

Background mortality trends in eastern and southern Africa: Evidence from the ALPHA Network of demographic and HIV surveillance sites

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Short abstract

Changes in HIV-related mortality have dominated adult mortality trends in populations with generalized epidemics, and our understanding of the underlying or background mortality is limited. Mortality among HIV negative men and women provides an empirical estimate of background mortality, and we study this using data from six demographic and HIV surveillances sites in eastern and southern Africa. We present (i) estimates of trends in summary indices of adult mortality (e.g., ${}_{45}q_{15}$, e_{15}) by gender and HIV status, (ii) describe changes in age-specific mortality rates, and (iii) use parametric survival analysis to test gender differences in the mortality trends of HIV negative adults. Estimates cover the period 2000-2013. Preliminary findings suggest that all study sites have registered important gains in adult life expectancy, some exceeding an average of one year per annum. The contribution of the HIV negative population to the overall reduction in adult mortality has, however, been small for women and negligible for men.

Extended abstract

Background

Mortality patterns in most eastern and southern African populations have been dominated by changes in HIV related mortality (Bor et al. 2013; Jahn et al. 2008; Reniers et al. 2014). There are no good empirical estimates of the underlying or *background* mortality from other causes, and these are essential for (i) understanding the health profile of a population, and (ii) modeling the impact of HIV on mortality and the mitigating effects of antiretroviral therapy (UN 2006). However, in demographic surveillance sites that also conduct HIV sero-surveillance, we can directly estimate the background mortality as the mortality of the HIV negative population.

Data & Methods

We use data from six rural study sites in five eastern and southern African countries with severe to very severe HIV epidemics (Table 1) (Maher et al. 2010). The rollout of ART in the study sites started between 2004 and 2007, and by 2009 all residents had access to free ART at a local facility. The demographic surveillance tracks the residency episodes and terminating events of residency episodes (death, migration and administrative censoring), and thus provides a measure of the events and person-time of exposure. HIV status information comes from community-based serological surveys, supplemented by self-reports, and from record-linkage with health facilities used by residents. In order to allocate person-time lived to the respective HIV status categories we classify time prior to the first recorded HIV test as HIV status unknown. Not doing so introduces downward bias in mortality estimates because survivors would be the only ones contributing person-time prior to the first test. The time following a negative test is considered negative for a duration corresponding to the 95% probability of their age group remaining uninfected given the sex-specific HIV incidence rates. Following that point, a person's HIV status is classified as unknown. Allowance of exposure time following a negative test is necessary to observe deaths to HIV negative individuals, but is kept short so that elevated mortality among seroconvertors would not bias results.

We first present trends in summary indices of adult mortality, including the probability of dying in adulthood ($_{45}q_{15}$). Second, we focus on HIV negative adults and report estimates of age-specific mortality by sex and period. Finally, we use parametric survival analysis – with individual age as a measure of time – to assess trends and sex differences in age-adjusted mortality hazards.¹ Among several possible distributions of the outcome, the Weibull model is chosen since mortality steadily increases with age.² Under the proportional hazards specification of the Weibull model and given a set of covariates, X_j , the age-specific mortality hazard is given by: $h(\text{age}_t | X_j) = pt^{p-1} \exp(\beta_0 + X_j \beta_x)$ where p represents the change in mortality by age. In this application, we expect that $p > 1$, which signifies that the hazard is monotone increasing with age. As covariates, we consider calendar year, gender and the interaction between both.

¹ Some of these analyses have yet to be completed and are not discussed in the results section of this extended abstract.

² By the time of the conference we will also consider other distributions, including the Gompertz model.

