Identifying deaths from AIDS in South Africa

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Objective: To quantify the HIV/AIDS deaths misclassified to AIDS-related conditions in South Africa.

Design: Retrospective analysis of vital registration data.

Methods: Cause-specific death rates for 1996 and 2000–2001 were calculated using vital registration cause-of-death profiles applied to a model (ASSA2000) estimate of total mortality rates by age and sex. The difference in the age-specific death rates for these two periods was examined to identify conditions where there was a noticeable increase in mortality following the same age pattern as the HIV deaths, thus likely to be misclassified AIDS deaths.

Results: The increase in the age-specific death rates for HIV-related deaths showed a distinct age pattern, which has been observed elsewhere. Out of the 22 potential causes of death investigated, there were nine that increased in the same distinct age pattern (tuberculosis, pneumonia, diarrhoea, meningitis, other respiratory disease, non-infective gastroenteritis, other infectious and parasitic diseases, deficiency anaemias and protein energy malnutrition) and could be considered AIDS-related conditions. The increase in these conditions accounted for 61% of the total deaths related to HIV/AIDS. When added to the deaths classified as HIV-related on the death certificate, the total accounts for 93% of the ASSA2000 model estimates of the number of AIDS deaths in 2000.

Conclusion: As a large proportion of AIDS deaths appear to be classified to AIDS-related conditions, without reference to HIV, interpretation of death statistics in South Africa cannot be made on face value as a large proportion of deaths caused by HIV infection are misclassified.

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Keywords: death statistics, AIDS, South Africa, HIV, AIDS-related conditions

Introduction

South Africa is currently experiencing a severe HIV/AIDS epidemic [1]. A seroprevalence of HIV infection of 26.5% was reported from a national survey among women attending public sector antenatal clinics in 2002 [2], a population-based survey conducted in 2002 reported a national HIV prevalence among people 2 years and older of 11.4% [3], and the numbers of reported deaths have shown an unabated rise, particularly among young adults [4].

Monitoring the actual number of AIDS deaths is challenging owing to both the under-registration and the misclassification of the causes of death, problems that occur in many developing countries. Death certification in South Africa has improved since 1994 and is now reasonably complete, with estimates of coverage of adult deaths currently over 90% [5]. Official publication of cause-specific mortality data is, however, slow. The last complete report was for 1996 [6], although a report on a 12% sample of deaths for 1997–2001 has been published [7]. Considerable and controversial debate has taken place

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in South Africa over the extent of AIDS mortality. A low estimate of the proportion of deaths from HIV/AIDS of 8.7% in 2001 takes into account only deaths explicitly reflecting HIV/AIDS on the death certificate [7]. Higher estimates for the same period of 30% are derived from mathematical modeling of the epidemic and include the deaths from other conditions as a result of underlying HIV infection [8].

The standard practice for classifying cause-of-death statistics is to identify the underlying cause of death, as this should be targeted for public health intervention. The *International Classification of Diseases* (ICD-10) defines the underlying cause of death as 'the disease or injury which initiated the train of morbid events leading directly to death' [9]. In the case of AIDS, the ICD-10 classifies a death as having HIV as an underlying cause when HIV is present and the person dies from a subsequent co-morbidity mediated by the HIV (codes B20–B24). For example, HIV with tuberculosis has code B20.0. The World Health Organization introduced a case definition for AIDS for developing countries that was initially based upon clinical criteria [10]. This was later expanded to include HIV serology and AIDS-defining illnesses [11]. In a country such as South Africa, where the HIV status of the deceased is often unknown or the medical certifier does not have access to a full medical history, mis-classification to the immediate cause of death rather than the underlying cause often takes place. Furthermore, since 1992 it has been possible for traditional headmen to complete an abbreviated death notification form, often resulting in misclassification of the cause of death to a generalized ill-defined rubric of ICD, in some rural areas.

