

# **Gender differences in AIDS mortality following the introduction of antiretroviral therapy in Ethiopia**

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## **0. Abstract**

The rollout of antiretroviral treatment (ART) in eastern and southern Africa will be one of the most important public health interventions in the years to come. Among the lingering dangers in that effort is that inequalities in infection rates will be compounded by inequities in the access to treatment. Because of a lack of vital registration systems, however, the settings where these concerns are probably most legitimate go without monitoring. We use 5-year data from an ongoing surveillance of burials at all cemeteries of Addis Ababa to investigate the population level impact of antiretroviral treatment on adult mortality trends. To that end, we compare projected with observed mortality trends and develop a method to estimate AIDS mortality based on lay reports of the causes of death. Our results suggest that AIDS mortality indeed declined since the introduction of ART, but more so for men than for women.

## **1. Introduction**

The provision of ART will be one of the most important public health interventions in sub-Saharan Africa in the decade to come. Among the lingering threats in the large scale provision of ART is that it will compound inequality in the risk of infection with inequity in the access to treatment [Loewenson & McCoy 2004 #2650] [Egger, Boule, et al. 2005 #20] [McCoy, Chopra, et al. 2005 #2640] [Rosen, Sanne, et al. 2005 #2720]. It is more common, however, to find this concern expressed in editorials or viewpoints rather than reports of research findings because most settings where ART has been and will be rolled-out most extensively simply lack the monitoring systems necessary to reach these conclusions [Cleland 1996 #1930] [Cooper, Rotimi, et al. 1998 #1690]; [Diaz, Loth, et al. 2005 #2630] [Mathers, Fat, et al. 2005 #3470]. HIV

prevalence figures no longer provide solace, as they have become a confounded measure of the scope of the epidemic as well as our success of combating it. The few studies on inequities in the impact of ART in developed countries as well as Brazil, have reached mixed conclusions [McNaghten, Hanson, et al. 2003 #2740] [Antunes, Waldman, et al. 2005 #10] [Gebo, Fleishman, et al. 2005 #2730]. Reports from sub-Saharan Africa are non-existing, or have not yet been published.

This new stage in the fight against AIDS thus poses new challenges to demographers and epidemiologists to review their set of methods to come up with reasonably timely data and reasonably accurate measures for monitoring the effectiveness of ART and biases in their delivery schemes. Population-based mortality data are the ultimate outcome measure in this respect and that is evocative of vital registration type data collection systems. These are, as most of us have come to realize, notoriously difficult to set up and maintain in resource constrained settings. In this contribution we use an ongoing registration of burials at all cemeteries of Addis Ababa as an exemplary alternative approach. A surveillance of burials is a relatively simple logistical endeavor as it taps into an existing infrastructure of cemeteries. In some of the cemeteries under surveillance, a rudimentary registry of burials existed prior to the initiation of our project (\*\*see sanders et al 2003\*\*\*\*).

Since February 2001 cemetery clerks collect background socio-demographic characteristics and the lay report of the cause of death from close relatives or friends while making the arrangements for burial. So far, we have used these data to document the high impact of HIV on adult mortality [Sanders, Araya, et al. 2003 #2340] [Araya, Reniers, et al. 2004 #1530] [Reniers, Araya, et al. Forthcoming #2330], and as a sampling frame for verbal autopsies that were conducted in 2001 and 2004. The current paper examines trends in AIDS mortality over five years during which ART was introduced. To that end we use ratios of projected and observed deaths and a method that relies on lay reporting of causes of death. We are particularly sensitive to diverging trends in AIDS mortality by sex because a previous study in Addis Ababa has pointed at a gender bias in hospital services utilization (Reniers et al. 2005).

## 2. Setting

Addis Ababa has an estimated population of close to 3 million and is one of the largest urban centers in East-Africa. As is the case for many urban areas in the region, Addis Ababa is severely affected by the HIV/AIDS epidemic. For 2003, urban HIV prevalence is estimated at 12.6% [MOH 2004 #2980], and this has obvious repercussions for the distribution of causes of death<sup>1</sup>. For 2001, between 60-70 % of adult deaths (aged 20-54) were attributed to AIDS [Araya, Reniers, et al. 2004 #1530] [Reniers, Araya, et al. Forthcoming #2330].

Since 1999, a limited number of AIDS patients have been receiving ART through the informal market and usually at a very high cost. In July 2003, the Ethiopian government launched a program for the provision of antiretrovirals through a co-pay

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<sup>1</sup> Rumors regarding the results of last years DHS survey in Ethiopia that included serostatus testing suggest that HIV prevalence is lower than initially thought or estimated. Official results have not yet been released.

scheme wherein the cost to the end user ranged from US\$28 to US\$80 per month depending on the combination of drugs. For most Ethiopians this is still a substantial amount because the monthly salary of an entry-level administrative government employee is less than US\$50. Nonetheless, well over 10,000 patients were receiving ART in Ethiopia by the end of 2004. In February 2005, the government launched a free ART program in which new patients are enrolled as well as transferred from the fee based schemes. Eligible patients need to present a physician report (including HIV test result) to the sub-city administration with a declaration that they cannot afford treatment. They have to produce three witnesses to that effect. After that the sub-city council may approve the free provision of ART. Because the supply of subsidized ART's increased, the Ministry of Health disclosed in October 2005 that it will provide free ART's in public hospitals regardless of individual's socioeconomic status. The clinical assessment remains the only screening mechanism.

