



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

Georges Reniers, Sylvia Blom, Clara Calvert, Alexandra Martin-Onraet, Abraham J Herbst, Jeffrey W Eaton, Jacob Bor, Emma Slaymaker, Zehang R Li, Samuel J Clark, Till Bärnighausen, Basia Zaba, Victoria Hosegood

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 9992 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.

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Introduction

The roll-out of antiretroviral therapy (ART) in populations with generalised epidemics has greatly improved the survival of people living with HIV and has been documented in both clinical cohorts and population-based research.^{1–7} Many studies report changes in all-cause mortality, but do not quantify how much of the overall mortality decline is due to a reduction in HIV-associated mortality. In addition, most studies are not in a position to estimate the residual burden of HIV on population-level adult mortality. We sought to remedy the above-mentioned shortcomings with data from the Africa Centre Demographic Information System (ACDIS) in rural KwaZulu-Natal, South Africa, where HIV status is known for a large portion of the population.

We report on trends in the life expectancy at age 15 years and the adult life expectancy by HIV status. Life expectancy is one of the most widely used summary measures of mortality and is well suited to quantify the effects of ART because it values the prolongation of life

in addition to the mere elimination of deaths from a particular cause. Other adult mortality measures, including the probability of dying in adulthood (45q15), are less sensitive to the shift in the age distribution of deaths and might underestimate the mortality reductions prompted by the roll-out of ART.

Our analyses focused on two measures of great public health interest: gains in adult life expectancy since ART introduction and trends in the adult life expectancy deficit. The second of these measures is defined as the shortfall of the population-wide adult life expectancy compared with that of the HIV-negative population, and quantifies the residual burden of HIV mortality in a population. Furthermore, we used demographic decomposition techniques to estimate the contribution of changes in HIV and other causes of death to recent trends in the adult life expectancy and the adult life expectancy deficit. With these analyses, we aimed to update and expand on previous work on adult mortality from the same study site.^{2,8–10} All our estimates are disaggregated by

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Department of Population Health, London School of Hygiene & Tropical Medicine, London, UK (G Reniers PhD, S Blom MSc, C Calvert PhD, E Slaymaker PhD,

Prof B Zaba MSc); School of Public Health, University of the Witwatersrand, Johannesburg, South Africa (G Reniers, Prof S J Clark PhD);

Instituto Nacional de Cancerología, Mexico City, Mexico (A Martin-Onraet MD);

Africa Health Research Institute, Durban, South Africa (A J Herbst MSc,

Prof T Bärnighausen MD, Prof V Hosegood PhD);

Department of Infectious Disease Epidemiology, Imperial College London,

London, UK (J W Eaton PhD);

Department of Global Health, Boston University, Boston, MA, USA (J Bor ScD);

Department of Statistics, University of Washington, Seattle, WA, USA (Z R Li MA);

Department of Sociology, The Ohio State University, Columbus, OH, USA

(Prof S J Clark); Institute of Public Health, University of Heidelberg, Heidelberg,

Germany

(Prof T Bärnighausen); Harvard TH Chan School of Public Health, Harvard University, Boston, MA, USA

(Prof T Bärnighausen); and

Social Statistics and Demography, University of Southampton, Southampton, UK (Prof V Hosegood)

Correspondence to:
Dr Georges Reniers, Department
of Population Health, London
School of Hygiene and Tropical
Medicine, London WC1E 7HT, UK
georges.reniers@lshtm.ac.uk

Research in context

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.

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.²

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.^{10,15} 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 classified 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

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