

ISSUES IN PUBLIC HEALTH

Limitations and potential bias in vital registration data and tuberculosis mortality reporting in South Africa

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Tuberculosis (TB) is a curable disease, but continues to contribute to large numbers of deaths globally and remains among the leading causes of death in South Africa (SA). Evaluating trends in TB deaths and progress towards the End TB strategy target of zero deaths is particularly important to guide policy and practice in SA. TB deaths are complicated by its relationship with HIV, and SA's initial slow response to HIV compounded this. In considering the reported deaths in SA that identify TB as the underlying cause of death, it is important to be aware of potential limitations and sources of bias. We have examined the relationship between TB and HIV and the recording of underlying and contributing causes of death, and clarified the World Health Organization's methodology for estimating TB deaths.

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In October 2019, Loveday *et al.*^[1] published 'Figures of the dead: A decade of tuberculosis mortality registrations in South Africa' and analysed published reports of routine mortality data from Statistics South Africa (Stats SA) between 2006 and 2016. Declining reported tuberculosis (TB) mortality rates and the changing profile of TB deaths were described in the context of overall changes in South African (SA) mortality and the impact of HIV and access to antiretroviral treatment (ART).^[1] Following this important publication, we would like to discuss some additional key considerations regarding the methodology of evaluating TB mortality, as well as the use of the World Health Organization (WHO) modelled estimates of TB deaths.

SA has been identified as the epicentre of the TB and HIV co-epidemics,^[2] where the effect of HIV on TB mortality with consideration of age, sex and CD4+ count^[3-6] has been well described. Modelling has been used to predict the anticipated benefits of the scale-up of ART on population mortality,^[7,8] but the limitations regarding reliable cause-of-death data and the impact of changes in the SA TB programme are recognised as limitations in the SA model.^[8]

The relationship between TB deaths and HIV deaths in SA

Using the Stats SA 2018 mortality report,^[9] we have plotted the number of TB deaths and the number of HIV deaths along with the proportion of all deaths due to TB or HIV among South Africans. The decline in reported TB deaths and the proportion of all reported deaths due to TB in SA is notable and has been reported.^[1] These decreases coincide with an increase in reported HIV deaths in the country, and a doubling of the proportion of all reported deaths due to HIV from 2.4% in 2006 to 4.8% in 2016 (Fig. 1). Considering SA's early response to HIV and the history of AIDS denialism,^[10,11] it is likely that in the earlier years, deaths due to HIV were attributed to

TB or other opportunistic infections, with HIV documentation on TB death certificates limited by the context and stigma at the time. A modest study conducted in 2004 confirmed under-reporting of HIV among deaths in hospital, with only 15/32 (46.9%) deaths due to HIV correctly recording HIV on the death certificate.^[12] The increase in reported deaths due to HIV from 2009 is likely to reflect changes in perceptions of HIV and improved documentation of underlying causes of death rather than an actual increase in HIV deaths. From 2009, SA has scaled up HIV testing and the provision of ART,^[10] and HIV-related mortality has decreased significantly.^[8,13-15]

Underlying cause of death

The Stats SA mortality reports document the underlying cause of death and contributing causes of death. Consistently, since 2006, where HIV appears on the death certificate, it is almost exclusively attributed to be the final cause of death. TB as an underlying cause of death has been consistently declining, and in 2016, of the 47 206 reported deaths that mention TB in the death certificate, only 29 513 (62.5%) documented TB as the underlying cause of death (Fig. 2). In a community-based study in Cape Town, independent validation of causes of death as reported on death certificates showed poor reporting for TB and HIV.^[16] With corrected reporting, HIV as the cause of death increased by 53.6%, from 11.9% (84/703) to 18.3% (129/703).^[16] In addition, studies from SA have documented that up to 24% of adults dying at home had undiagnosed TB that was only confirmed at autopsy, highlighting the under-ascertainment of TB in SA.^[17] Where both HIV and TB are recorded on death notifications, HIV is registered as the underlying cause of death and TB may be recorded as a contributory cause. As discussed previously, HIV and AIDS stigma may have contributed to the under-reporting of HIV during earlier years, and over time, the inclusion of HIV as the

