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Retention of HIV-infected children on antiretroviral treatment in HIV care and treatment programs in Kenya, Mozambique, Rwanda and Tanzania

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Abstract

Background—Retention of children in HIV care is essential for prevention of disease progression and mortality.

Methods—Retrospective cohort of children (0 to <15 years) initiating antiretroviral treatment (ART) at health facilities in Kenya, Mozambique, Rwanda and Tanzania, January 2005–June 2011. Retention was defined as the proportion of children known to be alive and attending care at their initiation facility; lost to follow-up (LTF) was defined as no clinic visit for > 6 months. Cumulative incidence of ascertained survival and retention after ART initiation was estimated through 24 months using Kaplan-Meier methods. Factors associated with LTF and death were assessed using Cox proportional hazard modeling.

Results—17,712 children initiated ART at 192 facilities: median age was 4.6 years (IQR: 1.9–8.3), median CD4 was 15% (IQR: 10–20) for children < 5 years and 265 cells/uL (IQR: 111–461) for children ≥ 5 years. At 12 and 24 months, 80% and 72% of children were retained with 16% and 22% LTF and 5% and 7% known deaths respectively. Retention ranged from 71–95% and 62–

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93% at 12 and 24 months across countries, and was lowest for children < 1 year (51% at 24 months). LTF and death were highest in children < 1 year of age and children with advanced disease.

Conclusion—Retention was lowest in young children and differed across country programs. Young children and those with advanced disease are at highest risk for LTF and death. Further evaluation of patient- and program-level factors is needed to improve health outcomes.

Keywords

HIV; retention; pediatric; antiretrovirals

INTRODUCTION

Scale up of pediatric HIV care and treatment across sub-Saharan Africa (SSA), where over 90% of children living with HIV reside[1], has been substantial with more than 387,000 children reported as initiating antiretroviral therapy (ART) by December 2010[2]. Treatment responses of children on ART in resource-limited settings have been robust[3–9] with high rates of viral suppression and immune reconstitution as well as improved survival[10–15]. However, the mortality rate of children on ART in resource-limited settings is considerably higher than the rate in developed countries, 8.0 versus 0.9 deaths per 100 child-years ($p < 0.001$) respectively[16]. Reasons for this disparity include both biomedical and programmatic factors such as advanced disease at time of presentation, fragility of infants and younger children, other infectious co-morbidities and malnutrition, delays in ART initiation, and suboptimal retention in care[4,13].

Retention of HIV-infected children in care is essential for prevention of HIV-related morbidity and mortality through timely ART initiation, monitoring and management of disease progression and treatment failure, and provision of medications and supportive care. Pediatric programs in SSA report retention ranging from 77–89% at 12 and 24 months[11,14,15,17–19] which may jeopardize long-term health outcomes[20]. Both patient and programmatic factors influencing retention need to be identified to improve outcomes and inform future interventions.

We examined retention, lost to follow-up (LTF) and death among 17,712 children, less than 15 years of age, initiating ART at 192 health facilities in Kenya, Mozambique, Rwanda, and Tanzania from January 2005 through June 2011. The objectives of this analysis were to determine the proportion of children who were retained, LTF and died at 12 and 24 months, to assess variation in retention outcomes by country, and to identify patient- and facility-level factors associated with these outcomes.

METHODS

Study Population

We conducted a retrospective cohort analysis of all children, < 15 years of age, initiating ART at 192 HIV care facilities in Kenya, Mozambique, Rwanda and Tanzania from January 2005–June 2011. All facilities received support from ICAP, a President's Emergency Plan

for AIDS Relief (PEPFAR) implementing partner that has been supporting HIV care and treatment in SSA since 2005. ICAP is a nongovernmental organization at the Mailman School of Public Health at Columbia University that supports scale-up of HIV care and treatment through facility mentorship of facility staff, renovation of laboratory and health facilities, creation and support of monitoring and evaluation tools and practices, and other technical assistance[21]. All health facilities included in this analysis participate in the Identifying Optimal Models of HIV Care and Treatment Study (5U2GPS001537-03)[22] which uses routinely collected patient- and facility-level data to measure patient and program outcomes. All facilities had electronic patient-level databases, which are password protected, and encrypted de-identified databases are transferred to ICAP offices every quarter where they are aggregated for analysis. Clinical and laboratory data was recorded by facility staff onto paper records and clerks then data was transferred from paper records into an electronic patient database; data quality assessments were done every 6 months to assess for completeness and accuracy of data entry.

Eligibility criteria for ART initiation followed each country's national guidelines which reflect WHO recommendations[23,24]. Per WHO 2006 guidelines, children < 5 years were eligible for ART if they had WHO Stage III/IV, CD4 percentage < 25% (<12 months), CD4 percentage <20 % (12–35 months) or CD4 percentage < 15% (36–59 months). For children > 5 years old, ART eligibility included 1) WHO Stage IV, 2) WHO stage III and CD4 < 350 cells/uL, or 3) CD4< 200 cells/uL irrespective of WHO Stage[23]. From 2006 to 2011, all four countries began adopting revised WHO guidelines, including recommendations for ART for all HIV-infected children < 1 year[25–28], later updated to < 2 years regardless of CD4 measurement[24,29,30]. Standard of care for HIV care and ART regimens followed national guidelines, which recommended ART for eligible children beginning in 2006[23]. Recommended facility follow-up was a minimum of every 3 months with semi-annual CD4 testing. Access to CD4 testing was not always available but improved over time with increased access to CD4 analyzers and decentralization of laboratories.

