	AIDS
4	AIDS/HIV-related (not TB)	Tuberculosis	AIDS
5	AIDS/HIV-related (not TB)	AIDS/HIV-related (not TB)	AIDS
6	AIDS/HIV-related (not TB)	Other	AIDS
7	Tuberculosis	Other	AIDS
8	Tuberculosis	AIDS/HIV-related (not TB)	AIDS
9	Tuberculosis	AIDS/HIV-related (not TB)	AIDS
10	Tuberculosis	Tuberculosis	AIDS
11	AIDS/HIV-related (not TB)	Tuberculosis	AIDS
12	AIDS/HIV-related (not TB)	Other	AIDS
13	AIDS/HIV-related (not TB)	AIDS/HIV-related (not TB)	AIDS
14	Tuberculosis	AIDS/HIV-related (not TB)	AIDS
15	AIDS/HIV-related (not TB)	AIDS/HIV-related (not TB)	AIDS
16	AIDS/HIV-related (not TB)	AIDS/HIV-related (not TB)	Other
17	Other	Other	AIDS
18	Tuberculosis	AIDS/HIV-related (not TB)	Other
19	AIDS/HIV-related (not TB)	AIDS/HIV-related (not TB)	AIDS
20	AIDS/HIV-related (not TB)	AIDS/HIV-related (not TB)	AIDS

*SmartVA 'AIDS' category includes death due to TB in an HIV-positive individual

Table 2: Agreement, expected agreement and Cohen's kappa when comparing causes of death assigned by NA to InterVA-4 and SmartVA

Methods compared	Agreement	Expected agreement	Cohen's kappa
Needle autopsy and InterVA-4	40%	42%	0.00
Needle autopsy and SmartVA	50%	50%	0.00

Figure 1: Venn diagram showing overlap of HIV and TB diagnoses between needle autopsy (NA) and InterVA-4 (IVA-4)

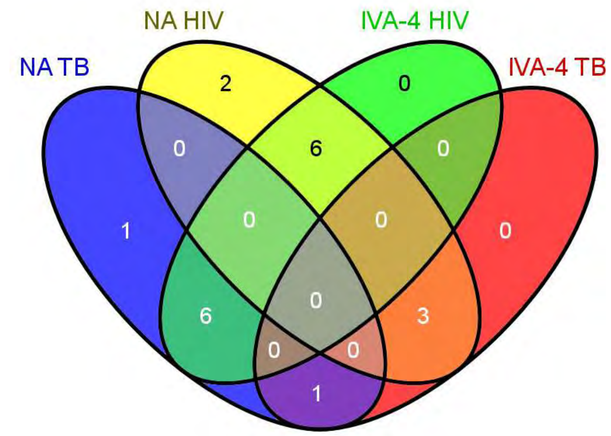


Figure 1 shows overlap between HIV and TB causes of death assigned by NA and InterVA-4: six cases assigned a TB cause of death by NA were assigned an HIV cause of death by InterVA-4; a further six cases were assigned an HIV cause of death by both NA and VA; only one case was assigned a TB cause of death by both NA and InterVA-4.

Conclusions

- These preliminary data suggest that current VA tools do not perform well at distinguishing between deaths due to TB vs. other HIV-related causes among individuals with advanced HIV disease: InterVA-4 appears to underestimate the incidence of TB deaths; and SmartVA does not attempt to distinguish between the two
- Alternative methods should be explored so that the burden of TB mortality can be more accurately recorded

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