Table 1: Alpha Network member sites contributing data to this study

Name	Short Name	Location, Country	Demographic surveillance:	Serological survey: start/interval
Kyamulibwa General Population Cohort	Masaka	Kalungu District (formerly Masaka), Uganda	1989 Annual	1989 Annual but from 2012 every 2 years
Rakai Community Cohort Study	Rakai	Rakai District Uganda	1995 12-16 months	1995 12-16 months
Magu Household Demographic Surveillance System	Kisesa	Magu District (Mwanza Region), Tanzania	1994 1-2 times per year	1994 3 years (approx)
Karonga Health and Demographic Surveillance System	Karonga	Karonga District, Malawi	2002 Continuous	Annual survey from 2007 to 2011; migrants and individuals with long testing interval since 2012
Africa Centre Demographic Information System (ACDIS)	uMkhanyakude	uMkhanyakude (formerly Hlabisa) District, South	2000 bi-annual	2003-2004 Annual
KEMRI/CDC Health and Demographic Surveillance System	Kisumu	Siaya county in former Nyanza Province, Kenya	2001 Tri-annual	2007 3 years (approx)

Preliminary results

The analytical dataset for this study contains close to 500,000 individuals, who jointly contribute over 2 million years of person-time of exposure and over 35,000 deaths (Table 2).

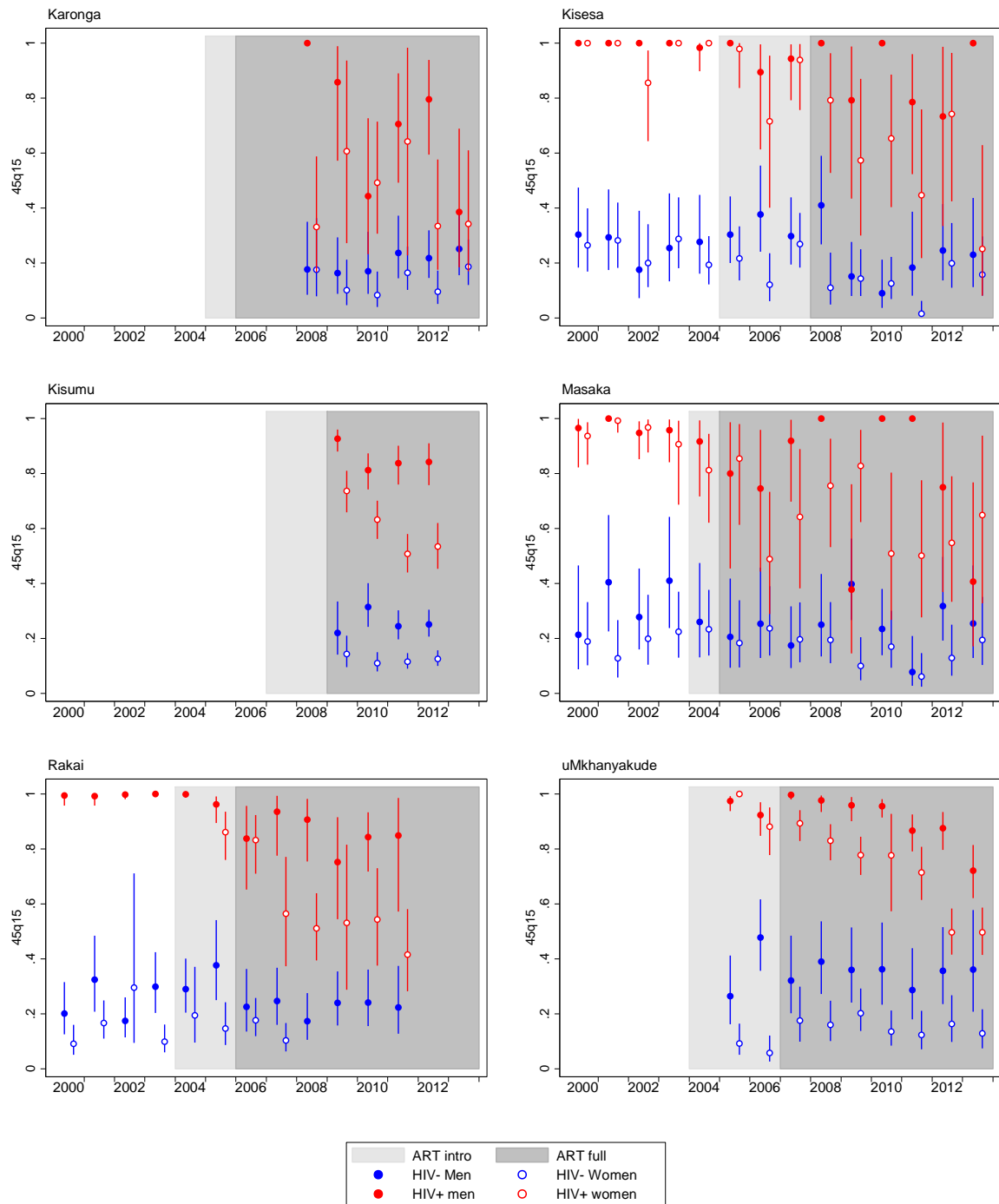
Table 2: Subjects, person years and death by study site (2000-2011)

