Age and cause decomposition of life expectancy changes following the introduction of antiretroviral therapy in South Africa (2000-2013)

Alexandra Martin-Onraet, Georges Reniers, Kobus Herbst, Clara Calvert, Emma Slaymaker and Vicky Hosegood

Extended abstract

Introduction

The southern Africa region represents one fifth of all HIV infections worldwide, and in South Africa (RSA) alone, more than 6 million people lived with HIV in 2014 (UNAIDS, 2014, Delva and Abdool Karim, 2014). The advent of antiretroviral therapy (ART) has brought great improvements in the survival of HIV positive individuals, and almost one decade after full introduction of combined ART, mortality rates of people living with HIV (PLHIV) have significantly declined (Reniers et al., 2014, Herbst et al., 2011). To date most studies of the impact of ART on mortality come from clinical cohorts, and are not population-based (Jahn et al., 2008, Johnson et al., 2013, Mills et al., 2011). One population-based study from Kwazulu-Natal reports an 11.3 year-gain in population-wide life expectancy (LE) between 2003 and 2011(Bor et al., 2013). In this study, we use the same data source to describe (i) changes in cause of death structure as mortality declined, and (ii) estimate the residual burden of HIV on adult mortality.

Methods

Data from an open population cohort of a DSS covering 93,650 individuals aged 15 and above in rural Kwazulu-Natal were analysed. This site is maintained by the Africa Centre for Health and Population studies; it covers an area of 434km^2 and is characterized by a high prevalence of HIV (29%), as well as high levels of cardiovascular risk factors, trauma-related mortality and temporary migration (Herbst et al., 2011, Reniers et al., 2014). The DSS started in 2000 and the population-based HIV testing was included annually in 2003-2004. Household surveys are done biannually and include data on household members, civil status, deaths description, migration, membership or residency. Data are collected from a key informant in the household. The serologic survey is done annually, directly to household residents, including information about the HIV status, reason for not testing and sexual behaviours (Tanser et al., 2008, Herbst et al., 2011). ART was introduced in 2004 and the program was fully implemented by 2006.

We describe mortality rates over time, by HIV status and age. We present non-parametric estimates of adult life expectancy by sex, year and HIV status. Adult life expectancy is defined as the number of additional years that a survivor to age 15 is expected to live beyond that age if subjected to the mortality pattern observed in a specific period. To limit bias associated with age over-reporting, we disregard person-years lived above age 100, so in effect we report the per-capita person years lived between ages 15 and 100, but hereafter we refer to these estimates as the adult LE (Bor et al., 2013).

The gross or total gains in adult LE since the introduction of ART are the mere difference in the LE between 2003 and the last year with available data(Reniers G., 2015). The adult LE deficit in 2013 is estimated as the difference between adult LE of HIV negative population and the whole population during that year and thus quantifies the public health impact of HIV conditional on the health profile of its population. This interpretation presumes that all of the differences in mortality between HIV negatives and the rest of the population are attributable to HIV, either directly or due to a correlation between HIV and other risk factors, such as socioeconomic status, violence, substance abuse or behaviour change (Reniers G., 2015).
To better understand the contribution of age and specific cause of death to the overall gains in adult LE and the current LE deficit, we decompose the differences following a method described by Arriaga (Arriaga, 1984). The decomposition of the LE gains to date highlights the contribution of mortality changes in each age to the overall change in life expectancy between 2 periods: the period pre-ART (2000-04) and the period post full ART implementation (2010-13). We decompose the LE deficit during the period 2011-13 by age and cause of death to assess how much of the life years lost is explained directly by HIV/AIDS related causes or indirectly by other probably associated causes. The age decomposition of the LE deficit is also done by 3-year interval after ART introduction to assess differences in age contribution to the deficit over time.

Information on the presumed causes of death comes from verbal autopsy interviews with relatives of deceased individuals. Cause of death assignment has been done with the interVA-4 instrument (Byass et al., 2012).). Data presented here were produced by individually matching CoD. The CoD are grouped as major categories adapted from the Global Burden of Disease, including HIV/AIDS, pulmonary tuberculosis, life-style related non-communicable diseases (NCD), other NCD, external injuries, maternal and nutritional causes, other infectious diseases and indeterminate (Herbst et al., 2011). [1]

Preliminary results [2]

