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Title:
"Outcomes of antiretroviral therapy over a 10-year period of expansion: a multicohort analysis of African and Asian HIV programmes"

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Running head:
ART outcomes over a 10-year expansion period

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ABSTRACT:

Objective: Little is known about the evolution of programme outcomes associated with rapid expansion of ART in resource-limited settings. We describe temporal trends and assess associations with mortality and loss to follow-up (LTFU) in HIV cohorts from 8 countries.

Design: Multi-cohort study using electronic health records.

Methods: Analysis included adults in twenty-five Médecins Sans Frontières supported programmes initiating ART between 2001 and 2011. Kaplan-Meier methods were used to describe time to death or LTFU, and proportional hazards models to assess associations with individual and programme factors.

Results: ART initiation (n=132 334; median age 35 years; 61% female) expanded rapidly. While 36-month mortality decreased from 22% to 9% over 5 years (≤2003-2008), LTFU increased from 11% to 21%. Hazard ratios (HR) of early (0-12 months) and late (12-72 months) LTFU increased over time, from 1.09 (95%CI 0.83-1.43) and 1.04 (95%CI 0.84-1.28) in 2004, to 3.29 (95%CI 2.42-4.46) and 6.86 (95%CI 4.94-9.53) in 2011, compared to 2001-2003. Rate of programme expansion was strongly associated with increased early and late LTFU, adjusted HR (aHR)=2.31 (95%CI 1.78-3.01) and HR=2.29 (95%CI 1.76-2.99), respectively, for ≥125 vs. 0-24 patients/month. Larger programme size was associated with decreased early mortality (aHR=0.49, 95%CI 0.31-0.77 for ≥20 000 vs. <500 patients), and increased early LTFU (aHR=1.77, 95%CI 1.04-3.04 for ≥20 000 vs. <500 patients).

Conclusion: As ART expands in resource-limited settings, challenges remain in improving access to ART and preventing programme attrition. There is an

urgent need for novel and sustainable models of care to increase long-term retention of patients.

Keywords: Antiretroviral therapy (highly active); loss to follow-up; mortality; programme outcomes; retention; survival analysis

INTRODUCTION

Over the past decade, there has been rapid expansion of antiretroviral therapy (ART) in resource-limited settings. By 2011, an estimated 9.7 million people in low- and middle-income countries were receiving ART[1]. During this growth, HIV programmes have adapted services to cope with the increasing numbers of patients requiring ART. As programmes mature and increase in size, the need to ensure long-term retention in care of patients receiving ART while continuing timely initiation of new patients onto treatment presents an ongoing challenge to policy makers and health care providers alike.

Over the past decade, the conditions in which ART programmes operate in low and middle-income countries have changed considerably. The numbers of patients has increased rapidly and often disproportionately to the number of health care workers providing care[2]. Guidelines for initiation of ART have been simplified and context specific recommendations have been adapted to facilitate improving and expanding access to treatment. Furthermore, eligibility criteria for ART initiation have evolved and recommended CD4 count thresholds for treatment start have recently been increased to improve patient outcomes[3].

The effectiveness of ART in reducing morbidity and mortality depends on patient adherence to therapy and on the ability of HIV programmes to retain patients in care. Previous analyses examining temporal trends in long-term programme outcomes in resource-limited settings have reported conflicting results. While data from South Africa showed increasing loss to follow-up (LTFU) by calendar year of enrolment [4-6]; systematic reviews of sub-Saharan African cohorts and

findings from a large Kenyan cohort reported improvements in patient retention in recent years [7-9]. Evaluating programme outcomes, assessing temporal trends in programme retention and investigating the factors associated with poor outcomes are essential to improve the long-term effectiveness of ART services in low and middle-income countries. Understanding associations between programme expansion and treatment outcomes are particularly relevant in the context of the Treatment 2.0 initiative to scale up HIV treatment through promoting innovation and efficiency gains, and of the ambitious goal of expanding ART to 15 million people by 2015[1, 10].

The objective of this study was to describe temporal trends in patient characteristics at ART initiation and in ART outcomes using data from resource-limited countries where Médecins Sans Frontières (MSF) supports the provision of HIV treatment. We also examined associations between individual level risk factors, absolute programme size, and rate of ART programme expansion, and mortality and loss to follow-up (LTFU).

METHODS

Study population

We analysed patient electronic health records from 25 sites in 8 countries where MSF supports the provision of ART care. Cohorts were located in Democratic Republic of Congo (DRC), India, Kenya, Malawi, Mozambique, Myanmar, Uganda and Zimbabwe. Details of these programmes have been described previously[11]. All programmes provided care and treatment free of charge. Criteria for ART initiation followed WHO guidelines. The analysis included all

adults aged 16 years or older who initiated ART between March 2001 and September 2011 in one of the programmes.

Data collection and definitions

Characteristics at ART initiation including sex, age, CD4 cell counts, WHO clinical stage, body mass index (BMI), and date of ART initiation, were prospectively collected with the FUCHIA software (Epicentre, Paris). Throughout, reference to baseline is a reference to time of ART initiation.

Patient follow-up began at the date of ART initiation and was censored at the earliest of: death, transfer out, last clinic visit, or analysis closure. Sites began initiating patients onto ART between 2001 and 2007. Only patients with a minimum of 6-months of follow-up were included with analysis closure preceding the database closure date by 6-months. The database closure ranged from 30 September 2011 to 20 March 2012. Deaths were events recorded before the analysis closure date. Loss to follow-up was defined as having no visit in the 6-months before analysis closure. Patients who initiated treatment but did not return were given 1-day of follow-up time so that they would contribute to survival analysis[12]. Programme retention was defined as being in care (i.e., not dead or LTFU) at the time of analysis closure.

To quantify the size of the ART programmes two variables, programme size and the rate of programme expansion, were defined. For each patient, programme size was calculated as the total number of both pre-ART and ART patients receiving care in the programme at the end of the calendar year of patient ART

initiation. To define the rate of programme expansion, the rank of each patient enrolled by site was divided by the duration of ART provision in the site up to the date of enrolment, in months. For example, if the one hundredth patient at the site was enrolled 4 months after the programme started, the rate of programme expansion for that patient would be 25 (100/4).

Statistical methods

Baseline characteristics were described by year of ART initiation using medians and interquartile ranges for continuous variables, and proportions for categorical variables. Kaplan-Meier methods were used to describe cumulative probabilities of death, LTFU and programme retention after ART initiation and were analysed overall, by calendar year of ART start, programme size, and rate of expansion.

Cox's proportional hazards models were used to assess associations between baseline patient characteristics and outcomes. Heterogeneity across sites was accounted for using random effects. To examine differences in risk factors over time, models were stratified by early (0-12 months) and late (12-72 months) follow-up time periods. Adjusted models were built first by including all baseline characteristics (model 1), and then adding the programme size variable (model 2), or the rate of expansion variable (model 3), or both (model 4). The primary analysis only included patients with complete data on baseline characteristics (complete case analysis).

