Abstract

Objective To investigate trends in adult mortality in a population serviced by a public-sector antiretroviral therapy (ART) programme in rural South Africa using a demographic surveillance system.

Methods Verbal autopsies were conducted for all 7930 deaths observed between January 2000 and December 2006 in a demographic surveillance population of 74 500 in the Umkhanyakude district of northern KwaZulu-Natal province, South Africa. Age-standardized mortality rate ratios (SMRRs) were calculated for adults aged 25 to 49 years, the group most affected by HIV, for the two years before 2004 and the three subsequent years, during which ART had been available.

Findings Between 2002–2003 (the period before ART) and 2004–2006 (the period after ART), HIV-related age-standardized mortality declined significantly, from 22.52 to 17.58 per 1000 person–years in women 25–49 years of age (P < 0.001; SMRR: 0.780; 95% confidence interval, CI: 0.691–0.881), and from 26.46 to 18.68 per 1000 person–years in men 25–49 years of age (P < 0.001; SMRR: 0.706; 95% CI: 0.615–0.811). On sensitivity analysis the results were robust to the possible effect of misclassification of HIV-related deaths.

Conclusion Overall population mortality and HIV-related adult mortality declined significantly following ART roll-out in a community with a high prevalence of HIV infection. A clear public health message of the benefits of treatment, as revealed by these findings, should be part of a multi-faceted strategy to encourage people to find out their HIV serostatus and seek care.

Introduction
Since 2003, there has been unprecedented global investment in delivering antiretroviral therapy (ART) for HIV infection to populations in resource-poor countries. The benefit of ART to an individual with advanced HIV infection is well established,1–5 and programmes for its widespread introduction6 can reduce the substantial increase in HIV-related adult mortality7,8 that has occurred as the HIV pandemic has developed. The effect of ART roll-out can be measured in many ways – treatment coverage, behaviour change, the emergence of resistance, etc.9,10 – but ultimately changes in population mortality are the most important measurable effect. In particular, national governments and international agencies faced with limited resources and competing demands need scientifically robust estimates of the potential effect at the population level of making a huge investment in ART roll-out.11

South Africa has over 5.5 million HIV-infected individuals and 14% of the world’s HIV+ population.8 The HIV pandemic is estimated to have reduced life expectancy in the country by about 13 years, from 64 in 1990 to 51 in 2005.12 The northern province of KwaZulu-Natal carries the greatest burden of infection, with an estimated12 1.54 million HIV+ residents, which is more than the combined total of HIV+ people in Botswana and Uganda.

We composed an open cohort within an ongoing demographic surveillance system to investigate adult all-cause and HIV-related mortality trends in 2000–2006 in a population serviced by a well-functioning, public-sector ART programme initiated in 2004.13

Methods

**Study area and population**

The Africa Centre for Health and Population Studies hosts a demographic surveillance programme in the district of Umkhanyakude in the province of KwaZulu-Natal, South Africa.13,14 Although it is largely rural, the demographic surveillance area (DSA), consisting of 435 square kilometres (km²), also includes a township and periurban informal settlements. Biannual surveillance visits to all homesteads within the DSA were performed by fieldwork teams to record births, deaths and any in- and out-migrations of household members. All household members reported during surveillance visits were
followed up, whether or not they were residing in the homestead in subsequent visits. Thus, at each surveillance visit a key household informant is presented with a list of the household members recorded at the previous visit, and the residential and household membership status of each individual – i.e. whether or not he or she still lived in the homestead or had moved or died since the last visit – is recorded. The preferred key informant is the household head or a senior household member if the household head is absent. If by the fourth repeat visit to a homestead no suitable key informant is present, the case is referred to a tracking team that makes three more attempts, after hours or over weekends, to contact the key informant. The identity of the key informant is recorded and attempts are made to contact the same one for every visit. Household membership is self-defined on the basis of links to other household members. A resident is a member of a household who normally lives in the same homestead as the other members, whereas a non-resident household members normally lives elsewhere but retain links to the household. Individuals cease to be members of households when they terminate such links or die. Migrations to or from places outside the DSA (external migrations) were distinguished from those within the DSA (internal migrations). On average, 99.5% of all households participated in the biannual surveillance rounds, and the constant review of household members ensured high data quality and reduced the likelihood that any death would be missed.

