Adult mortality in East and Southern Africa in the era of antiretroviral therapy

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Abstract

Monitoring the impact of AIDS and the mitigating effects of interventions in developing countries is notoriously difficult because the populations that are hardest hit by the epidemic tend to have poor registration of vital events. In this contribution, we use data from seven demographic surveillance sites with repeated testing for HIV and continuous monitoring of mortality. These studies also collect self-reported and/or facility data on ART uptake and establish causes of death via verbal autopsy. We use survival analysis techniques to study the time to diagnosis following seroconversion (with death as a competing risk), the time to ART initiation following diagnosis (with death as a competing risk), and death following ART uptake. We disaggregate these analyses by sex, region, and (seroconversion, diagnosis or treatment) cohort. Preliminary results suggest that HIV testing and ART coverage are have increased rapidly. Despite delayed ART scale-up, Southern African sites now achieve better treatment coverage and lower mortality on treatment than Eastern African sites.

Extended abstract

Background and data

The expansion of HIV testing and AIDS treatment services are one of the largest public health interventions in developing countries in recent times. Monitoring the impact of AIDS and the mitigating effects of interventions is notoriously difficult because the countries that are hardest hit by the epidemic tend to have the poorest registration of vital events. Clinical cohort studies fill part of that knowledge gap, and testify to the efficacy of ART for prolonging the lives of HIV positives. A clinical cohort study from Uganda [1], for example, demonstrates that the life expectancy of model patients (i.e., patients who start treatment early and do not default) is hardly distinguishable from that of HIV negative individuals of the same age. This and similar studies do not, however, provide insight into the population-level impact of ART. To do so, we also need to quantify pre-treatment mortality and the mortality of those lost to follow up. Demographic Surveillance Sites (DSS) that monitor HIV status and the uptake of services are well positioned to study these.

In this contribution, we use data from seven DSS with repeated testing for HIV and continuous monitoring of mortality. All of these sites are members of the ALPHA network [2].[1] The dataset includes a total number of 45,898 individuals who have ever been identified as HIV positive. This has generated 152,906 total person-years of follow-up of HIV positives. In total 7,524 deaths of known HIV positives have been recorded and included in the analyses. The seven sites are listed in Figure 1 along with their follow up time of HIV positives in the site. The relative size of the sites is quantified by the average number of HIV positives over the period of observation and captured in the height of the bars. The different shades of the bars represent the various phases of ART rollout in the sites. Kisesa (TZ) and Masaka (UG) have been monitoring HIV serostatus for the longest, but have relatively small populations under surveillance. The uMkhanyakude (SA), Manicaland (ZW) and Kisumu (KE) sites are much larger and have much higher HIV prevalence. The (sero)surveillance in these sites started more recently. In Kisumu (KE) and Karonga (MW), no data are available from the pre-ART era.

First, we present trends in adult life expectancy (e_{15}) and compute the adult life expectancy deficit due to HIV by substracting the life expectancy in the population as a whole from the life expectancy of the HIV negatives. This measure gives us an indication of the demographic impact of HIV and the mitigating effects of ART in these populations. We also present adult life expectancy trends of HIV positive individuals. These analyses demonstrate the effect of HIV on adult mortality, but they do not highlight the programmatic bottlenecks that prevent further reductions in HIV related mortality. To that end we revert to a cohort perspective and use a competing risks framework to study the time from seroconversion to diagnosis (with death as a competing risk), the time to ART initiation following diagnosis (with death as a competing risk), and death following ART uptake. Successful programs reduce the time to the first event and minimize the number of deaths without experiencing that event. We

[1] http://www.lshtm.ac.uk/eph/dph/research/alpha/

disaggregate these analyses by sex[2], region[3], and cohort. Depending on the analysis, these are seroconversion, diagnosis or treatment cohorts.

Preliminary results

In the Masaka DSS in Uganda, adult life expectancy has increased by 14-20 years in since its low point in the mid-1990s (Figure 2). The most recent estimate is almost 60 years for women and somewhat lower for men. To put these estimates in perspective, they are still about 10 years lower than contemporary estimates for the US. Interestingly, adult life expectancy started to increase well before the introduction of ART.

