



Published in final edited form as:

Pediatr Infect Dis J. 2013 August ; 32(8): e341–e347. doi:10.1097/INF.0b013e31828c2744.

High Retention Among HIV-infected Children in Rwanda During Scale-up and Decentralization of HIV Care and Treatment Programs, 2004 to 2010

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Abstract

Background—Efforts to scale-up HIV treatment in high burden countries have resulted in wider access to care, improved survival and decreased morbidity for HIV-infected children. The country of Rwanda has made significant achievements in expanding coverage of pediatric HIV services.

Methods—We describe the extent of and factors associated with mortality and lost to follow-up (LTF) in children (<15 years) enrolled in HIV care at 39 ICAP-supported facilities across Rwanda from 2004 to 2010 by antiretroviral treatment (ART) status. We estimated the 1-year cumulative incidence of death and LTF among all children enrolled in care (pre-ART) and children on ART. Survival analysis was used to evaluate factors associated with death and LTF in both groups.

Results—Between January 2004 and June 2010, 3244 children with a median age of 5.7 years (interquartile range 2.8–9.6) enrolled in HIV care. One-year cumulative incidence for death and LTF among pre-ART children was 4% (95% confidence interval [CI]: 3–5%) and 5% (95% CI: 4–6%), respectively. Overall, 2035 (63%) children initiated ART, median age 6.3 years (interquartile range 3.3–10.4): 1-year Kaplan–Meier estimates of death and LTF were 3% (95% CI: 3–4%) and 1% (95% CI: 1–2%), respectively. Factors associated with an increased hazard for death among pre-ART children included being <18 months old versus ≥5 years (adjusted sub hazard ratio [aSHR] = 4.4, 95% CI: 2.9–6.8) and World Health Organization stage IV versus I (aSHR = 4.1, 95% CI: 2.0–8.4), whereas children entering care through prevention of mother-to-child transmission had lower hazard than those from voluntary counseling and testing (aSHR = 0.50, 95% CI: 0.25–1.0). Markers of advanced disease, including severe immunosuppression (aSHR = 0.25, 95% CI: 0.12–0.54), and enrollment in care in rural versus urban clinics (aSHR = 0.71, 95%

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The authors have no other funding or conflicts of interest to disclose.

CI: 0.53–0.97) were protective against LTF. For children on ART, factors associated with hazard of death included younger age (adjusted hazard ratio [aHR] <18 months versus 5 years = 2.1, 95% CI: 1.3–3.6), severe malnutrition versus not malnourished (aHR = 3.2, 95% CI: 1.3–8.1), advanced World Health Organization stage (aHR IV versus I = 9.8, 95% CI: 3.5–27.4) and severe immunodeficiency versus no evidence (aHR = 2.3, 95% CI: 1.7–3.3). No associations were observed with LTF among children on ART.

Conclusions—The results demonstrate very high retention among children enrolled in HIV care in Rwanda. Younger children continue to be particularly vulnerable, underscoring the urgent need for early identification, rapid treatment initiation and long-term retention in care.

Keywords

Rwanda; HIV; retention; pediatric; antiretrovirals

The country of Rwanda has made outstanding achievements toward the goal of universal access to antiretroviral therapy (ART) for both adults and children with HIV. Of the estimated 22,000 children in Rwanda living with HIV in 2011, 11,000 were estimated to qualify for ART, and more than 7500 (68%) had been initiated on treatment.¹ In efforts to increase uptake of ART and to improve retention in care, the Rwandan Ministry of Health decentralized pediatric HIV services in 2006 to lower level health facilities² and has worked with implementing partners to expand HIV services from 31 facilities in 2004 to 336 in 2011.¹ However, little has been described on the outcomes of children living with HIV in Rwanda.

Despite the known efficacy of ART, deaths in children after the start of ART remain high in sub-Saharan Africa, attributed to treatment initiation at advanced immunologic and clinical disease stages.^{3–9} Loss to follow-up (LTF) is also a significant barrier to achieving optimal outcomes, although data on retention in children are limited, particularly for children not on ART (pre-ART). Reported rates of LTF for pediatric cohorts range widely; in a pooled analysis of children on ART at 10 clinical sites in Southern Africa, LTF rates ranged from 1.9% to 14.2%.¹⁰ Age and whether the child is on ART or awaiting treatment have been associated with LTF in other African settings.^{7,11}

Given the high ART coverage achieved among HIV-infected children in Rwanda, the outcomes of children enrolled in HIV care might be different compared with other sub-Saharan African countries. In this article, we describe the extent of and factors associated with mortality and LTF in children less than 15 years of age enrolled in HIV care at 39 healthcare facilities in Rwanda from 2004 to 2010.

METHODS

Study Design and Study Population

Analysis was performed on de-identified routinely collected data on ART-naïve HIV-infected children (<15 years old) enrolled at 39 healthcare facilities in Rwanda from January 2004 to June 2010. These facilities, located in Kigali and the western provinces, represented 12% of all clinics providing ART in the country and approximately one-third of the children

enrolled in HIV care by June 2011.¹² All facilities included in this analysis received support from ICAP, a President's Emergency Plan for AIDS Relief implementing partner that has been supporting HIV prevention, care and treatment in sub-Saharan Africa since 2005. Routinely collected information from patient charts was recorded at each clinic visit by clinicians on national forms. Data were entered into an electronic database at the health facility by trained data clerks, with information de-identified for analysis. Data quality assessments were conducted every 6 months to assess completeness and accuracy of the database.

