Mortality in HIV-negative adults in Kwazulu-Natal: trends, causes and gender differences

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Short abstract

For the past few decades adult mortality in South Africa has been shaped by the HIV epidemic. Whilst much is known about the impact of HIV there is little empirical data on the underlying or 'background' mortality. Background mortality can be studied as the mortality of the HIV negative population, and to that end we use longitudinal data produced by the HIV and demographic surveillance system in KwaZulu Natal. We report on mortality trends, age patterns of mortality and causes of death in the known HIV negative adults (aged 15 and above) for the period between 2007 and 2013. Preliminary results are indicative of relatively stable mortality levels over the 7-year period and bring about gender differences in adult life expectancy that average 12.5 years. This difference exceeds the typical gender disparity in adult mortality, and will be decomposed by age and cause using verbal autopsy data.

Extended abstract

Introduction

For the past few decades mortality in South Africa has been shaped by the HIV epidemic. Whilst much is known of the impact of HIV, there is little empirical data on the underlying or 'background' mortality. From a public health perspective it is important to understand the health profile of the HIV negative population, especially as HIV mortality begins to fall following the introduction of anti-retroviral therapy (ART). Furthermore background mortality estimates are used in the UN's HIV epidemic projections. To understand background mortality in South Africa we will be examining mortality of the known HIV negative population of the demographic surveillance system (DSS) in KwaZulu-Natal, with the aim of understanding mortality trends and causes between men and women.

Methods

Data

Data for this study come from the Africa Centre Demographic Information System (ACDIS), a DSS situated in the uMkhanyakude district of northern KwaZulu-Natal, South Africa. ACDIS was established in 1997 to produce high quality longitudinal data for monitoring the health and demographic impacts of the HIV epidemic in South Africa. The study area covers 438 km^2 of predominantly rural land and has a population characterised by high HIV prevalence (Welz et al., 2007), a young age structure, and high levels of circulatory migration (Tanser et al., 2008).

Demographic household surveys have been conducted in ACDIS between two and three times a year since January 2000. These surveys consist of household visits and interviews with a key household member who provides information on births, deaths and movements in and out of the study area for all household members within the inter-survey period. Information is collected on both resident and non-resident members of the household. The surveys produce residence episodes for each individual, an episode is initiated through either birth or in-migration and ended through either death or out-migration. As this study is focusing on adult mortality the earliest episodes included in the data-set begin at a subject's 15^{th} birthday. Since 2000 each reported death has been followed up with a verbal autopsy. The verbal autopsy aims to determine the underlying and immediate causes of deaths and in short consists of an interview with a close caregiver of the deceased regarding the details of the death. The data produced in each interview has been processed by the probabilistic Inter-VA4 model to produce up to 3 potential causes of death compatible with the International Classification of Disease version 10 (ICD-10). The InterVA-4 HIV prevalence was set to high and malaria prevalence was set to low.

In addition to the demographic surveys, population-based serological surveys have been conducted annually in the study area since 2003. For the first three surveys (2003-2006) only women aged 15-49 and men aged 15-54 resident in the study area were eligible for HIV testing but in 2007, the eligibility criteria have been extended to all resident adults aged 15 plus, and that will therefore be the starting year for most of our analyses. A 12.5% sample of non-residents is also included in each serosurvey round. In addition to the serosurveys the local HIV treatment and care clinic records have been linked to the DSS therefore allowing continuous HIV status updates from this source (Tanser et al., 2008).

The serosurvey and clinic results have been linked to the demographic and residency data to allow allocation of deaths and person-time to separate HIV statuses. Classification of HIV negative status in relation to a HIV negative test date in the data-set is as follows. In the time preceding a HIV negative test result an individual is classified as HIV status unknown. In the time following a HIV negative result, an individual's status is classified as negative until the cumulative probability of seroconversion exceeds 5%, at which point they are classified as unknown. This probability is calculated using observed age and sex-specific incidence rates specific to the ACDIS.

Statistical analysis

We first present time trends in adult life expectancy for the known HIV population 2007-2013 and total population 2000-2013. Adult life expectancy is the average number of years a person aged 15 can expect to live if the mortality rates of the period in question remain unchanged throughout their lifetime. Unchanging mortality rates are highly unlikely and thus life expectancy provides a summary measure of mortality for a period in time rather than a predictive estimate for any real cohort. Data were restricted to an upper limit of 100 years to prevent bias due to age over-reporting (Bor et al., 2013). Due to this a more accurate description of the estimates is the average number of years a person would live between 15 and 100 if the mortality rates for the year in question remained stable. The adult life expectancy estimates were calculated as the area under the Kaplan-Meier produce-limit survivor curve between 15 and 100 for each sex, year and HIV status separately. The average difference between male and female HIV negative life expectancies was calculated as the mean of the 7 yearly gender differences.