Since the beginning of 2003, the HIV infection status of local residents of Umkhanyakude district aged 15–49 years (females) and 15–54 years (males) has been determined through separate annual serosurveillance. In the study population, the prevalence of HIV infection has increased steadily since the early 1990s. In 2004, it had reached 21.5% among residents aged 15–49 years and was highest among women aged 25–29 years (51%) and men aged 30–34 years (44%). But while in 2007 prevalence was essentially unchanged, mortality appears to have decreased steadily. In 2000, 74% of deaths among women and 61% of deaths among men aged 15–44 years were due to HIV-related causes, but an analysis of mortality trends by HIV serostatus in the population under HIV surveillance showed a progressive decline in mortality among HIV-infected individuals from 2004 to 2006.
Mortality data
All deaths notified in both residents and non-residents were followed up by a verbal autopsy interview conducted an average of 6 months after the person’s death by a trained nurse. The closest caregiver of the deceased was interviewed and asked to provide a narrative of the circumstances leading up to the death of the individual and to reply to a checklist of signs and symptoms and a standard structured questionnaire based on the INDEPTH standard questionnaire for verbal autopsies. Two clinicians independently assigned the cause of death on the basis of the information collected during the verbal autopsy and their clinical judgement. A third clinician reviewed and codified the causes of death using the International classification of disease, 10th revision (ICD-10). If the two clinicians disagreed, the third one organized a consensus meeting among all three clinicians. If consensus on the cause of death could not be reached in this meeting, the cause of death was recorded as “undefined”. This was also done if no consent was given for the verbal autopsy interview or no suitable interviewee could be found. The ICD-10 codes were mapped into global burden of disease groups I, II and III with the exception of tuberculosis and AIDS diagnoses, which were classified together into a separate group as HIV-related deaths, given the considerable overlap in mortality from HIV infection and tuberculosis. Details on the verbal autopsy methods and their validation have been published previously by Hosegood.

Permission for demographic and HIV serologic surveillance and for the use of data regarding clinic attendees was obtained from the University of KwaZulu-Natal Research Ethics Committee and the Research Committee of the KwaZulu-Natal Department of Health.

Analysis
Deaths and person–years of observation were aggregated annually for the period from 1 January 2000 to 31 December 2006 for all individuals in the study population. Individuals contributed to the person–years denominator from 1 January 2000, or from any later date of birth or in-migration, until 31 December 2006, and they ceased to contribute to the denominator at death, termination of household membership, household out-migration or the last surveillance visit in which household membership was
confirmed. Thus, individuals who were previous homestead residents continued to be followed when they became non-residents for as long as they remained a member of – i.e. retained links with – the household under surveillance. Over 2000-2006, approximately 90% of external out-migrants continued to be followed as non-resident household members. The previously published mortality analysis\textsuperscript{20} was restricted to resident deaths and residential exposure only. As a result, the mortality rates given in that article are not directly comparable to those recorded in this one.

We stratified mortality rates by sex and four age groups (< 15, 15–24, 25–49 and > 49 years). The age-group boundaries were chosen to separate groups distinctly different in their rates of HIV infection prevalence,\textsuperscript{15} risk of dying from an HIV-related cause and rates of enrolment in the local ART programme. To control for changes in the age composition over time within each stratum, we adjusted mortality rates in the different periods to the stratum-specific age distribution across all periods (using 5-year age groups). The remainder of the analysis was restricted to the 25–49-year-old group, as it had the highest AIDS-related burden of disease and also included the majority of the patients in the ART programme.

Table 1 summarizes the 25–49 year old open age cohort and the changes to this cohort during the course of each year. Cohort members were lost to follow-up if they ceased to be members of a household after external out-migration. In 90% of the cases, loss to follow-up occurred sometime after out-migration, rather than at the time out-migration took place. Cause-specific age-standardised mortality rates (SMRs) were calculated for (i) communicable, maternal, perinatal, and nutritional conditions (excluding any that were HIV-related); (ii) non-communicable diseases; (iii) injuries; (iv) HIV-related conditions (AIDS and tuberculosis) and (v) undefined cause.