Pediatric Guidelines for HIV Care and Treatment

National guidelines in place during this period recommended a comprehensive history, physical examination and CD4+ cell count (CD4+) at the first visit followed by monthly evaluations and twice yearly CD4+ monitoring.^{13–15} The coverage in CD4+ machines has been gradual over the observation period, and by 2011 all referral and district hospitals had a CD4 machine. Health centers coordinated with their district hospitals to transport the samples on specific days for CD4+ measurement. CD4+ percentages were generally not available as laboratories were not equipped to provide those values until recently. All HIV services were provided free of charge. National guidelines for ART eligibility were revised in 2007 and 2010.^{14,15} According to the 2010 guidelines, ART eligibility criteria included the following: (1) all children <18 months, (2) World Health Organization (WHO) stages III/IV, (3) WHO stage I/II and CD4+ <1500 cells/μL for children 19–36 months of age and (4) CD4+ count <1000 cells/μL for children 36–59 months of age or CD4+ count <350 cells/μL for children ≥60 months of age.¹⁵ ART was prescribed by a physician according to national protocols, and follow-up was conducted by trained nurses. An appointment list was used to schedule monthly appointments. At the end of each day, the appointment list was checked to identify appointment defaulters who were traced by phone or home visits by the facility team or by peer educators. If recovered, defaulters were assessed for the reasons of missing their appointments, appropriately counseled and readmitted in the program.

Definitions

LTF was defined as not having had a clinic, laboratory or pharmacy visit in the 12 months before the date of closure of the database for pre-ART children (ie, July 2010 to June 2011) and in the 6 months before the date of closure of the database for children on ART (ie, Jan 2011 to June 2011). Follow-up time on pre-ART was defined as the time between date of enrollment into care and ART initiation, transfer, known death, LTF or completion of the observation period. Follow-up time on ART was defined as the time between date of ART initiation and transfer, known death, LTF or completion of the observation period. For characteristics at enrollment into care (ie, weight, WHO stage, CD4+), any value within 3 months of enrollment was used. For characteristics at ART initiation, we considered the closest value using a window period of 3 months before and 1 month after the date of ART initiation. Immunodeficiency was defined based on age-adjusted CD4+ according to the Centers for Disease Control and Prevention 1994 classification system: no evidence of immune suppression (<12 months: ≥1500 cells/μL; 1–5 years: ≥1000 cells/μL; ≥5 years: ≥500 cells/μL); evidence of moderate suppression (<12 months: 750–1499 cells/μL; 1–5 years: 500–999 cells/μL; ≥5 years: 200–499 cells/μL); and severe suppression (<12 months:

<750 cells/ μ L; 1–5 years: <500 cells/ μ L; 5 years: <200 cells/ μ L).¹⁶ Weight-for-age Z scores were calculated based on the Centers for Disease Control and Prevention standards; children were classified as not malnourished (Z score > -2), moderately malnourished (-2 Z score -3) and severely malnourished (Z score < -3).¹⁷ A substantial proportion of children had missing information on CD4+, WHO stage and weight; they were included in our analyses and assigned to “missing” categories.

Statistical Analysis

We describe characteristics at enrollment into care of all children enrolled between January 2004 and June 2010 and at ART initiation among the subset that subsequently started ART between January 2004 and December 2010. For each group, we stratified characteristics by the age groups specified in the national Rwanda guidelines (<18 months, 18–59 months and 5 years). We then examined factors associated with LTF and known deaths among pre-ART children and ART children. In the pre-ART model, children who initiated ART were censored at the date of ART initiation. In both models, children who were LTF were censored 15 days after their last recorded visit and children having transferred to another clinic were censored at their recorded date of transfer. For pre-ART children, we constructed subdistribution hazards models using the methods outlined by Fine and Grey to account for the competing risk of initiating ART.¹⁸ ART initiation was treated as a competing risk in the pre-ART analysis as it alters the probability of being dead or LTF.¹⁹ For children who started ART, the Cox proportional hazards models accounting for within-clinic correlation were used to examine factors associated with LTF and known deaths among children on ART. Variables significant at the 0.20 level in the bivariate models were included in the multivariate survival analyses and retained if significant at the 0.05 level based on the likelihood ratio test using a backward stepwise procedure. We report 1-year and 2-year death and LTF cumulative incidence estimates for pre-ART and Kaplan–Meier (KM) estimates for ART. The log-rank test was used to compare differences on the estimates for death and LTF by age and type of facility among pre-ART children and ART children. Data were analyzed using SAS 9.2 (SAS Institute, Cary, NC) and STATA 11 (StataCorp, College Station, TX) for the competing risk model.

