Time from HIV sero-conversion to death: What factors affect survival?

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Abstract.

Survival following HIV infection in adults is around 10 years in all countries, irrespective of income. We used a large dataset from a population-based cohort in rural Uganda to estimate the median survival among adults following HIV seroconversion and to assess several risk factors. Kaplan-Meier functions were used to estimate survival patterns, and Weibull distributions to compare survival estimates. In this cohort, survival times varied by age, but not sex. The median survival was 9.6 years (95% CI 8.2-10.2). For those infected between 15 and 24 years of age, median survival was over 13 years, while in those infected at 45 years or more, median survival was under 6 years. There were no significant differences in survival by sex, tribe, religion, marital status, or sexual behaviour. The finding that survival is largely independent of social and environmental factors reinforces the importance of universal access to antiretroviral therapy to extend survival.

Introduction.

HIV/AIDS is a major cause of death in many low and middle income countries. In high income countries the overall survival, following HIV sero-conversion and prior to the general availability of anti-retroviral therapy (ART) was estimated at 11.2 years by the CASCADE collaboration [1]. The median survival in developed countries varied by age at seroconversion, but not by sex and route of infection.

In low and middle income countries (LMC), survival following HIV seroconversion was reported from eight longitudinal cohorts in seven countries showed a median survival of 10.2 years [2]. Survival varied by age at seroconversion, but not by sex, and survival across the five African sites was very similar. However the minimum dataset used in that analysis did not allow the exploration of further risk factors for survival. Other analyses in Uganda have shown a similar survival post HIV seroconversion, but have been too small to investigate other factors of interest [3]. The collection of data over 20 years from a rural cohort in south-western Uganda allows us to examine a wide range of other risk factors for survival post HIV-infection.

Methods.

We identified new HIV seroconverters from annual, cross-sectional, serological surveys in a population cohort of around 18,000 people in south-west Uganda. Annual, demographic follow up was conducted for vital registration and to ascertain mortality. More details of the population cohort, follow-up procedures and the serological testing for HIV can be obtained from other publications [4-5].

Participants were eligible for this analysis if they were adult (at least 15 years of age), had less than four years between the last seronegative HIV test, and the first seropositive HIV test. The date of seroconversion was defined as half way between the last negative and first positive HIV test, and participants were included in the analysis if they had at least 2 years of follow-up following seroconversion.

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Age at seroconversion was grouped into ten-year age groups, 15-24, 25-34, 35-44 and 45 years and above. All subjects were censored at the date of death, the end of the study, or when they were last known to be alive. Data on ART initiation was not recorded for individual subjects, but survival was limited to before 2004, when anti retroviral therapy became available to cohort members.

Demographic and other risk factors were taken from responses to questionnaires administered from the first occasion after seroconversion through to the end of follow up. We analysed all responses and categorised participants as to whether they reported any casual sexual partner, or any extra-marital partner from the date of sero-conversion to the end of the study.

Analysis methods

The analysis calculated survival since the estimated date of sero-conversion, but individuals entered the analysis at the time of the first positive test, resulting in up to 2 years of left censoring. Kaplan-Meier functions were used to calculate survival patterns, and the log-rank test to compare survival between groups. The Weibull distribution was fitted using parametric regression techniques and used to model survival and to compare the effects of age at infection, sex and other risk factors. Crude and adjusted hazard rate ratios (HRR) are presented, with 95% CI and p-values to compare differences. All analysis was undertaken in Stata 9.0 (Stata Corp, Texas, USA). Estimated survival times were taken from the model parameters.

Results.

A total of 341 people have been recorded as sero-converting to HIV positive in the Masaka cohort prior to March 2006. Of these 294 had a seroconversion date prior to 1st January 2004, and have been included in this analysis. The characteristics of the seroconverters are shown in Table 1. In total 84 deaths were observed over a period of 1425 person-years of follow up, with a median survival time of 9.6 years (95% CI 8.2-10.2 years).

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Table 1 Characteristics of 294 subjects who sero converted to HIV positive prior to 1`st Jan 2004.

		Frequency
Sex	Male	138 (47%)
	Female	156 (53%)
Age groupings (at sero conversion)	15-24 years	143 (49%)
	25-34 years	73 (25%)
	35-44 years	44 (15%)
	45 or more years	34 (12%)
Tribe	Muganda	183 (62%)
	Other Ugandan tribes	15 (5%)
	Tribes originating elsewhere	86 (29%)
	Missing	10 (3%)
Religion	Catholic	212 (72%)
	Protestant	32 (11%)
	Muslim	40 (14%)
	Missing	10 (3%)
Following sero-conversion (at some time during the follow up).	Reported being married	115 (39%)
	Reported being widowed	43 (15%)
	Reported being separated	179 (61%)
	Reported casual sexual partner	63 (21%)
	Reported extra marital partner	114 (39%)
Deaths		83 (28%)

The survival curves (Figure 1) differed by age at seroconversion (p<0.001), but not by sex (p=0.7).