To compare mortality before and after ART became available (2002–2003 and 2004–2006, respectively), we calculated the age-standardised mortality rate ratio (SMRR). To obtain the SMRR, the crude mortality rate observed after ART introduction is divided by the rate that would have been expected had the 5-year age group-specific mortality rates remained the same as before ART was introduced.\textsuperscript{26} SMRRs were calculated separately for males and females aged 25–49 years for all-cause mortality,
HIV-related cause-specific mortality and non-HIV-related cause-specific mortality. All analyses were performed with STATA release 10.1 (StataCorp, College Station, TX, USA).27

**ART programme**

As in the rest of South Africa,28 ART first became widely available in the study area in 2004 through local private practitioners with support from employers, individual medical benefit contributions or local non-governmental organizations. The local public ART programme enrolled its first patient in August 2004. This government programme receives support through grants from the United States’ Presidential Emergency Fund for AIDS Relief (PEPFAR) administered through Elizabeth Glazer Paediatric AIDS Fund and, more recently, through Priorities in AIDS Care and Treatment. It is managed as a partnership between the local department of health and the Africa Centre for Health and Population Studies of the University of KwaZulu-Natal, in Mtubatuba, and delivers care and treatment to those who are HIV+ through a decentralised network of primary health care clinics.

Since late 2004, between 40 and 100 patients a month have initiated treatment through the local ART programme, and by the end of 2006 1092 patients were being treated at clinics within the surveillance area. If one assumes that 15% of the HIV+ population requires ART,29 the estimated crude treatment coverage in the surveillance area had reached 84% at the end of 2006. Treatment follows South African government guidelines,30 which recommend stavudine and lamivudine combined with either nevirapine or efavirenz as a first-line regimen. Patients with a CD4+ lymphocyte (CD4) count < 200 cells per mm³ and/or WHO clinical stage IV disease are eligible for enrolment in the programme. All patients in the programme are eligible for CD4 counts every 6 months, either before or after the initiation of antiretrovirals.

**Results**

**Mortality**

A total of 7930 deaths were recorded over 517 856 person–years of observation from January 2000 to December 2006. HIV-related causes accounted for 49.0% of the total
number of deaths in the overall population and for 71.5% of the deaths in the 25–49 year age group. Of HIV-related deaths, 65% occurred in the 25–49 year age group, and 12% in the group 50 years of age and older. Table A1 (in Appendix A, available at: http://www.africacentre.ac.za/Portals/0/Publications/2009_AppendixAR.pdf) shows the data broken down by year (2000–2006), 5-year age groups and sex, as well as the person–years of observation and the deaths by cause.

In the 25–49 year age group, standardised all-cause mortality increased from a low of 24.0 (95% CI: 21.5–26.5) deaths per 1000 person–years in 2000 (Fig. 1) to a high of 33.0 (95% CI: 30.4–35.6) in 2003, and then declined to a low of 23.9 (95% CI: 21.8–26.1) in 2006. The HIV-related cause-specific mortality rate in the 25–49 year age group over the same period increased from 19.3 (95% CI: 17.1–21.5) deaths per 1000 person–years in 2000 (Fig. 2) to a high of 24.3 (95% CI: 22.0–26.6) in 2003, and then declined to 14.6 (95% CI: 12.9–16.3) by 2006.

From 2002–3 (pre-ART period) to 2004–6 (post-ART period), HIV-related age-standardised mortality declined significantly from 22.5 to 17.6 per 1000 person–years in women 25–49 years old ($P < 0.0001$; SMRR: 0.780; 95% CI: 0.691–0.881) (Table 2 and Table 3) and from 26.5 to 18.7 per 1000 person–years in men 25–49 years old ($P < 0.0001$; SMRR: 0.706; 95% CI: 0.615–0.811). Non-HIV-related SMRs increased in 2004 for women 25–49 years old from 4.5 per 1000 person–years before ART to 7.3 per 1000 person–years after ART ($P = 0.0004$; SMRR: 1.615; 95% CI: 1.275–2.045). There was no significant change in non-HIV-related SMRs for men aged 25–49 years old ($P = 0.1236$; SMRR: 1.157; 95% CI: 0.957–1.400).