Definitions and Outcomes

Follow-up time on ART was estimated as the time between date of ART initiation and either documented transfer, death, LTF, or completion of the observation period. Children were considered retained if they were known to be alive and continuing ART at their initiation facility. Mortality was passively ascertained from documentation of death in patient records. LTF was defined as having no recorded visit for 6 months with no visits after the last missed visit, as per by Chi et al[31], and non-retention was defined as either death or LTF. Children who were LTF were censored 15 days after their last recorded visit. Children documented to have transferred to another facility were censored at their recorded date of transfer.

Individual-level factors were chosen based on available data across all country datasets and factors known or suspected through previous research to influence retention and survival. The CD4 percent or cell count and WHO stage taken closest to the date of ART initiation, within a window of 3 months prior to or up to one month after ART initiation, was used to determine disease severity at ART initiation. Clinical stage and immunologic category were defined according to 2006 WHO guidelines: severe immunodeficiency is defined as CD4 <

25% or < 1500 cells/uL in children ≤ 11 months, CD4 < 20% or < 750 cells/uL in children age 12 to 35 months, CD4 < 15% or < 350 cells/uL in children age 36 to 59 months and CD4 < 15% or < 200 cells/uL in children > 5 years[23]. To investigate the potential influence of malnourishment in our population, we constructed weight-for-age z- scores and categorized children as z-score ≤ or > −2 standard deviations[32]. No reliable data was available for TB status or treatment at the time of ART initiation. A new category of "severe illness" was created to include any child with severe immunodeficiency, defined above, or WHO Stage IV at time of ART initiation because of the high proportion of missing CD4 measurements and WHO stage.

Facilities were defined as primary or secondary/tertiary. A primary facility is any health center; secondary and tertiary facilities are district, regional, or national hospitals. Facility location was categorized into urban (capital and other large cities with city administration and political bodies), semi-urban (big and small towns, peri-urban areas, growth areas, and mining communities), and rural (small towns, and farming areas).

Statistical Analysis

Cumulative incidence of non-retention, LTF, and reported death through 24 months after ART initiation were estimated using Kaplan-Meier techniques. In the primary analysis, Cox Proportional Hazards models accounting for within-clinic correlation between patients with robust sandwich error terms were used to assess the association between measured patient and facility-level characteristics and LTF and documented death after ART initiation. Individual-level factors include age, point of entry, weight-for-age z-score at ART initiation, CD4 measure at ART initiation, WHO stage at ART initiation, and year of ART initiation; facility-level factors include country, facility type and setting.

Ethical Considerations

This study is part of the Identifying Optimal Models of HIV Care and Treatment, which was approved by the Columbia University Medical Center IRB, the US Centers for Disease Control and Prevention, PEPFAR's Office of the Global AIDS Coordinator (OGAC), and each participating country's national ethics committee.

RESULTS

Characteristics of HIV Care Programs

From January 2005 through June 2011, 37,154 children were enrolled in HIV services at 192 facilities in Kenya, Rwanda, Tanzania, and Mozambique (Table 1). A total of 17,712 children initiated ART with the largest cohort in Mozambique (7,226) and the smallest in Rwanda (2,170). The number of children initiated on ART increased annually from 585 in 2005 to 3,653 in 2010, the last full year of observation, with the number of facilities increasing from 75 to 192. Half of the facilities (54%) were in primary-level health centers as compared to secondary (district/regional hospitals) or tertiary-level facilities (teaching or national referral hospitals). Half of facilities (49%) were in rural locations (Table 1) and the majority of facilities were government-supported.

Patient Characteristics

Median follow-up time for children initiated on ART was 598 days (IQR: 245–1,106). The median age at ART initiation was 4.6 years (IQR: 1.9–8.3) with a similar distribution of females (51%) and males. Forty-eight percent of children had WHO Stage III/IV disease, and 32% of children had severe immunodeficiency (67% of children < 5 years and 38% of children ≥ 5 years). Thirty-three percent of children had a weight-for-age z-score of ≤ −2. Among the 8,263 children with recorded CD4 measurements (33% for children < 5 years and 62% of children ≥ 5 years) at ART initiation, the median CD4 was 15% (IQR: 10–20) for children < 5 years and 265 cells/uL (IQR:111–461) for children ≥ 5 years (Table 1). Overall, 34.5% of children were classified with severe illness at time of ART initiation (Table 1) and the proportion of children < 1 year classified with severe illness decreased from 56% in 2006 to 18% in 2011 (Supplemental Table 1). Over time, the proportion of children < 2 years of age initiated on ART increased from 12% of all children in 2005 to 33% in 2011 (Figure 1). The majority of all children reported entry into HIV care through voluntary counseling and testing or provider initiated counseling and testing (Table 1). First-line ART regimens for 95% of children included two nucleoside reverse transcriptase inhibitors plus one non-nucleoside reverse transcriptase inhibitor.

Country programs varied in the proportion of young (< 2 years) and severely ill children. Rwanda reported the smallest proportion of young children, 15.6% as compared to 38.7% in Mozambique. Rwanda also reported the smallest proportion of children with severe illness at 18.6% compared to 44.5% in Mozambique, 36.5% in Tanzania, and 26.9% in Kenya. Tanzania had the largest proportion of children with documented WHO Stage IV, 26.2%, as compared to Kenya (4.5%); however over 30% of children in Mozambique did not have WHO stage recorded.