In sensitivity analyses, models including patients with missing baseline CD4 cell counts, clinical stage, and/or BMI as separate categories were used. We also assessed different measures of programme size including the number of patients who had previously initiated ART by site and the number of ART patients in care at each site at the end of the calendar year. Kaplan-Meier survival proportions and hazard ratios (HRs) stratified by site were assessed and compared with the primary results. Finally, to account for non-differential censoring (e.g. higher risk of death among patients LFTU early after ART start), models of time to death and LTFU were calculated using competing risks methods[13].

Data was analysed with STATA 12.0 (STATA Corporation, College Station, Texas, USA). All FUCHIA sites obtained agreement from health ministries for the prospective collection of data. No patient identifiers were included in datasets. The International Ethics Review Board of MSF reviewed the study and determined it did not require formal approval. The Human Subjects Research Ethics Committee of the Faculty of Health Sciences from the University of Cape Town reviewed and approved the data usage and analysis plan.

RESULTS

Characteristics at ART initiation

Between 2001 and 2011, 132 334 individuals contributed 299 658 person-years of follow-up (median per patient, 1.75 years, interquartile range (IQR), 0.57-3.56). At ART initiation, the median age was 35 years, 61% of patients were female, 69% had CD4 cell counts <200 cells/μL and less than 5% had CD4 count >350 cells/μL (Table 1). Twenty-five percent of patients had clinical stage 4

disease and a third had a BMI below 18.5 kg/m^2. More than half of patients received treatment in Malawi (n=37 657) or Zimbabwe (n=30 783); Asian cohorts contributed 14% of patients.

Temporal changes in patient baseline characteristics and outcomes

The number of patients initiating ART increased substantially each calendar year (Table 2), from 4 427 in 2001-2003 to 22 863 in 2010. Median age was 35 years and remained constant over time. Median CD4 cell count increased over time from 97 in 2003 or earlier to 184 cells/μL in 2011 (see **Web Appendix 1, Supplemental Digital Content,** http://links.lww.com/QAI/A547). However, every year approximately 30% of patients initiated ART with a CD4 count <100 cells/μL (see **Web Appendix 2, Supplemental Digital Content,** http://links.lww.com/QAI/A547); the range across countries being 22-48%. The proportion of patients with clinical stage 4 disease at the time of ART initiation decreased from 44% to 14%.

Mortality decreased over the study period (Figure 1A), from 17% to 5% at 12 months; and from 22% to 9% at 36 months (Table 3). Larger programmes (Figure 1C) and those with greater rate of expansion (Figure 1D) had lower rates of mortality. In contrast, LTFU increased substantially over time, from 6% to 15% at 12 months; and from 11% to 21% at 36 months (Figure 1B). LTFU increased with programme size up to a number of 7 500 patients (Figure 1D). Programme retention was highest between 2006 and 2009. Trends in outcomes were homogeneous across sites (see **Web Appendix 3, Supplemental Digital Content,** http://links.lww.com/QAI/A547).

The contribution of LTFU to overall programme attrition increased with duration of ART (see **Web Appendix 4, Supplemental Digital Content,** http://links.lww.com/QAI/A547). During the first year of treatment, approximately half of the programme losses were LTFU (6% of patients had died compared to 8% who were LTFU). However, after five years, two thirds of the losses were LTFU patients (24% compared to 13% of deaths). Programme retention decreased from 82% at 12 months, to 73% at 36 months and 66% at 60 months. The smallest programmes had the largest estimates of 12-month mortality: 12%, 11% and 9% in sites with less than 500, 500-999 and 1 000-2 499 people, respectively. However, 12 month LTFU was largest in medium size programs. Similarly, programmes with a slow rate of expansion had double the risk of 12-month mortality compared those with fastest expansion (10.0% vs. 5.3%). LTFU was lowest in programmes with a slow rate of expansion compared to those with medium or fast expansion (Figure 1F).

Risk factors for mortality

The risk of death decreased with each successive calendar year of enrolment (Table 3). After adjusting for programme size and rate of expansion this association was only seen for the 0-12 month period and up to 2007 (aHR=0.76, 95%CI 0.61-0.95 for 2007; and aHR=1.00, 95% CI 0.76-1.33, for 0-12 months, and aHR=1.21, 95% CI 0.73-2.00, for 12-72 months, vs. ≤2003).

Larger programme size was associated with decreased early mortality (aHR=0.49, 95% CI 0.31-0.77, for ≥20 000 vs. <500 patients). This association was not significant for late mortality (aHR=0.34, 95% CI 0.09-1.27).

Fully adjusted models did not show evidence of association between rate of expansion and early or late mortality (aHR=1.13, 95%CI 0.87-1.48, and aHR=0.85, 95%CI 0.55-1.31, respectively, for ≥125 vs. <25 patients/month).

Increased early and late mortality was associated with male gender (aHR=1.30, and 1.57, respectively), older age (aHR=1.46, and 1.48, respectively, for ≥45 vs. 16-25 years), and low BMI (aHR=2.59, and 1.56, respectively, for ≤18.5 vs. 18.6-25.0 kg/m^2). Death was also strongly associated with advanced clinical stage and lower CD4 count level, with the strongest associations observed with early mortality (aHR=2.65 for stage 4 vs. stages 1 or 2; and aHR=0.29, 0.26-0.32 for 200-349 vs. <25 CD4 cells/μL).

Risk factors for lost to follow-up

Increased risk of early and late LTFU was observed with each successive calendar year of ART initiation (Table 4). Adjusted hazard ratios for early LFTU increased from 1.09 (95%CI 0.83-1.43) in 2004 to 3.29 (95%CI 2.42-4.46) in 2011, compared to the 2001-2003 period; and adjusted hazard ratio for late LTFU from 1.04 (95%CI 0.84-1.28) to 6.86 (95%CI 4.94-9.53), respectively.

Larger programme size was associated with a 7-fold increase in the risk of early (HR 7.35, 95% CI 5.55-9.73) and late LTFU (HR 7.03, 95% CI 4.30-11.48) but the association in final models attenuated for early LTFU (aHR 1.77, 95% CI 1.04-3.04) and was not observed for late LTFU (aHR 0.53, 95% CI 0.27-1.04). Rate of programme expansion was strongly associated with an increased risk of early

and late LTFU (early aHR increased from 1.26 in programmes with rates of 25-59 patients/month to 2.31 in those with ≥125 patients/month; and late aHR from 1.22 to 2.29 compared to programmes with rates of 0-24 patients/month respectively). Late LTFU was only higher among patients who received treatment in programmes with 500-4999 HIV patients in care (aHR=1.34, 95%CI 1.00-1.80 for 2500-4999 vs. <500 programme size).