**ART programme**

ART was initiated at a median age of 35 years (inter-quartile range, IQR: 29–43) and 77% of patients, mostly women, were 25–49 years of age at initiation. The median CD4 count before the initiation of ART was 115 cells/mm$^3$ (IQR 52–173). By the end of 2004, 2005 and 2006, 24, 298 and 859 patients aged 25–49 years, respectively, were enrolled at the clinics within the surveillance area. These figures do not include ART accessed through other channels, such as private practitioners. Thus, they can be considered the
lower-bound estimate of true coverage, although local data suggests that the numbers of people who access care through these channels is small since ART was introduced free of cost in the public sector.

**Estimated mortality and ART programme coverage**

To estimate HIV-related mortality in people 25–49 years of age in the absence of ART, we assumed that 15% of HIV-infected individuals were eligible for treatment. The prevalence of HIV infection in this population for the years 2003–2006 was actually measured through ongoing HIV surveillance activities; for the years 2000–2002 it was extrapolated from the measured prevalence by using the Actuarial Society of South Africa (ASSA) 2003 AIDS and Demographic model. For the extrapolation, the measured prevalence in 2003 was multiplied by the ratio of the modelled prevalence for KwaZulu-Natal Blacks in 2003 to the modelled prevalence in the corresponding earlier year. An annual mortality rate of 44.5% was assumed for individuals who were eligible for but did not receive ART. An annual baseline mortality rate was calculated under the assumption that ART was not available in the period 2000–2006. In Table 4, the counterfactual estimated mortality rates are compared with the actual mortality rates observed. As noted, mortality did not change significantly over time before ART was introduced in this population, but it dropped significantly beginning in 2004, and particularly in 2005 and 2006. Under the assumption that 15% of HIV-infected individuals are eligible for ART, from 2004 to 2006 the public ART programme covered 2%, 30% and 84%, respectively, of the estimated need for ART in patients 25–49 years old. We did not explore the effect of changing the assumptions underlying the ASSA model regarding prevalence estimates prior to 2003 because some of them, such as those relating to ART rollout rates, were not relevant in our case, as we were only interested in overall mortality in the absence of ART.

**Sensitivity analysis**

To determine if the significant reductions in HIV-related mortality in the period after the ART programme was introduced could be due to misclassification of HIV-related deaths in the verbal autopsies, we re-calculated the annual mortality rates in the following three scenarios: (a) All deaths in the communicable, maternal and nutritional diagnostic
group were re-classified as HIV-related deaths in individuals who were known to be HIV+ (from the population-based HIV surveillance); (b) all deaths as in (a), in addition to deaths in the undefined diagnostic group, were re-classified as HIV-related deaths in individuals who were known to be HIV+ (from the population-based HIV surveillance); (c) all deaths were reclassified according to (b) and, in addition, deaths with an underlying cause (ICD-10 codes A09 [diarrhoea and gastroenteritis of presumed infectious origin], G03 [meningitis due to other and unspecified causes], G04 [encephalitis, myelitis and encephalomyelitis], G04.9 [encephalitis, myelitis and encephalomyelitis, unspecified], J22 [unspecified acute lower respiratory infection]) that could be HIV-related but did not fulfil all the criteria to be classified as an AIDS death in the original verbal autopsy assessment were re-classified as HIV-related. The sensitivity analysis showed that ascertainment bias could not have accounted for the observed reduction in mortality. In females, the HIV-related cause-specific SMRR (post-ART/pre-ART) increased to a maximum of 0.833 (95% CI: 0.742–0.942; \( P = 0.003 \)) in scenario (c), while in males, it increased to a maximum of 0.741 (95% CI: 0.647–0.836; \( P < 0.0001 \)) in scenario b. In scenario c, a significant increase in non-HIV-related mortality was also noted in males aged 25–49 years (SMRR: 1.287; 95% CI: 1.035–1.540; \( P = 0.0259 \)).