The present study used available cause-of-death data to estimate cause-specific mortality rates and the changing age-specific distribution of deaths between 1996 and 2000–2001. The characteristics of the distribution were then utilized to estimate the contribution of HIV to mortality, even in the face of misclassification of deaths. Although deaths certified as AIDS accounted for 2.2% of all deaths in the 1996 data, this dataset is used as a baseline as it displayed significantly less under-registration of deaths than in earlier years [5].

Methods

The cause-of-death data for 1996 were obtained as individual microdata records from Statistics South Africa; these records had been used to compile the 1996 official report on deaths in South Africa [6]. The cause-of-death data for the years 2000–2001 combined were obtained as the microdata records for the 12% sample of deaths officially analysed by cause of death for the period 1997 to 2001 [7]. The underlying causes were coded by Statistics South Africa using the ICD-10 classification at three-character level [9] for both datasets and were subsequently aggregated according to the South African Burden of Disease list for analysis [8]. Data were broadly grouped in the analysis owing to lack of precision in the data even to the three-character rubric; this was a result of limited specificity on death certificates.

Cause-specific death rates were calculated for 1996 and 2000–2001 by age and sex. The most recent data for years 2000 and 2001 were used in combination in order to get a more robust estimate from a larger number of deaths. The estimated total number of deaths and the South African population by age and gender for the years analysed were obtained from the ASSA2000 Demographic and AIDS model of the Actuarial Society of South Africa [12]. The ASSA2000 model corrects for underestimation in the 1996 census as well as for incomplete registration of deaths in a consistent manner across all years. The model is, among other parameters, calibrated to the total adult deaths recorded by the Department of Home Affairs and is adjusted for under-reporting. The cause-specific mortality rates were calculated from the ASSA2000 model estimate of the all-cause mortality rate, multiplied by the observed proportion of deaths from a specified cause in that age and sex group, from the death registration datasets mentioned above.

Table 1 shows the causes of death from the South African Burden of Disease list, selected for investigation for an underlying cause of death of HIV. Based on the literature, AIDS indicator conditions, including tuberculosis, pneumonia, diarrhoea, meningitis, wasting, septicaemia, lymphoma, cervical cancer, candidiasis, cryptococcosus and other opportunistic infections, were selected [11,13]. Clinical and autopsy surveys suggested that myocarditis (I40) and cardiomyopathy (I42) [14] should also be considered potential candidates for investigation as HIV-related deaths. On the basis of experience in Zimbabwe, which suggested that many HIV deaths were misclassified to malaria [15], malaria was also investigated. Maternal deaths were also selected on the basis of the most recent confidential inquiry into maternal deaths, which showed that the proportion of deaths from non-pregnancy-related infections (mainly AIDS) had increased dramatically between 1998 and 1999–2001 [16]. Kaposi's sarcoma (C46) was added to the HIV-related deaths (B20–B24) as the 1985 Bangui definition for AIDS considered the presence of Kaposi's sarcoma as sufficient for the diagnosis of AIDS for surveillance purposes [11]. Causes of death with no known association with AIDS, which had shown a marked rise during this period, were also investigated to ascertain whether this rise could be attributed to AIDS.

The difference in the cause-specific mortality rates between 1996 and 2000–2001, as well as the difference in the age-specific distributions of the death rates in these

Table 1. Conditions selected for investigation.