Male gender (aHR=1.25 and 1.21, for early and late periods), younger age (aHR=0.58 and 0.48, respectively, for ≥45 vs. 16-25 years) and advanced clinical stage (aHR=1.56 and 1.28, respectively, for stage 4 vs. stages 1 or 2) were also associated with an increased risk of LTFU. Patients with a CD4 cell count of less than 25 cells/μL had a higher risk of early LTFU (adjusted hazard ratio decreased from 0.89 among patients with 25-49 cells/μL to 0.60 among those with 200-349 cells/μL). No association between CD4 cell count and late LTFU was observed.

Sensitivity analyses including patients with missing data (see **Web Appendix 5 and 6, Supplemental Digital Content,** http://links.lww.com/QAI/A547) and stratification by site provided similar results. Estimates from competing risks models were slightly reduced but did not change results (see **Web Appendix 7 and 8, Supplemental Digital Content,** http://links.lww.com/QAI/A547).

DISCUSSION

This multicentre cohort study included over 130 000 HIV-infected patients initiated on ART in 8 low and middle-income countries where the provision of

ART has rapidly expanded over the last 10-years. In this challenging context where programmes needed to adapt to the growing numbers of patients in need for care, we observed a gradual improvement in measures of disease severity at ART initiation and a decrease in mortality over time. Despite this finding, every year 30% of the total number of patients who initiated ART had CD4 cell counts less than 100 cells/μL. Furthermore, twelve, 24 and 36-month LTFU rates among patients initiating ART in successive calendar years doubled between the periods 2001-2003 and 2008.

Over the 10-year study period, ART provision was rapidly implemented and programmes expanded to reach a growing number of people infected with HIV. Expansion rates ranged from 0-25 to 125-192 new patients/month, and programme size from <500 to 20 000-23 995 patients. Mortality gradually improved with 6-month estimates decreasing from 14% in the years before 2004 to less than 4% in 2011, which is consistent with reports from South Africa[14]. The observed decreased estimates of mortality may result from improved access to ART, as suggested by the increased number of patients initiating ART with less severe disease. The rapid growth of programmes might have also led to poorer outcome ascertainment, with greater number of deaths occurring in recent years misclassified as LTFU[15]. Linkage to national death registries is not available in these cohorts highlighting the need to improve outcome ascertainment for programme evaluation in resource-limited countries.

The rapid growth of ART programmes is related to a combination of several factors including the long-term availability of antiretroviral drugs, the

implementation of new simplified guidelines for ART, and the widespread availability of CD4 enumeration to identify ART-eligible individuals. A third of patients initiated ART with a CD4 cell count below 100, placing a substantial strain on the health-care system requiring intensive support from clinically trained staff [16, 17]. Our findings do not suggest that increases in treatment guideline thresholds prevent patients with more advanced HIV disease from accessing care, but rather that all programmes still face challenges in timeously seeking, testing, and linking patients to ART care.

Even with continued challenges to improving access to ART, LTFU appears to present a ubiquitous challenge to the long-term effectiveness of ART programmes. After 2-years of ART, 15% of the cohort was LTFU and retention was 77% and after 5-years of treatment two-thirds of patients remained in care. This is slightly less than the estimate from 23 countries with cohorts of more than 2000 people which reported 72% retention after 5-years[1]. A temporal trend of increasing LTFU was observed with LTFU contributing an increasing proportion of overall programme attrition[14, 18]. These findings confirm the urgent need to refocus efforts to improve long-term retention and contradict systematic reviews from sub-Saharan Africa suggesting that programme outcomes are improving[7, 18]. A novel finding of our study is that the rate of programme expansion, more than the size of the HIV programme, was associated with the high levels of LTFU. This is likely to relate to the need for timely adjustments in programmes to cope with the increase in activity, independently of financial and human resource allocation. Associations observed between

LTFU and male gender, younger age, and advanced clinical stage are consistent with previous reports[14, 19-21].

This analysis of long-term outcomes was based on substantial follow-up of a large number of patients treated in several resource-limited ART programmes. All sites offered care and treatment free of charge, followed WHO recommendations for ART initiation, and site heterogeneity was accounted for using random effects in the Cox's models. These data are not likely to be representative of all ART programmes since MSF provides additional resources and technical support. For example, quality and completeness of routine electronic data are challenging but MSF provides considerable means to address these concerns[2]. Without linkage to death registries, estimates of programme attrition may misclassify some proportion of deaths as losses to follow-up[5, 15, 19, 22, 23]. LTFU may be overestimated further due to administrative errors, incomplete records of patient decentralization and unrecorded transfers and the contribution of treatment interrupters [2, 21, 24-26]. Furthermore, we were unable to minimize this bias as we did not have data on tracing for all or a sample of those who were LTFU[27]. Our focus was limited to programme outcomes after ART acknowledging that a substantial proportion of patients were lost during pre-ART care[28-31]. While programme size and the rate of expansion were adjusted for, residual confounding may be present if important internal organisational aspects were not sufficiently captured and from unmeasured factors. Sensitivity analyses confirmed our results investigating differences by programme, including patients with missing covariate data, and adjusting for site heterogeneity. A competing risks approach led to very similar

findings corroborating that the traditional Cox's proportional hazards models are appropriate[32, 33].

Our findings explore the tension and challenges involved in pursuing the ambitious goals of expanding ART to 15 million people by 2015 and implementing "Treatment 2.0" strategies in high prevalence, resource-limited settings[1, 10]. Recent Treatment as Prevention models assumed a long-term drop-out rate of 1.5% annually, which appears optimistic considering our estimates of long-term retention[34]. With a high burden of acutely ill patients, ART programmes will struggle to expand access to patients in earlier stages of HIV disease without additional resources. With new 2013 WHO guidelines to expand ART access to an additional 9.2 million people in low- and middle-income countries, we need to fully understand the individual and programmatic implications of earlier initiation[1].

Over a decade, ART programmes have expanded in high prevalence, resource-limited settings with a focus to increase access to care and thus patient numbers. Today, many sites hold high numbers of HIV-infected patients, above 20,000 at some sites. The quality of ART services and psychosocial counselling at these large sites may be taking a back seat as the drive for expansion continues. The conscious trade-off between numbers and quality deserves more discussion and close monitoring as the targets for expansion of treatment continue to increase. The findings of our study suggest that, potentially, ART sites should be capped at a maximum number of patients and the rate of enrolment restricted in favour of balancing growth with quality care. Site human resource capacity and

programme organisation characteristics are likely to be important determinants to consider in achieving this balance and deserve further investigation to provide effective recommendations regarding maximum patient volume and expansion rate at programme level.