The time series for the South African site are not sufficiently long to establish the inflection point, but other studies have shown that the increase in adult life expectancy in uMknanyakude coincided with the introduction of ART in the area [3]. The life expectancy deficit is an expression of the years of life lost due to HIV related mortality, and dependent on epidemic severity (and maturity), ART coverage, and competing mortality risks. As overall adult life expectancy increased, the adult life expectancy deficit in Masaka reduced from 15-20 years in the early 1990s to under 5 years for the most recent set of estimates. In contrast, the contemporary life expectancy deficit is still about 15 years in the South African site today. Reasons for that include a later and more severe epidemic in South Africa, and a delayed scale-up of ART. Common to both sites is the higher adult life expectancy deficit for women compared to men. This is probably related to higher HIV prevalence in women, a younger age at infection and death [4], and more competing mortality risks for men in adulthood (e.g., due to external injuries).

Figure 2b shows that life expectancy of HIV positive men and women has been increasing in the last 5 years or so. The estimates have much wider confidence bounds because of the relatively small number of observations. They also come with the disclaimer that their interpretation can be complex, primarily because the stage of infection at which individuals are tested may be changing over time. Increasing life expectancy estimates among HIV positives is thus not just a matter of prolonged survival due to ART, but also of earlier testing [note to self: fig2b should be relegated to an annex].

Figure 3 is the result of a competing risks survival analysis whereby we model the time from seroconversion to diagnosis, with death prior to diagnosis as a competing event. ALPHA Network sites typically use a study testing protocol of informed consent without automatic disclosure of the results (although some provision is usually made to provide HTC in parallel with the study tests). Study participants are also asked whether they ever had HTC so that we can determine the time between seroconversion and diagnosis. The date of seroconversion is estimated as the midpoint between the last negative and first positive HIV test. Given the outreach efforts that take place in parallel with the study

[2] Analyses disaggregated by sex have not yet been completed.
[3] Eastern Africa: Uganda (Masaka & Rakai), Tanzania (Kisesa), Kenya (Kisumu), Malawi (Karonga). Southern Africa: Zimbawe (Manicaland) and South Africa (uMkanyakude).

tests, we expect that our estimates give an optimistic picture of the HTC coverage in the DSS sites, but the trends may be informative nonetheless. In Eastern Africa, we find that up to 20% of the seroconvertors of the 1990s died without ever been diagnosed. HTC coverage improved considerably in successive seroconversion cohorts as 75-90% of those who seroconverted after 2005, had received a diagnosis within 5 years. Southern Africa (the analysis is restricted to the Manicaland site) has made up a lot of ground in this respect, but still lags the Eastern African sites in terms of HTC coverage.

Figure 4 uses a similar approach, and portrays the progression from diagnosis to ART uptake and death. Compared to the previous analysis, we do not require information on the date of the last negative test, and the cohort sizes are therefore larger. This analysis demonstrates that ART uptake has been increasing rapidly in successive cohorts of diagnosed HIV positives About 80% of diagnosed HIV positives have started treatment 5 years after receiving their first positive diagnosis. The more sobering observation from this illustration is that 6-8% of the diagnosed die within 5 years without ever receiving ART. In other words, these statistics underline that there is still room for improvement in the linkage of HIV positives to care and treatment services. As is the case for the coverage of HTC, the Southern African sites have made up a lot of ground in terms of ART coverage, and even seem to produce slightly more advantageous statistics in the most recent cohort.

Figure 5 shows the survival after the initiation of treatment. It illustrates that death after starting ART is still considerable, but improving: In early treatment cohorts, about 10% died within one year of starting ART; 20% died within seven years but In the latest ART initiation cohort, under 5% died the first year. Differences between Eastern and Southern Africa are small in this respect.

Finally, Figure 6 portrays the progression from seroconversion to ART uptake with death prior to treatment initiation as a competing event. It confirms the important improvements that have been made in successive seroconversion cohorts in terms of ART uptake as well as the reduction of pre-treatment mortality. It also confirms that the Southern African sites now perform better in terms of these two program performance indicators than the Eastern African sites.