\*\*\*\*Exhaustive and detailed data on the number of patients on ART's are not easy to come by, but in 13 governmental and private hospitals in the capital for which data are available, a combined number of 6,605 patients have been receiving ART between July 2003 and December 2004<sup>2</sup>. The sex ratio of these patients is 1.19 suggesting that men have privileged access to ART; most likely because of greater control over the necessary economic resources.\*\*\* An alternative explanation is that there are more male than female AIDS patients and that a random selection from this pool would result in more men on ART than women. This is unlikely to explain the full extent of the difference: 10 years prior to the initiation of ART, the ratio of male to female infections was 0.97 (95%-CI: 0.70-1.35) [Fontanet, Messele, et al. 1998 #2240].

### 3. The data

In this paper, we use data from a surveillance of burials as well as the results from verbal autopsy interviews that were carried out for a random sample of the burial records. The burial surveillance was initiated at all cemeteries of Addis Ababa in February 2001 and records information for an average of over 20,000 deaths a year. The surveillance currently covers 55 Orthodox, 9 Muslim, 1 Catholic, 1 Jewish and 8 municipal cemeteries. The number of cemeteries under surveillance fluctuates a little over the period of observation because some of them are sometimes temporarily closed during the rainy season or for restructuring when they are full. A few new cemeteries were established over the period of observation and included in the surveillance. All of this implies that bodies are sometimes registered in one church and subsequently transported to another cemetery where they may be registered again. We have set up a system at the database level of filtering out the potential duplicate registration of bodies.

The largest of the municipal cemeteries, *Baytewar*, buries persons without close relatives or friends to facilitate a funeral<sup>3</sup>. *Baytewar* alone accommodates approximately 15% of burials. Over 40% of burials at *Baytewar* concern infants and young children; many of which are delivered by obstetrics wards of hospitals and can be separated out from the rest. Most persons (61.5%) buried at *Baytewar* remain unidentified and often

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<sup>2</sup> Data provided by the Addis Ababa City Administration Health Bureau.

<sup>3</sup> *Baytewar* is an Ethiopian Amharic word that is used to refer to a stranger or someone who is socially isolated.

come without full information and that means that cases from this cemetery often need to be singled out for special treatment in the analyses that follow. Another important characteristic of the *Baytewar* cemetery is that the sex ratio of burials is 2.3 to 1.

The surveillance is facilitated by cemetery clerks who were trained in a two-day workshop. Twelve supervisors closely monitor the work of the clerks and report to the project office on a weekly basis. The cemetery clerks collect information on the date of burial, age, name, sex, address, and presumed cause of death (i.e. the lay report of the cause of death) from relatives or close friends while they are making arrangements for burial. Marital status, region of birth, ethnicity and religion were added to this list in 2002.

It would be a mistake to claim that the quality of the data from the burial surveillance lives up to the standards that demographers working in western countries are used to, but it is encouraging nonetheless. For the first year of the surveillance, 6.3% of the records have missing values for age. Excluding Baytewar, only 1.5% of cases have missing values for age. Age heaping is serious (Whipple Index of 283) and more severe than in the census (Whipple Index 206) [CSA 1999 #1910]. Age over-reporting is a potentially more problematic because it leads to underestimates of mortality [Ewbank 1981 #2130] [Coale & Kisker 1986 #2140]. Both in the burial surveillance data as well as in other published reports on mortality for Addis Ababa, there is evidence of age over-reporting<sup>4</sup>, and this casts doubt on the utility of old age mortality schedules for analytical purposes.

Because infant deaths occurring before the naming ceremony (40 days for boys and 80 days for girls) are often not given an official funeral, the burial surveillance is prone to underreporting of infant mortality. The under-reporting of infant deaths is the main reason why we concentrate on adult mortality. After correcting for the underreporting of early childhood deaths, the crude death rate (CDR) estimated from the burial surveillance oscillates between 9 and 10 per 1000 [Reniers, Araya, et al. Forthcoming #2330]. This figure is higher than Central Statistical Authority (CSA) estimate of 7.6 [CSA 1999 #1910], but is still on the low side for a population that is severely affected by the HIV/AIDS epidemic and suggest that there may be sources for the under-reporting of adult deaths as well<sup>5</sup>. Potential sources for under-reporting are the burial of residents beyond the city administration limits<sup>6</sup>; the return of terminally sick migrants to their families for care [Urassa, Boerma, et al. 2001 #2160], the repatriation of bodies for burial; cemetery clerks that fail to register burials; and possibly also illegal

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<sup>4</sup> For example, the reported value of 13.5 for  $e_{70}$  in a life table for 1984 for males [CSA 1987 #2150] would imply an  $e_0$  value of 76 and 80 years in the North and West model life tables respectively. This is an unrealistic value and probably not only due to age over-reporting but also to the under-reporting of deaths.

<sup>5</sup> Unfortunately, we do not have a solid estimate of the degree of underreporting in the burial surveillance. There are two potentially useful strategies for identifying the completeness of the burial registration that will not be further explored in this paper. Indirect methods often assume stability and/or that the population is closed to migration [Bennet & Horiuchi 1981 #2170] [Preston 1984 #2180] and these assumptions are too stringent for the current context. A second approach is to identify deaths in the community through an independent system and assess to what extent these deaths can be traced in the burial registration system. Preston [Preston 1984 #2180 /d] labeled this a direct method for assessing the completeness of a death registration system and it has previously been applied in Abidjan and Dakar [Garenne & Zanou B. 1995 #2190]. We hope to pursue a similar effort in the future.