Study Site (country)	Start date	N	Person-Years	Deaths
Karonga (MAW)	2002/2007	30,397	144,479	1,486
Kisesa (TAZ)	2000/2000	45,402	165,349	1,725
Kisumu (KEN)	2001/2008	229,177	901,590	17,289
Masaka (UGA)	2000/2000	22,001	105,864	1,412
Rakai (UGA)	2000/2000	68,247	303,276	3,840
uMkhanyakude (RSA)	2000/2005	88,230	467,619	9,560
Total		483,454	2,088,177	35,312

Notes: Two start dates are given per site: the start year of the demographic surveillance data used in this study, and the start year of the population-based HIV surveillance. Records are administratively censored on 31 December 2011 (but will be extended to 31 December 2013 by the time of the conference). MAW: Malawi; TAZ: Tanzania; KEN: Kenya; UGA: Uganda; RSA: South Africa

Figure 1 summarizes trends in adult mortality by HIV status and sex. The shaded background represents the year wherein ART was first introduced in the study site (light grey) and the year wherein rollout was considered complete (dark grey). These estimates clearly bring about the mortality reductions among HIV positive men and women following the introduction of ART. This is most clearly visible in the study sites where the time series start by the year 2000. Prior to the availability of treatment, the life table probability that a 15 year-old HIV positive person would survive to age 65 was close to zero. At current rates, the probability that an HIV positive 15-year old would survive to age 65 are often in excess of 50 percent. Even though the confidence intervals around these estimates are fairly large because of the relatively small number of HIV positives in these populations, the downward trend in the mortality of HIV positive adults is clearly pronounced in all study sites.

Figure 1: trends in the probability of dying in adulthood ($_{45}q_{15}$) by HIV status, sex and study site



The steep mortality declines among people living with HIV (PLHIV) contrasts with that of the HIV negative population. In their case, the probability of dying in adulthood varies between 15 and 30 percent depending on the sex and study site, and there is no clear upward or downward trend in the estimates. This stagnation in background mortality thus supports an earlier finding that adult life expectancy increases in these populations (often exceeding 1 year per annum) are largely driven by a reduction in HIV related mortality; a phenomenon that is the combined result of (i) earlier declines in new infections and (ii) a reduction of the mortality rates of PLHIV (Reniers et al. 2015).

In the full paper that will be prepared for the conference, we will also explore age patterns of mortality among HIV negative adults, including adults above age 65.

In Table 3, we present (preliminary) results from the Weibull regression of the mortality among HIV negative adults aged 15 and above. The age term, p , is greater than 1 indicating that adult mortality is monotone increasing with age as we expect in human populations. The model includes main effects for sex, calendar year and study site, and interactions between sex and calendar year, and sex and study site.