Mortality trends:
There were 93645 individuals aged 15 to 100 years and 10340 deaths from 2000 to 2013. Verbal autopsy interviews were completed for 9830 of these deaths, and a cause of death could be assigned for 9659 cases with a completed VA. Overall mortality rate decreased from 22.3 per 1000 person-years in 2000-04 (CI95% 21.6-22.9) to 19.7 per 1000 person-years in 2005-09 (CI95% 19.1-20.3) and 14.5 per 1000 person-years in 2010-13 (CI95% 13.9-15.1). Comparing to the first period, overall mortality rate was reduced by 35% in 2010-13 (RR= 0.65, 95%CI 0.62-0.68). Mortality rate differed by sex: in men, the rate was 21.5 per 1000 (CI95% 20.9-22.1)) for all periods and in women 17.3 per 1000 (CI95% 16.9-

[1] This classification might change with further analysis
[2] By the time of the conference, we will be in a position to extend our analysis to include data for 2014. We will also discuss the methods and results with far greater detail.
[3] In the full paper we will quantify in detail how much of the total difference(s) in adult is explained by the different CoD categories.

17.8). Overall, women had 20% lower mortality compared to men (RR=0.81, CI95% 0.78-0.84). The adjusted mortality rate ratio did not change stratifying by period.
When comparing age-specific mortality rates by period, there is evidence of increased mortality in age-groups 20-59 years in 2000-04 compared to 2010-13. These mortality rates were more than halved for young adults (age-groups from 20 to 34 years) from period 1 to period 3 (see table 1).
Mortality rate was 12.2 per 1000 (CI95% 11.4-12.9) in HIV negative individuals compared to 35.8 per 1000 (CI95% 34.1-37.5) in HIV positive individuals and 13.9 per 1000 (CI95% 13.4-14.4) in individuals with HIV status unknown. Overall, between 2006 and 2013, HIV positive individuals had 3.1 times higher mortality rates than HIV negative (RR=3.1, CI95% 2.87-3.35).

LE trends:
Figure 1 shows the overall adult life expectancy by calendar year from 2000 to 2013. In women, LE decreased from 43.5 years in 2000 (CI95% 41.1-45.9) to 37.1 years in 2003 (CI95% 35.5-39.5) when it reached its lowest point. After the ART introduction it increased to 53.7 years in 2013 (CI95% 51.2-55.9) (figure 1). For men, it decreased from 34.5 years (CI95% 32.5-36.6) to 30.9 years (CI95% 29.1-32.4) from 2000 to 2003 and then increased to 41.8 years (CI95% 39.7-43.9) in 2013. Life expectancy for HIV positive individuals increased from 25.8 years in 2006 (CI95% 22.7-29.4) to 39.6 years in 2013 (CI95% 37.3-44.6) in women and from 24.1 years (CI95% 20-29.5) to 33.6 years (CI95% 29.4-39.1) in men (figure 2).

LE gains:
Compared to 2003, population-wide gains in adult LE by 2013 amount to 10.9 and 16.6 years for men and women, respectively. Individuals aged 25-39 years contributed the most to the LE gain. By period, LE gains by 2010-13 are 11.9 and 8.2 years in women and men respectively, compared to 2000-04. Persons aged 25-39 years contribute the most to the gains in life expectancy and account for 60% of the LE change between both periods in men and women. Across all ages, changes in TB and HIV/AIDS-related mortality explain most of the LE gain between the two periods under consideration: 85.6% in men and 95.8% in women when using the first cause of death (see figure 3). [3]

LE deficit:
Despite these impressive mortality reductions, the LE deficit is still 5.1 years for men and 9.7 years for women in 2013 (figure 1). For the period of 2011-13, it amounts 8.7 years in men and 13 years in women. Variability in TB and HIV/AIDS-related mortality explains most of the LE deficit in both men and women during that period. When adding the contribution of each cause of death across all age groups, the four main causes that contribute to the LE deficit in women in 2011-13 are: pulmonary TB (35%), HIV/AIDS (23.5%), lifestyle associated NCD (17%) and other NCD (7.5%). In men, the four main causes are: pulmonary TB (64%), HIV/AIDS (9%), other NCD (9%) and external injuries (9%). This suggests that HIV positive men not only have higher mortality from HIV related causes, but also from external injuries (see figure 2).

When comparing by three-year interval since the introduction of ART, there is a shift to a larger contribution of older ages to the LE deficit in women in recent years: in 2005-07, women aged 50+ contributed 36%. This decreased to 30% in 2008-10 and increased to 44% in 2011-13. This is not the case in men, where the contribution of men aged 50+ to the LE deficit was 17% in 2005-07 and 8% in 2011-13.