Retention, LTF and Mortality at 12 and 24 months

Among those initiated on ART, 80% and 72% of children were retained at 12 and 24 months (Table 2, Figure 2a). At 12 and 24 months, 16% and 22% of children were LTF, while 5% and 7% had documented deaths (Table 2). LTF and mortality rates were highest in the first 6 months after ART initiation (26.3 and 9.1 per 100 person-years, respectively), declining through 12 months (18.4 and 6.3 per 100 person-years) and 24 months (14.2 and 4.5 per 100 person-years). Retention varied substantially across countries, ranging from 71–95% at 12 months and 62–93% at 24 months (Table 2, Figure 2b). Compared to children in Rwanda, children in Mozambique had 16 fold higher rate of LTF (adjusted HR 16.8, 95% CI 8.9–32.0) and children in Tanzania had over two times higher death rate (adjusted HR 2.6, 95% CI 1.8–3.6). All country programs experienced the largest drop in retention during the first six months after ART initiation. Across all age groups and time periods, the proportion of children who were LTF was higher than the proportion of known deaths, except for Rwanda. The overall proportion of documented transfers was similar across programs: 18% Kenya, 12% Mozambique, 19% Rwanda, and 15% Tanzania.

Retention was lowest among children < 1 year, 61% and 51% at 12 and 24 months, and highest in children age 5 to < 10 years, 87% and 80% respectively (Table 2, Figure 2c). There was no consistent improvement in retention, LTF or death in children < 1 year over

time by calendar year although LTF appeared to be marginally lower in later years (Supplemental Table 2).

Factors associated with LTF and death

Multivariable analysis was done to assess factors associated with LTF and death including country, age at ART initiation, severe illness at ART initiation, weight-for-age z-score at ART initiation, year of ART initiation, point of entry into HIV care, and facility type and location. The adjusted hazard ratio for LTF and death were highest in children < 1 year (HR_{LTF} =2.0, 95% CI 1.7–2.4; HR_{Death}= 3.4, 95% CI: 2.6–4.6) (Table 3). Compared to children with less advanced disease, children with severe illness had higher rate of death (HR_{Death} =1.6, 95% 1.4–1.9) but similar rate of LTF (HR_{LTF} = 0.99, 95% CI 0.86–1.13) (Table 3). Among older children, CD4 count was a strong predictor of LTF and death; children ≥ 5 years with CD4 < 100 cells/uL had nearly three times higher death rates compared with children initiating ART at CD4 > 350 cells/uL. Children with missing CD4 counts had 2.3 times the rate of death compared to children with a CD4 > 350 cells/uL; and children missing WHO stage or severe illness information were also more likely than other children to be LTF or to be documented deaths. There was no evidence of differences in LTF, or death by point of entry or facility type (Table 3). There was no consistent evidence for reduced LTF, or death by year of ART initiation. No facility-level factors were found to have a significant impact on the risk of LTF or death.

Results were also stratified by country (Supplemental Table 3) and similar factors are associated with increased risk of LTF and death across all countries. Sensitivity analyses using random effects multilevel Cox Proportional Hazards models, in addition to the fixed effects model presented, yielded no substantial differences in the magnitude of the hazard ratios presented in Table 3.

DISCUSSION

To our knowledge, this is the largest reported cohort of children on ART across multiple African countries, which reflects the scale-up of HIV care and treatment across Sub Saharan Africa. At 12 and 24 months, 80% and 72% of children were retained in care, 16% and 22% were LTF and 5% and 7% were known to have died. The true proportion of children who have died is likely much higher than reported values given some children who are categorized as LTF are undocumented deaths[18,33]. While this study's outcomes are similar to other cohorts[7,11,14,15,17–19,22,34,35], there was substantial variation within specific populations of children, particularly the youngest (< 1 year) and those with advanced disease, and across country programs.

One of the most striking findings of this study is the outcomes seen among the youngest children initiating ART (< 1 year of age). While young age, as well as advanced disease, has been associated with increased risk of LTF and death[4,7,13–15,17,36–39], the fact that only half of children who initiated ART during infancy were retained in care at 24 months and 18% have died is sobering (Table 2). While these estimates can be considered an improvement from the reports in the pre-ART era (50% mortality at 24 months), the mortality rates remain unacceptably high in the context of ART[40].

From 2005 through 2011 we observed an increase in the proportion of young children (both infants < 1 year and young children 1 to 2 years) initiating ART (Figure 1) and a concomitant decrease in the severity of illness among infants (Supplemental Table 1). These findings reflect improved access to early diagnostic testing in the four countries[41], as well as implementation of the WHO guidelines recommending treatment of all children < 1 year of age, later revised to < 2 years of age. However, despite a decrease in the proportion of infants categorized as severely ill at time of ART initiation from 2005 to 2011, as noted, there was no concurrent improvement in retention or mortality over time (Supplemental Table 2). We would anticipate improved outcomes with the enrollment of healthier children and the accrual of benefits from early treatment[5,6,10]. While it is encouraging to see greater numbers of young children initiating earlier treatment, further research is needed to identify other factors impacting health outcomes among this highly vulnerable group of children. These findings also underscore the ongoing need for special attention for infants to be promptly diagnosed, initiated on treatment and retained in care.

Another striking finding of this study is the fact that country programs contributing to this analysis achieved vastly different outcomes, with retention at 24 months ranging from 62–93%. Moreover, within countries we observed substantial heterogeneity in both retention and mortality. All facilities received technical support through ICAP and implemented the same general model of care, which emphasizes early infant diagnosis, family-focused care, involvement of peer-educators, and active follow-up. However, possible reasons explaining such differences in country outcomes likely include a combination of national influences, such as national leadership, access to health services and requirements for medical record documentation, as well as epidemiological and program factors such as HIV seroprevalence (ranging from 2.9% in Rwanda to 11.5% in Mozambique[42]), patient caseload, provider-patient ratios, and decentralization of services. Since the proportion of documented transfers is fairly similar across programs, variability in quality of documentation of transfers may explain some but not all of the variation seen in retention.