Ethical Considerations

This study is part of the Identifying Optimal Models of HIV Care and Treatment Collaboration, which was approved by the Rwandan National Ethics Committee, the Columbia University Medical Center Institutional Review Board, the US Centers for Disease Control and Prevention and President’s Emergency Fund for AIDS Relief Office of the Global AIDS Coordinator.

RESULTS

Children Enrolled in HIV Care

Between January 2004 and June 2010, 3244 ART-naïve children enrolled in HIV care at 39 facilities, including 26 health centers, 9 district hospitals, 3 referral hospitals and 1 private hospital. Nearly two-thirds (60%) of the facilities were in rural settings and 44% of the children received care in rural settings (Table 1). Annual enrollment of children increased

from 107 in 2004 to 783 in 2007 and then declined each year thereafter. At enrollment, 50% of subjects were female, the median age was 5.7 (interquartile range [IQR] 2.8–9.6), 363 (11%) were <18 months old, 1057 (33%) were 18–59 months old and 1824 (56%) were ≥5 years old. Four percent of the children were transferred in from another facility, and 72% of them were ≥5 years old. Only 7% of children enrolled in care through prevention of mother-to-child transmission (PMTCT), of which 54% were <18 months old. Of children with a WHO stage at enrollment (91%), 47% had a WHO stage III/IV. Among the 2820 (87%) children with a CD4+ recorded at enrollment, 870 (31%) had evidence of immunodeficiency and 442 (16%) had severe immunodeficiency. The median follow-up time during the pre-ART period was 5.2 months (IQR 1.0–20.3). Of those pre-ART, 143 (4%) died, 334 (10%) transferred to another facility, 2035 (63%) initiated ART, 191 (6%) were LTF and 541 (17%) remained in pre-ART care at the end of the observation period (Fig. 1). One-year cumulative incidence for death and LTF among all children enrolled in care was 4% (95% confidence interval [CI]: 3–5%) and 5% (95% CI: 4–6%), respectively. Two-year cumulative incidence for death and LTF among all children enrolled in care were 5% (95% CI: 4–5%) and 6% (95% CI: 5–7%), respectively. Among the 1209 who did not initiate ART during this period, 293 (24%) were severely immunosuppressed or had a WHO stage III/IV at their last visit, of which 81 (28%) died and 48 (16%) were LTF (results not shown).

Children on ART

Overall, 2035 (63%) children initiated ART; 48% were female, the median age was 6.3 years [IQR 3.3–10.4] and 8% were <18 months old (Table 2). The number of children starting ART was highest in 2007 with 477 children newly initiating ART. Fifty-seven percent of the children had a recorded weight at ART initiation, of which 503 (43%) were severely malnourished based on weight-for-age Z scores. Of those with a WHO stage at ART initiation (98%), 65% were WHO stage III or IV. Among those with a CD4+ at ART initiation (84%), 24% were severely immunosuppressed. ART regimens at initiation were AZT/D4T/ABC+3TC+NVP (84%), AZT/D4T/ABC+3TC+EFV (14%) and others (2%). With a median time on ART of 2.6 years [IQR 1.4–3.8], 1449 (71%) children were still on ART at the facility at the end of the observation period, 437 (21%) transferred to another facility, 108 (5%) were known deaths and 41 (2%) were LTF (Fig. 1). KM estimates 1 year after ART initiation were 3% (95% CI: 3–4%) for death and 1% (95% CI: 1–2%) for LTF. Significantly higher 1 year KM estimates for death were observed among children <18 months old 1 and 2 years after ART initiation (1-year KM estimates: <18 months: 8%, 18–59 months: 4%, ≥5 years: 3%; 2-year KM estimates: <18 months: 10%, 18–59 months: 5%, ≥5 years: 4%; log-rank *P* value = 0.004). No statistically significant differences were observed for LTF after ART initiation by age group. KM estimates 2 years after ART initiation were 5% (95% CI: 4–6%) for death and 2% (95% CI: 1–3%) for LTF.

Factors Associated With Death and LTF Among pre-ART Children

Multivariate competing risks models for known death among pre-ART children are presented in Table 3. Factors associated with an increased hazard for death among this group included being <18 months old versus ≥5 years (adjusted subhazard ratio [aSHR] = 4.4, 95% CI: 2.9–6.8), being severely malnourished versus not malnourished (aSHR = 1.9, 95% CI: 1.1–3.2), WHO stage IV and missing versus WHO stage I (aSHR = 4.1, 95% CI: 2.0–8.4;

aSHR = 3.7, 95% CI: 1.9–7.4, respectively) and no recorded CD4+ (aSHR = 3.0, 95% CI: 1.9–4.6). Children who entered care through PMTCT programs had a lower risk of death versus those from voluntary counseling and testing (aSHR = 0.50, 95% CI: 0.25–1.0]. Pre-ART children had a higher hazard of being LTF if they were <18 months old versus 5 years (aSHR = 1.6, 95% CI: 1.0–2.4) and had a missing WHO stage versus WHO stage I (aSHR = 2.4, 95% CI: 1.6–3.6) (results not shown). A lower hazard for being LTF was observed among pre-ART children with more advanced disease (WHO stage III versus WHO stage I aSHR = 0.48, 95% CI: 0.31–0.75), severe immunosuppression versus none (aSHR = 0.25, 95% CI: 0.12–0.54, respectively) and those attending facilities located in rural versus urban settings (aSHR = 0.71, 95% CI: 0.53–0.97) (results not shown).