<sup>6</sup> This may particularly a problem around at the fringe of the city. We tried to compensate for this problem by also registering burials from non-residents within the city limits.

burials<sup>7</sup>. The only category of burials outside the capital that are represented in the surveillance is that of Orthodox Christians that are referred to sacred burial sites outside Addis Ababa because they are usually first registered in one of the local churches.

From January to March 2004 we carried out 1226 verbal autopsy interviews (adult and children) for a random sample of the deaths recorded in the burial registration. As the sampling frame we used all burials registered in November and December 2003 and with presumably valid identifying information (name, age, sex and address.). Most records from the *Baytewar* cemetery were therefore de-facto excluded for VA selection. Of the cases that were selected for verbal autopsy, 78.6% was completed, 4.5% refused, 13.8% of the households could not be retrieved, and 2.9% of the VA's were not completed for other reasons.

The verbal autopsy interviews were carried out by experienced community health workers who received one week training. The interviewers were assigned in pairs to each household, and completed interviews were checked for internal consistency and against the information reported in the burial surveillance. Causes of death were assigned using physician review for just over half of the completed questionnaires. In that process, two physicians independently assigned one or more underlying causes of death. They were asked to explicitly indicate whether they suspected the death to be HIV/AIDS related or not. Physician diagnoses were subsequently coded following ICD10 principles and guidelines. In case the two physicians did not agree on the cause of death, the VA interview was assigned to a third physician. When none of the three physician reports were concordant, the case was settled by consensus by two of the three physicians who earlier reviewed the questionnaire<sup>8</sup>.

## 4. Results

To demonstrate trends in adult (AIDS) mortality, we use two methods. In the first approach, we simply compare age-specific observed deaths with those implied in population projections. The second method is based on the lay reports of causes of death. Each of these methods is discussed below.

### 4.1 Observed versus projected deaths

To project the annual number of deaths excluding the mortality impact of HIV/AIDS, we emulated population projections from the CSA [CSA 1999 #1910 /d]. These use 1994 census population as the baseline and assume that life expectancy increases steadily from  $e_0^m$ : 57 and  $e_0^f$ : 60 to  $e_0^m$ :64 and  $e_0^f$  67.7 between 1995 and 2005. For fertility, we use observed values up to the DHS survey of 2000 [CSA and ORC Macro 2001 #1950], and following the medium variant projections, we assume a constant

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<sup>7</sup> We are aware of one cemetery where burials continued even though it was officially closed. In that case, youngsters from the neighbourhood arranged with relatives of the deceased to prepare the grave against a small compensation.

<sup>8</sup> An addition 227 verbal autopsy interviews were carried out for patients that had visited or been admitted to one governmental hospital where we had set up a surveillance that included serostatus testing. These data will be used for validating the diagnostic accuracy of the physician review for identifying AIDS deaths (report forthcoming). Preliminary results suggest that the physician review has a PPV of 95.2%, a sensitivity of 90.9% and a specificity of 73.0% in the age group 20-64.

TFR of 1.9 thereafter<sup>9</sup>. For migration, we follow the high variant CSA assumption of a constant number of internal migrants at the 1994 level<sup>10</sup>. With the exception of the implied effect of AIDS on the population age structure of Addis Ababa in the 1994 census, these projections thus ignore AIDS mortality. Among the most obvious consequences is that this procedure underestimates deaths in early adulthood and overestimates the number of deaths at older age.

In figure 1, trends in projected deaths –by broad age ranges– are compared with observed deaths<sup>11</sup>. The ratio of observed over projected child deaths is below unity for the whole period and confirms our suspicion of the under-reporting of early childhood mortality in the burial surveillance. The ratio of deaths in old age (65+) hovers between .7 and .8 without a clear trend over the period of observation. Even though this is also suggestive of underreporting, the projected number of deaths in old age is most likely an overestimate. Because the projections do not reflect the impact of HIV/AIDS, many of those that have died in early adulthood survive under the projection assumptions until old age and thus depress the ratio of observed over projected deaths. It is therefore not unlikely that the coverage of the burial surveillance for adult deaths is well above 80%.

Most interesting for the current discussion is the ratio of deaths in early adulthood because this is most suggestive of trends in AIDS mortality. Despite possible underreporting in the burial surveillance, the ratio is above unity for the whole period of observation and that reflects the impact of HIV/AIDS. The higher ratio for women compared to men may have different causes: it could reflect the sex ratio of HIV incidence in the early 1990s<sup>12</sup>; it may be the result of underestimates of female migration in the population projections; or could be the result of greater underreporting of male mortality [Reniers, Araya, et al. Forthcoming #2330]. Underreporting of male mortality in particular is possibly linked with the return of terminally sick migrants to their families for care (i.e., a salmon effect) as well as by the return of bodies for burial in their region of origin. Such an explanation accommodates sex differences because it rests on the idea that male migrants retain greater ties with their families while women in patrilineal societies become more fully absorbed by the households they marry into. None of these explanations can be substantiated at this stage and remain purely hypothetical.