For the first time, the WHO guidelines acknowledge the challenge of long-term retention in ART programmes with explicit guidance on operations and service delivery, including adherence, retention, decentralization and task shifting[3]. Additional resources are needed to strengthen monitoring systems to ascertain true outcomes of children and adults lost to care pre- and post-ART initiation[15, 35]. Identification of ART patients disengaged from care is critical as they are at an increased risk of developing and transmitting drug resistant strains of HIV[18]. There is an urgent need to determine sustainable and optimal models of care for stable patients on lifelong ART, especially in large programmes in high-prevalence, resource-limited settings. Decreasing visit frequency by expanding intervals between prescription refills, decentralizing ART delivery into community-based patient led groups, and introducing flexible systems to support mobile populations are all interventions that could be considered and assessed on a large-scale[36-39].

In summary, ART programmes in resource-limited settings have grown rapidly over the last decade. However, significant work remains to continue expanding access while addressing the growing challenge of programme attrition. Sustainable models of care for long-term retention of patients in large, high-prevalence, resource-limited settings are urgently needed.

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Figure Legends:

Figure 1. Cumulative probability of death and LTFU stratified by year of ART initiation, programme size, or rate of expansion
A) Mortality by year of ART initiation
B) LTFU by year of ART initiation
C) Mortality by programme size
D) LTFU by programme size
E) Mortality by rate of expansion
F) LTFU by rate of expansion

Table 1: Patient characteristics at ART initiation

Characteristics	No. of patients N=132 334
Sex, n (%)	
Females	80 456 (60.8)
Age (years)	
Median [IQR]	35.0 [29.4-42.0]
Age group, n (%)	
16-25	11 840 (9.0)
25-34	53 332 (40.3)
35-44	42 894 (32.4)
45+	24 268 (18.3)
CD4 cell count (cell/µ/L)	n=103 197 (78.0)
Median [IQR]	142 [63-220]
Level, n (%)	
<25	10 890 (10.6)
25-49	10 054 (9.7)
50-99	16 826 (16.3)
100-149	16 220 (15.7)
150-199	17 253 (16.7)
200-349	27 484 (26.6)
≥350	4 470 (4.3)
Clinical stage, n(%)	n=129 859 (98.1)
1 & 2	41 105 (31.7)
3	56 619 (43.6)
4	32 135 (24.8)
BMI group (kg/m^2), n (%)	n=121 809 (92.0)
Underweight (≤18.5)	40 122 (32.9)
Normal (18.6-25.0)	72 217 (59.3)
Overweight (25.1-30.0)	7 727 (6.4)
Obese (>30.0)	1 733 (1.4)
Country, n (%)	
DRC	4 140 (3.1)
India	1 526 (1.2)
Kenya	19 353 (14.6)
Malawi	37 657 (28.5)
Mozambique	12 492 (9.4)
Myanmar	16 784 (12.7)
Uganda	9 599 (7.3)
Zimbabwe	30 783 (23.3)

IQR, interquartile range

Table 2: Baseline characteristics and 6-, 12- and 36-month Kaplan-Meier cumulative mortality, loss to follow-up and overall programme retention stratified by calendar year of ART initiation

	Year of ART initiation								
	≤2003 n=4 427	**2004** n=8 410	**2005** n=10 974	**2006** n=15 383	**2007** n=19 826	**2008** n=18 991	**2009** n=19 410	**2010** n=22 863	**2011** n= 12 050
Age (years), median [IQR]	34.7 [29.4-41.1]	35.1 [29.4-42.1]	35.0 [29.5-41.9]	34.9 [29.4-41.8]	35.0 [29.8-42.1]	35.1 [29.4-42.1]	35.1 [29.3-42.0]	35.0 [29.3-42.0]	35.0 [29.4-42.0]
CD4 cell count (cell/μ/L), median [IQR]	97 [42-162]	114 [51-178]	116 [50-182]	112 [48-189]	132 [58-205]	150 [72-221]	155 [74-224]	171 [80-248]	184 [77-276]
Clinical stage 4, n(%)	1 914 (44.4)	3 659 (44.3)	4 276 (40.3)	5 254 (35.0)	5 266 (27.0)	3 814 (20.7)	3 253 (17.0)	3 030 (13.4)	1 669 (14.0)
Underweight, n(%)	1 567 (38.9)	2 672 (27.9)	3 744 (38.5)	5 470 (38 2)	6 254 (33.3)	5 594 (31.5)	5 703 (31.3)	5 785 (27.7)	3 333 (30.1)
Cumulative mortality, (95% CI)									
6-month	14.1 (13.1-15.2)	9.3 (8.7-9.9)	8.1 (7.6-8.6)	8.0 (7.6-8.5)	5.4 (5.1-5.7)	5.2 (4.9-5.5)	4.5 (4.2-4.8)	4.1 (3.8-4.3)	3.7 (3.3-4.2)
12-month	17.3 (16.2-18.5)	11.8 (11.1-12.6)	10.2 (0.6-10.8)	9.9 (9.4-10.4)	6.8 (6.4-7.2)	6.5 (6.1-6.9)	5.6 (5.2-5.9)	5.1 (4.8-5.4)	-
36-month	21.5 (20.3-22.8)	15.4 (14.6-16.3)	13.7 (13.0-14.4)	12.8 (12.2-13.3)	9.5 (9.1-10.0)	8.8 (8.4-9.2)	-	-	-
Cumulative LTFU, (95% CI)									
6-month	4.0 (3.4-4.6)	6.9 (6.4-7.5)	6.2 (5.8-6.7)	5.9 (5.5-6.3)	7.6 (7.2-8.0)	8.4 (8.0-8.8)	7.3 (7.0-7.7)	9.2 (8.8-9.6)	11.3 (10.4-12.2)
12-month	5.9 (5.2-6.7)	9.3 (8.7-9.9)	8.9 (8.4-9.5)	8.1 (7.7-8.5)	10.3 (9.8-10.7)	11.5 (11.0-11.9)	10.3 (9.9-10.7)	14.6 (14.1-15.2)	-
36-month	11.4 (10.4-12.5)	16.3 (15.5-17.2)	14.6 (13.9-15.3)	14.6 (14.0-15.2)	17.1 (16.6-17.7)	21.2 (20.5-21.8)	-	-	-
Cumulative programme retention in care, (95% CI)									
6-month	82.4 (81.3-83.5)	84.5 (83.7-85.2)	86.2 (85.6-86.9)	86.6 (86.0-87.1)	87.4 (87.0-87.9)	86.8 (86.3-87.3)	88.5 (88.1-89.0)	87.1 (87.7-87.6)	85.5 (84.5-86.4)
12-month	77.8 (76.6-79.0)	80.0 (79.1-80.8)	81.8 (81.1-82.5)	82.8 (82.2-83.4)	83.6 (83.1-84.2)	82.8 (82.2-83.3)	84.7 (84.2-85.2)	81.0 (80.5-81.6)	-
36-month	69.6 (68.2-70.9)	70.8 (69.8-71.7)	73.8 (72.9-74.6)	74.5 (73.8-75.2)	75.0 (74.4-75.6)	71.9 (71.2-72.6)	-	-	

CI, confidence interval; IQR, interquartile range; LTFU, lost to follow-up.