Improvements to be made prior to PAA 2014

- More comprehensive literature review
- More detailed description of the datsets, methods and possible sources of selection bias
- Update analysis with new data provided by the sites in early 2014
- Disaggregate the analyses by sex (Figures 3-6)
- Disaggregate deaths by cause (using diagnosis established by verbal autopsy) (Figures 3-6)
- Figure 6: show the deaths after ART initiation as a separate category

Acknowledgements

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References

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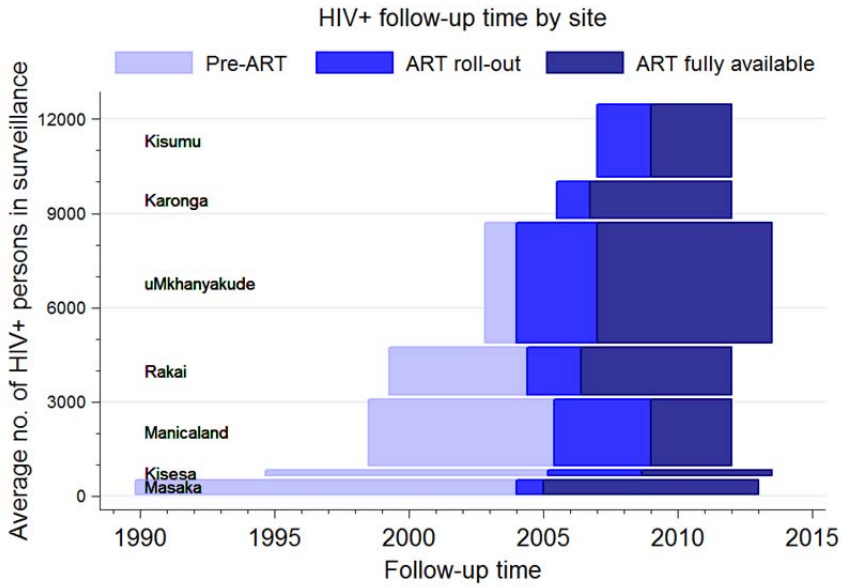
3. Bor J, Herbst AJ, Newell M-L, Bärnighausen T (2013) Increases in adult life expectancy in rural South Africa: valuing the scale-up of HIV treatment. Science 339: 961-965.
4. Todd J, Glynn JR, Marston M, Lutalo T, Biraro S, et al. (2007) Time from HIV seroconversion to death: a collaborative analysis of eight studies in six low and middle-income countries before highly active antiretroviral therapy. AIDS 21: S55-S63.

Illustrations

Figure 1: HIV positive follow up time by site and ART rollout phase.



Notes: Height of the bars represent the average number of HIV+ persons under surveillance

Figure 2a: Adult life expectancy (e15), and the adult life expectancy deficit due to HIV in Masaka (UG) and umKhanyakude (SA)

