Estimating trends in life expectancy in HIV-positive individuals

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Estimates of life expectancy are of obvious importance to people with HIV-1, and are essential to monitor and predict the progress of the HIV/AIDS epidemic and to plan health services. The Rwandan study reported by Sabin Nsanzimana and colleagues[1] in *The Lancet Global Health* is the first from sub-Saharan Africa to focus on the evolution of HIV-positive life expectancy during the scale-up of antiretroviral therapy, and is a welcome addition to a small body of data. The investigators show that the scale-up of antiretroviral therapy resulted in substantial gains in life expectancy, with near-normal life expectancy in individuals enrolled in care with little immunodeficiency.[1]

How reliable are estimates of life expectancy in people living with HIV? Life expectancy is the number of years that a person of a particular age would live, assuming that current age-specific mortality rates remain constant. Calculations might thus seem straightforward, but for people living with HIV in sub-Saharan Africa they are not. First, analyses rely on data for patients in treatment and care programmes, which might not be representative of all individuals living with HIV-1.[2] Second, loss to follow-up of patients after the start of antiretroviral therapy is common.[3] In the absence of functioning systems for vital statistics or outreach programmes to trace patients who were lost, mortality for these individuals remains unknown. To ignore the deaths in patients lost to follow-up substantially biases mortality downwards: death accounts for a substantial proportion of patients lost to follow-up.[4] Last, the duration of follow-up needs to be standardised across calendar periods. The risk of death is not uniform after initiation of antiretroviral therapy, but falls with increasing duration of therapy.[5]

Nsanzimana and colleagues[1] addressed all of these issues. The researchers limited the duration of follow-up to 3 years in all calendar periods, by contrast with other studies (eg, an analysis from the UK[6] and a collaborative study in high-income countries[7]). The Rwandan study therefore controlled at least to some extent for survivor bias, although how similar lengths of follow-up were in the two calendar periods is unclear. Many patients from a nationally representative sample of clinics were included, which is an important strength of the study. Unfortunately, no information about mortality in patients lost to follow-up was obtained, but statistical adjustment was made assuming that about half of patients lost to follow-up had died. In Rwanda and many other countries in sub-Saharan Africa, vital statistics function poorly, with only a small number of deaths registered.[8] The exception is South Africa, where coverage of vital registration is near universal and data from treatment and care programmes for HIV can be linked with mortality records to obtain accurate mortality estimates.[9] The importance of the deaths among patients lost to follow-up in the Rwandan study is underlined by the much-higher estimates of life expectancy obtained when no adjustment was made, and uncertainty remains in this regard.

How do the increases in life expectancy estimated for Rwanda compare with those of other studies, and how should they be interpreted? In Rwanda, the improvements were probably driven by changes over time in eligibility criteria for antiretroviral therapy and associated increases in CD4 counts at antiretroviral therapy initiation. Indeed, in a large-scale analysis of the International Epidemiologic Databases to Evaluate AIDS (IeDEA)[10] that included patients starting antiretroviral therapy in 23 countries between 2002 and 2009, Rwanda had the highest annual increase in CD4 cell count at the start of therapy.[11] However, whether any improvement in life expectancy would remain after

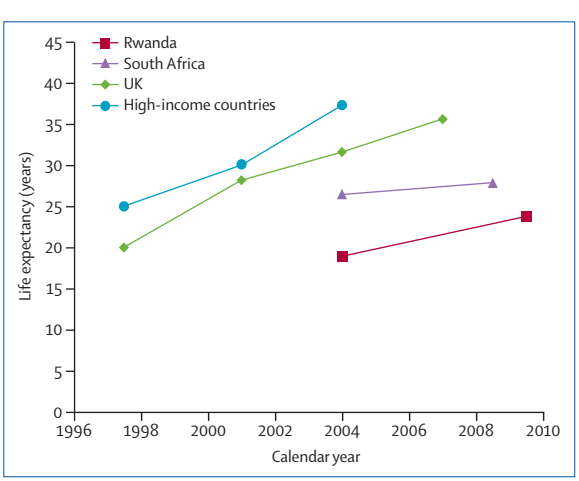

Figure: **Trends in life expectancy for individuals initiating antiretroviral therapy at age 35 years**
Life expectancy estimates from Rwanda,[1] South Africa,[9] the UK,[6] and high-income countries in North America and Europe[7] are plotted at the midpoint of the calendar periods for which they are reported.