All-cause age-specific mortality rates have been produced for each sex over two periods, 2007-2009 and 2011-2013, for the known HIV negative population. The population was broken down into 10-year age groups, 15 to 25, 25 to 34, 35 to 44, 45 to 54, 55 to 64, 65 to 74, 75 to 84 and 85 plus.

To determine sex differences in age-adjusted mortality hazards of the HIV negative population parametric survival analysis was undertaken with individual age acting as the measure of time. A Weibull model was selected as mortality hazards steadily increase with age, and this demonstrated to provide the best fit. Calendar year and sex have been considered as covariates.

Finally, the verbal autopsy data has been linked to the data-set for use in an age-cause decomposition of the difference in mortality between men and women in the total period 2007-2013 following a method first described by Arriaga (Arriaga, 1984). The Inter-VA4 produced up to three causes per death, each with a corresponding likelihood between 0 and 100. For any death in which the likelihoods did not sum up to 100 the remaining likelihood was categorised as ‘indeterminable’. Cause-specific mortality fractions (CSMF) were produced for each cause and later grouped into communicable, maternal and nutritional diseases; non-communicable disease; injuries and indeterminable.

Results

Of the total 68,744 subjects surveyed between 2007 and 2013, 24,712 subjects were classified at any point as known HIV negative. Collectively they contribute 73,450 HIV negative person-years (PY) of observation and 965 deaths, resulting in an overall HIV negative mortality rate of 13.14 deaths per 1,000 PY (95% CI: 12.34-14.00).

Figure 1 demonstrates adult life expectancy changes for HIV negative men and women in comparison to the total population, which also comprises HIV positive individuals and individuals with an unknown HIV status. Whilst adult life expectancy in the total population shows a clear rise from 2005 for both sexes (following the introduction of ART) this is not mirrored in the HIV negative population. The adult life expectancy of HIV negative women stays fairly steady around 62 years. The male adult life expectancy varies between 46 and 52 years, without a clear increase or decline. Figure 1 clearly demonstrates the wide gender differences in adult life expectancy in uMkhanyakude, both within the HIV negative and total population. The average 2007-2013 gender difference in adult life expectancy is 8.5 years for the total population and 12.5 years for the HIV negative population.

Figure 2 compares the age-specific mortality rates by sex over two periods, 2007-2009 and 2011-2013. There is little change in mortality rates over the two periods for men and women which supports the earlier life expectancy results. In 2007-2009 mortality rates were significantly higher in men in ages 45 to 84, and in 2011-2013 mortality rates were significantly higher in men from age 45 onwards.

Table 1 provides the output of the Weibull regression model. Age-adjusted mortality of HIV negative men is roughly 2.5 times that of HIV negative women (Hazard ratio=2.55; 95% CI=2.25-2.89) and mortality of the total HIV negative population shows no association with calendar year (0.97; 0.94 – 1.01). An interaction between calendar year and sex was investigated but proved not to be significant and therefore was not included in the final model.

Figure 3 provides the cause-specific mortality fractions (CSMFs) for men and women of the known HIV negative population for the period 2007-2013. Roughly 5% of mortality has been attributed to HIV although all of the known HIV negative deaths occurred before the probability of seroconversion exceeded 5%. This may be due to false positives as some error is always to be expected with InterVA4, or there may be subjects that were HIV positive by the time of their death (Byass et al., 2013). The CSMFs were categorised by the most common causes of death (COD). Deaths from cardiovascular, respiratory and nutritional diseases account for more mortality in the female HIV negative population than in the male population, whilst in men pulmonary tuberculosis and external injuries account for a larger proportion of mortality than in women.

Figure 4 provides a preliminary age-cause decomposition of the difference between male and female mortality in the 2007 – 2013 period. The overall adult life expectancy for the 7 year period was 50.1 years for men and 62.8 for women, thus the gender gap in life expectancy was 12.7 years. As might be expected elevated rates of external injuries among men are a key factor in gender differences in mortality below age 45. The majority (approximately 70%) of the female life expectancy gains occur at older ages (45-74 years), where pulmonary tuberculosis, malignant neoplasms and cardiovascular disease dominate. This corroborates the pattern of higher male mortality at older ages seen in the age-specific mortality rates. Table 2 provides a breakdown of the total contribution of each COD grouping to the overall life expectancy gender gap. Male mortality from pulmonary tuberculosis accounts for almost a third of the total mortality difference (4.35 years).