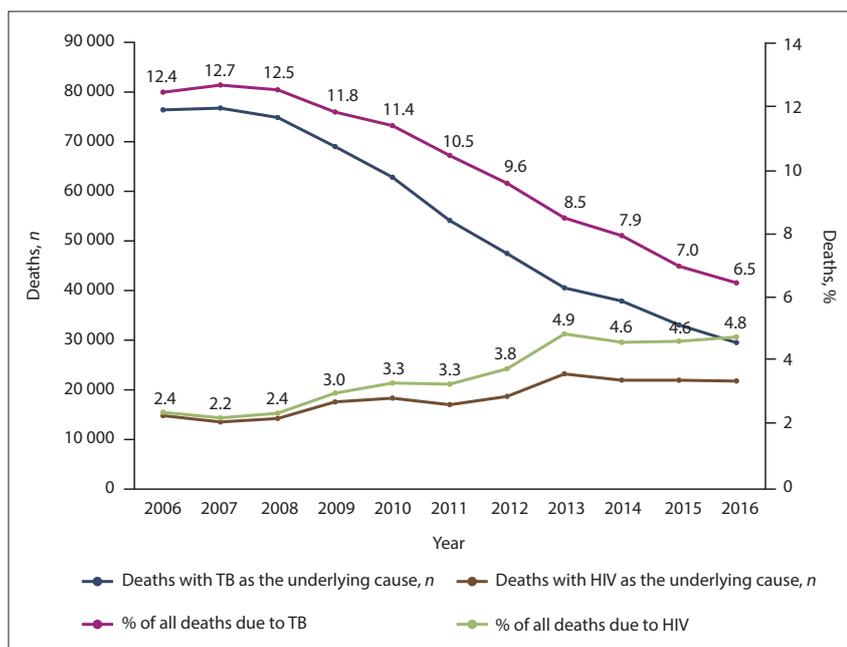


Fig. 1. Number of reported TB and HIV deaths as a proportion of total reported deaths in South Africa using Statistics South Africa reports, 2006 - 2016. (TB = tuberculosis.)

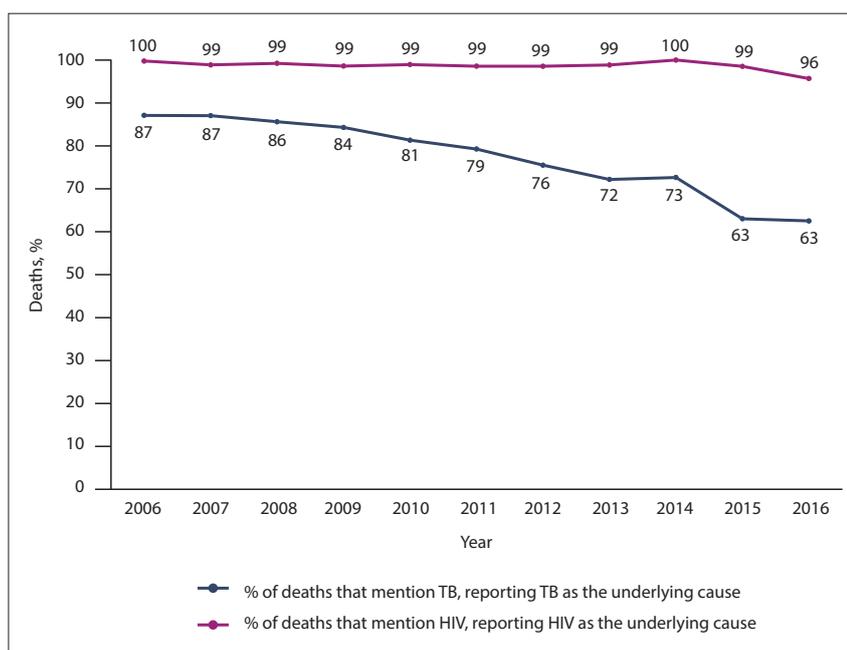


Fig. 2. The proportion of TB and HIV (underlying causes of death) as a proportion of all deaths where TB and HIV are mentioned on death notification forms, South Africa, 2006 - 2016. (TB = tuberculosis.)

underlying cause will decrease the proportion of TB deaths reported in people co-infected with HIV, as more deaths will be attributed to HIV.