Amongst individuals older than 75 years, HIV negative have a mortality rate of 65.8 per 1000 (CI95% 59.4-73.0) compared to 90.7 per 1000 (CI95% 85.5-96.2) for the rest of the population above that age. The difference in mortality rates in old age is, however, only apparent for women (RR= 1.6, CI95% 1.38-1.86). For men the relative rate of mortality is the same for HIV negative and the rest of the population (RR=0.97, CI95% 0.80-1.17). This could be due to the fact that relatively few HIV positive men have survived until old age. We will explore this phenomenon in greater detail by the time of the conference.

Preliminary Conclusions

After full ART expansion, there has been a substantial increase in adult LE. Most of these gains are due to mortality reductions in young adults, and a reduction of HIV/AIDS (including TB) related deaths. Despite these important mortality reductions, the adult LE in this population still falls short of the LE among HIV negative individuals. Again, it is HIV related mortality among young adults that contribute most to that difference. These results are highly relevant to evaluate the population impact of ART and support continuing improvement in early HIV detection and ART coverage.

By the time of the conference we will be able to present and compare LE estimates for HIV individuals on ART and not on ART. We will also present the results of weighted cause decomposition by using population-based cause-specific mortality fractions and compare them to the individually matched cause decomposition. We will also produce HIV-cause deleted LE estimates to evaluate the impact of HIV as a cause of death on life years lived (Bor et al., 2013).

Table 1: Age specific mortality rates and Rate Ratios for periods 2000-04 and 2010-13										
	2000-04				2010-13				Rate Ratio 2010-13/2000-04	
Age	Individuals	Deaths	PY	Rate*	Individuals	Deaths	PY	Rate*	RR	95%CI
15-19	20046	108	42388	2.6	16784	69	32360	2.1	0.84	0.62-1.13
20-24	15346	262	29840	8.8	14350	104	25935	4.0	**0.46**	0.36-0.57
25-29	10677	498	21071	23.6	11022	199	20662	9.6	**0.41**	0.35-0.48
30-34	8135	533	17011	31.3	7813	212	15015	14.1	**0.45**	0.38-0.53
35-39	6777	454	15000	30.3	5879	209	12334	16.9	0.56	0.48-0.66
40-44	5976	415	13972	29.7	4780	170	10165	16.7	0.56	0.47-0.67
45-49	4597	332	10780	30.8	4212	153	9262	16.5	0.54	0.44-0.65
50-54	3578	227	8845	25.7	3910	153	8913	17.2	0.67	0.55-0.82
55-59	2828	189	6403	29.5	2980	126	6725	18.7	0.64	0.51-0.79
60-64	2638	240	7018	34.2	2341	145	5551	26.1	0.76	0.62-0-94
65-69	2176	219	5212	42.0	1745	135	3747	36.0	0.86	0.69-1.06
70-74	2019	253	5347	47.3	1604	197	3899	50.5	1.07	0.89-1.29
75-79	1100	164	2712	60.5	1101	152	2422	62.8	1.04	0.83-1.29
80-84	586	122	1493	81.7	921	160	2124	75.3	0.92	0.73-1.17
85+	459	177	1232	143.7	540	140	1356	103.2	0.72	0.58-0.90

* per 1000 person-years

Table 1: Age specific mortality rates and rate ratios by periods

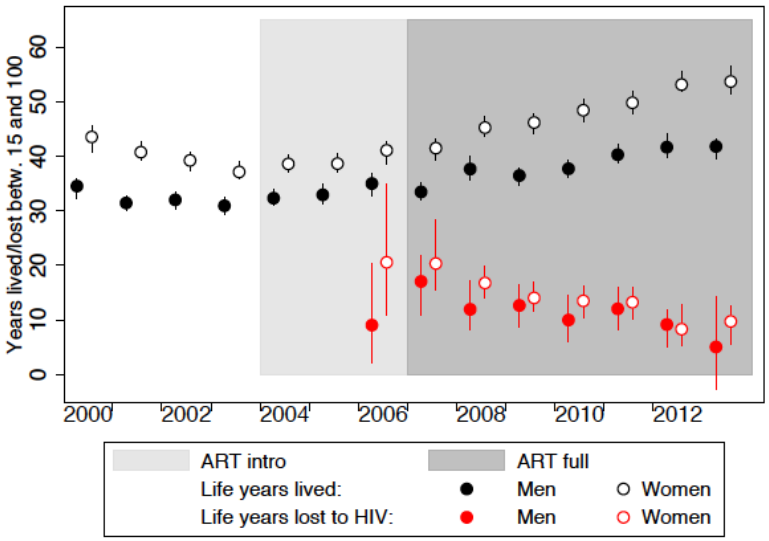

Figure 1: Life years lived and Life years lost to HIV, from 2000 to 2013.