The high retention observed in Rwanda is consistent with other studies investigating retention in HIV programs in this country[43–46]. The ICAP-supported program in Rwanda, in comparison to the other country programs included in this study, had a smaller proportion of young (age < 2 years) and severely ill children at time of ART initiation. Also, the Rwanda program is smaller with a lower patient caseload, 2,170 children in Rwanda as compared to 7,226 children in ICAP-Mozambique (Table 1), that has been associated with lower LTF in resource limited settings[47,48]. Smaller programs may have higher staff to patient ratios, shorter wait times, and more staff and time for active patient follow-up, which has been shown to significantly decrease LTF[49–51]. Finally, better documentation may explain some of the differences seen among countries. In Rwanda, the proportion of children who are LTF is lower than the proportion of known deaths, for which the reverse is true in other country programs. The category of LTF serves as a combination category of children who have been truly lost to follow-up and others who have undocumented deaths or transfers. Rwanda's results are encouraging as they illustrate what is achievable in public programs and suggest that improvement is obtainable. Additional evaluation of program and facility-level factors, not available in this dataset, to explain variations seen across countries is clearly warranted.

There are a number of strengths to this analysis. The first is that it is the largest, single program, multi-country analysis reporting outcomes of children on ART over the period of PEPFAR scale-up beginning in 2005. The results are likely generalizable to other PEPFAR-supported pediatric HIV programs and reflect the diversity in outcomes from rapid scale-up of ART for children across SSA. The use of patient-level data allows analysis within age categories and links patient-level data to facility data. Finally, we were able to assess retention, LTF and death across a relatively long follow-up period of 24 months.

An important limitation of this analysis is the amount of missing data for patient characteristics at time of ART initiation, which may be due to poor documentation as well as lack of clinical staging and limited access to CD4 testing. The large amount of missing data prevented the use of imputation techniques. Instead, we chose to include “missing” as a separate category in our regression analyses to investigate whether children with missing information differed from children with complete information in outcomes of interest, and indeed children with missing data appear to be at increased risk for LTF or death. This is not surprising as clinicians report that some children entering HIV care programs attend only one clinic visit and do not return to complete full enrollment evaluation including CD4 assessment. Second, this study only includes ICAP-supported pediatric HIV facilities that have capacity for electronic patient-level database, which may represent higher-resourced facilities as compared to others. A total of 192 facilities were included representing 31% of ICAP-supported care and treatment facilities in Kenya (24%), Rwanda (88%), Mozambique (47%), and Tanzania (39%) and regional differences within countries were not analyzed. Finally, this analysis does not include HIV-exposed infants, HIV-infected children who have not enrolled in care, or those who have enrolled in care but have not initiated ART—all groups which have lower estimated retention rates[12,22,34,52–54].

It is established that the benefits of ART on children in resource-limited settings are comparable with those in developed countries[3–9]; yet, these benefits are not currently realized in many pediatric HIV programs, such as those presented in this analysis. This study builds upon the evidence that overall retention, LTF and death are suboptimal, and young children and those with advanced disease are at highest risk for LTF and death. Despite encouraging results suggesting enrollment of a larger proportion of younger children and a smaller proportion of those with severe illness, we do not yet see substantial improvement in reported retention, LTF or death of young children. The vast differences across country programs illustrate that improved retention is achievable. However, additional attention to prompt diagnosis, early ART initiation, active follow-up of children who miss appointments and improved documentation of known transfers and deaths are urgent priorities for pediatric HIV programs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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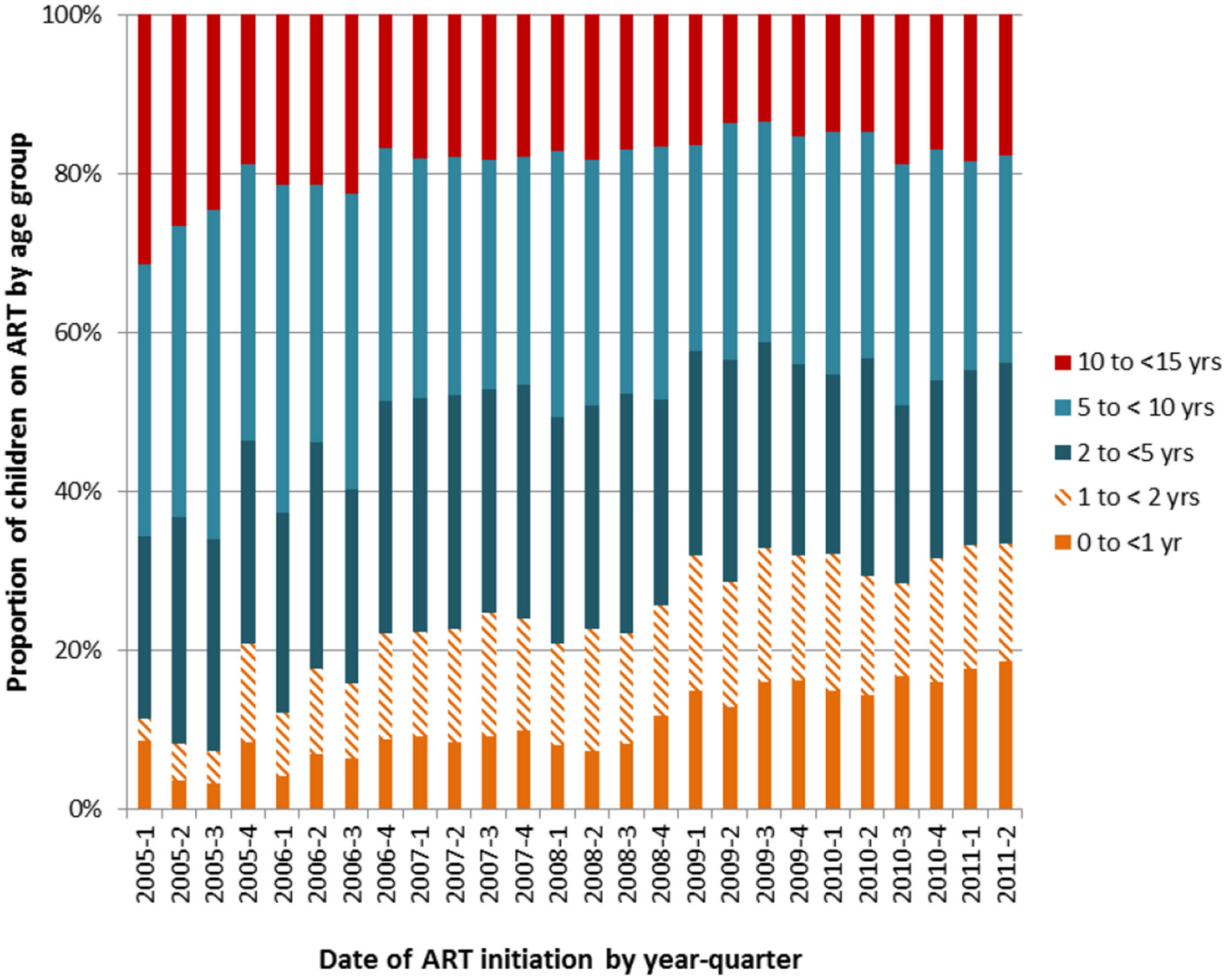