Factors Associated With Death and LTF Among Children on ART

Multivariate Cox proportional models for known death among children on ART are presented in Table 3. Factors associated with an increased hazard for death among children on ART included children <18 months versus 5 years (adjusted hazard ratio [aHR] = 2.1, 95% CI: 1.3–3.6), severe malnutrition versus not malnourished (aHR = 3.2, 95% CI: 1.3–8.1), advanced WHO stage and missing versus WHO stage I (aHR_{stageII} = 3.6, 95% CI: 1.3–9.6; aHR_{stageIII} = 2.6, 95% CI: 0.96–6.8; aHR_{stageIV} = 9.8, 95% CI: 3.5–27.4; aHR_{stage missing} = 6.0, 95% CI: 1.8–19.6) and severe immunosuppression versus no evidence of immunosuppression (aHR = 2.3, 95% CI: 1.7–3.3). No associations were observed with LTF among children on ART.

DISCUSSION

Our results demonstrate very high retention among a cohort of 3244 HIV-infected children enrolled in care at 39 health facilities in Rwanda. Among pre-ART children, we found that the 1-year cumulative incidence for death and LTF were 4% and 5%, respectively, considerably lower than the rates of 7–10% mortality and 10–20% LTF reported among children in HIV care in Cote d'Ivoire⁷ and the Democratic Republic of Congo.¹¹ Overall, 2035 (63%) children in care were initiated on ART, of whom 3% died and only 1% were LTF 1 year after ART initiation. Although the proportion of documented deaths among children on ART is similar to other programs in sub-Saharan Africa,^{3–5,10,11,20,21} the proportion LTF is substantially lower than what has been previously described in the region (range 7% to 23%).^{4,10,11,20,21}

There are several reasons that could explain the high rates of retention observed in this study compared with other sub-Saharan African countries. First, it is noteworthy that high rates of retention have also been observed among adults on ART in Rwanda.²² The prevalence of HIV in Rwanda (3%) is considerably lower than many other sub-Saharan Africa countries, ART coverage among children is estimated to be 68%¹ and the success of the PMTCT program has substantially reduced the number of new HIV infections in infants in recent years.²³ Other factors that might have contributed to the high rates of retention among children in Rwanda are a good mentoring system for clinic staff, which was intensified during decentralization, a strong defaulter tracking system linking the facilities and the communities through peer educators, a regular drug and commodities supply system with

very limited stock outs and an efficient monitoring and evaluation system. In fact, the good documentation of children in this cohort transferring to another facility may also contribute to the low rates of LTF in pre-ART and ART children. However, it is important to note that the data available could not confirm whether these children were successfully engaged in care at another facility and whether there were treatment interruptions during this process. As a result, it is possible that the rates of LTF could indeed be higher than reported here.

Given that mortality and LTF are poorly understood during the pretreatment phase of HIV care among children, we examined the factors associated with these outcomes among pre-ART children. Among this group, those entering care through PMTCT had half the risk of death of those identified through voluntary testing and counseling services. This finding supports the importance of linking PMTCT programs to pediatric HIV services to optimize pediatric outcomes. The hazard of LTF was lower among those with advanced HIV disease, as the sickest patients initiated ART. Additionally, we observed a lower hazard of LTF among those in rural settings, probably due to better links between the community and the health facility. LTF is a heterogeneous mix of withdrawals from care as well as undocumented transfers and deaths.²⁴ Our findings suggest that in this cohort, those LTF are most likely to be either undocumented transfers or withdrawals, as their healthier disease status at enrollment suggests they are less likely to be undocumented deaths. The finding that healthier children are more likely to be lost is consistent with results from some adult cohorts, which have shown greater loss among subjects with less advanced disease at enrollment.^{25,26} We speculate that parents as well as health providers likely prioritize keeping children in care when they are receiving ART compared with children who are only being monitored prior to initiation. Earlier treatment of children, even among those with less advanced disease, could be a strategy to improve retention.

Similar to other studies in the region, younger age was strongly associated with death among pre-ART children and children on ART, highlighting the particular vulnerability of HIV children <18 months and the need to rapidly initiate ART.^{4,6,10,27,28} Initiating children on ART at a younger age could have potential benefits both for survival and program retention. The 2010 WHO ART guidelines for infants and children recommend that all patients <24 months should be started on ART immediately regardless of CD4 count or clinical staging. Earlier treatment initiation is also now being recommended in older children.²⁹ As expected, severe malnutrition and advanced HIV disease were also associated with higher risk of death in this cohort, in keeping with other studies.^{4,7,10}