**Discussion**

There is evidence the public-sector ART roll-out in rural South Africa is beginning to affect adult population mortality, with an approximate reduction of 22% and 29% in HIV-related mortality rates in women and men, respectively. This reduction occurred in a community with a very high prevalence of HIV infection and high mortality attributable to HIV.\(^{19}\) Importantly, the longitudinal demographic surveillance system records all-cause mortality and cause-specific mortality and provides information about the coverage of the ART roll-out in the population. Because all births, deaths and migrations are recorded, the total population at any given moment is known, and this allows for a precise denominator with which to calculate mortality rates. Because the majority of out-migrants were followed as non-resident household members, the potential effect of any differential out-migration on the reported results was reduced. Further, the cause-specific
mortality information obtained through verbal autopsies made it possible to distinguishing changes over time in AIDS/tuberculosis-related mortality from changes in mortality unrelated to AIDS/tuberculosis. It is important to distinguish between different categories of cause of death because an ART programme would be expected to reduce HIV-related mortality primarily.

Recent work from Malawi has shown a decline in population mortality shortly after the introduction of ART in the study population. Our study assessed the effect of ART in a different environment, with a larger population (74 500 versus 32 000), a higher prevalence of HIV infection in adults (21.5% versus 11.4%), higher HIV-related adult mortality (11.4 versus 6.3) before ART availability and stricter criteria for treatment eligibility (CD4 count of < 200 cells/mm³ versus 250 cells/mm³).

**Effect of ART on population mortality**

It is highly plausible that the widespread availability of ART has led to the substantial decline in mortality observed in the study population. Not only does the decline show a temporal correspondence with the introduction of ART, but no other major health interventions were introduced in the study area during the same period. As in Malawi, the effect of ART on mortality at the population level was seen soon after ART roll-out and increased with expanding coverage, perhaps because, under current South African government guidelines, patients start treatment later than they should and they experience high mortality both while waiting for ART and after initiating it. Thus, many patients who survived while on ART would have died within a short time had they not been treated. Data from the Western Cape province of South Africa during the pre-ART era show that without ART, 22.2% of patients with stage 4 disease (WHO classification) and a CD4 count of < 200 cells/mm³ would have died within 6 months.

Second, the decline in HIV-related mortality over time is unlikely to have resulted from differential increases in the out-migration rates of HIV+ people. The out-migration rates of both HIV+ and HIV− individuals and of those with unknown HIV status remained constant over the three complete years for which data on HIV status were available (2004, 2005, and 2006).
Third, the prevalence of HIV infection measured through antenatal surveillance has not declined since the late 1990s, the current population incidence rate of HIV infection is high, and the prevalence of HIV infection in the study community has increased steadily. Thus, it is unlikely that the observed decrease in overall population mortality is the late result of a sudden decline in the incidence of HIV infection. Furthermore, non-HIV-related mortality did not decline overall, so that our findings cannot be attributed to a general improvement in health and survival due to secular changes.

In the early years of our surveillance, both overall and HIV-associated mortality were still on the rise, as was expected in light of the trend in the HIV epidemic. According to estimates based on the ASSA2003 AIDS and Demographic model, mortality in KwaZulu-Natal increased sharply after the mid-1990s and levelled off only after 2006, as incidence declined. Contrary to the assumptions in the South Africa model, there is as yet no evidence that incidence is declining in our area, which makes the decrease in mortality even more intriguing.

Although only a small part of one of the districts in the KwaZulu-Natal province was included in this study, the findings should apply on a larger scale: the measured epidemiological distribution of HIV infection and the mortality pattern in this population resemble those for the province as a whole and do not differ much from those observed in other sub-Saharan populations heavily affected by the HIV pandemic. The additional funds received via the PEPFAR initiative allowed for a faster, more comprehensive roll-out of the ART programme in this area, but solely within existing public health facilities and under the operational control of the provincial government’s public health services.