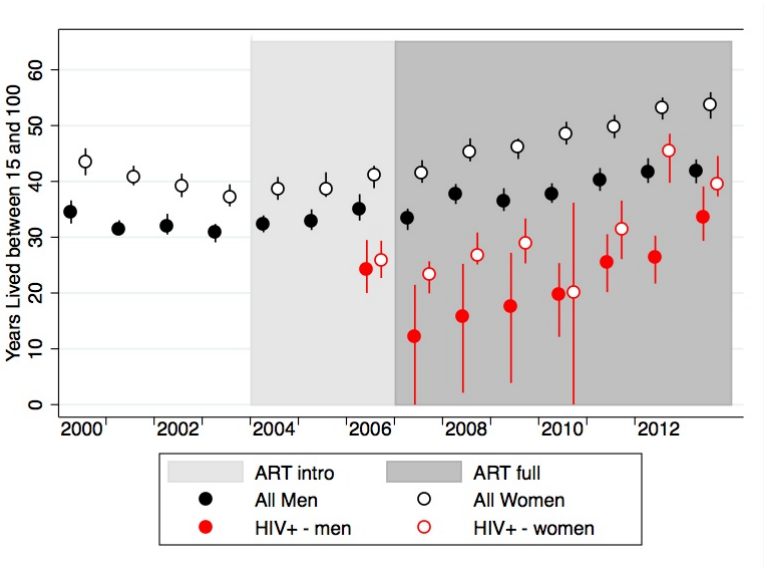

Figure 2: Life years lived, all individuals and HIV positive, from 2000 to 2013

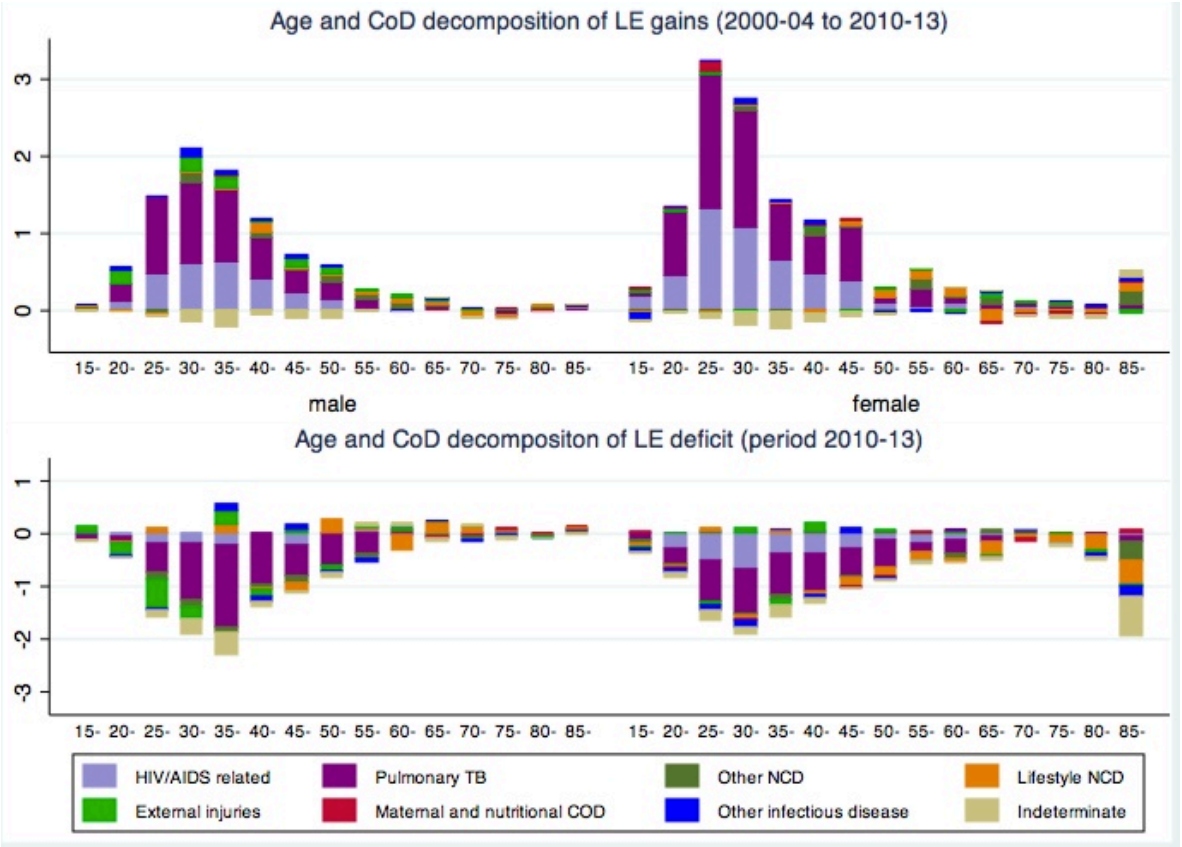

Figure 3: Age and cause decomposition of LE gain and LE deficit

References:

ARRIAGA, E. E. 1984. Measuring and explaining the change in life expectancies. *Demography,* 21**,** 83-96.