The WHO modelled estimates of TB deaths

The WHO publishes an annual global TB report providing an assessment of the TB epidemic using data collected from 202 countries and modelled estimates for specific parameters.^[18] For the estimations of

incidence and mortality, a detailed document describing methods^[19] and country-specific data^[20] are publicly available. To inform these estimates, the WHO uses country data as reported through vital registers and adjusts estimates obtained from the Institute of Health Metrics and Evaluation to fit the overall WHO mortality estimates.^[19] The model then adjusts the estimates upwards to account for incomplete coverage of reporting of deaths, and ill-defined causes of death. Stats SA have documented that unreported

deaths declined from 7% in 2006^[21] to 4% in 2016,^[9] estimating >19 000 deaths unreported in SA in 2016. Ill-defined causes of death as reported using *International Classification of Diseases and Related Health Problems*, 10th revision (ICD-10) R00 - R99 include ill-defined conditions with no diagnosis classifiable elsewhere.^[9] In SA, between 2006 and 2016, ill-defined causes of death have consistently contributed to ~13% of reported deaths, with >60 000 deaths with unknown causes recorded in 2016.^[9] The WHO model assumes deaths among unreported deaths and ill-defined causes of death to be the same as the observed proportion of TB deaths in recorded deaths.^[19] This could be a conservative estimate of TB among unreported and ill-defined causes of death, as it is plausible that the proportion of TB deaths among ill-defined causes of death is in fact higher than the proportion of TB deaths among reported deaths. In addition, the WHO has noted the complexity of HIV and TB deaths, with HIV being recorded as the underlying cause among all HIV TB deaths.^[19] A correction has been applied for SA, with estimates of mortality among HIV-infected TB patients considering the gap between the estimated TB incidence and treated TB patients.^[19] SA is estimated to have notified only 75% of the estimated incident TB cases in 2018,^[18] and the probability of unreported TB among HIV deaths remains high. Fig. 3 documents the WHO estimates of TB mortality and case notification with a calculated proportion of TB deaths. A downward trend in estimated TB deaths is noted, but the absolute numbers from the WHO model vary significantly from the reported TB deaths by Stats SA.

Future directions

While we have demonstrated the complexity of the relationship between HIV and TB in the context of routine reporting of deaths in SA, we used secondary analysis of routine data sources only to substantiate this. We have identified that rigorous studies validating the Stats SA and WHO reports of death are required in SA, given the history of stigma and AIDS denialism. Despite the availability of an SA guide on the completion of death certificates including the process of death notification, the information required, and details on medical certification,^[22] implementation appears incomplete. Further research is required on the implementation of these guidelines, including a validation of death notification forms and medical records and an evaluation of healthcare workers' knowledge, attitudes and practices around death recording and reporting.

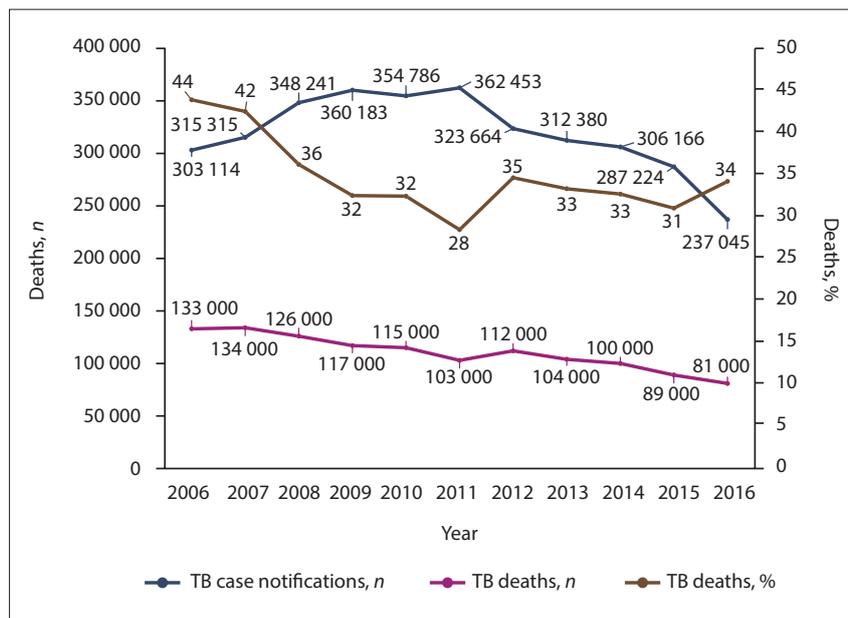


Fig. 3. World Health Organization estimates of TB deaths* and TB case notifications, with a calculated proportion of TB deaths per case notifications per year. (TB = tuberculosis; *TB deaths refer to any death in a patient with TB, regardless of the underlying or contributing cause.)

In summary, while reported TB mortality rates in SA have declined during the past decade, we need to consider changes in reporting of deaths that have occurred over the same period in the country. The SA history of HIV stigma and denialism and the complex interaction between TB and HIV need to be considered carefully before reported TB deaths are viewed in isolation. Global strategies have provided estimates of TB mortality considering some of the nuances described. These should be considered as we re-evaluate the SA progress towards the End TB strategy targets.

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