Figure 1.

Trends in age distribution among children age < 15 years (N=17,712) at ART initiation at 192 facilities in Kenya, Mozambique, Rwanda, and Tanzania, January 2005 through June 2011

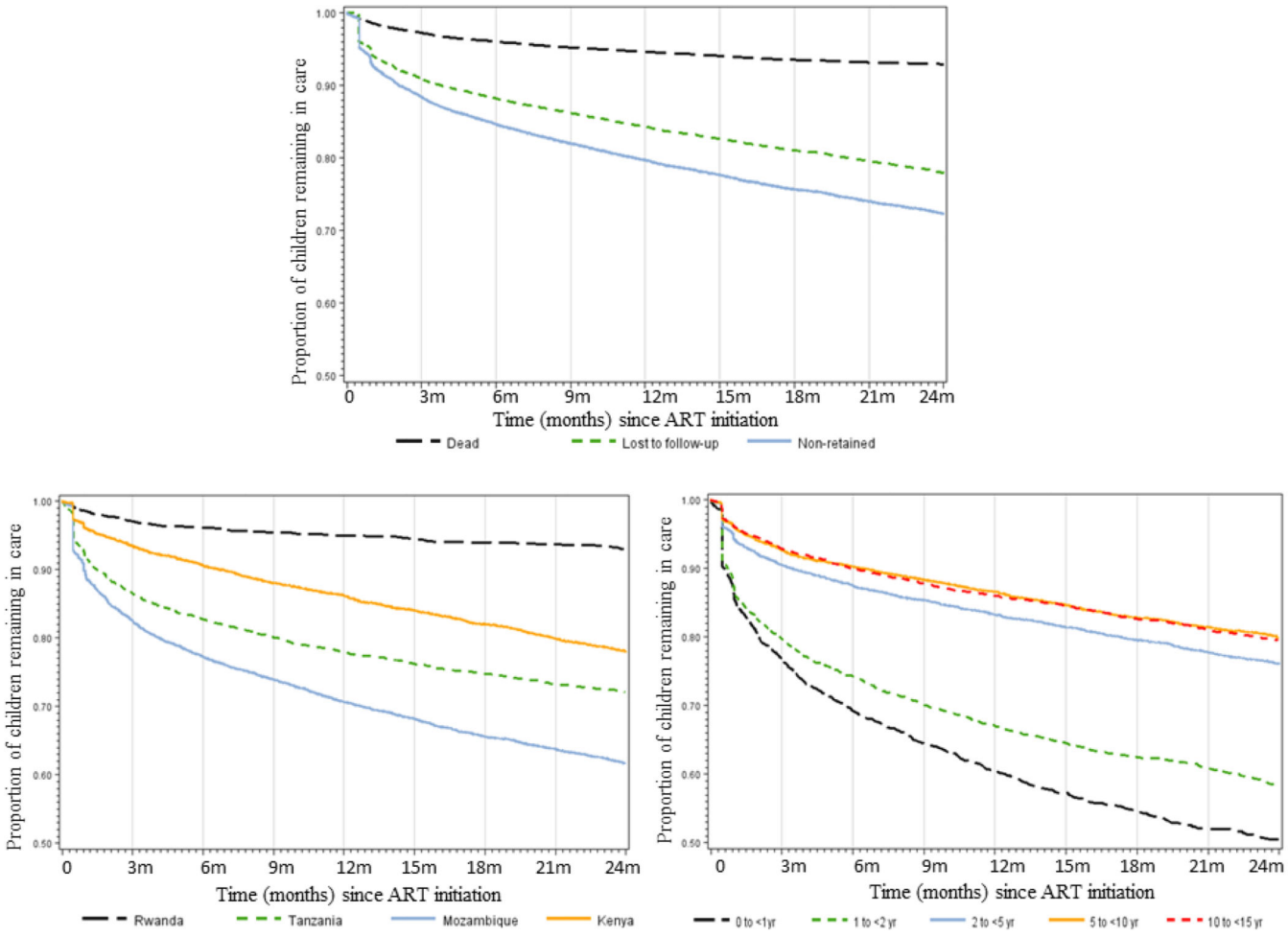

Figure 2.