Cause of death	ICD-10 codes	Notes
HIV/AIDS and related conditions		
HIV/AIDS	B20–B24,C46	C46: Kaposi sarcoma
Tuberculosis	A15–A19, B90, J90	
Diarrhoeal disease	A00–A04, A06–A09	A09: Diarrhoea of presumed infectious origin
Bacterial meningitis	A39, G00–G03	G03: Meningitis caused by other and unspecified causes
Other infectious and parasitic disease	A05, A20–A28, A31, A32, A38, A42–A49, A65–A69, A70–A74, A75–A79, A81–A89, A90–A99, B00–B02, B04, B07–B09, B25–B34, B35–B37, B38–B45, B46–B49, B57–B64, B66–B73, B75, B82–B89, B94–B99	A81: includes progressive multifocal leukoencephalopathy B00: herpes simplex infections B25: cytomegaloviral disease B37: candidiasis B38: coccidiomycosis B39; histoplasmosis B45: cryptococcosus B58: toxoplasmosis B59: pneumocystosis
Lower respiratory infections	J10–J18, J20–J22	
Protein energy malnutrition	E40–E46	
Deficiency anaemias	D50–D53, D64	D64: other anaemias including unspecified
Cervix cancer	C53	
Lymphoma + multiple myeloma	C81–C90, C96	
Septicaemia	A40–A41	
Alzheimer's disease and other dementias	F01–F02, F03–F09, G30–G31	F03: unspecified dementia G31: other degenerative diseases of nervous system
Other nervous system disorders	G08, G10–G12, G23–G25, G36–G37, G43–G47, G50–G58, G60–G64, G70–G72, G80–G83, G90–G93, G94–G98	G37: other demyelinating diseases of CNS
Inflammatory heart disease	I30, I33, I38, I40, I42	I40: myocarditis I42: cardiomyopathy
Conditions with increased mortality rates		
Trachea/bronchus/lung carcinoma	C33–C34	
Melanoma	C43	
Epilepsy	G40–G41	
Other endocrine and metabolic disease	D55–D63, D65–D89, E03–E07, E15–E16, E20–E34, E65–E68, E71–E86, E87–E89	E86: volume depletion E87: other disorders of fluid, electrolyte, and acid–base balance
Other non-infectious gastroenteritis and colitis	K50–K52	K52: other non-infective gastroenteritis and colitis
Other respiratory disease	J30–J39, J47, J60–J68, J70, J80, J82–J84, J92–J98	J98: other respiratory disorders
Other conditions		
Maternal conditions	O00–O99	
Malaria	B50–B54	

two periods, was examined to identify those conditions where there was both a noticeable increase in mortality and the increase followed the same pattern as the HIV deaths; these conditions, therefore, were likely to be misclassified HIV deaths. Death rates were considered up to 59 years for women and 64 years for men, based on the gender differences in the age distribution of HIV prevalence. The excess deaths in the conditions following the distinct age profile in increase were attributed to AIDS. The number of deaths attributed to AIDS for each of these conditions was calculated by multiplying the rate difference by the population size for each age and sex group. The proportion attributed to AIDS for each of these conditions was calculated. Finally, the percentage contribution from each condition to the total excess deaths attributed to AIDS was calculated.

Results

According to the ASSA2000 model, the total annual number of deaths in South Africa in 1996 was 387 784 and in 2000–2001 was 556 585 [12]. The crude death rate per 1000 population increased from 9.4 to 12.4 for the respective periods. Only 326 186 deaths were registered in 1996 (84%); there were 117 773 deaths in the 2000–2001 period within the 12% sample of deaths from Statistics South Africa.

The increase in the age-specific death rates for HIV/AIDS, as recorded on the death certificate (Fig. 1), showed a distinct age pattern, with a marked increase of almost 7 per 1000 in child deaths and a peak increase of 2.7 per 1000 at age 30–34 years for women and 2.6 per