We observed a steady increase in the number of children enrolling into care and initiating ART from 2004 to 2007, with a decrease in new enrollments and ART initiations after 2008. Although we cannot fully explore these trends with the available data, we hypothesize that these findings reflect decreasing numbers of new pediatric infections as a result of wider access and the success of PMTCT services. Recent data from the Rwanda Ministry of Health estimates that 98% of all pregnant HIV-positive mothers attending PMTCT services in Rwanda receive antiretroviral treatment.²³ Interestingly, a high proportion of children in our study entered care through non-PMTCT services. Rwanda has recommended systematic HIV testing for all children of unknown HIV status in pediatric wards, malnutrition and tuberculosis units as well as at other entry points in order to identify HIV-positive children

for enrollment into care.²³ Furthermore, an additional explanation could be that the facilities included in the analysis were not enrolling as many HIV-infected children in more recent years as a result of decentralization and altered referral patterns. It is therefore possible that fewer children are newly enrolling in care at the facilities included in this analysis in the period after 2008 as a result of more facilities offering pediatric HIV services in Rwanda.

There are several important strengths of this analysis. First, this analysis includes more than 3000 children from 39 health facilities in different settings and levels of care from 2004 to 2010. Secondly, this analysis fills an important gap in the knowledge regarding outcomes of HIV-infected children before ART initiation who are enrolled in large scale HIV care and treatment programs. Finally, although this analysis used routinely collected data, there was good documentation of deaths, which, as noted above, may have contributed to a more accurate accounting for LTF and may also explain the somewhat high rates of death in children who were not on ART, particularly among younger children.

There are also limitations to this analysis, including missing data for individual subjects and lack of CD4+ percentage for all children <5 years old. These data were collected as part of routine clinical care at public facilities, so there is a high proportion of missing data compared with research studies. Another limitation is the lack of confirmation that children who were transferred to care to other facility did in fact enroll in care, so a subset of those transfers could indeed be LTF. Finally, while these sites represent 12% of facilities providing ART Rwanda and almost one-third of children in care by June 2011, results might not be generalizable to all sites in Rwanda, although we include facilities from different settings and type of care.

Overall, this study highlights the success of the Rwanda national program to rapidly scale-up and decentralize access to pediatric HIV care and treatment while maintaining very high retention rates after ART initiation. Our results also emphasize the need to optimize transfers of care, improve documentation of transfers across sites and ensure uninterrupted treatment during this process. Younger children continue to be particularly vulnerable, underscoring the urgent need for early identification and engagement in long-term HIV care and treatment.

Acknowledgments

This publication has been supported by the United States President's Emergency Plan for AIDS Relief (PEPFAR) through the Centers for Disease Control and Prevention under the terms of Cooperative Agreement Number 5U62PS223540 and 5U2GPS001537. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of PEPFAR or the Centers for Disease Control and Prevention.

We want to thank all children and staff at the HIV care and treatment facilities included in this analysis. We also want to acknowledge the efforts of the ICAP staff in-country and clinic staff tasked with collecting the data used for this analysis.

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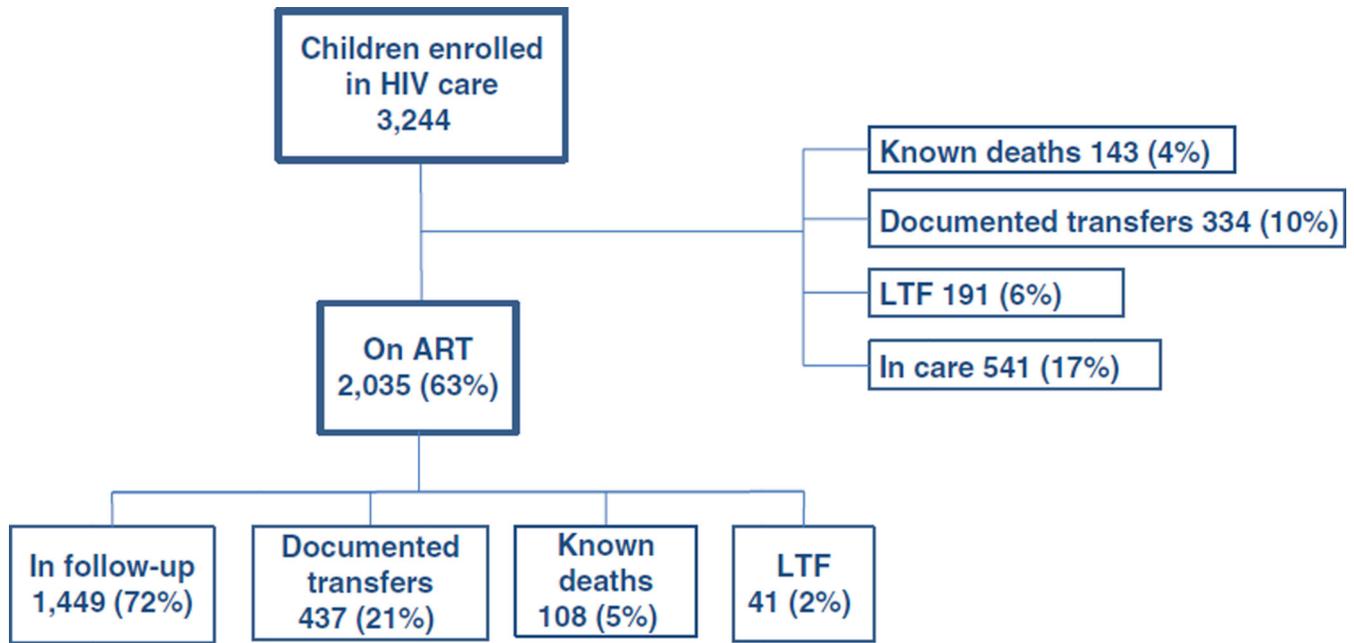


FIGURE 1. Outcomes among 3244 HIV-infected children <15 years of age enrolled in HIV care and treatment in Rwanda, January 2004 to June 2010.