Figure (1) Trends in adult life expectancy by sex, comparing known HIV individuals to the total population

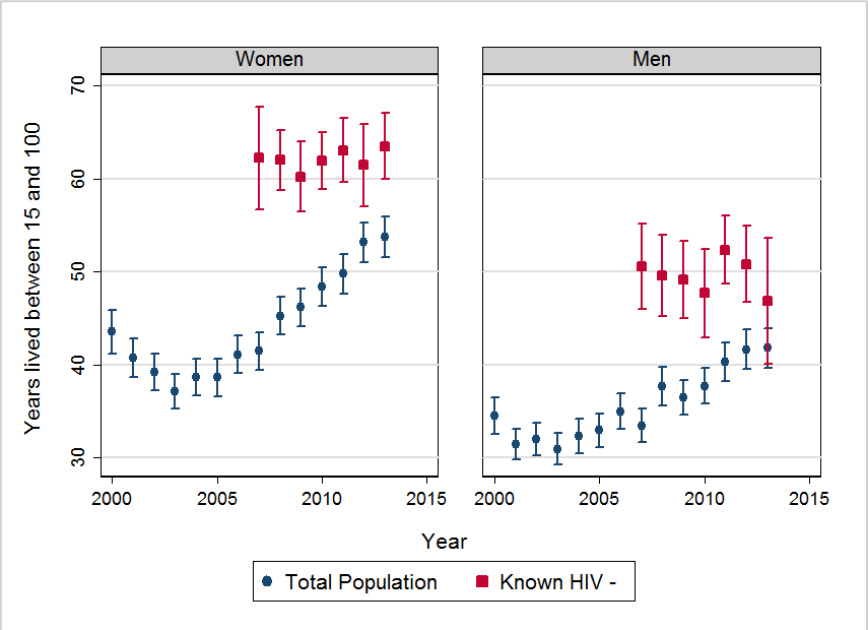

Figure (2) All-cause age-specific mortality rates in 2007-2009 and 2011-2013 of the known HIV negative population

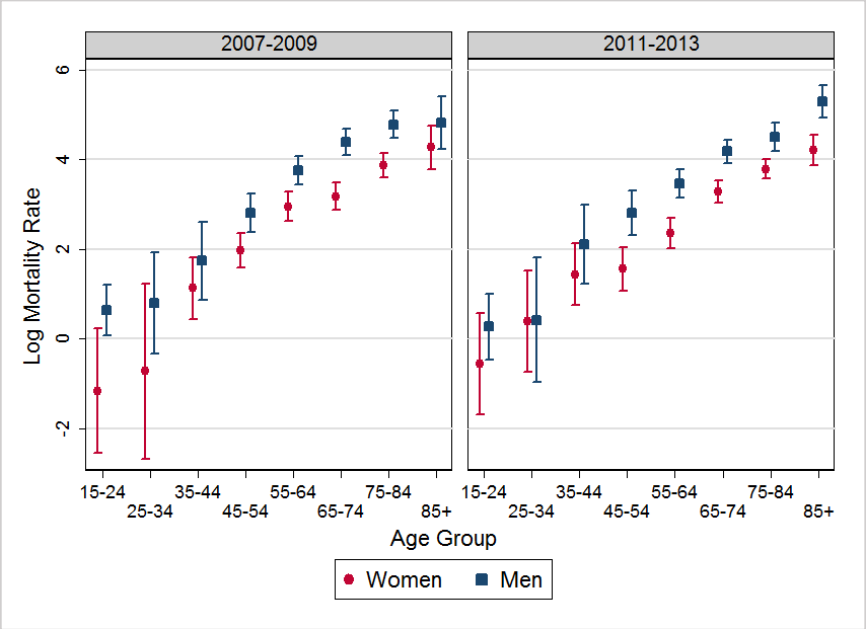

Table (1) Age-adjusted trends in mortality hazard of the known HIV negative population (2007-2013)

	Hazard Ratio (95% CI)	p-value
Calendar year	0.97 (0.94 – 1.01)	0.114
Women	1 (baseline)	
Men	2.55 (2.25 – 2.89)	<0.001
Age (p)	4.65 (4.41 – 4.89)	

Figure (3) Cause-specific mortality fractions (CSMFs) by sex of the known HIV negative population (2007-2013)