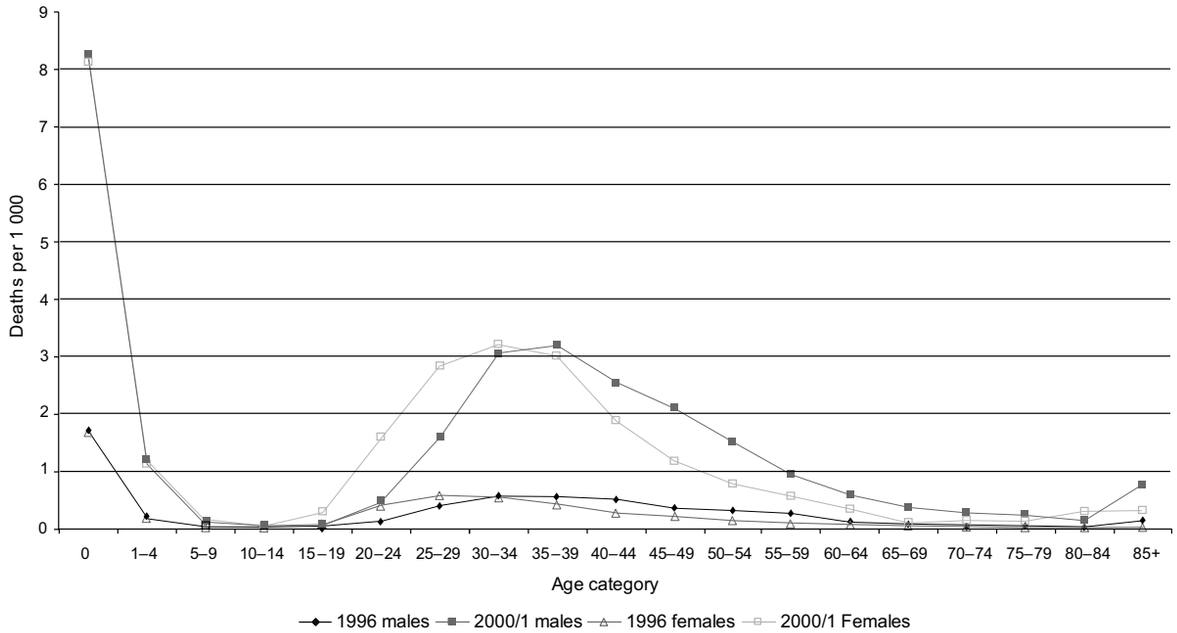

Fig. 1. Estimates of HIV/AIDS death rates in 1996 and 2000–2001 by age and sex in South Africa.

1000 at 35–39 years for men. The extreme older ages were omitted from the figure as the data displayed a small increase among those 85 years and older, which was considered an artefact.

Out of the potential 22 causes of death investigated, there were 11 that had increases following the same distinct age pattern typical of HIV/AIDS. Of these, nine were selected for estimating the excess caused by AIDS, as the increase in actual numbers of deaths for two of the causes (other endocrine and metabolic diseases and inflammatory heart disease) were small. It was interesting to note that the single ICD-10 codes that increased in other endocrine and metabolic diseases were non-specific clinical signs, namely E86 (volume depletion) and E87 (other disorders of fluid electrolyte and acid–base balance). The difference in rates for adults for the selected AIDS-related conditions are presented in Fig. 2. In all of these AIDS-related conditions, the difference peaks for women at a younger age than for men. Some conditions that had displayed an increase during the study period were considered not to be AIDS-related conditions because the characteristic age pattern was not observed. For example, melanomas displayed an increase across the age range greater than 60 years and no change in younger adult ages (Fig. 3). The fact that the characteristic age pattern seen in all the AIDS-related conditions was not observed for melanoma demonstrates that this characteristic pattern is not an artefact of the estimation procedure used in this study.

The estimated contribution from the identified AIDS-related conditions to the total HIV adult deaths is given in Table 2. For males, AIDS-related conditions contributed 60.2% (31 999 out of 53 185 deaths) and for females 57.8% (34 345 out of 59 445 deaths) of the total HIV-linked adult deaths. Tuberculosis, the majority of which is pulmonary, and lower respiratory infections accounted for approximately 80% of the excess deaths attributed to AIDS in adult males and 70% in adult females. In children under 5 years of age, AIDS-related conditions contributed 65.6% (26 715 out of 40 724) of the total deaths from HIV infection (Table 3). In contrast to adults, lower respiratory infections, diarrhoea and protein–energy malnutrition accounted for approximately 85% of the excess deaths in children. The total HIV deaths for all ages estimated using this method accounted for 93% of the estimates derived using the ASSA2000 model.