Characteristics of 3244 HIV-infected Children <15 Years Old at Enrollment Into Care by Age at 39 Health Facilities in Rwanda (January 2004 to June 2010)

TABLE 1

| | Total | | <18 mo | | 18–59 mo | | 5 yr | |
|-----------------------------------------|-------|-------|--------|-------|----------|-------|------|-------|
| | n | % | n | % | n | % | n | % |
| Total (row %) | 3244 | | 363 | 11.2% | 1057 | 32.6% | 1824 | 56.2% |
| Sex (column %) | | | | | | | | |
| Female | 1613 | 49.7% | 196 | 54.0% | 519 | 49.1% | 898 | 49.2% |
| Male | 1631 | 50.3% | 167 | 46.0% | 538 | 50.9% | 926 | 50.8% |
| Year of enrollment | | | | | | | | |
| 2004 | 107 | 3.3% | 5 | 1.4% | 18 | 1.7% | 84 | 4.6% |
| 2005 | 493 | 15.2% | 36 | 9.9% | 166 | 15.7% | 291 | 16.0% |
| 2006 | 697 | 21.5% | 46 | 12.7% | 235 | 22.2% | 416 | 22.8% |
| 2007 | 783 | 24.1% | 83 | 22.9% | 246 | 23.3% | 454 | 24.9% |
| 2008 | 570 | 17.6% | 69 | 19.0% | 209 | 19.8% | 292 | 16.0% |
| 2009 | 437 | 13.5% | 89 | 24.5% | 144 | 13.6% | 204 | 11.2% |
| Jan–Jun 2010 | 157 | 4.8% | 35 | 9.6% | 39 | 3.7% | 83 | 4.6% |
| Care entry points | | | | | | | | |
| VCT | 2048 | 63.1% | 109 | 30.0% | 688 | 65.1% | 1251 | 68.6% |
| PMTCT | 237 | 7.3% | 129 | 35.5% | 78 | 7.4% | 30 | 1.6% |
| TB clinic | 9 | 0.3% | 1 | 0.3% | 0 | 0.0% | 8 | 0.4% |
| PICT | 950 | 29.3% | 124 | 34.2% | 291 | 27.5% | 535 | 29.3% |
| Transferred from another facility | | | | | | | | |
| No | 3126 | 96.4% | 359 | 98.9% | 1028 | 97.3% | 1739 | 95.3% |
| Yes | 118 | 3.6% | 4 | 1.1% | 29 | 2.7% | 85 | 4.7% |
| Malnutrition* | | | | | | | | |
| Not malnourished (Z score > -2) | 947 | 29.2% | 95 | 26.2% | 310 | 29.3% | 542 | 29.7% |
| Moderately malnourished (-2 Z score -3) | 513 | 15.8% | 39 | 10.7% | 134 | 12.7% | 340 | 18.6% |
| Severely malnourished (Z score < -3) | 918 | 28.3% | 121 | 33.3% | 329 | 31.1% | 468 | 25.7% |
| Missing | 866 | 26.7% | 108 | 29.8% | 284 | 26.9% | 474 | 26.0% |
| WHO stage at ART initiation | | | | | | | | |

| | Total | | <18 mo | | 18–59 mo | | 5 yr | |
|-------------------------------|-------|-------|--------|-------|----------|-------|------|-------|
| | n | % | n | % | n | % | n | % |
| Stage 1 | 743 | 22.9% | 81 | 22.3% | 218 | 20.6% | 444 | 24.3% |
| Stage 2 | 807 | 24.9% | 41 | 11.3% | 252 | 23.8% | 514 | 28.2% |
| Stage 3 | 1193 | 36.8% | 152 | 41.9% | 415 | 39.3% | 626 | 34.3% |
| Stage 4 | 203 | 6.3% | 47 | 12.9% | 78 | 7.4% | 78 | 4.3% |
| Missing | 298 | 9.2% | 42 | 11.6% | 94 | 8.9% | 162 | 8.9% |
| Immunodeficiency [†] | | | | | | | | |
| No evidence | 1508 | 46.5% | 132 | 36.4% | 457 | 43.2% | 919 | 50.4% |
| Evidence of immunodeficiency | 870 | 26.8% | 90 | 24.8% | 307 | 29.0% | 473 | 25.9% |
| Severe immunodeficiency | 442 | 13.6% | 39 | 10.7% | 148 | 14.0% | 255 | 14.0% |
| Missing | 424 | 13.1% | 102 | 28.1% | 145 | 13.7% | 177 | 9.7% |
| Type of setting | | | | | | | | |
| Urban | 1808 | 55.7% | 235 | 64.7% | 531 | 50.2% | 1042 | 57.1% |
| Rural | 1436 | 44.3% | 128 | 35.3% | 526 | 49.8% | 782 | 42.9% |
| Type of facility | | | | | | | | |
| Health center (N = 26) | 1230 | 37.9% | 126 | 34.7% | 376 | 35.6% | 728 | 39.9% |
| District hospitals (N = 9) | 1508 | 46.5% | 166 | 45.7% | 537 | 50.8% | 805 | 44.1% |
| Referral hospitals (N = 3) | 491 | 15.1% | 71 | 19.6% | 142 | 13.4% | 278 | 15.2% |
| Private (N = 1) | 15 | 0.5% | 0 | 0.0% | 2 | 0.2% | 13 | 0.7% |