Table 3: Cox proportional hazards estimates of mortality by baseline characteristics and year of ART initiation, adjusted by cohort. *

	0-12 months					12-72 months				
	Univariate	Model 1 (n=94 571)	Model 2 (n=94 571)	Model 3 (n=94 571)	Model 4 (n=94 571)	Univariate	Model 1 (n=62 080)	Model 2 (n=62 080)	Model 3 (n=62 080)	Model 4 (n=62 080)
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Year of ART initiation										
≤2003	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
2004	0.67 (0.61-0.74)	0.67 (0.58-0.78)	0.74 (0.62-0.88)	0.75 (0.64-0.87)	0.78 (0.65-0.94)	0.77 (0.66-0.91)	0.78 (0.63-0.97)	0.85 (0.66-1.09)	0.88 (0.70-1.10)	0.87 (0.68-1.13)
2005	0.53 (0.48-0.58)	0.62 (0.54-0.71)	0.77 (0.64-0.94)	0.75 (0.64-0.88)	0.82 (0.65-0.94)	0.69 (0.59-0.81)	0.72 (0.58-0.88)	0.84 (0.64-1.11)	0.82 (0.65-1.04)	0.85 (0.64-1.11)
2006	0.51 (0.47-0.56)	0.61 (0.54-0.69)	0.77 (0.64-0.93)	0.76 (0.65-0.89)	0.80 (0.66-0.97)	0.58 (0.50-0.68)	0.63 (0.52-0.77)	0.75 (0.57-0.98)	0.74 (0.58-0.94)	0.75 (0.57-0.99)
2007	0.36 (0.33-0.40)	0.47 (0.42-0.53)	0.71 (0.57-0.88)	0.60 (0.51-0.71)	0.76 (0.61-0.95)	0.53 (0.46-0.62)	0.64 (0.53-0.78	0.75 (0.55-1.03)	0.76 (0.59-0.98)	0.76 (0.55-1.04)
2008	0.34 (0.31-0.38)	0.55 (0.48-0.62)	0.85 (0.68-1.07)	0.72 (0.60-0.86)	0.91 (0.72-1.14)	0.46 (0.38-0.54)	0.58 (0.47-0.72)	0.69 (0.49-0.97)	0.71 (0.53-0.99)	0.72 (0.51-1.01)
2009	0.29 (0.26-0.32)	0.54 (0.48-0.61)	0.94 (0.74-1.19)	0.71 (0.59-0.85)	0.98 (0.77-1.26)	0.43 (0.35-0.52)	0.60 (0.47-0.76)	0.73 (0.50-1.06)	0.72 (0.53-0.99)	0.74 (0.51-1.08)
2010	0.27 (0.24-0.29)	0.58 (0.51-0.65)	0.95 (0.74-1.21)	0.76 (0.63-0.91)	1.00 (0.78-1.29)	0.50 (0.35-0.72)	0.83 (0.56-1.23)	1.19 (0.72-1.96)	1.01 (0.65-1.56)	1.21 (0.73-2.00)
2011	0.28 (0.24-0.32)	0.60 (0.50-0.71)	0.95 (0.72-1.25)	0.78 (0.63-0.97)	1.00 (0.76-1.33)	-	-	-	-	-
Programme size (patients)										
<500	1.0 (ref)		1.0 (ref)		1.0 (ref)	1.0 (ref)		1.0 (ref)		1.0 (ref)
500-999	0.90 (0.79-1.03)		1.19 (0.98-1.45)		1.15 (0.94-1.40)	0.83 (0.69-1.00)		0.99 (0.77-1.27)		0.99 (0.77-1.27)
1000-2499	0.64 (0.57-0.72)		1.17 (0.95-1.42)		1.14 (0.94-1.40)	0.77 (0.65-0.91)		1.07 (0.83-1.39)		1.08 (0.83-1.40)
2500-4999	0.51 (0.45-0.57)		0.99 (0.78-1.24)		0.97 (0.77-1.24)	0.59 (0.49-0.71)		0.84 (0.62-1.14)		0.87 (0.63-1.21)
5000-7499	0.31 (0.27-0.35)		0.65 (0.49-0.86)		0.61 (0.45-0.82)	0.42 (0.34-0.52)		0.75 (0.51-1.11)		0.76 (0.50-1.16)
7500 – 9999	0.26 (0.23-0.30)		0.57 (0.42-0.76)		0.48 (0.34-0.68)	0.38 (0.29-0.51)		0.70 (0.44-1.10)		0.72 (0.42-1.22)
10000-14999	0.22 (0.19-0.25)		0.75 (0.54-1.03)		0.61 (0.41-0.90)	0.42 (0.33-0.54)		0.95 (0.59-1.53)		1.02 (0.59-1.77)
15000-19999	0.15 (0.12-0.18)		0.50 (0.34-0.73)		0.41 (0.26-0.63)	0.35 (0.25-0.50)		0.88 (0.49-1.57)		1.00 (0.51-1.96)
≥20000	0.18 (0.15-0.22)		0.61 (0.41-0.89)		0.49 (0.31-0.77)	0.18 (0.06-0.55)		0.29 (0.08-1.06)		0.34 (0.09-1.27)
Rate of expansion (patients/month)										
<25	1.0 (ref)			1.0 (ref)	1.0 (ref)	1.0 (ref)			1.0 (ref)	1.0 (ref)
25-59	0.64 (0.59-0.69)			0.93 (0.83-1.04)	0.93 (0.83-1.05)	0.74 (0.65-0.84)			0.89 (0.75-1.05)	0.93 (0.78-1.10)
60-89	0.43 (0.40-0.47)			0.75 (0.64-0.87)	0.88 (0.74-1.04)	0.56 (0.49-0.65)			0.75 (0.61-0.93)	0.87 (0.68-1.12)
90-124	0.37 (0.34-0.41)			0.75 (0.63-0.89)	1.06 (0.86-1.30)	0.52 (0.45-0.61)			0.84 (0.65-1.08)	1.02 (0.74-1.40)
≥125	0.21 (0.20-0.24)			0.70 (0.58-0.85)	1.13 (0.87-1.48)	0.39 (0.32-0.47)			0.74 (0.54-1.02)	0.85 (0.55-1.31)
Sex										
Female	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Male	1.61 (1.54-1.68)	1.29 (1.22-1.36)	1.30 (1.23-1.37)	1.29 (1.22-1.37)	1.30 (1.22-1.37)	1.77 (1.64-1.91)	1.57 (1.42-1.73)	1.57 (1.42-1.73)	1.57 (1.42-1.73)	1.57 (1.42-1.73)
Age group (years)										
16-25	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
25-34	1.07 (0.99-1.17)	1.11 (0.99-1.25)	1.10 (0.99-1.23)	1.11 (0.99-1.24)	1.10 (0.99-1.23)	0.94 (0.81-1.09)	0.85 (0.70-1.03)	0.85 (0.70-1.02)	0.85 (0.70-1.03)	0.85 (0.70-1.02)