Discussion

Mortality rates in South Africa have increased between 1996 and 2000–2001. This appears to be mainly a result of an increase in mortality related to HIV; the change followed a distinct age pattern, with the increase in mortality concentrated amongst young children, women aged 25–39 years and men aged 30–49 years. There was a peak in mortality rates approximately 5 years earlier in women than in men [4,5]. The age pattern is consistent with the age pattern observed for HIV seroprevalence in South Africa, with an age lag [3]. A similar mortality age pattern has been observed in northern Namibia [17], Zimbabwe [15] and Uganda [18] and has been attributed to AIDS. These findings are also corroborated by Africa

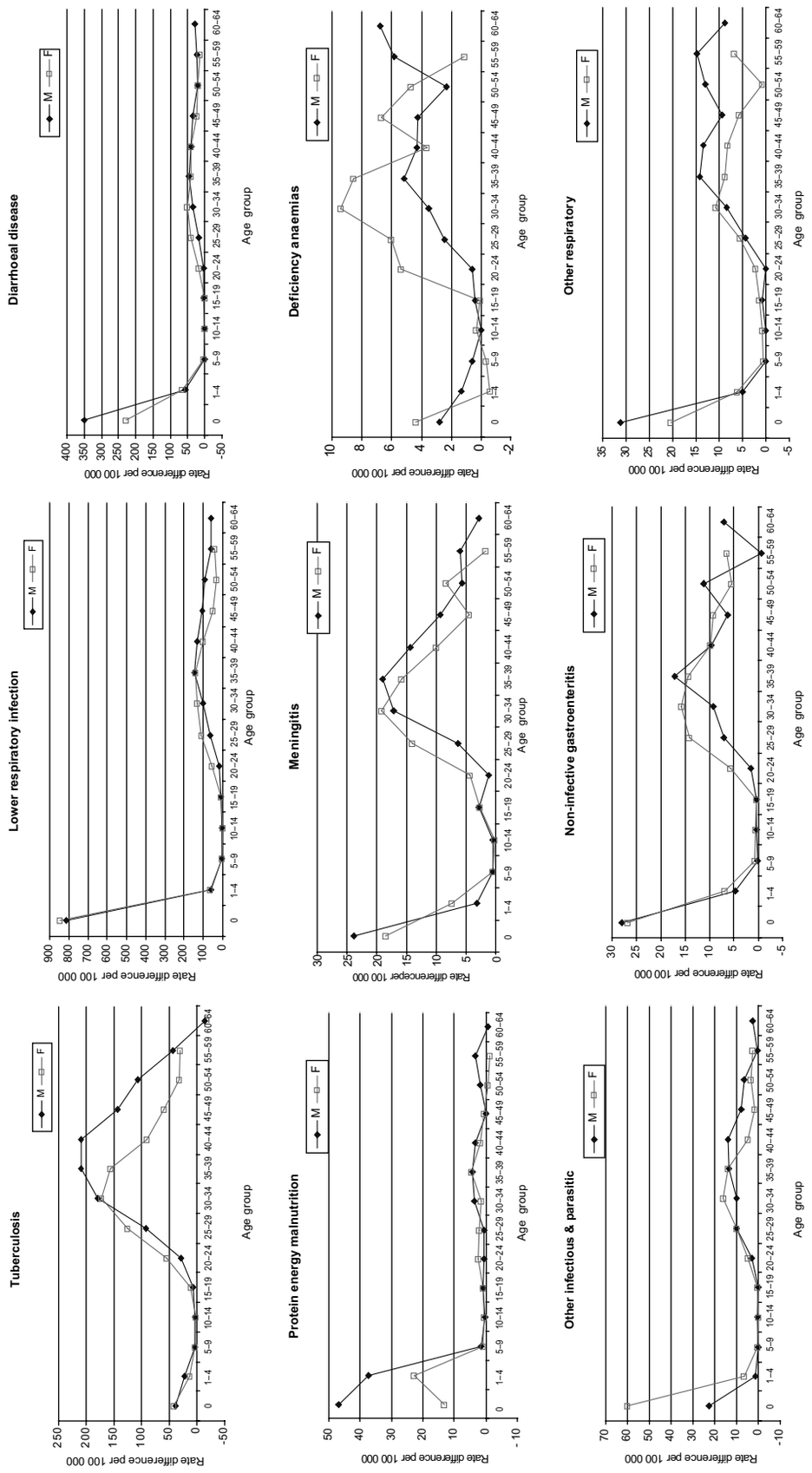

Fig. 2. Differences in age-specific death rates for selected HIV/AIDS related conditions between 1996 and 2000–2001 in South Africa.