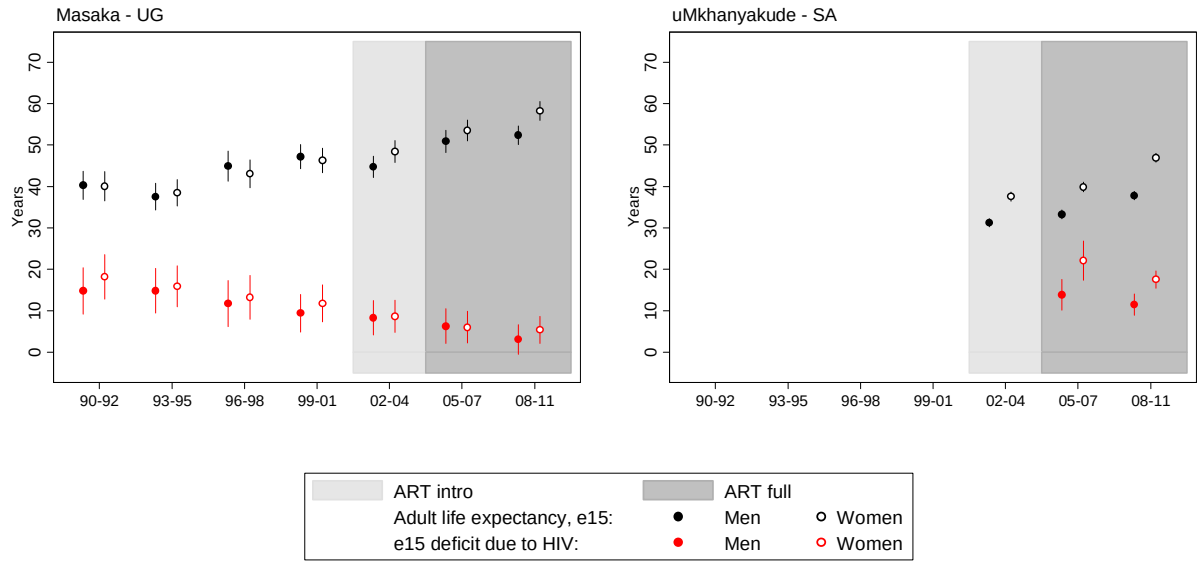


Figure 2b: Adult life expectancy (e_{15}), and the adult life expectancy of HIV positives in Masaka (UG) and umKhanyakude (SA)

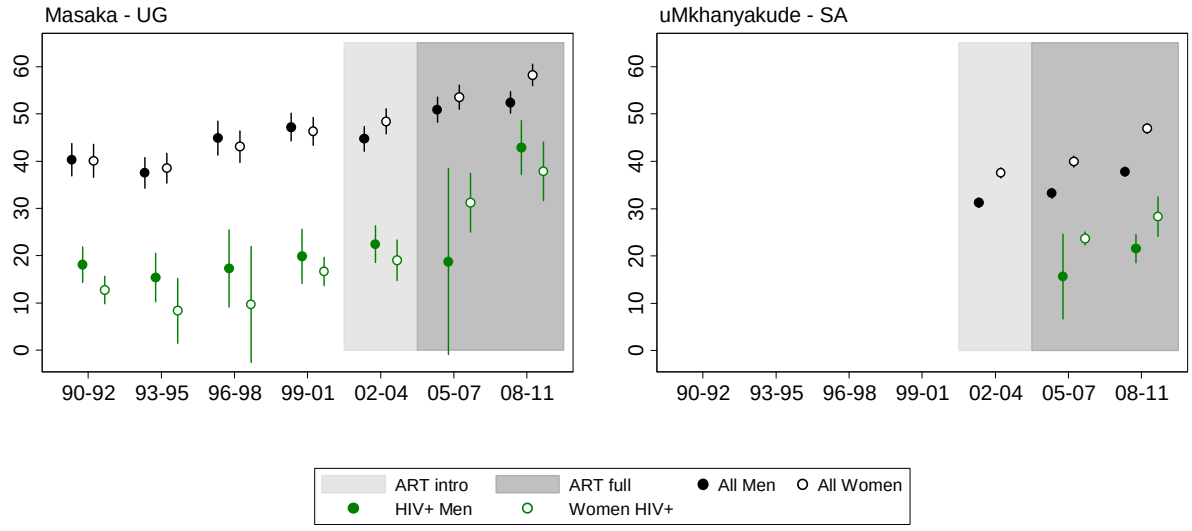
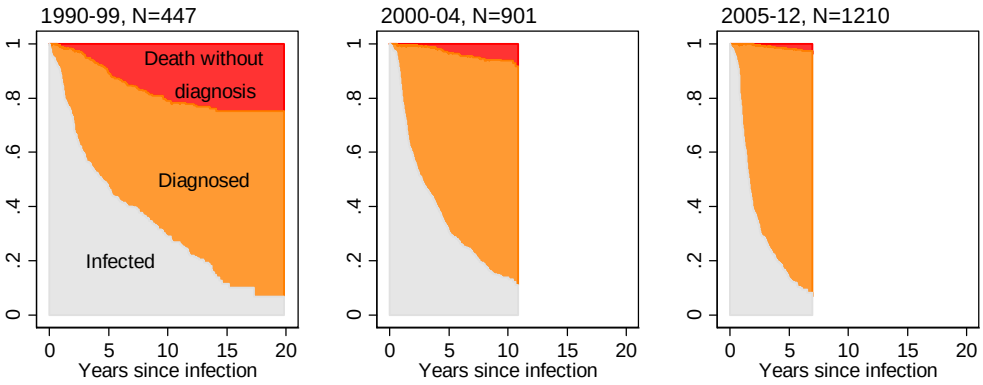