* Weight-for-age Z scores were calculated based on the Centers for Disease Control and Prevention standards [19].

[†]Based on the Centers for Disease Control and Prevention age-adjusted CD4 count classification [18].

VCT indicates voluntary counseling and testing; TB, tuberculosis; PICT, provider-initiated counseling and testing.

Characteristics of 2035 HIV-infected Children <15 Years Old at Antiretroviral Initiation by Age at 39 Health Facilities in Rwanda (January 2004 to December 2010)

TABLE 2

| | Total | | <18 mo | | 18–59 mo | | 5 yr | |
|-----------------------------------------|-------|-------|--------|-------|----------|-------|------|-------|
| | n | % | n | % | n | % | n | % |
| Total (row %) | 2035 | | 167 | 8.2% | 633 | 31.1% | 1235 | 60.7% |
| Sex | | | | | | | | |
| Female | 979 | 48.1% | 92 | 55.1% | 306 | 48.3% | 581 | 47.0% |
| Male | 1056 | 51.9% | 75 | 44.9% | 327 | 51.7% | 654 | 53.0% |
| Year of ART initiation | | | | | | | | |
| 2004 | 43 | 2.1% | 0 | 0.0% | 6 | 0.9% | 37 | 3.0% |
| 2005 | 172 | 8.5% | 7 | 4.2% | 40 | 6.3% | 125 | 10.1% |
| 2006 | 343 | 16.9% | 7 | 4.2% | 116 | 18.3% | 220 | 17.8% |
| 2007 | 477 | 23.4% | 29 | 17.4% | 160 | 25.3% | 288 | 23.3% |
| 2008 | 403 | 19.8% | 29 | 17.4% | 139 | 22.0% | 235 | 19.0% |
| 2009 | 339 | 16.7% | 59 | 35.3% | 111 | 17.5% | 169 | 13.7% |
| 2010 * | 258 | 12.7% | 36 | 21.6% | 61 | 9.6% | 161 | 13.0% |
| Care entry points | | | | | | | | |
| VCT | 1262 | 62.0% | 39 | 23.4% | 386 | 61.0% | 837 | 67.8% |
| PMTCT | 147 | 7.2% | 67 | 40.1% | 62 | 9.8% | 18 | 1.5% |
| TB clinic | 9 | 0.4% | 1 | 0.6% | 0 | 0.0% | 8 | 0.6% |
| PICT | 617 | 30.3% | 60 | 35.9% | 185 | 29.2% | 372 | 30.1% |
| Transferred from another facility | | | | | | | | |
| No | 1975 | 97.1% | 165 | 98.8% | 621 | 98.1% | 1189 | 96.3% |
| Yes | 60 | 2.9% | 2 | 1.2% | 12 | 1.9% | 46 | 3.7% |
| Malnutrition [†] | | | | | | | | |
| Not malnourished (Z score > -2) | 376 | 18.5% | 36 | 21.6% | 112 | 17.7% | 228 | 18.5% |
| Moderately malnourished (-2 Z score -3) | 283 | 13.9% | 15 | 9.0% | 68 | 10.7% | 200 | 16.2% |
| Severely malnourished (Z score < -3) | 503 | 24.7% | 37 | 22.2% | 178 | 28.1% | 288 | 23.3% |
| Missing | 873 | 42.9% | 79 | 47.3% | 275 | 43.4% | 519 | 42.0% |
| WHO stage at ART initiation | | | | | | | | |