**Figure 1: ratio of observed to projected (excl. AIDS mortality) deaths by sex and broad age groups**

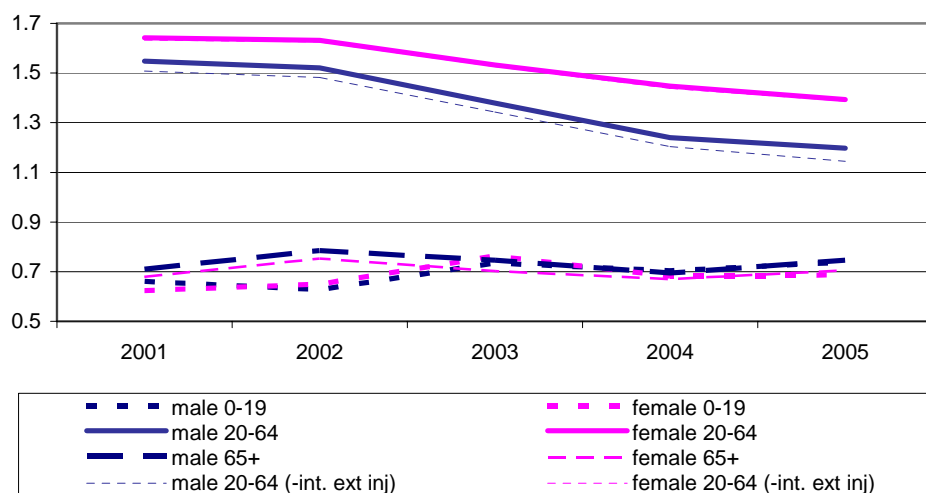
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<sup>9</sup> Addis Ababa is a special case of below replacement fertility in Africa [Kinfu 2000 #3500] [Sibanda, Woubalem, et al. 2003 #3490].

<sup>10</sup> A curious phenomenon in Ethiopia, again, is that the female rural-urban migration is more important than male migration [Reniers 2000 #2200].

<sup>11</sup> Observed deaths with missing sex and/or age are distributed proportionally to the share of each sex and age group.

<sup>12</sup> This is not the most likely of explanations: in a 1994 community survey, the ratio of infections was still close to 1 [Fontanet, Messele, et al. 1998 #2240].



Because of the uncertainty surrounding the level and nature of under-reporting in the burial surveillance, our primary attention should go to trends in mortality since these are unlikely to be affected as long as the underreporting remains stable over time. In that regard, it is of interest that the ratio of observed to projected deaths seems to have peaked in 2001-2002. In 2003, when a government program of ART has been introduced, the ratio of observed over projected deaths in adulthood dropped from 1.52 to 1.38 (or a 9.5% annual decline) for men and from 1.63 to 1.53 for women (or a 6.0% decline). The same rate of change in adult mortality by sex extended into 2004, thereby increasing the gap between male and female (AIDS-) mortality. In 2005, when a government program to provide free ART's was initiated, adult mortality continued to decline, with a slight attenuation of the difference between male and female mortality. However, part of that attenuation is due to increased male mortality following the political turmoil in Addis Ababa after the May 2005 elections. The same trend, but this time excluding intentional external injuries as causes of death documents a more modest catch-up of the rate of decline in female adult mortality in 2005. In sum, excess adult mortality compared to AIDS-free projections declined since the introduction of the ART program, but more so for men than for women. The reduction in adult mortality is most likely a reduction in AIDS mortality. To seek confirmation on trends in cause-specific mortality, we turn to trends in lay reports of causes of deaths.

#### 4.2 Extrapolations from lay reports of causes of death

The second and more uncommon method for estimating trends in AIDS mortality is based on the lay report of the cause of death. Table 1 provides a description of the distribution of lay reports (by sex) for the 5 year period. Among others, it indicates that over 80% of the diagnoses are sufficiently specific to be classified under one of the main disease groups. The share of weakly defined diagnoses is higher for men than for women. The table also highlights that few deaths are explicitly attributed to AIDS.

Though few deaths are explicitly ascribed to HIV/AIDS, lay reports of causes of death do not seem to be assigned at random, and some of the lay diagnoses are very suggestive of AIDS. This is demonstrated in table 2. In this table, groups of lay diagnoses

are mapped against the cause of death attributed by physicians (i.e. the ‘gold standard’) in the sample with a reviewed verbal autopsy (N=413). The gold standard in this case is constructed as a TB/AIDS death rather than solely AIDS deaths versus non-AIDS deaths, because both layman and physicians tend to have difficulty disentangling both causes.

The diagnostic indicators are presented for each group of lay diagnoses as well as their cumulative values. Deaths explicitly labeled as *TB/AIDS* deaths have a positive predictive value (PPV) of 89%, but only account for 7% of the total number of TB/AIDS deaths. *Herpes zoster*, *diarrhea*, *uterine cancer*, *mental problem*, and *emaciation* account for another 8% of TB/AIDS deaths, but their PPV is only 71%. *Lung disease*, and to a lesser extent *cough disease* are other good predictors of TB/AIDS mortality and about 40% of all adult TB/AIDS cases are labeled as such. *Cold* is a fair predictor of AIDS and accounts for just under a quarter of all TB/AIDS deaths. Together these lay reports accurately predict a TB/AIDS death in 80% of the time and have a sensitivity of 78%. Their cumulative specificity is 77%. In the remainder of this paper all these lay reports will be labeled TB/AIDS indicative lay diagnoses (LD+). Other lay reports of causes of death are much less predictive of AIDS (PPV: 25%, Sensitivity 22%, specificity 23%).