Figure 1. Survival by sex and age.
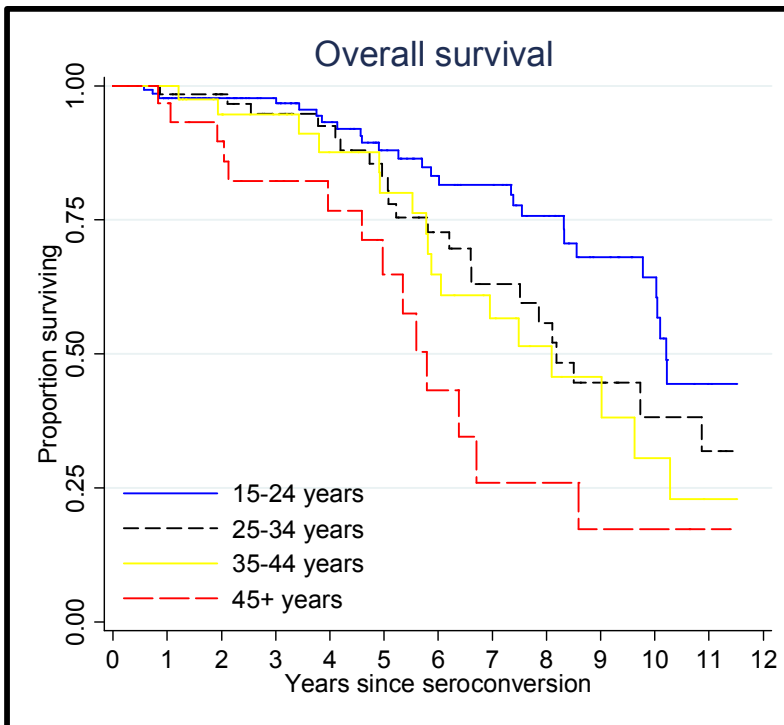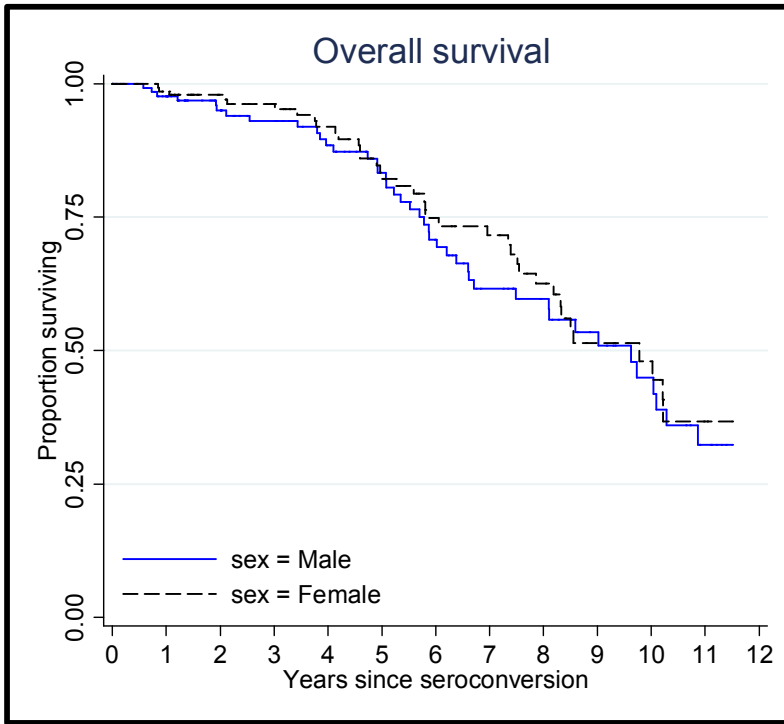
After adjusting for age at sero-conversion there was no significant difference in survival by sex (p=0.4), tribe (p=0.9), or religion (p=0.13). Similarly after adjusting for age there was no significant difference in those who reported being married after sero-conversion (p=0.22), widowed (p=0.9) or separated (0.6). We also considered the effect of sexual behaviour on survival, but after adjusting for age, there was no significant difference in survival for those who reported polygamous marriages (p=0.160), casual sexual partners (p=0.2), extra-marital sexual partners (p=0.3) or more than one sexual partner in the past year (p=0.085).

Discussion

Previous papers have shown that age is significantly associated with survival after HIV sero-conversion, with those who sero-convert at 25-29 years of age surviving almost twice as long as those who sero-convert at 50 years of age [2,6]. However previous reports have not look at the influence of other socio-demographic factors on survival, nor the effect of sexual behaviour on survival.

This paper reports survival from almost 300 people who sero-convereted over 13 years prior to the general availability of ART. None of the factors investigated showed significant association with survival, which indicates that survival post HIV infection may be independent of social and environmental factors. Although this study followed up almost 300 sero-converters for up to 13 years, the power of the study was insufficient to identify as significant, effects that produced small differences in survival, of less than 2 years difference in survival, or when less than 25% of the population reported the characteristics. Another consideration is that some factors, such as religion, and marital status change over time, and we have not taken these changes into consideration in this analysis. Others have shown that survival may differ by the sub-type of the virus [7-9], but this has not been analysed in this presentation.

The importance of age in determining survival following HIV seroconversion must be used in education messages to all age groups. The consequence of HIV infection is drastically reduced survival, and ART is the only way to extend survival. These data will

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give us some accurate benchmarks to gauge the effect of ART on the survival of HIV positive people in sub-Saharan Africa.

The definition of seroconversion was based on two HIV tests taken from a population based cohort with annual serological testing for HIV. Although most sero-converters are seen with less than three years between the last HIV negative test, and the first HIV test, a few have considerably longer between the two tests, making it difficult to assess an accurate date for sero-conversion. Some sero-converters were lost to follow up as the moved out of the area. All follow up was censored at 1st January 2004 when anti-retroviral therapy (ART) became generally available to the population. At present over 80% of cohort members in need of ART are receiving this through the cohort clinic.

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