**Increase in non-HIV-related mortality**

A significant increase in non-HIV-related mortality was observed among women after ART became available. Among males, the increase in non-HIV-related mortality during the same period was not statistically significant in the base analysis but became significant in scenario c of the sensitivity analysis. These findings require further analysis but could have several explanations: non-AIDS-related causes could have defined the
mortality profile among the large group of HIV-infected people in this population who were not yet eligible for ART;\textsuperscript{39,40} the competing risk of HIV-related mortality could have declined,\textsuperscript{41} or the ART programme could have been expanded at the expense of health care in other areas.

**Verbal autopsies**

Physician-coded verbal autopsies have known limitations,\textsuperscript{32} and misclassification could have occurred. However, the sensitivity analysis presented here has shown that even if all deaths from undefined causes and from infectious diseases had been, in reality, misclassified HIV-related deaths, the main results of the analysis remained significant. Changes in mortality from tuberculosis among HIV– individuals are unlikely to have influenced the results, since 80\% of the patients who present with active tuberculosis in the province of KwaZulu-Natal, South Africa, are co-infected with HIV\textsuperscript{25} and this percentage is likely to be higher still among tuberculosis patients who die.

**Public health and operational aspects of the ART programme**

The programme that delivers ART to the study population is administered through the public primary health care facilities of the South African Department of Health. Although it receives support through PEPFAR, the programme is overseen, managed and staffed largely by public sector employees, which ensures operational continuity after cessation of external support. Nevertheless, the sustainability of this large-scale ART programme faces the same challenges as in any developing country: a rapidly increasing need for health workers who can deliver ART,\textsuperscript{42} due in part to treatment success;\textsuperscript{43} the need to ensure long-term treatment adherence and to retain patients in the programme;\textsuperscript{44} the unsolved question of the optimal relationship between ART programmes and the overall health care system.\textsuperscript{45} Currently, many of these issues are being addressed in ongoing studies in our community and other sites.

In summary, we have found a substantial fall in population mortality, particularly from HIV-related causes, following the widespread availability of ART in a rural community with a high prevalence of HIV infection and high HIV-related mortality. However, this should not be a cause for complacency. Although nearly 15\% of all HIV-infected individuals are receiving ART, HIV infection remains the leading cause of death
in the study community. A much larger proportion of HIV-infected individuals will need to start treatment before HIV-related mortality falls to the levels seen in developed countries. These findings should be part of a clear public health message of the benefits of treatment within the context of a multi-faceted strategy to encourage people to find out their HIV serostatus and seek care.

Acknowledgements
We thank the community members in the demographic surveillance area who have contributed their data to the study since 2000. We appreciate the contribution of the research operations staff of the Africa Centre in collecting the data used in this paper. We thank the staff of the KwaZulu-Natal provincial government health care facilities in this area for providing the ART programme.

Funding
The Africa Centre’s contribution to the government ART programme is funded by grants from the Presidential Emergency Fund for AIDS Relief, administered through the Elizabeth Glazer Paediatric Aids Fund (EGPAF) and, more recently, through Priorities in AIDS Care and Treatment (PACT).

Competing interests
None declared.

References


5. The Antiretroviral Therapy in Lower Income Countries (ART-LINC) Collaboration. ART Cohort Collaboration (ART-CC) groups. Mortality of


Table 1. **Open cohort of adults aged 25–49 years created to investigate overall mortality trends in 2000–2006, KwaZulu-Natal, South Africa**

<table>
<thead>
<tr>
<th>Adults</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under surveillance at start of year</td>
<td>16 921</td>
<td>17 831</td>
<td>18 308</td>
<td>18 828</td>
<td>19 435</td>
</tr>
<tr>
<td>Entered age group during year</td>
<td>1 201</td>
<td>1 131</td>
<td>1 414</td>
<td>1 506</td>
<td>1 473</td>
</tr>
<tr>
<td>In-migrated(^a) during year</td>
<td>2 010</td>
<td>1 310</td>
<td>1 079</td>
<td>1 071</td>
<td>1 027</td>
</tr>
<tr>
<td>Died during year</td>
<td>521</td>
<td>591</td>
<td>588</td>
<td>526</td>
<td>464</td>
</tr>
<tr>
<td>Exited age group during year</td>
<td>435</td>
<td>354</td>
<td>430</td>
<td>418</td>
<td>407</td>
</tr>
<tr>
<td>Lost to follow-up during year</td>
<td>1 345</td>
<td>1 019</td>
<td>955</td>
<td>1 026</td>
<td>1 184</td>
</tr>
</tbody>
</table>

\(^a\) From outside the demographic surveillance area.