Figure 3: Diagnosis and survival by region and seroconversion cohort

Eastern Africa



Southern Africa

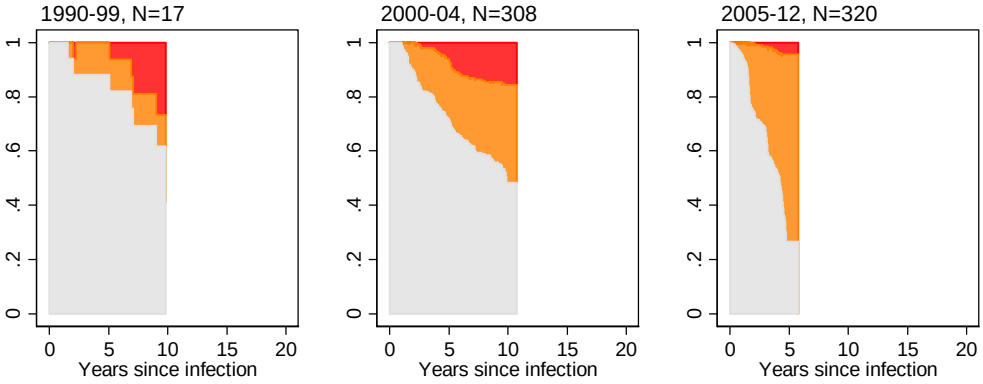


Figure 4: ART initiation and survival following diagnosis, by region and diagnosis cohort