controlling for these changes in baseline CD4 counts is unclear. Such an analysis addresses the question of whether or not the quality of HIV care has improved over time, which is important in view of the ever-increasing patient burden that treatment and care programmes for HIV face in sub-Saharan Africa.[10]

Unfortunately, no trends in retention in care were presented by Nsanzimana and colleagues, and the method used to estimate life expectancy—the abridged life table method—is not well suited to answering questions about trends in quality of care, because it allows little scope for multivariate analysis. Using an alternative method—the relative survival model—we have recently shown that some improvement in life expectancy is likely to have occurred in South Africa, after controlling for both differences in baseline CD4 count and antiretroviral therapy duration across different calendar years.[9] However, the improvement was small when compared with the more substantial improvements reported in studies from high-income countries and the Rwandan study, which did not fully control for baseline CD4 count and duration of antiretroviral therapy (figure). Finally, as the investigators point out,[1] the improvements in life expectancy in Rwanda might partly be due to improvements in non-HIV mortality.

The study by Nsanzimana and colleagues contributes to a growing evidence base on the successes and challenges of scaling up antiretroviral therapy in resource-limited settings. The reasons for the observed increases in life expectancy in people living with HIV in Rwanda are not entirely clear, however, and further research is needed to disentangle the effects of loss to follow-up, changing eligibility criteria for antiretroviral therapy, patient management systems, drug regimens, and non-HIV mortality.

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1 Nsanzimana S, Remera E, Kanters S, et al. Life expectancy among HIV-positive patients in Rwanda: a retrospective observational cohort study. *Lancet Glob Health* 2015; **3:** e169–77.
2 Stover J, Bertozzi S, Gutierrez JP, et al. The global impact of scaling up HIV/AIDS prevention programs in low- and middle-income countries. *Science* 2006; **311:** 1474–76.
3 Rosen S, Fox MP, Gill CJ. Patient retention in antiretroviral therapy programs in sub-Saharan Africa: a systematic review. *PLoS Med* 2007; **4:** e298.
4 Egger M, Spycher BD, Sidle J, et al. Correcting mortality for loss to follow-up: a nomogram applied to antiretroviral treatment programmes in sub-Saharan Africa. *PLoS Med* 2011; **8:** e1000390.
5 Egger M, May M, Chene G, et al, for the ART Cohort Collaboration. Prognosis of HIV-1-infected patients starting highly active antiretroviral therapy: a collaborative analysis of prospective studies. *Lancet* 2002; **360:** 119–29.
6 May M, Gompels M, Delpech V, et al. Impact of late diagnosis and treatment on life expectancy in people with HIV-1: UK Collaborative HIV Cohort (UK CHIC) Study. *BMJ* 2011; **343:** d6016.
7 The Antiretroviral Therapy Cohort Collaboration. Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies. *Lancet* 2008; **372:** 293–99.
8 Boerma T. Moving towards better cause of death registration in Africa and Asia. *Glob Health Action* 2014; **7:** 1–2.
9 Johnson LF, Mossong J, Dorrington RE, et al. Life expectancies of South African adults starting antiretroviral treatment: collaborative analysis of cohort studies. *PLoS Med* 2013; **10:** e1001418.
10 Egger M, Ekouevi DK, Williams C, et al. Cohort Profile: the international epidemiological databases to evaluate AIDS (IeDEA) in sub-Saharan Africa. *Int J Epidemiol* 2012; **41:** 1256–64.
11 Avila D, Althoff KN, Mugglin C, et al. Immunodeficiency at the start of combination antiretroviral therapy in low-, middle-, and high-income countries. *J Acquir Immune Defic Syndr* 2014; **65:** e8–16.