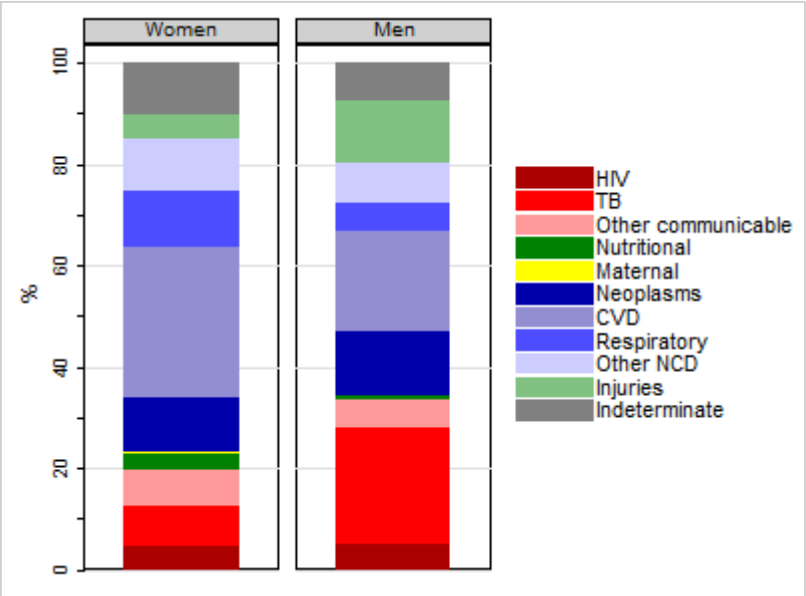

Figure (4) Age-sex decomposition of gender differences in mortality of the known HIV negative population (2007-2013)

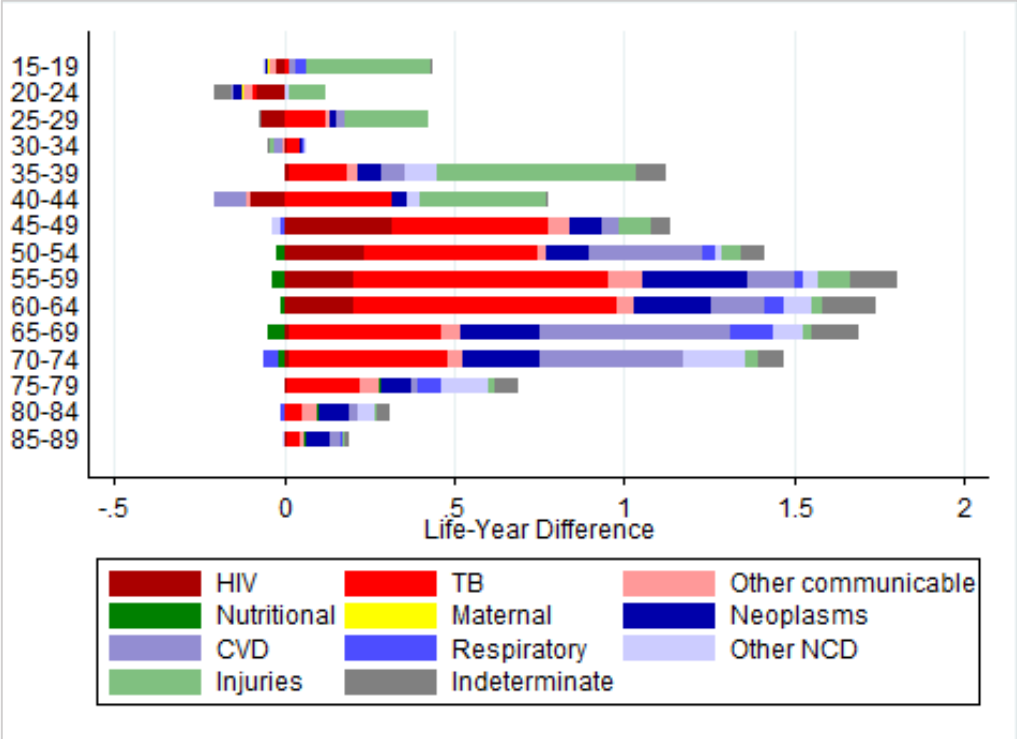

Table (2) Cause of death contributions to the gender difference in adult life expectancy

Cause of Death	Life-year Difference
All	12.68
HIV/AIDS related	0.77
Pulmonary Tuberculosis	4.35
Other communicable disease	0.44
Nutritional disorders	-0.11
Maternal related	-0.01
Malignant neoplasms	1.57
Cardiovascular disease	1.73
Respiratory disease	0.29
Other non-communicable disease	0.73
External Injuries	2.03
Indeterminate	0.80

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