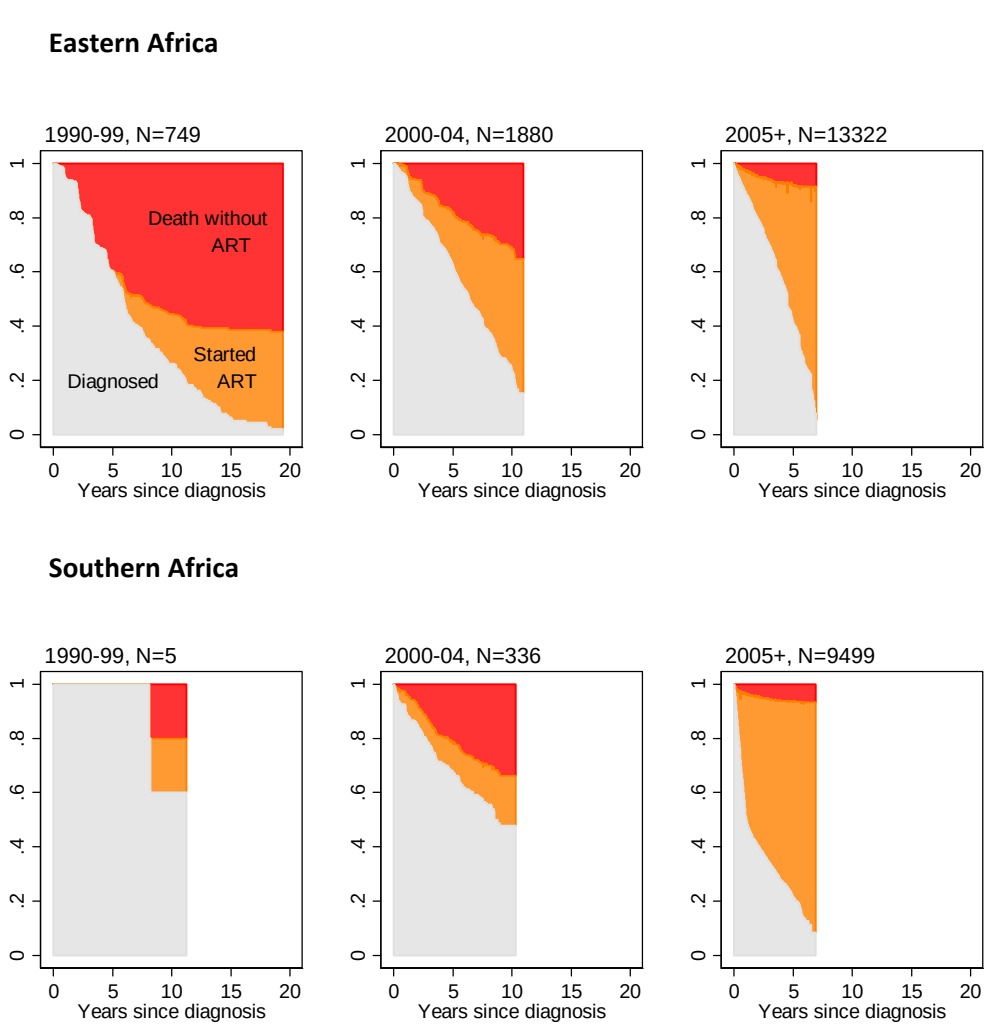


Figure 5: Survival following ART initiation, by region and ART initiation cohort

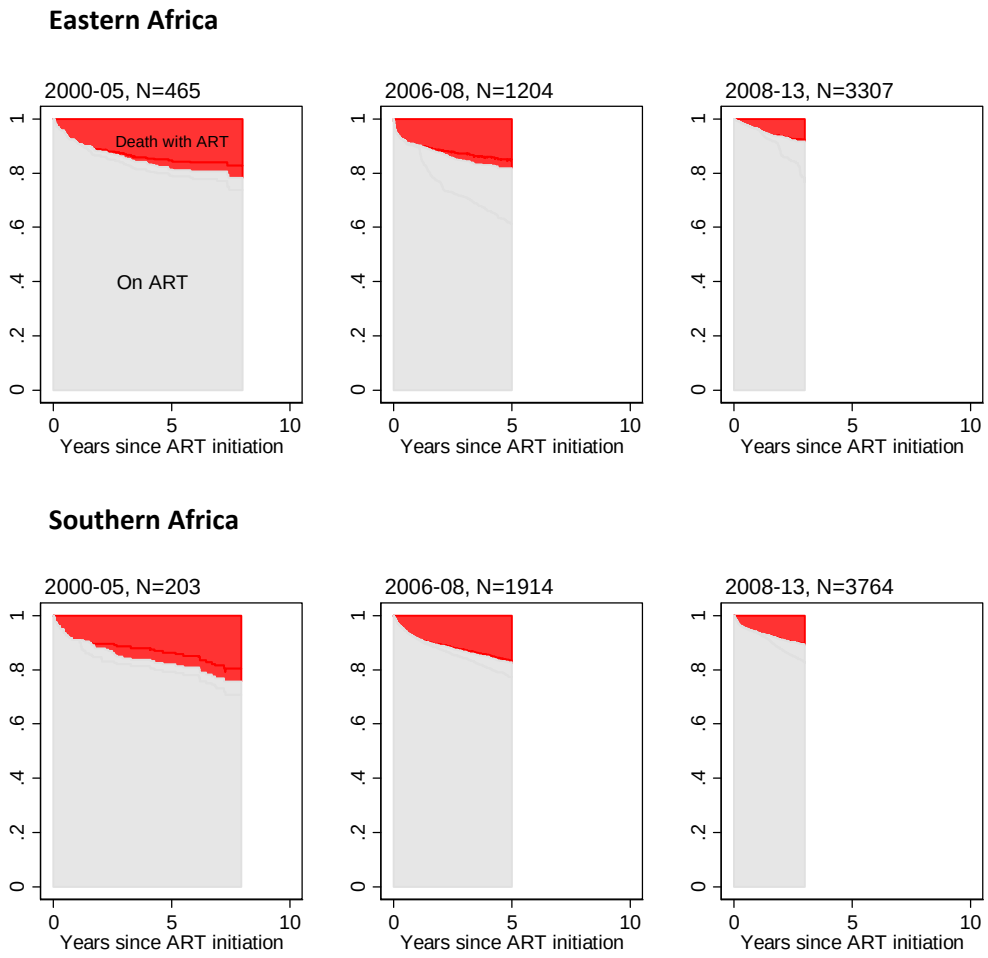


Figure 6: ART initiation and survival following seroconversion cohort, by region and seroconversion cohort