Trends in the burden of HIV mortality after roll-out of antiretroviral therapy in KwaZulu-Natal, South Africa: an observational community cohort study

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Summary

Background: Antiretroviral therapy (ART) substantially decreases morbidity and mortality in people living with HIV. In this study, we describe population-level trends in the adult life expectancy and trends in the residual burden of HIV mortality after the roll-out of a public sector ART programme in KwaZulu-Natal, South Africa, one of the populations with the most severe HIV epidemics in the world.

Methods: Data come from the Africa Centre Demographic Information System (ACDIS), an observational community cohort study in the uMkhanyakude district in northern KwaZulu-Natal, South Africa. We used non-parametric survival analysis methods to estimate gains in the population-wide life expectancy at age 15 years since the introduction of ART, and the shortfall of the population-wide adult life expectancy compared with that of the HIV-negative population (ie, the life expectancy deficit). Life expectancy gains and deficits were further disaggregated by age and cause of death with demographic decomposition methods.

Findings: Covering the calendar years 2001 through to 2014, we obtained information on 93,903 adults who jointly contribute 535,428 person-years of observation to the analyses and 9,992 deaths. Since the roll-out of ART in 2004, adult life expectancy increased by 15.2 years for men (95% CI 12.4–17.8) and 17.2 years for women (14.5–20.2). Reductions in pulmonary tuberculosis and HIV-related mortality account for 79.7% of the total life expectancy gains in men (8.4 adult life-years), and 90.7% in women (12.8 adult life-years). For men, 9.5% is the result of a decline in external injuries. By 2014, the life expectancy deficit had decreased to 1.2 years for men (–2.9 to 5.8) and to 5.3 years for women (2.6–7.8). In 2011–14, pulmonary tuberculosis and HIV were responsible for 84.9% of the life expectancy deficit in men and 80.8% in women.

Interpretation: The burden of HIV on adult mortality in this population is rapidly shrinking, but remains large for women, despite their better engagement with HIV-care services. Gains in adult life-years lived as well as the present life expectancy deficit are almost exclusively due to differences in mortality attributed to HIV and pulmonary tuberculosis.

Funding: Wellcome Trust, the Bill & Melinda Gates Foundation, and the National Institutes of Health.
sex and add a new perspective to the scientific literature wherein women are routinely considered to have disproportionately benefited from the expansion of treatment.11,12

Methods

Study design and population

In this observational community cohort study, we used data from the Africa Centre Demographic Information System (ACDIS) in the uMkhanyakude district in northern KwaZulu-Natal, South Africa, covering 434 km² of predominantly rural area with a resident adult population of around 45,000 adults (aged 15 years and older).13 The population is characterised by high HIV prevalence (29% in adults aged 15–49 years in 2011),14 high levels of cardiovascular risk factors, and high mortality from external injuries.15

The public sector ART programme in the study area enrolled its first patients in August, 2004. By the end of 2006, more than 1000 patients were receiving treatment, and by mid-2011, an estimated 37% of people living with HIV in the study population were on ART.10 Further details about the expansion of the treatment programme in South Africa and changes to the ART eligibility criteria have been described previously.16

Ethical approvals for this study were obtained from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal and the Observational Research Ethics Committee of the London School of Hygiene & Tropical Medicine. Household representatives gave verbal informed consent for the demographic surveillance, and individual written consent was required for the HIV surveillance.

Data collection

Demographic surveillance was done through household visits three times a year, and population-based HIV testing of resident adults was done annually since 2003–04 for men and women of reproductive age and since 2007 for all adults. HIV status information was also obtained through record linkage with health facilities providing ART in the area covered by the ACDIS.

Individuals contributed person-time to the analyses from their 15th birthday or from when they moved into one of the villages under surveillance until they moved out, died, or turned 100 years old. The data extraction from the ACDIS database was done in August, 2015, and observations were administratively censored at the end of 2014.

To allocate person-time to HIV status categories, we classified the time before the first recorded HIV test as HIV status unknown. The time after a positive test remained positive until censoring or death. The time after the last negative test was considered negative for a duration of 5 years, after which it was classed as unknown. This procedure allowed for the estimation of mortality rates in HIV-negative individuals, but the exposure time was sufficiently short to ensure that

Evidence before this study

We searched PubMed and MEDLINE on June 15, 2016, for studies on the effect of antiretroviral therapy (ART) and the residual burden of HIV on adult mortality. We did not apply any language or date restriction, and used combinations of the search terms “HIV”, “AIDS”, “life expectancy”, “population”, “antiretroviral therapy”, and “burden”. Several studies reported on the life expectancy of HIV-positive individuals who started ART, and a number of institutions regularly report on mortality estimates that are the result of more complex modelling exercises. Two studies, one from Uganda and one from South Africa, provided direct non-parametric estimates of population-wide changes in adult life expectancy after the roll-out of antiretroviral therapy in generalised HIV epidemics. The South African study is based on the same data source used here, and reported an increase of 11.3 years in the life expectancy for both sexes at age 15 years between 2003, the year before ART was rolled out, and 2011.

Added value of this study

We extended the analyses for KwaZulu-Natal from 2011 to 2014 and documented adult life expectancy gains of 1.38 years per year for men and 1.58 years for women, for a total gain since ART of 15.2 years and 17.2 years for men and women, respectively. We expanded on these findings in two novel ways. First, we quantified the residual burden of HIV-associated mortality as the shortfall or deficit of the population-wide life expectancy compared with the life expectancy of the HIV-negative population. This shows that the remaining burden of HIV has become relatively small, especially in men. In women, the adult life expectancy deficit in 2014 was still 5.3 years. Second, we used verbal autopsy data and a new verbal autopsy interpretation tool (InSilicoVA) to establish that differences in mortality from pulmonary tuberculosis and HIV explain most of the gains in adult life expectancy as well as the remaining life expectancy deficit.

Implications of all the available evidence

Unprecedented increases in adult life expectancy associated with a reduction in HIV-related mortality underscore the success of the ART programme in this population. However, the burden of HIV mortality remains sizable for women, despite their better engagement with HIV care services. Women, who have so far gained more adult life-years than men, continue to bear the highest burden of HIV mortality, which is a finding that adds a new perspective to published work wherein men are often portrayed as the so-called losers of the ART scale-up.
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