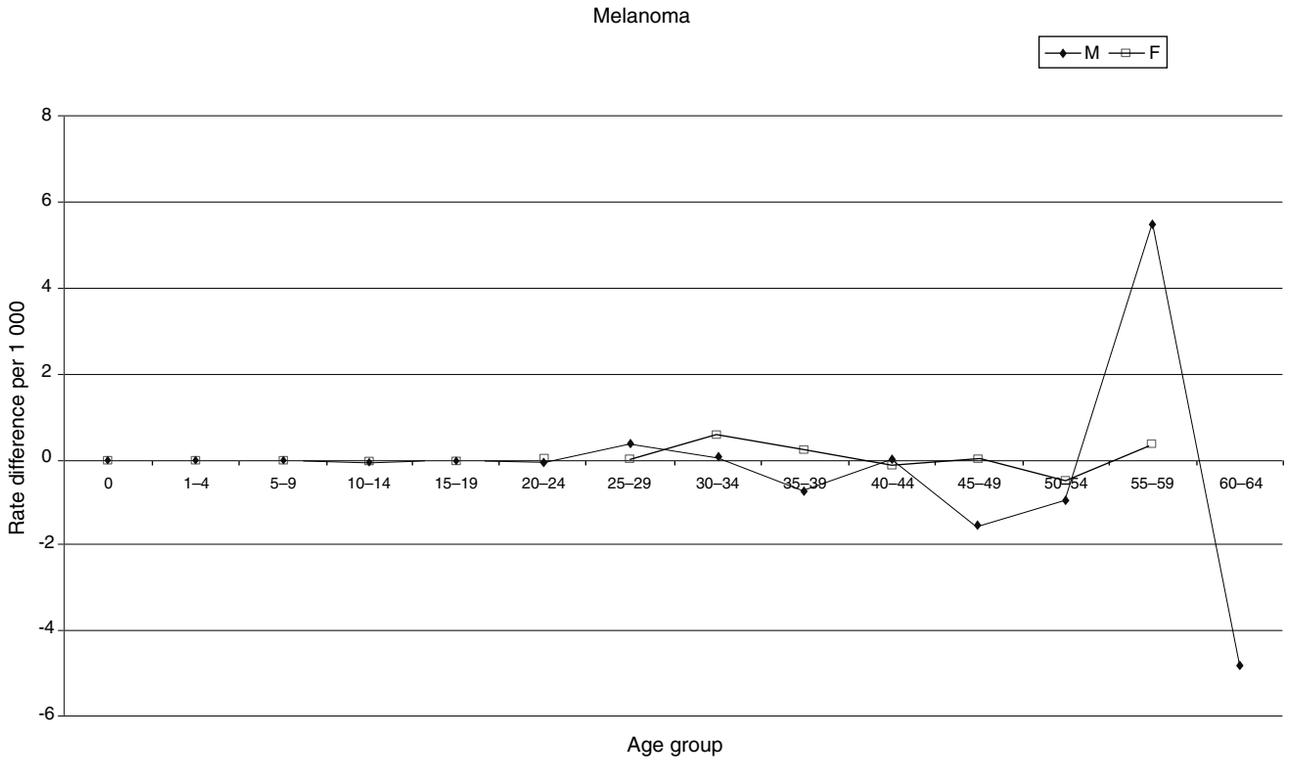

Fig. 3. Differences in age-specific death rates for melanoma between 1996 and 2000–2001 in South Africa.

Table 2. Estimation of HIV/AIDS deaths in adults, 2000–2001.