Cumulative incidence curves of retention, lost to follow-up and death among children age < 15 years initiating ART in Kenya, Mozambique, Rwanda, and Tanzania (2a), retention by country (2b) and retention by age group (2c)

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Table 1

Characteristic of children age < 15 years initiating ART (N = 17,712) and HIV treatment facilities (N=193) in Kenya, Mozambique, Rwanda and Tanzania, January 2005 through June 2011

	Overall		**Kenya**		**Mozambique**		**Rwanda**		**Tanzania**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Total population	456,192	(100%)	105,313	(23.1%)	242,045	(53.1%)	44,450	(9.7%)	64,384	(14.1%)
Adult	419,038	(91.9%)	94,064	(89.3%)	225,036	(93.0%)	40,476	(91.1%)	59,462	(92.4%)
Children	37,154	(8.1%)	11,249	(10.7%)	17,009	(7.0%)	3,974	(8.9%)	4,922	(7.6%)
Children initiating ART	**17,712**	**(47.7%)**	**5,710**	**(50.8%)**	**7,226**	**(42.5%)**	**2,170**	**(54.6%)**	**2,606**	**(52.9%)**
Individual-level characteristics										
Female	9,026	(51.0%)	2,870	(50.3%)	3,809	(52.7%)	1,047	(48.2%)	1,330	(51.0%)
Age										
0 to < 1 yr	2,151	(12.1%)	441	(7.7%)	1,301	(18.0%)	147	(6.8%)	262	(10.1%)
1 to < 2 yrs	2,526	(14.3%)	532	(9.3%)	1,499	(20.7%)	191	(8.8%)	304	(11.7%)
2 – < 5 yrs	4,641	(26.2%)	1,509	(26.4%)	1,942	(26.9%)	577	(26.6%)	613	(23.5%)
5 to < 10 yrs	5,335	(30.1%)	2,041	(35.7%)	1,734	(24.0%)	707	(32.6%)	853	(32.7%)
10 to < 15 yrs	3,059	(17.3%)	1,187	(20.8%)	750	(10.4%)	548	(25.3%)	574	(22.0%)
Point of entry into HIV care										
PMTCT	862	(4.9%)	247	(4.3%)	177	(2.4%)	198	(9.1%)	240	(9.2%)
TB clinic	444	(2.5%)	381	(6.7%)	25	(0.3%)	12	(0.6%)	26	(1.0%)
VCT/PICT *	13,791	(77.9%)	4,512	(79.0%)	5,798	(80.2%)	1,960	90.3%)	1,521	(58.4%)
Missing	2,615	(14.8%)	570	(10.0%)	1,226	(17.0%)	-	-	819	(31.4%)
Weight-for-age z-score (CDC Standard)										
≤ −2	5,866	(33.1%)	2,070	(36.2%)	1,605	(22.2%)	795	(36.6%)	1,396	(53.6%)
>2	5,624	(31.8%)	2,208	(38.7%)	2,075	(28.7%)	432	(19.9%)	909	(34.9%)
Missing	6,222	(35.1%)	1,432	(25.1%)	3,546	(49.1%)	943	(43.5%)	301	(11.6%)
WHO stage prior to ART initiation										
I	1,970	(11.1%)	782	(13.7%)	723	(10.0%)	316	14.6%)	149	(5.7%)
II	3,829	(21.6%)	1,808	(31.7%)	1,191	(16.5%)	440	(20.3%)	390	(15.0%)

	Overall		Kenya		Mozambique		Rwanda		Tanzania	
	N	%	N	%	N	%	N	%	N	%
III	6,672	(37.7%)	2,219	(38.9%)	2,331	(32.3%)	1,036	(47.7%)	1,086	(41.7%)
IV	1,845	(10.4%)	257	(4.5%)	734	(10.2%)	172	(7.9%)	682	(26.2%)
Missing	3,396	(19.2%)	644	(11.3%)	2,247	(31.1%)	206	(9.5%)	299	(11.5%)
CD4 % at ART initiation among patients < 5 years of age (N = 9,318)										
median (IQR)	3,029	15% (10–20%)	576	16% (10–21%)	2,453	15% (10–19%)	.	.	.	.
Missing	6,289	(67%)	1,906	(77%)	2,289	(48%)		(100%)		(100%)
CD4 count (cells/mL) at ART initiation among patients 5–15 years of age (N = 8,394)										
median (IQR)	5,234	265 (111–461)	1,972	222 (77–397)	1,491	289 (127–499)	1061	337 (206–574)	710	196 (81–378)
< 100	1,229	(14.6%)	571	(17.7%)	327	(13.2%)	131	(10.4%)	200	(14.0%)
100–200	816	(9.7%)	337	(10.4%)	198	(8.0%)	120	(9.6%)	161	(11.3%)
200–350	1,305	(15.5%)	479	(14.8%)	357	(14.4%)	325	(25.9%)	144	(10.1%)
≥ 350	1,884	(22.4%)	585	(18.1%)	609	(24.5%)	485	(38.6%)	205	(14.4%)
Missing	3,160	(37.6%)	1,256	(38.9%)	993	(40.0%)	194	(15.5%)	717	(50.2%)
Severe illness at ART initiation**										
No	9,864	(55.7%)	3757	(65.8%)	2985	(41.3%)	1667	(76.8%)	1455	(55.8%)
Yes	6,103	(34.5%)	1534	(26.9%)	3216	(44.5%)	403	(18.6%)	950	(36.5%)
Missing	1,745	(9.9%)	419	(7.3%)	1025	(14.2%)	100	(4.6%)	201	(7.7%)
Year of ART initiation										
2005	585	(3.3%)	160	(2.8%)	177	(2.4%)	139	(6.4%)	109	(4.2%)
2006	1,846	(10.4%)	620	(10.9%)	666	(9.2%)	325	(15.0%)	235	(9.0%)
2007	2,970	(16.8%)	945	(16.5%)	1202	(16.6%)	468	(21.6%)	355	(13.6%)
2008	3,180	(18.0%)	1074	(18.8%)	1213	(16.8%)	411	(18.9%)	482	(18.5%)
2009	3,760	(21.2%)	1298	(22.7%)	1536	(21.3%)	331	(15.3%)	595	(22.8%)
2010	3,653	(20.6%)	1112	(19.5%)	1653	(22.9%)	365	(16.8%)	523	(20.1%)
2011 (Jan–June)	1,718	(9.7%)	501	(8.8%)	779	(10.8%)	131	(6.0%)	307	(11.8%)
Facility-level characteristics										
Number of facilities	192	(100%)	69	(35.9%)	31	(16.1%)	42	(21.9%)	50	(26.0%)