35-44	1.16 (1.07-1.26)	1.18 (1.05-1.32)	1.16 (1.04-1.31)	1.17 (1.05-1.32)	1.17 (1.04-1.31)	1.10 (0.92-1.27)	0.99 (0.82-1.20)	0.99 (0.81-1.20)	0.99 (0.81-1.20)	0.99 (0.81-1.20)
45+	1.33 (1.22-1.46)	1.48 (1.31-1.67)	1.46 (1.29-1.65)	1.47 (1.31-1.66)	1.46 (1.29-1.65)	1.66 (1.42-1.95)	1.49 (1.22-1.82)	1.48 (1.21-1.81)	1.49 (1.22-1.82)	1.48 (1.21-1.82)
Body Mass Index										
Underweight	3.65 (3.47-3.83)	2.58 (2.43-2.74)	2.60 (2.45-2.76)	2.58 (2.43-2.74)	2.59 (2.44-2.75)	1.67 (1.54-1.82)	1.57 (1.42-1.73)	1.57 (1.42-1.74)	1.56 (1.31-1.73)	1.56 (1.41-1.73)
Normal	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Overweight	0.59 (0.50-0.69)	0.75 (0.62-0.90)	0.74 (0.61-0.90)	0.75 (0.62-0.90)	0.74 (0.61-0.90)	0.85 (0.69-1.03)	1.01 (0.80-1.27)	1.01 (0.80-1.27)	1.01 (0.80-1.28)	1.01 (0.80-1.28)
Obese	0.88 (0.67-1.17)	1.23 (0.90-1.69)	1.22 (0.88-1.67)	1.24 (0.90-1.71)	1.22 (0.89-1.68)	0.93 (0.62-1.39)	0.76 (0.43-1.34)	0.76 (0.43-1.34)	0.77 (0.43-1.36)	0.76 (0.43-1.35)
CD4 cell count (cells/μL)										
<25	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
25-49	0.61 (0.57-0.66)	0.71 (0.65-0.78)	0.71 (0.65-0.78)	0.71 (0.65-0.78)	0.71 (0.65-0.78)	0.93 (0.78-1.10)	0.98 (0.82-1.18)	0.98 (0.81-1.18)	0.98 (0.82-1.18)	0.98 (0.81-1.18)
50-99	0.39 (0.36-0.42)	0.52 (0.48-0.56)	0.52 (0.48-0.56)	0.52 (0.48-0.560	0.52 (0.48-0.56)	0.86 (0.72-1.00)	1.00 (0.85-1.18)	1.00 (0.85-1.18)	1.00 (0.85-1.18)	1.00 (0.84-1.18)
100-149	0.26 (0.24-0.28)	0.41 (0.37-0.45)	0.41 (0.37-0.45)	0.41 (0.37-0.45)	0.41 (0.37-0.45)	0.63 (0.54-0.75)	0.79 (0.66-0.95)	0.79 (0.66-0.95)	0.80 (0.67-0.95)	0.79 (0.66-0.95)
150-199	0.19 (0.18-0.21)	0.35 (0.31-0.39)	0.35 (0.31-0.39)	0.35 (0.31-0.39)	0.35 (0.31-0.39)	0.65 (0.55-0.76)	0.89 (0.74-1.07)	0.89 (0.74-1.06)	0.90 (0.75-1.07)	0.89 (0.74-1.06)
200-349	0.15 (0.13-0.16)	0.29 (0.26-0.32)	0.29 (0.26-0.32)	0.29 (0.26-0.32)	0.29 (0.26-0.32)	0.52 (0.44-0.61)	0.74 (0.62-0.89)	0.74 (0.62-0.88)	0.75 (0.62-0.89)	0.74 (0.62-0.89)
≥350	0.24 (0.21-0.28)	0.42 (0.36-0.49)	0.43 (0.36-0.50)	0.42 (0.36-0.49)	0.42 (0.36-0.49)	0.78 (0.60-1.03)	0.98 (0.72-1.33)	0.98 (0.72-1.34)	0.98 (0.72-1.33)	0.98 (0.72-1.33)
Clinical stage										
1 and 2	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
3	2.60 (2.42-2.79	1.65 (1.51-1.80)	1.61 (1.47-1.76)	1.54 (1.50-1.79)	1.61 (1.47-1.76)	1.54 (1.38-1.73)	1.20 (1.05-1.38)	1.19 (1.04-1.37)	1.19 (1.04-1.37)	1.19 (1.03-1.36)
4	5.70 (5.31-6.11)	2.73 (0.48-2.99)	2.65 (2.41-2.91)	2.69 (2.45-2.96)	2.65 (2.41-2.92)	2.26 (2.01-2.53)	1.54 (1.32-1.79)	1.51 (1.30-1.76)	1.52 (1.31-1.76)	1.51 (1.30-1.75)

* All models accounted for site heterogeneity using random effects. Model 1 – demographics and baseline variables, Model 2 - Model 1 + programme size, Model 3 – Model 1 + rate of expansion, Model 4 – Model 1 + programme size and rate of expansion

Table 4: Cox proportional hazards estimates of LTFU by baseline characteristics and year of ART initiation, adjusted by cohort. *