	Males 15–64 years				Females 15–59 years			
Cause of death	Total deaths from condition (A)	Excess deaths attributed to AIDS (B)	Percentage attributed to AIDS (B/A)	Excess deaths as percentage of total excess deaths	Total deaths from condition (A)	Excess deaths attributed to AIDS (B)	Percentage attributed to AIDS (B/A)	Excess deaths as percentage of total excess deaths
Conditions								
Tuberculosis	29 167	15 026	51.5	47.0	19 768	13 329	67.4	38.8
Lower respiratory infections	14 861	9747	65.6	30.5	14 521	11 350	78.2	33.0
Diarrhoeal diseases	4493	2823	62.8	8.8	5251	4080	77.7	11.9
Bacterial meningitis	1966	1101	56.0	3.4	1898	1406	74.1	4.1
Other respiratory disease	2047	879	43.0	2.7	1378	832	60.4	2.4
Non-infective gastroenteritis	1146	875	76.4	2.7	1603	1299	81.0	3.8
Other infectious and parasitic disease	1215	956	78.7	3.0	1205	989	82.1	2.9
Deficiency anaemias	524	331	63.2	1.0	1064	766	72.0	2.2
Protein energy malnutrition	533	260	48.8	0.8	420	294	70.0	0.9
Total (I)	55 949	31 999	57.2	100.0	47107	34 345	72.9	100.0
HIV AIDS (explicitly certified) (2000–2001) (II)		21 186				25 100		
HIV/AIDS (empirical) (I+II)		53 185				59 445		
HIV/AIDS (from ASSA2000 model)		57 887				64 130		

Table 3. Estimation of HIV/AIDS deaths in children under 5 years, 2000–2001.

Cause of death	Total deaths from condition (A)	Excess deaths attributed to AIDS (B)	Percentage attributed to AIDS (B/A)	Excess deaths as percentage of total excess deaths
Condition				
Lower respiratory infections	19 866	12 783	64.3	47.8
Diarrhoeal diseases	19 982	7453	37.3	27.9
Protein–energy malnutrition	7789	2784	35.7	10.4
Tuberculosis	2231	1449	64.9	5.4
Bacterial meningitis	1952	632	32.4	2.4
Other respiratory diseases	1000	575	57.5	2.2
Non-infective gastroenteritis	554	325	58.7	1.2
Other infectious and parasitic disease	778	644	82.8	2.4
Deficiency anaemias	161	73	45.3	0.3
Total (I)	54 313	26 718	49.2	100.0
HIV AIDS (explicitly certified) (2000–2001) (II)		14 009		
HIV/AIDS (empirical) (I+II)		40 727		
HIV/AIDS (ASSA 2000)		42 749		

Centre demographic surveillance data, which showed a recent massive rise in adult mortality in rural KwaZulu Natal, South Africa, following a similar age pattern and accounted for by AIDS deaths [19].

This study identified nine causes of death that clearly display a characteristic age pattern in the increase, suggesting that these conditions are HIV related. The proportion of AIDS deaths attributed to these conditions was similar between males and females but differed in cause-of-death profile. Respiratory conditions accounted for the majority of the excess deaths attributed to AIDS. Diarrhoea accounted for a relatively low proportion of these deaths in adults, but this may reflect preferential death certification to respiratory causes. Differences were also observed between adults and children, with tuberculosis ranking highest amongst adults and lower respiratory tract infections ranking highest amongst children. Data based on autopsy surveys in West Africa [20,21] and Botswana [22] have shown similar findings, with tuberculosis being the most common cause of death in HIV-positive adults and respiratory tract diseases and malnutrition being the most dominant causes of death in HIV-positive children. Clinical reports have also emphasized the importance of pulmonary infections, diarrhoea and malnutrition as causes of death in HIV-positive children [21].