**Table 1: Distribution of lay diagnoses of causes of death by sex (2001-2005), age 20-64 (in %)\***

	Women	Men	Total (N)
<b>Communicable diseases</b>	<b>59.6</b>	<b>57.5</b>	<b>30,105</b>
Tuberculosis/Lung disease	27.2	28.2	14,228
Cold	22.9	20.0	11,036
Acute febrile illness	3.1	4.2	1,874
AIDS	2.6	1.8	1,122
Diarrhoeal diseases	1.6	1.5	808
Herpes Zoster	1.1	0.8	471
Other communicable diseases	1.2	1.0	566
<b>Maternal causes</b>	<b>2.1</b>		<b>532</b>
<b>Non-communicable diseases</b>	<b>29.7</b>	<b>30.3</b>	<b>15,455</b>
Cardiovascular disorders	7.2	6.7	3,597
Liver cirrhosis**	4.6	7.6	3,144
Neoplasms	4.7	2.2	1,784
Renal disorders	3.2	3.2	1,657
Diabetes	1.7	2.5	1,081
Other non-communicable diseases	8.2	8.1	4,192
<b>Symptoms, signs and syndromes</b>	<b>5.6</b>	<b>5.6</b>	<b>2,888</b>
Mental problem	2.1	2.7	1,250
Emaciation	0.0	0.0	13
Cough/Coughing disease	0.2	0.2	99
Other symptoms signs and syndromes	3.2	2.7	1,526
<b>External causes</b>	<b>3.0</b>	<b>9.9</b>	<b>3,313</b>
<b>Subtotal of specific diagnoses (N)</b>	<b>25,720</b>	<b>26,573</b>	<b>52,293</b>
<b>Subtotal of specific diagnoses (%)</b>	<b>87.5</b>	<b>83.2</b>	
<b>Unknown - weakly specified</b>	<b>12.5</b>	<b>16.8</b>	<b>9,029</b>
No COD assigned, unknown, found dead	5.5	9.3	4,561
Sickness / accidental sickness	5.4	6.5	3,674
Medically not recognized community beliefs	1.3	0.9	676
Aged	0.3	0.1	117
<b>Total</b>	<b>29,381</b>	<b>31,941</b>	<b>61,322</b>

Notes:

\* Percentages have been calculated using the subtotal of sufficiently 'specific' diagnoses as the denominator

\*\* It was not always clear whether lay diagnoses referred to communicable or non-communicable diseases. In these cases arbitrary decisions had to be made. For example, all liver problems not explicitly referred to as *hepatitis* (in the community known as 'ye wof beshita' and here classified under 'other communicable diseases') were interpreted as *liver cirrhosis*. The lay diagnosis in Amharic these cases usually mentioned 'gubet beshita', which literally means *liver disease*.

Table 2: Diagnostic values for lay reports of causes of death for identifying TB/AIDS mortality (both sexes, age 20-64)

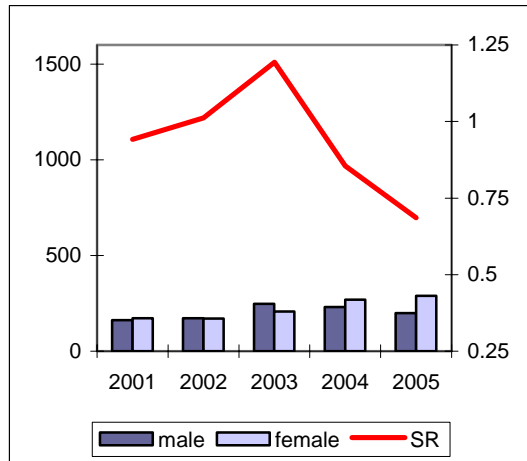
Gold Standard (physician review of VA)	Lay report					
	TB/AIDS	Herpes zoster / Diarrhea / Uterine cancer / Mental problem / Emaciation	Lung disease/ Cough disease	Cold	Other	Total
AIDS	16	17	88	52	48	221
NoAIDS	2	7	14	20	143	186
Undetermined	0	0	0	1	5	6
<b>Diagnostic indicators</b>						
PPV	0.89	0.71	0.86	0.72	0.25	
Sensitivity	0.07	0.08	0.40	0.24	0.22	
Specificity	0.99	0.96	0.92	0.89	0.23	
<b>Cumulative values for the diagnostic indicators</b>						
PPV	0.89	0.79	0.84	0.80		
Sensitivity	0.07	0.15	0.55	0.78		
Specificity	0.99	0.95	0.88	0.77		

The results thus far suggest that, while far from perfect, lay diagnoses may be useful for monitoring AIDS mortality. One of the assumptions we need to make for that purpose is that the diagnostic validity of the lay reports does not vary over time. We cannot substantiate that claim at this stage, but since the range over which we want to make estimates is short; we do not expect this to introduce important bias. Also, we are primarily interested in trends in AIDS mortality by gender and if lay reports vary over time, they are likely to do so for men as well as women.