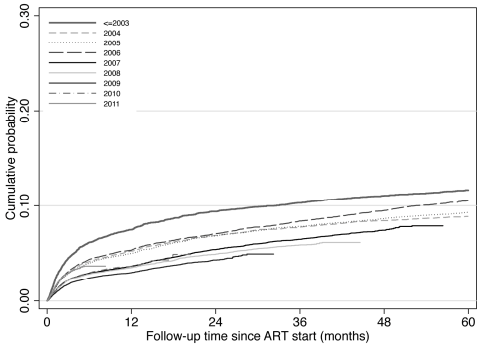
	0-12 months					12-72 months				
	Univariate HR (95% CI)	Model 1 (n=94 571) HR (95% CI)	Model 2 (n=94 571) HR (95% CI)	Model 3 (n=94 571) HR (95% CI)	Model 4 (n=94 571) HR (95% CI)	Univariate HR (95% CI)	Model 1 (n=62 080) HR (95% CI)	Model 2 (n=62 080) HR (95% CI)	Model 3 (n=62 080) HR (95% CI)	Model 4 (n=62 080) HR (95% CI)
Year of ART initiation										
≤2003	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
2004	1.62 (1.40-1.88)	1.52 (1.22-1.90)	1.06 (0.81-1.39)	1.36 (1.08-1.72)	1.09 (0.83-1.43)	1.31 (1.16-1.49)	1.19 (1.02-1.40)	1.03 (0.84-1.27)	1.09 (0.92-1.29)	1.04 (0.84-1.28)
2005	1.69 (1.46-1.95)	1.99 (1.61-2.45)	1.34 (1.03-1.76)	1.74 (1.39-2.18)	1.37 (1.04-1.80)	1.19 (1.05-1.35)	1.20 (1.03-1.40)	1.03 (0.83-1.28)	1.00 (0.85-1.19)	0.94 (0.76-1.17)
2006	1.62 (1.41-1.86)	2.18 (1.79-2.66)	1.54 (1.19-1.98)	1.80 (1.43-2.26)	1.43 (1.09-1.88)	1.47 (1.31-1.66)	1.67 (1.44-1.93)	1.45 (1.18-1.80)	1.27 (1.07-1.51)	1.17 (0.94-1.46)
2007	2.04 (1.78-2.34)	3.25 (2.68-3.93)	2.25 (1.71-2.96)	2.60 (2.07-3.26)	2.19 (1.64-2.93)	1.82 (1.62-2.05)	2.37 (2.05-2.74)	2.19 (1.72-2.80)	1.76 (1.47-2.11)	1.83 (0.94-1.46)
2008	2.26 (1.98-2.59)	3.58 (2.95-4.33)	2.43 (1.83-3.21)	2.66 (2.10-3.35)	2.31 (1.72-3.09)	2.44 (2.15-2.75)	3.30 (2.83-3.84)	3.02 (2.34-3.89)	2.33 (1.92-2.83)	2.48 (1.91-3.23)
2009	2.14 (1.87-2.45)	3.58 (2.95-4.34)	2.37 (1.77-3.16)	2.52 (2.00-3.19)	2.14 (1.58-2.89)	3.60 (3.16-4.10)	4.71 (4.01-5.53)	4.54 (3.46-5.95)	3.26 (2.65-4.01)	3.58 (2.70-4.75)
2010	2.99 (2.62-3.42)	5.46 (4.51-6.61)	3.52 (2.62-4.72)	3.74 (2.96-4.73)	3.29 (2.42-4.46)	6.50 (5.45-7.76)	8.47 (6.92-10.53)	8.50 (6.18-11.68)	5.94 (4.62-7.46)	6.86 (4.94-9.53)
2011	3.64 (3.15-4.21)	6.17 (5.03-7.56)	3.61 (2.65-4.92)	4.06 (3.17-5.19)	3.51 (2.55-4.83)	-	-	-	-	-
Programme size (patients)										
<500	1.0 (ref)		1.0 (ref)		1.0 (ref)	1.0 (ref)		1.0 (ref)		1.0 (ref)
500-999	1.71 (1.29-2.26)		2.01 (1.32-3.06)		1.86 (1.23-2.82)	1.64 (1.34-2.00)		1.45 (1.13-1.85)		1.40 (1.09-1.79)
1000-2499	3.02 (2.33-3.92)		2.66 (1.75-4.05)		2.36 (1.55-3.58)	2.35 (1.94-2.86)		1.55 (1.19-2.02)		1.44 (1.10-1.88)
2500-4999	3.29 (2.54-4.27)		2.80 (1.81-4.32)		2.29 (1.48-3.55)	2.66 (2.19-3.22)		1.64 (1.23-2.18)		1.34 (1.00-1.80)
5000-7499	4.36 (3.36-5.67)		2.54 (1.61-4.00)		1.97 (1.24-3.10)	3.80 (3.11-4.65)		1.39 (1.00-1.92)		1.03 (0.74-1.43)
7500 – 9999	4.60 (3.53-5.99)		2.72 (1.72-4.32)		1.67 (1.04-2.69)	5.47 (4.42-6.77)		1.44 (1.02-2.03)		0.83 (0.57-1.20)
10000-14999	6.17 (4.73-8.04)		4.07 (2.53-6.53)		2.02 (1.22-3.34)	4.06 (3.22-5.12)		1.34 (0.90-1.99)		0.83 (0.54-1.27)
15000-19999	5.97 (4.49-7.93)		4.52 (2.73-7.47)		2.27 (1.34-3.87)	4.89 (3.69-6.48)		1.11 (0.71-1.74)		0.74 (0.46-1.19)
≥20000	7.35 (5.55-9.73)		3.66 (2.20-6.10)		1.77 (1.04-3.04)	7.03 (4.30-11.48)		0.81 (0.42-1.57)		0.53 (0.27-1.04)
Rate of expansion (patients/month)										
<25	1.0 (ref)			1.0 (ref)	1.0 (ref)	1.0 (ref)			1.0 (ref)	1.0 (ref)
25-59	1.57 (1.41-1.75)			1.36 (1.16-1.60)	1.26 (1.07-1.49)	1.48 (1.33-1.64)			1.24 (1.08-1.41)	1.22 (1.06-1.39)
60-89	1.94 (1.73-2.18)			1.39 (1.14-1.69)	1.36 (1.10-1.67)	1.96 (1.75-2.18)			1.43 (1.21-1.68)	1.56 (1.31-1.85)
90-124	2.16 (1.92-2.4)			1.61 (1.31-1.98)	1.70 (1.35-2.14)	2.79 (2.48-3.14)			1.86 (1.55-2.23)	2.22 (1.81-2.72)
≥125	3.09 (2.74-3.48)			2.21 (1.78-2.75)	2.31 (1.78-3.01)	3.72 (3.25-4.27)			1.65 (1.33-2.05)	2.29 (1.76-2.99)
Sex										
Female	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Male	1.31 (1.27-1.36)	1.26 (1.20-1.32)	1.26 (1.20-1.32)	1.25 (1.19-1.31)	1.25 (1.2-1.31)	1.16 (1.11-1.21)	1.21 (1.14-1.28)	1.21 (1.15-1.28)	1.21 (1.14-1.28)	1.21 (1.15-1.29)
Age group (years)										
16-25	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
25-34	0.72 (0.69-0.76)	0.72 (0.67-0.77)	0.72 (0.67-0.77)	0.72 (0.67-0.77)	0.72 (0.67-0.77)	0.63 (0.59-0.67)	0.66 (0.60-0.72)	0.66 (0.60-0.72)	0.66 (0.60-0.72)	0.66 (0.60-0.72)