	Overall		Kenya		Mozambique		Rwanda		Tanzania	
	N	%	N	%	N	%	N	%	N	%
Facility-type										
Primary	103	(53.6%)	35	(50.7%)	18	(58.1%)	31	(73.8%)	19	(38.0%)
Secondary/tertiary	89	(46.4%)	34	(49.3%)	13	(41.9%)	11	(26.2%)	31	(62.0%)
Facility location										
Urban	35	(18.2%)	1	(1.4%)	23	(74.2%)	11	(26.2%)	0	(0.0%)
Semi-Urban	63	(32.8%)	21	(30.4%)	2	(6.5%)	2	(4.8%)	38	(76.0%)
Rural	94	(49.0%)	47	(68.1%)	6	(19.4%)	29	(69.0%)	12	(24.0%)

*Voluntary counseling and testing (VCT), Provider initiated counseling and testing (PICT)

**Severe illness includes any child with WHO stage IV or severe immunodeficiency, defined as CD4 < 25% or < 1500cells/uL for children < 12 months, CD4 < 20% or < 750 cells/uL in children 12–35 months, CD4 < 15% or <350 cells/uL in children 36–59 months, and CD4 < 15% or < 200 cells/uL in children > 5 years (WHO 2006 guidelines)

Table 2

Retention, loss to follow-up, and death at 12 and 24 months after ART initiation: overall, by country, and by age group

		Retention after ART initiation											
		overall		<1 year		1 to <2 years		2 to <5 years		5 to <10 years		10 to <15 years	
	N	12 months	24 months	12 months	24 months	12 months	24 months	12 months	24 months	12 months	24 months	12 months	24 months
Overall	17,712	80%	72%	61%	51%	67%	58%	83%	76%	87%	80%	86%	80%
Kenya	5,710	86%	78%	70%	58%	81%	69%	87%	80%	89%	82%	88%	80%
Mozambique	7,226	71%	62%	54%	43%	60%	51%	78%	69%	81%	73%	78%	68%
Rwanda	2,170	95%	93%	86%	82%	91%	88%	96%	94%	97%	95%	96%	94%
Tanzania	2,606	78%	72%	65%	58%	63%	56%	80%	73%	83%	78%	83%	78%
		Loss to follow-up after ART initiation											
		overall		<1 year		1 to <2 years		2 to <5 years		5 to <10 years		10 to <15 years	
	N	12 months	24 months	12 months	24 months	12 months	24 months	12 months	24 months	12 months	24 months	12 months	24 months
Overall	17,712	16%	22%	30%	39%	26%	34%	14%	20%	11%	17%	10%	15%
Kenya	5,710	11%	19%	26%	37%	17%	28%	11%	18%	9%	16%	9%	16%
Mozambique	7,226	24%	32%	36%	44%	33%	41%	19%	27%	16%	24%	19%	27%
Rwanda	2,170	1%	2%	4%	6%	2%	2%	1%	1%	1%	2%	1%	1%
Tanzania	2,606	14%	18%	24%	30%	23%	27%	13%	19%	11%	15%	10%	14%
		Measured death after ART initiation											
		overall		<1 year		1 to <2 years		2 to <5 years		5 to <10 years		10 to <15 years	
	N	12 months	24 months	12 months	24 months	12 months	24 months	12 months	24 months	12 months	24 months	12 months	24 months
Overall	17,712	5%	7%	13%	18%	9%	12%	4%	5%	3%	4%	4%	6%
Kenya	5,710	3%	3%	6%	7%	3%	4%	2%	2%	2%	3%	4%	4%

Mozambique	7,226	7%	9%	16%	23%	10%	13%	4%	6%	3%	4%	4%	7%
Rwanda	2,170	3%	5%	9%	11%	6%	9%	3%	4%	2%	3%	3%	4%
Tanzania	2,606	9%	11%	14%	17%	19%	23%	7%	10%	7%	9%	8%	10%

Table percentages obtained using product-limit estimates. LTF defined as not having a recorded clinic visit within the last 6 months of clinic follow-up. Children who were LTF were censored 15 days after their last recorded visit. Children documented to have transferred to another facility were censored at their recorded date of transfer.