The main effect of sex (HR=2.01) represents the male-female difference in the age-adjusted mortality hazard in uMkhanyakude (RSA). Gender differences in adult mortality are much smaller in the other study sites and vary between $HR=2.01*0.58=1.17$ in Karonga (MAW) and $HR=2.01*0.65=1.31$ in Kisumu (KEN).

Gender differences in adult mortality also seem to have increased over time as women's age-adjusted mortality hazards declined by about 3 percent a year ($HR=0.97$, 95% CI:0.96-0.98), while men's stagnated ($HR=0.97*1.02=0.99$).

Table 3: Weibull regression output

N = 209,250; D = 6,328	Main effects			Interaction with sex = male		
	hazard ratio	95% CI		hazard ratio	95% CI	
female	1					
male	2.01	1.69	2.39			
year (cont)	0.97	0.96	0.98	1.02	1.01	1.04
uMkhanyakude	1			1		
Karonga	0.81	0.69	0.96	0.58	0.46	0.73
Kisesa	1.01	0.89	1.15	0.64	0.53	0.77
Kisumu	1.15	1.04	1.28	0.65	0.56	0.75
Masaka	1.07	0.94	1.22	0.61	0.50	0.73
Rakai	0.94	0.80	1.10	0.62	0.51	0.77
age term (Weibul)	1.37	1.35	1.39			

Preliminary conclusions

In a period characterized by important reductions in HIV-related mortality, changes in the background mortality have been at best modest. This is evidenced by mortality trends among HIV negative adults in six rural populations in eastern and southern Africa. Among women we have registered small reductions in adult mortality over the last decade; among HIV negative men adult mortality rates have stagnated.

Acknowledgements

This study is funded by the Wellcome Trust (085477/Z/08/Z) and the Bill and Melinda Gates Foundation (BMGF- OPP1082114).

References

- Bor, J., A.J. Herbst, M.-L. Newell, and T. Bärnighausen. 2013. "Increases in adult life expectancy in rural South Africa: valuing the scale-up of HIV treatment." *Science* 339(6122):961-965.
- Jahn, A., S. Floyd, A.C. Crampin, F. Mwaungulu, H. Mvula, F. Munthali, N. McGrath, J. Mwafilaso, V. Mwinuka, and B. Mangongo. 2008. "Population-level effect of HIV on adult mortality and early evidence of reversal after introduction of antiretroviral therapy in Malawi." *The Lancet* 371(9624):1603-1611.
- Maher, D., S. Biraro, V. Hosegood, R. Isingo, T. Lutalo, P. Mushati, B. Ngwira, M. Nyirenda, J. Todd, and B. Zaba. 2010. "Translating global health research aims into action: the example of the ALPHA network." *Tropical Medicine and International Health* 15(3):321-328.
- Reniers, G., J. Eaton, J. Nakiyingi-Miir, C. Kabudula, A. Crampin, K. Herbst, M. Urassa, A. Nyaguara, E. Slaymaker, A. Cori, S. Gregson, S. Macquins, D. Michael, V. Hosegood, A. Price, X. Gomez-Olive, I. Kasamba, E. Mclean, and B. Zaba. 2015. "The Impact of Antiretroviral Therapy on Adult Life Expectancy in sub-Saharan Africa." in *Annual Conference on Retroviruses and Opportunistic Infections (CROI)*. Seattle.
- Reniers, G., E. Slaymaker, J. Nakiyingi-Miir, C. Nyamukapa, A.C. Crampin, K. Herbst, M. Urassa, F. Otieno, S. Gregson, M. Sewe, D. Michael, T. Lutalo, V. Hosegood, I. Kasamba, A. Price, D. Nabukalu, E. McLean, B. Zaba, and A. Network. 2014. "Mortality trends in the era of antiretroviral therapy: evidence from the Network for Analysing Longitudinal Population based HIV/AIDS data on Africa (ALPHA)." *AIDS* 28 Suppl 4:S533-542.
- UN. 2006. "World Population Prospects. The 2004 Revision. Volume III: Analytical Report." New York.