Figure 2 highlights trends in the frequency of reporting of four groups of AIDS indicative lay diagnoses as well as the sex ratio of therein. The number of deaths attributed to *TB/AIDS* declined for men since 2003 and increased for women over the whole period. The number of deaths due to the second group of lay diagnoses (*herpes zoster, diarrhea, uterine cancer, mental problem, emaciation*) decreased since the introduction of ART for both men and women. The most important lay diagnosis for identifying AIDS deaths is *lung disease* (and *cough disease*) and the frequency with which it is reported peaked in 2002 for men and in 2003 for women. *Cold*, the least specific of the AIDS indicative lay diagnoses seems to be increasingly more often reported. Worth noting is that the sex ratio of deaths for each of these TB/AIDS indicative lay reports is higher in 2005 than in 2001. In 2005, the absolute number of deaths attributed to each of these TB/AIDS indicative diagnoses is also higher for women than for men.

**Figure 2: trends in the frequency of four groups of AIDS indicative lay diagnoses and the sex ratio therein, 2001-2005 (age 20-64)**

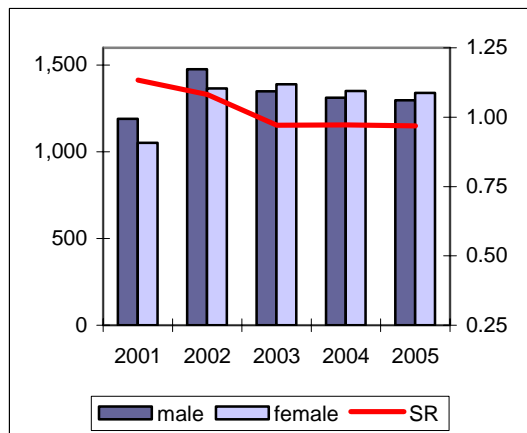
a. TB/AIDS



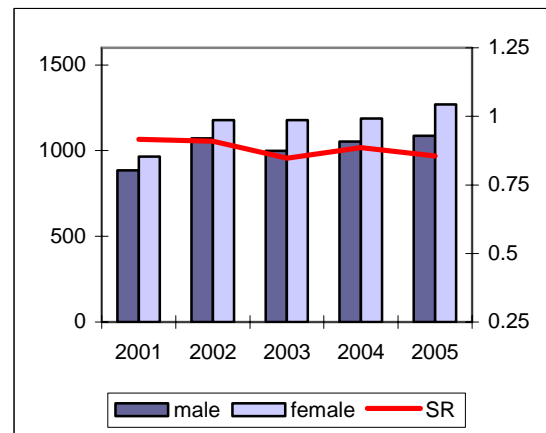
b. Herpes zoster, Diarrhoea, Uterine cancer, Mental problem, Emaciation



c. Lung disease, cough disease



d. Cold



Even though not immediately suggestive of a clear tendency in the frequency of AIDS deaths, the changing sex ratio in TB/AIDS deaths is more obvious. These hypotheses are further investigated using a method to estimate the frequency of AIDS deaths (by age and sex) based on the lay reports of causes of death. To do so, we first estimate the age and sex specific values for the PPV and sensitivity and subsequently use the diagnostic indicators from that analysis to extrapolate estimates of AIDS mortality to the total population of Addis Ababa. This method was first explored in Araya et al. [Araya, Reniers, et al. 2004 #1530 /d], and here extended to allow for sex and age-specific variation in the diagnostic validity of the lay diagnoses. In the sub-sample with a verbal autopsy diagnosis of the cause of death (i.e. the 'gold standard'), the PPV and sensitivity of lay reports are estimated by means of a probit regression model<sup>13</sup> (results presented in Annex I). Under the assumption that these diagnostic indicators are

<sup>13</sup> As it turned out, only age had a significant effect on the PPV of the lay diagnoses: The PPV of the AIDS indicative lay diagnoses (LD+) decreases linearly from 88% in early adulthood to 65% in late adulthood.

unbiasedly estimated in the sub-sample with a verbal autopsy diagnosis of the cause of death, the sex and age specific share of TB/AIDS attributable mortality can be estimated as:

$$(\text{LD}^+_{\text{x}} * \text{PPV}_{\text{x}}) / (\text{Sensitivity}_{\text{x}} * \text{D}_{\text{x}}) * 100$$

Where  $LD^+$  is the number of deaths with a TB/AIDS indicative lay reports and  $D$  is total number of deaths with a ‘sufficiently specific’ lay diagnosis<sup>14</sup>. By ‘sufficiently specific’ lay diagnosis, we mean that we excluded cases that came without a lay report of the cause of death, or where the cause of death is stated as *unknown*, *sickness* or *accidental sickness*<sup>15</sup> (see also table1). For calculating the absolute number of AIDS deaths, we again include these non-valid lay diagnoses, thereby assuming that their distribution of causes of death is the same as for the better specified lay reports.

Figure 3 summarizes the estimated trend in AIDS mortality by sex based on the extrapolation from lay reports. The estimated number of AIDS deaths dropped from around 8500 in 2001 to just above 7200 in 2005. Worth noting is that our estimates of the absolute number of deaths are roughly half of those reported by the Ministry of Health [MOH 2004 #2980]. Admittedly, our estimates of AIDS deaths are dependent on the completeness of the burial surveillance and are rather conservative. Yet, suppose the burial surveillance is 80% complete (for adult mortality), then this would translate into an estimate ranging from 9,000 to 10,500 annual adult AIDS deaths; still barely half of the estimated number in the MOH-report<sup>16</sup>. The large discrepancy in these estimates suggest that AIDS mortality estimates based on extrapolations from antenatal sentinel surveillance sites (the method used by the MOH) need to be interpreted with the necessary caution<sup>17</sup>.