A recent study at a paediatric teaching hospital in Cape Town, South Africa revealed that the undercertification rate for HIV-related deaths was 11.4% and that a further 29.5% of HIV-related deaths were classified using non-specific terms that could lead to inaccurate classification of the deaths by nosologists [23]. In an ideal setting, such cases would have HIV recorded as the underlying cause of death on the death notification form to ensure coding of these deaths to HIV/AIDS. There are a number of factors that could explain these discrepancies, which also extend to adult ages. First, the HIV status of the patient may be unknown and the immediate cause of death may be reported. Second, there is a strong social stigma attached to HIV/AIDS in South Africa and many patients are reluctant to reveal their HIV status and request their doctors not to do so. In addition, many funeral and life insurance policies specifically exclude cover for death from HIV/AIDS, and patient's families may exert pressure on doctors not to certify the death as such in order to claim the benefits. There are anecdotal reports of doctors being threatened by family members in such cases. Doctors' concerns about the maintenance of confidentiality of cause-of-death details on the death certificate have also been cited as a reason for incomplete details being given on the medical certification of the cause of death [24]. These factors must be seen against a background of heightened politicization of the debate about the size of, and the government's response to, the AIDS epidemic in South Africa. This debate has unfortunately sown confusion about the urgency of the epidemic, delayed the implementation of interventions aimed at reducing transmission and mortality, and contributed to the stigma attached to the disease. Given the political climate and the resultant disincentives for reporting HIV/AIDS in the South African setting, it is probably not surprising that the level of reporting HIV or AIDS as a cause of death is low. This is in stark contrast to Brazil, where a policy of universal access to free treatment [highly active antiretroviral therapy (HAART)] was implemented early in the epidemic, and the level of reporting of HIV on the death certificate is over 85%, as shown in a study of death certificates for females aged 10–49 years of age [25]. It is hoped that the level of reporting will improve in South Africa now that a HAART programme has been introduced.

Unlike many countries in sub-Saharan Africa, South Africa has prioritized the collection of reliable cause-of-death statistics to inform health policy [26] and extensive efforts have been made to improve vital registration [27].

However, this study has shown that the data need careful interpretation and there is a need to take the current levels of misclassification of causes of death into account. Efforts need to be made to reduce tendencies to misclassify causes of death in the future and identify ways in which the confidentiality of information regarding cause of death can be maintained.

The lack of reliable AIDS death statistics has led to debate about the value of making HIV infection a notifiable condition with mandatory anonymous reporting to a national database [28]. The proponents for this approach consider that it is the only way to obtain reliable statistics, while the opponents argue that, based upon the poor performance of other notification systems in South Africa, it is unlikely to achieve this goal and will yield limited public health value. Building complementary surveillance systems such as population-based prevalence surveys and sentinel surveillance among groups such as attendees at tuberculosis clinics and risk-behaviour surveys is more likely to provide data that can be used together with models to inform policy. With the implementation of the comprehensive treatment plan in the South African public sector, including antiretroviral therapy, there is clearly an opportunity to develop the HIV/AIDS surveillance system. This will require mechanisms to ensure confidentiality. Furthermore, it must be expected that the data will still be incomplete and that it will be essential to analyse carefully the various data sources to obtain meaningful estimates of the disease burden of HIV and AIDS, and that there will be a need to align the clinical case definition and surveillance case definition.

This study highlights the importance of rapid surveillance of the age and sex profile of deaths. If death registration were complete, the effects of a severe epidemic would be reflected in a change in both the overall number and age distribution of total deaths, regardless of any misclassification of or protocol defining a death from HIV or AIDS. Even in the situation where registration of deaths has been improving, tracking the number of registered deaths has enabled us to discern the rapid change in adult mortality [4].

Nine conditions, some of which are known to be opportunistic infections associated with HIV, displayed an increase in age-specific death rates when compared with those experienced 5 years earlier that followed a characteristic AIDS age distribution. The excess deaths based on the increased mortality rates for these conditions, together with the deaths explicitly classified as HIV, agree with the ASSA2000 model estimates of the total number of AIDS deaths and enables us to estimate the actual proportion of deaths from AIDS despite inadequate information about the underlying causes. The study demonstrates that cause-of-death statistics in South Africa cannot be interpreted on face value because a high proportion of AIDS deaths appear to be classified as AIDS-related conditions without reference to HIV as an underlying cause. This highlights the importance of surveillance of the age pattern of mortality in such a setting.

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