Table 2. **Comparison of population mortality rates in 25–49 year olds before and after the ART delivery programme was introduced in KwaZulu-Natal, South Africa, 2002–2006**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>PYO</td>
<td>21 116</td>
<td>14 191</td>
</tr>
<tr>
<td>Total deaths</td>
<td>572</td>
<td>540</td>
</tr>
<tr>
<td>HIV-related deaths</td>
<td>476</td>
<td>377</td>
</tr>
<tr>
<td>All-cause SMR(^a) (CMR)</td>
<td>27.07(27.09)</td>
<td>37.89</td>
</tr>
<tr>
<td>HIV-related cause-specific SMR (CMR)</td>
<td>(22.54)</td>
<td>(26.56)</td>
</tr>
<tr>
<td>Non-HIV-related cause-specific SMR (CMR)</td>
<td>4.54</td>
<td>11.43</td>
</tr>
</tbody>
</table>

\(^a\) Per 1000 PYO.

ART, antiretroviral therapy; CMR, crude mortality rate; PYO, person–years of observation; SMR, age-standardised mortality rate.
### Table 3. Ratio of pre-ART and post-ART programme SMRs, KwaZulu-Natal, South Africa, 2002–2006

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th></th>
<th>P-value</th>
<th>Male</th>
<th></th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SMRR</td>
<td>95% CI</td>
<td></td>
<td>SMRR</td>
<td>95% CI</td>
<td></td>
</tr>
<tr>
<td>All-cause SMRR</td>
<td>0.920</td>
<td>0.828–1.024</td>
<td>0.097</td>
<td>0.842</td>
<td>0.754–0.941</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HIV-related SMRR</td>
<td>0.780</td>
<td>0.691–0.881</td>
<td>&lt; 0.001</td>
<td>0.706</td>
<td>0.615–0.811</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Non- HIV-related SMRR</td>
<td>1.615</td>
<td>1.275–2.045</td>
<td>&lt; 0.001</td>
<td>1.157</td>
<td>0.957–1.400</td>
<td>0.124</td>
</tr>
</tbody>
</table>

ART, antiretroviral therapy; CI, confidence interval; SMRR, age-standardised mortality rate ratio.

### Table 4. Ratio of observed to estimated HIV-related SMR for adults 25–49 years old in the assumed absence of an ART programme, KwaZulu-Natal, South Africa, 2002–2006

<table>
<thead>
<tr>
<th>Year</th>
<th>Observed SMR</th>
<th>Estimated SMR</th>
<th>SMRR (95% CI, P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>19.2</td>
<td>21.1</td>
<td>1.08</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.91–1.24, 0.356)</td>
</tr>
<tr>
<td>2001</td>
<td>21.2</td>
<td>22.6</td>
<td>1.06</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.92–1.21, 0.398)</td>
</tr>
<tr>
<td>2002</td>
<td>23.9</td>
<td>23.8</td>
<td>1.10</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.87–1.12, 0.942)</td>
</tr>
<tr>
<td>2003</td>
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<td>(0.91–1.16, 0.602)</td>
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<td>(1.04–1.34, 0.016)</td>
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<tr>
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<td>18.5</td>
<td>24.4</td>
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<td>(1.16–1.51, &lt; 0.001)</td>
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<tr>
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<td>14.5</td>
<td>24.2</td>
<td>1.69</td>
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<td>(1.45–1.92, &lt; 0.001)</td>
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ART, antiretroviral therapy; CI, confidence interval; SMR, age-standardised mortality rate; SMRR, age-standardised mortality rate ratio.
Fig. 1. All-cause SRS by age group, for males and females, KwaZulu-Natal, South Africa, 2000–2006
Fig. 2. Cause-specific SMRs for adults aged 25–49 years, KwaZulu-Natal, South Africa, 2000–2006