35-44	0.60 (0.57-0.64)	0.60 (0.55-0.64)	0.59 (0.55-0.64)	0.60 (0.55-0.64)	0.59 (0.55-0.64)	0.50 (0.47-0.54)	0.51 (0.46-0.56)	0.51 (0.46-0.56)	0.51 (0.46-0.56)	0.51 (0.46-0.56)
45+	0.60 (0.56-0.64)	0.58 (0.53-0.63)	0.58 (0.53-0.63)	0.58 (0.53-0.63)	0.58 (0.53-0.63)	0.51 (0.47-0.56)	0.49 (0.44-0.54)	0.49 (0.44-0.54)	0.49 (0.44-0.54)	0.48 (0.44-0.54)
Body Mass Index										
Underweight	1.70 (1.63-1.77)	1.53 (1.45-1.60)	1.52 (1.45-1.59)	1.52 (1.45-1.60)	1.52 (1.45-1.60)	1.12 (1.07-1.18)	1.06 (1.00-1.13)	1.07 (1.00-1.13)	1.06 (1.00-1.13)	1.07 (1.00-1.13)
Normal	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Overweight	0.91 (0.83-0.99)	0.93 (0.84-1.03)	0.93 (0.84-1.03)	0.93 (0.84-1.03)	0.93 (0.83-1.03)	0.99 (0.90-1.109)	1.08 (0.96-1.20)	1.08 (0.96-1.20)	1.08 (0.97-1.21)	1.08 (0.97-1.21)
Obese	1.21 (0.96-1.31)	1.14 (0.94-1.39)	1.14 (0.94-1.39)	1.14 (0.94-1.39)	1.14 (0.93-1.38)	0.86 (0.70-1.07)	0.98 (0.77-1.25)	0.98 (0.76-1.25)	0.98 (0.76-1.25)	0.97 (0.76-1.25)
CD4 cell count (cells/μL)										
<25	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
25-49	0.81 (0.74-0.87)	0.89 (0.82-0.97)	0.88 (0.81-0.97)	0.89 (0.81-0.97)	0.89 (0.81-0.97)	0.93 (0.84-1.04)	0.98 (0.8-1.10)	0.99 (0.88-1.11)	0.98 (0.88-1.10)	0.99 (0.88-1.11)
50-99	0.61 (0.57-0.66)	0.73 (0.67-0.79)	0.72 (0.66-0.78)	0.72 (0.67-0.78)	0.72 (0.66-0.78)	0.87 (0.79-0.95)	0.95 (0.85-1.05)	0.95 (0.86-1.05)	0.94 (0.85-1.04)	0.95 (0.85-1.05)
100-149	0.56 (0.52-0.60)	0.70 (0.64-0.76)	0.69 (0.66-0.78)	0.69 (0.64-0.75)	0.69 (0.64-0.75)	0.85 (0.77-0.94)	0.97 (0.88-1.08)	0.98 (0.88-1.08)	0.97 (0.87-1.07)	0.97 (0.88-1.08)
150-199	0.47 (0.44-0.51)	0.60 (0.55-0.66)	0.60 (0.64-0.75)	0.60 (0.55-0.65)	0.59 (0.55-0.65)	0.88 (0.80-0.97)	0.98 (0.88-1.09)	0.98 (0.89-1.09)	0.97 (0.88-1.08)	0.98 (0.88-1.09)
200-349	0.51 (0.48-0.55)	0.60 (0.56-0.66)	0.60 (0.55-0.65)	0.60 (0.56-0.65)	0.60 (0.55-0.65)	0.92 (0.84-1.01)	0.91 (0.82-1.01)	0.92 (0.83-1.02)	0.91 (0.82-1.01)	0.92 (0.83-1.02)
≥350	0.78 (0.71-0.87)	0.76 (0.68-086)	0.77 (0.68-0.86)	0.77 (0.68-0.86)	0.77 (0.68-0.86)	1.13 (0.96-1.32)	1.07 (0.91-1.27)	1.09 (0.92-1.29)	1.05 (0.89-1.25)	1.05 (0.89-1.25)
Clinical stage										
1 and 2	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
3	1.10 (1.05-1.14)	1.15 (1.09-1.22)	1.17 (1.11-1.24)	1.17 (1.11-1.24)	1.17 (1.10-1.23)	1.05 (0.99-1.11)	1.21 (1.13-1.30)	1.21 (1.13-1.29)	1.20 (1.12-1.28)	1.18 (1.10-1.27)
4	1.51 (1.44-1.59)	1.52 (1.42-1.62)	1.55 (1.45-1.65)	1.56 (1.46-1.67)	1.56 (1.46-1.66)	1.11 (1.04-1.18)	1.29 (1.19-1.40)	1.29 (1.19-1.40)	1.29 (1.19-1.40)	1.28 (1.18-1.39)

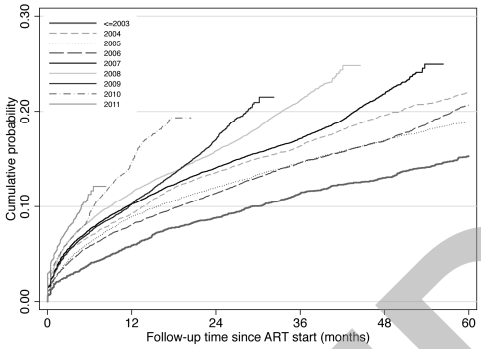
* All models accounted for site heterogeneity using random effects. Model 1 – demographics and baseline variables, Model 2 - Model 1 + programme size, Model 3 – Model 1 + rate of expansion, Model 4 – Model 1 + programme size and rate of expansio

Figure 1. Cumulative probability of death and LTFU stratified by year of ART initiation, programme size, or rate of expansion

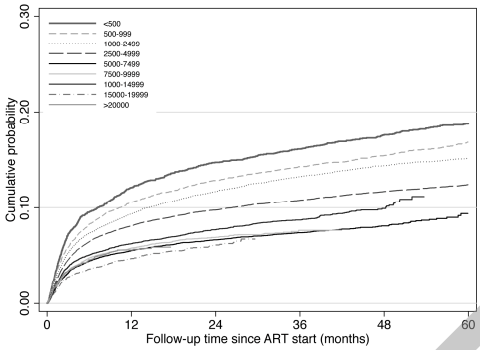
A) Mortality by year of ART initiation



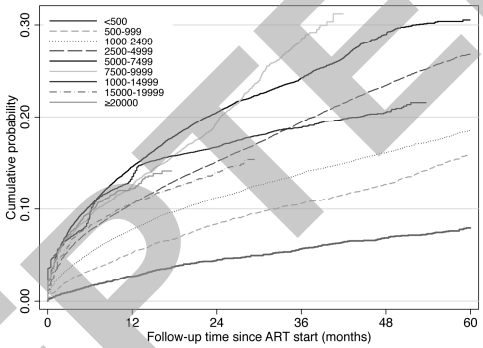
1B) LTFU by year of ART initiation



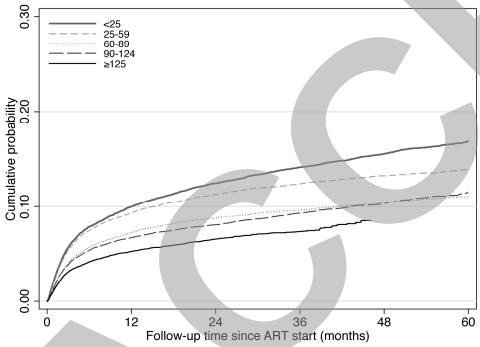
1C) Mortality by programme size



1D) LTFU by programme size



1E) Mortality by rate of expansion



1F) LTFU by rate of expansion