Table 3

Factors associated with loss to follow-up and death among children age < 15 years (N=17,712) in Kenya, Mozambique, Rwanda, and Tanzania

	Loss to follow-up				Measured Death			
	Crude		Adjusted[1]		Crude		Adjusted[1]	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Country								
Kenya	12.57	(6.88–22.98)	9.53	(4.96–18.33)	0.81	(0.61–1.07)	0.84	(0.61–1.16)
Rwanda								
Tanzania	10.72	(5.86–19.63)	7.83	(3.77–16.26)	2.67	(2.1–3.39)	2.57	(1.82–3.62)
Mozambique	19.82	(10.33–38.01)	16.83	(8.86–31.96)	2.13	(1.52–2.97)	1.71	(1.30–2.26)
Age at ART initiation								
0 to < 1yr	2.59	(2.24–2.99)	2.02	(1.73–2.36)	4.08	(2.96–5.63)	3.41	(2.55–4.56)
1 to < 2 yrs	2.13	(1.83–2.48)	1.71	(1.47–1.98)	2.68	(2.14–3.35)	2.16	(1.74–2.68)
2 to < 5 yrs	1.23	(1.10–1.37)	1.13	(1.00–1.28)	1.11	(0.91–1.36)	1.11	(0.91–1.35)
5 to < 10 yrs								
10 to < 15 yrs	0.95	(0.84–1.08)	1.04	(0.93–1.16)	1.41	(1.12–1.75)	1.23	(0.97–1.54)
Point of entry								
PMTCT	0.88	(0.63–1.23)	0.82	(0.67–0.99)	1.56	(1.15–2.11)	1.03	(0.78–1.36)
TB clinic	0.92	(0.63–1.36)	1.07	(0.80–1.44)	0.86	(0.51–1.44)	1.62	(1.02–2.55)
Other HCT								
missing	1.11	(0.94–1.32)	0.90	(0.78–1.03)	1.44	(1.12–1.86)	1.10	(0.86–1.41)
Weight-for-age z-score (CDC Standard)								
≤ −2	1.18	(1.04–1.33)	1.34	(1.21–1.47)	2.62	(2.19–3.13)	2.36	(1.98–2.80)
>2	reference							
Missing	1.56	(1.15–2.13)	1.42	(1.19–1.70)	2.80	(2.21–3.55)	2.42	(1.89–3.09)
WHO stage prior to ART initiation								
I	1.12	(0.89–1.41)	1.03	(0.87–1.21)	0.61	(0.46–0.82)	0.65	(0.47–0.88)
II	0.92	(0.76–1.12)	0.90	(0.78–1.02)	0.60	(0.48–0.75)	0.75	(0.59–0.94)
III								

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	Loss to follow-up				Measured Death			
	Crude		Adjusted[1]		Crude		Adjusted[1]	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
IV	1.34	(1.12–1.6)	1.16	(0.98–1.36)	2.20	(1.78–2.7)	1.60	(1.34–1.92)
Missing	2.24	(1.34–3.75)	1.75	(1.21–2.53)	1.82	(1.24–2.66)	1.49	(1.07–2.06)
CD4 count (cells/uL) at ART initiation for children > 5 years of age[2]								
< 100	0.79	(0.58–1.06)	1.16	(0.95–1.41)	1.87	(1.41–2.48)	2.78	(1.92–4.03)
100–199	0.72	(0.55–0.94)	0.96	(0.78–1.18)	1.14	(0.84–1.55)	1.28	(0.81–2.05)
200–349	0.65	(0.53–0.80)	0.84	(0.70–1.02)	0.85	(0.62–1.17)	1.36	(0.94–1.98)
>350								
Missing	1.05	(0.75–1.48)	1.23	(0.90–1.68)	1.38	(1.00–1.92)	2.27	(1.62–3.19)
Severe illness at ART initiation[3]								
Severe	1.30	(1.07–1.57)	0.99	(0.86–1.13)	1.96	(1.61–2.40)	1.60	(1.36–1.89)
Not severe								
Missing	2.33	(1.64–3.32)	1.71	(1.37–2.14)	2.27	(1.57–3.28)	1.70	(1.27–2.27)
Year of ART initiation								
2005	0.73	(0.52–1.04)	0.86	(0.62–1.19)	1.21	(0.8–1.82)	1.30	(0.82–2.07)
2006	0.78	(0.65–0.94)	0.83	(0.69–0.99)	0.95	(0.68–1.33)	1.07	(0.80–1.43)
2007								
2008	1.17	(1.03–1.34)	1.24	(1.10–1.39)	0.95	(0.76–1.18)	0.99	(0.80–1.22)
2009	1.18	(0.86–1.62)	1.09	(0.80–1.49)	1.07	(0.84–1.36)	0.98	(0.77–1.25)
2010	1.28	(0.85–1.95)	1.19	(0.77–1.84)	0.98	(0.75–1.28)	0.94	(0.73–1.21)
2011	0.97	(0.61–1.52)	0.87	(0.54–1.42)	1.19	(0.87–1.64)	1.11	(0.80–1.54)
Facility type								
Primary	1.22	(0.64–2.33)	1.08	(0.60–1.96)	1.17	(0.78–1.74)	1.00	(0.74–1.36)
Secondary/Tertiary	reference							
Facility location								
Rural	0.43	(0.24–0.79)	0.84	(0.56–1.26)	0.75	(0.5–1.12)	1.29	(0.96–1.73)
Semi-Urban	0.85	(0.5–1.44)	1.61	(0.96–2.69)	0.81	(0.56–1.18)	1.09	(0.76–1.55)
Urban	reference							

[1]Unless otherwise notes, predictors in adjusted models include country, age at ART initiation, point of entry, severe sickness at ART initiation (see below), year of ART initiation, facility type, and facility location.

[2]Analyses for CD4 count at ART initiation are restricted to children 5 years and older, and adjusted analyses include country, age at ART initiation, point of entry, year of ART initiation, facility type, and facility location.

[3]Severe illness includes any child with WHO Stage IV illness or severe immunodeficiency, defined as CD4 < 25% or < 1500 cells/uL in children ≤ 11 months, CD4 < 20% or < 750 cells/uL in children age 12 to 35 months, CD4 < 15% or < 350 cells/uL in children age 36 to 59 months and CD4 < 15% or < 200 cells/uL in children > 5 years (WHO Guidelines 2006)

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