The two most important conclusions to be drawn from this figure are the same as those that can be read into figure 1: AIDS mortality declined since the large scale introduction of ART, and AIDS mortality declined faster for men than for women. The latter is visible in the declining sex ratio of AIDS deaths. For illustrative purposes, we compare these estimates with those obtained via population projections that incorporate the impact of AIDS (excluding the effect of ART) using the Spectrum software package. The assumptions underlying these projections are –to the extent possible– based on those in Mekonnen et al. [Mekonnen, Jegou, et al. 2002 #1600 /d]<sup>18</sup>. As mentioned earlier, the sex ratio in AIDS mortality in the absence of ART is likely to drop as the AIDS epidemic matures but not necessarily as fast we observe here: the estimated sex ratio of adult AIDS mortality dropped from 1.10 in 2001 to 0.95 in 2005, and from 1.10 to 1.03 under the projections excluding ART. Note also that the averted number of AIDS deaths since the

<sup>14</sup> In principle it is possible to extrapolate from the diagnostic indicators using any pair of indicators. Here we only present results using the PPV and sensitivity.

<sup>15</sup> Since the beginning of the burial surveillance we have undertaken some efforts to improve the lay reporting of causes of death and the share of non-valid lay diagnoses has dropped from 15 to just under 6% in the age group 20-64.

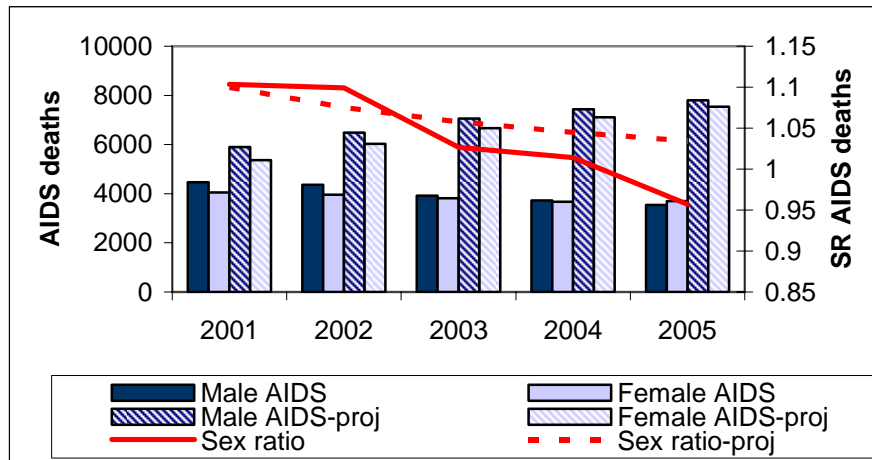
<sup>16</sup> In the MOH report the total annual number of adult AIDS deaths (age 15+) is estimated above 20,000 for the period 2002-2005. The reported sex ratio of adult AIDS deaths is between .82 and .84 for the same period. [MOH 2004 #2980].

<sup>17</sup> See also footnote 1.

<sup>18</sup> For determining the epidemiology of HIV, these projections rely heavily on the results from a 1994 community-based study involving the HIV serostatus testing [Fontanet, Messele, et al. 1998 #2240 /pt " Cfr." ] rather than on extrapolations from ANC sentinel surveillance data.

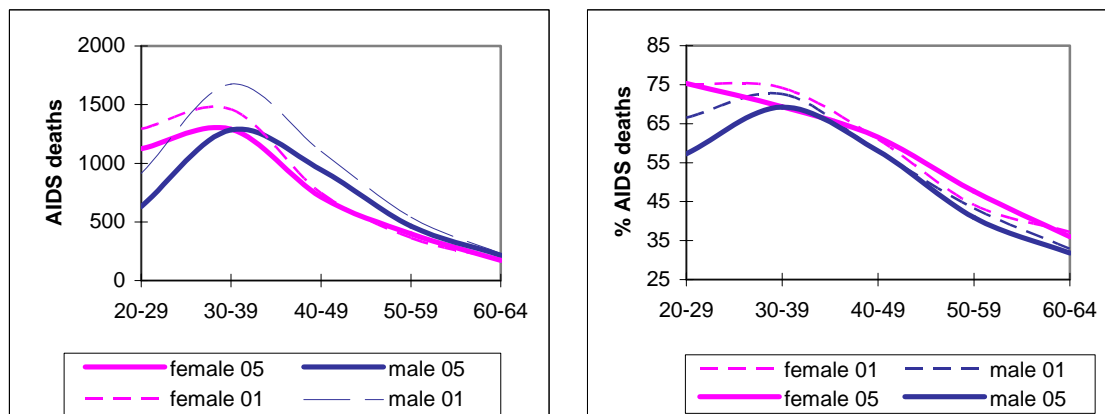
introduction of ART is probably greater than the difference between the number of AIDS deaths in 2001 and 2005, as the number of AIDS deaths are expected to have increased significantly in the absence of ART.

**Figure 3: estimated number of AIDS deaths 20-64 and the sex ratio of AIDS deaths (2001 – 2005), based on extrapolations from lay reports of causes of death compared to projections including an AIDS effect (without ART)**



The age pattern in the decline of AIDS mortality since 2001 is illustrated in figure 4. Both in terms of the absolute number of AIDS deaths and in terms of the share of AIDS mortality, the greatest progress seems to have been made in early adulthood (i.e. below age 40), and this appears to be true for both men and women. This is also the age range where the greatest fraction of deaths is attributable to AIDS and with the greatest number of AIDS deaths. The overall share of AIDS attributable mortality in the age group 20-64 declined between 2001 and 2005 from 59.2% to 55.3% for men and from 64.9% to 63.4% for women<sup>19</sup>.