| | Total | | <18 mo | | 18–59 mo | | 5 yr | |
|-------------------------------|-------|-------|--------|-------|----------|-------|------|-------|
| | n | % | n | % | n | % | n | % |
| Stage 1 | 287 | 14.1% | 37 | 22.2% | 82 | 13.0% | 168 | 13.6% |
| Stage 2 | 415 | 20.4% | 11 | 6.6% | 99 | 15.6% | 305 | 24.7% |
| Stage 3 | 1123 | 55.2% | 88 | 52.7% | 376 | 59.4% | 659 | 53.4% |
| Stage 4 | 169 | 8.3% | 30 | 18.0% | 67 | 10.6% | 72 | 5.8% |
| Missing | 41 | 2.0% | 1 | 0.6% | 9 | 1.4% | 31 | 2.5% |
| Immunodeficiency [‡] | | | | | | | | |
| No evidence | 536 | 26.3% | 57 | 34.1% | 172 | 27.2% | 307 | 24.9% |
| Evidence of immunodeficiency | 762 | 37.4% | 49 | 29.3% | 225 | 35.5% | 488 | 39.5% |
| Severe immunodeficiency | 415 | 20.4% | 26 | 15.6% | 127 | 20.1% | 262 | 21.2% |
| Missing | 322 | 15.8% | 35 | 21.0% | 109 | 17.2% | 178 | 14.4% |
| First ART regimen | | | | | | | | |
| AZT/D4T/ABC+3TC+NVP | 1713 | 84.2% | 155 | 92.8% | 566 | 89.4% | 992 | 80.3% |
| AZT/D4T/ABC+3TC+EFV | 291 | 14.3% | 4 | 2.4% | 58 | 9.2% | 229 | 18.5% |
| Others | 31 | 1.5% | 8 | 4.8% | 9 | 1.4% | 14 | 1.1% |
| Type of setting | | | | | | | | |
| Rural | 1078 | 53.0% | 107 | 64.1% | 304 | 48.0% | 667 | 54.0% |
| Urban | 957 | 47.0% | 60 | 35.9% | 329 | 52.0% | 568 | 46.0% |
| Type of facility | | | | | | | | |
| Health center (N = 26) | 769 | 37.8% | 58 | 34.7% | 222 | 35.1% | 489 | 39.6% |
| District hospitals (N = 9) | 945 | 46.4% | 68 | 40.7% | 316 | 49.9% | 561 | 45.4% |
| Referral hospitals (N = 3) | 316 | 15.5% | 41 | 24.6% | 95 | 15.0% | 180 | 14.6% |
| Private (N = 1) | 5 | 0.2% | 0 | 0.0% | 0 | 0.0% | 5 | 0.4% |

* Only includes children who were enrolled between January and June 2010.

[‡] Weight-for-age Z scores were calculated based on the Centers for Disease Control and Prevention standards [19].

[‡] Based on the Centers for Disease Control and Prevention age-adjusted CD4 count classification [18].

VCT indicates voluntary counseling and testing; TB, tuberculosis; PICT, provider-initiated counseling and testing.

TABLE 3

Factors Associated With Documented Death Among HIV-infected Children <15 Years of Age Enrolled in Care and on Antiretroviral Treatment in the Survival Analyses

| | Pre-ART* (N = 3244) | | ART† (N = 2035) | |
|--------------------------------------------|------------------------|----------|--------------------|----------|
| | aSHR | 95% CI | aHR | 95% CI |
| Age | | | | |
| <18 mo | 4.4 | 2.9–6.8 | 2.1 | 1.3–3.6 |
| 18–59 mo | 1.2 | 0.77–1.7 | 1.3 | 0.93–1.8 |
| 5 yr | 1 | | 1 | |
| Care entry points | | | | |
| VCT | 1 | | — | — |
| PMTCT | 0.50 | 0.25–1.0 | — | — |
| TB/HIV | — | | — | — |
| PICT | 1.06 | 0.72–1.6 | — | — |
| Malnutrition‡ | | | | |
| Not malnourished (Z score > -2) | 1 | | 1 | |
| Moderately malnourished (-2 Z score -3) | 0.72 | 0.31–1.6 | 0.29 | 0.06–1.4 |
| Severely malnourished (Z score < -3) | 1.9 | 1.1–3.2 | 3.2 | 1.3–8.1 |
| Missing | 1.7 | 0.97–2.8 | 2.4 | 0.98–5.9 |
| WHO stage | | | | |
| Stage I | 1 | | 1 | |
| Stage II | 1.2 | 0.6–2.6 | 3.6 | 1.3–9.6 |
| Stage III | 1.7 | 0.94–3.2 | 2.6 | 0.96–6.8 |
| Stage IV | 4.1 | 2.0–8.4 | 9.8 | 3.5–27.4 |
| Missing | 3.7 | 1.9–7.4 | 6.0 | 1.8–19.6 |
| Immunodeficiency§ | | | | |
| No evidence | 1 | | 1 | |
| Evidence of immunodeficiency | 1.1 | 0.65–1.7 | 0.9 | 0.62–1.3 |
| Severe immunodeficiency | 1.6 | 0.93–2.8 | 2.3 | 1.7–3.3 |
| Missing | 3.0 | 1.9–4.6 | 1.3 | 0.68–2.7 |

* Competing risk using subdistribution hazards models (adjusted subdistribution hazards ratios [aSHRs]).

† Cox proportional hazards models (adjusted hazard ratios [aHRs]).

‡ Weight-for-age Z scores were calculated based on the Centers for Disease Control and Prevention standards [19].

§ Based on the Centers for Disease Control and Prevention age-adjusted CD4 count classification [18].

VCT indicates voluntary counseling and testing; TB, tuberculosis; PICT, provider-initiated counseling and testing; —, too few to compare.