BOR, J., HERBST, A. J., NEWELL, M. L. & BARNIGHAUSEN, T. 2013. Increases in adult life expectancy in rural South Africa: valuing the scale-up of HIV treatment. *Science,* 339**,** 961-5.

BYASS, P., CHANDRAMOHAN, D., CLARK, S. J., D'AMBRUOSO, L., FOTTRELL, E., GRAHAM, W. J., HERBST, A. J., HODGSON, A., HOUNTON, S., KAHN, K., KRISHNAN, A., LEITAO, J., ODHIAMBO, F., SANKOH, O. A. & TOLLMAN, S. M. 2012. Strengthening standardised interpretation of verbal autopsy data: the new InterVA-4 tool. *Glob Health Action,* 5**,** 1-8.

DELVA, W. & ABDOOL KARIM, Q. 2014. The HIV epidemic in Southern Africa - Is an AIDS-free generation possible? *Curr HIV/AIDS Rep,* 11**,** 99-108.

HERBST, A. J., MAFOJANE, T. & NEWELL, M. L. 2011. Verbal autopsy-based cause-specific mortality trends in rural KwaZulu-Natal, South Africa, 2000-2009. *Popul Health Metr,* 9**,** 47.

JAHN, A., FLOYD, S., CRAMPIN, A. C., MWAUNGULU, F., MVULA, H., MUNTHALI, F., MCGRATH, N., MWAFILASO, J., MWINUKA, V., MANGONGO, B., FINE, P. E., ZABA, B. & GLYNN, J. R. 2008. Population-level effect of HIV on adult mortality and early evidence of reversal after introduction of antiretroviral therapy in Malawi. *Lancet,* 371**,** 1603-11.

JOHNSON, L. F., MOSSONG, J., DORRINGTON, R. E., SCHOMAKER, M., HOFFMANN, C. J., KEISER, O., FOX, M. P., WOOD, R., PROZESKY, H., GIDDY, J., GARONE, D. B., CORNELL, M., EGGER, M., BOULLE, A. & INTERNATIONAL EPIDEMIOLOGIC DATABASES TO EVALUATE, A. S. A. C. 2013. Life expectancies of South African adults starting antiretroviral treatment: collaborative analysis of cohort studies. *PLoS Med,* 10**,** e1001418.

MILLS, E. J., BAKANDA, C., BIRUNGI, J., CHAN, K., FORD, N., COOPER, C. L., NACHEGA, J. B., DYBUL, M. & HOGG, R. S. 2011. Life expectancy of persons receiving combination antiretroviral therapy in low-income countries: a cohort analysis from Uganda. *Ann Intern Med,* 155**,** 209-16.

RENIERS, G., SLAYMAKER, E., NAKIYINGI-MIIRO, J., NYAMUKAPA, C., CRAMPIN, A. C., HERBST, K., URASSA, M., OTIENO, F., GREGSON, S., SEWE, M., MICHAEL, D., LUTALO, T., HOSEGOOD, V., KASAMBA, I., PRICE, A., NABUKALU, D., MCLEAN, E., ZABA, B. & NETWORK, A. 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**,** S533-42.

RENIERS G., E. J., NAKIYINGI-MIIRO J., CRAMPIN A.C., CHODZIWADZIWA KABUDULA, HERBST K., URASSA M., NYAGUARA A., SLAYMAKER E. 2015. The Impact of Antiretroviral Therapy on Adult Life Expectancy in Sub-Saharan Africa. *CROI, abstract 161.* Seattle.

TANSER, F., HOSEGOOD, V., BARNIGHAUSEN, T., HERBST, K., NYIRENDA, M., MUHWAVA, W., NEWELL, C., VILJOEN, J., MUTEVEDZI, T. & NEWELL, M. L. 2008. Cohort Profile: Africa Centre Demographic Information System (ACDIS) and population-based HIV survey. *Int J Epidemiol,* 37**,** 956-62.

UNAIDS. 2014. *HIV and AIDS estimates* [Online]. www.unaids.org/en/regionscountries/countries/southafrica.