**Figure 4: change in the estimated number of AIDS deaths and the share of AIDS attributable mortality by sex and age (2001 & 2005)**



<sup>19</sup> Using different methods (life tables and verbal autopsy results), we estimated the share of AIDS attributable mortality in 2001 to be between 50.3% and 60.5% for men and between 59.8% and 67.2% for women [Reniers, Araya, et al. Forthcoming #2330].

## 5. Discussion

The evidence presented here is very suggestive of the mortality impact of HIV/AIDS in Addis Ababa. It is also pretty suggestive of a reversal in mortality trends since the introduction of ART. This reversal of adult AIDS mortality is indicated by a declining ratio of observed to projected deaths (all-cause mortality) as well as by estimates of the trend in AIDS-specific mortality. Though the absolute decline of the number of adult AIDS deaths is minimal (a difference of just 1000 AIDS deaths between 2001 and 2005), it is encouraging to note that this happened in a period where AIDS mortality could still be expected to have increased in the absence of ART. Less comforting is that male AIDS mortality appears to have declined faster than female AIDS mortality. Again this is visible in the trends of all-cause mortality and in AIDS specific mortality trends. This is the likely result of the privileged access of men to ART; most likely because they have greater control over the necessary economic resources to cover treatment costs.

The observation that women experience barriers to accessing ART is plausible as it mirrors available figures on ART enrolment. This situation is not unique for Ethiopia either, as it is observed in high income settings as well [Shannon, Bright, et al. 2005 #3510] [Gebo, Fleishman, et al. 2005 #2730]. In considering these results, we need to be aware of competing explanations. Gender differences in adherence while on therapy is one possible explanation for diverging mortality trends and some evidence to that effect has been collected in the US and Canada [Berg, Demas, et al. 2004 #3520] [Kuyper, Wood, et al. 2004 #3530], but the opposite has been shown in studies in Italy [Manfredi, Calza, et al. 2004 #3540], South Africa [Orrell, Bangsberg, et al. 2003 #2970], and recently also in Addis Ababa [Tadios & Davey forthcoming #3550]. The pharmacokinetics of ART may also differ between males and females [Kappelhoff, van Leth, et al. 2005 #3560], but the evidence so far suggests, if anything, a lower risk of clinical progression during ART among adherent women compared to men [Nicastri, Angeletti, et al. 2005 #3570].

The most plausible explanation for the gender differences in AIDS mortality trends is thus related to gender differences in the access to ART. Worth noting is that it is perhaps not just a matter of financial resources as the free provision of ART did not seem to reverse the gender imbalance. This program is, however, still young and may be revised to better suit the demands and inhibitions of patients as we go on.

The data and methods used in this paper are not highly refined and rely on a few crucial assumptions, but the relative consistency with other estimates strengthens our belief that they capture the order of the magnitude of the epidemic (a notable exception being the discrepancy with the MOH in the estimate of the absolute number of AIDS deaths)<sup>20</sup>. Regardless of its accuracy in providing a reliable point estimate of the level of AIDS mortality, burial surveillance data will prove useful for monitoring trends in AIDS mortality as well as the population level impact of the provision of antiretroviral treatment.

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<sup>20</sup> In the near future, we hope to strengthen our estimates of trends in AIDS mortality based on population projections (including and excluding an AIDS effect) and life table methods following a methodology developed in Reniers et al. [Reniers, Araya, et al. Forthcoming #2330 /d].

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**Annex I: estimating age (and sex) specific values of for the PPV and Sensitivity of the LD+ lay reports for identifying the AIDS deaths (using the physician diagnosis of the VA as ‘gold standard’)**

Table annex 1a: Probit parameter estimates for predicting the PPV and Sensitivity of the LD+ lay reports for diagnosing TB/AIDS

	PPV		Sensitivity	
	model 1	model 2	model 1	model 2
VAage	-0.064 (0.96)	-0.020** (2.14)	-0.051 (0.85)	
VAage2	0.001 (0.66)		0.000 (0.67)	
Vasex	-0.001 (0.01)		0.322* (1.77)	
Constant	2.459* (1.85)	1.613*** (4.28)	1.642 (1.42)	0.613*** (7.02)
Observations	216	216	237	237
LL	-105.29	-105.52	-136.00	-138.24
df	3.00	1.00	3.00	0.00
AIC	216.58	213.03	278.01	276.48

Notes: z statistics in parentheses; \*  $p < .1$ ; \*\*,  $p < .05$ ; \*\*\*  $p < .001$

After defining the most parsimonious model for estimating the PPV and the Sensitivity (model 2 in both cases), the parameter estimates are used to predict age specific values for the PPV and Sensitivity (sex is not significant and omitted). These are summarized in the table below:

Table annex 1b: Age-specific values of the PPV and Sensitivity

Age-group	PPV (both sexes)	Sensitivity (both sexes)
20-24	0.877	0.770
25-29	0.858	0.770
30-34	0.835	0.770
35-39	0.809	0.770
40-44	0.784	0.770
45-49	0.752	0.770
50-54	0.720	0.770
55-59	0.683	0.770
60-64	0.649	0.770

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