HHS Public Access

Author manuscript

Trop Med Int Health. Author manuscript; available in PMC 2024 November 07.

Published in final edited form as:

Trop Med Int Health. 2017 April ; 22(4): 474–484. doi:10.1111/tmi.12834.

Outcomes among HIV-infected children initiating HIV care and antiretroviral treatment in Ethiopia

Zenebe Melaku[1], **Sileshi Lulseged**[1], **Chunhui Wang**[2], **Matthew R. Lamb**[2,3], **Yoseph Gutema**[1], **Chloe A. Teasdale**[2,3], **Solomon Ahmed**[4], **Tsigereda Gadisa**[1], **Zelalem Habtamu**[5], **Abubaker Bedri**[4], **Ruby Fayorsey**[2], **Elaine J. Abrams**[2,3,6]

[1]ICAP in Ethiopia, Addis Ababa, Ethiopia

[2]ICAP, Mailman School of Public Health, Columbia University, New York, NY, USA

[3]Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA

[4]Centers for Disease Control and Prevention, Addis Ababa, Ethiopia

[5]Oromia Regional Health Bureau, Addis Ababa, Ethiopia

[6]College of Physicians & Surgeons, Columbia University, New York, NY, USA

Abstract

OBJECTIVE—To describe pediatric ART scale-up in Ethiopia, one of the 21 global priority countries for elimination of pediatric HIV infection.

METHODS—A descriptive analysis of routinely collected HIV care and treatment data on HIV-infected children (<15 years) enrolled at 70 health facilities in four regions in Ethiopia, January 2006–September 2013. Characteristics at enrollment and ART initiation are described along with outcomes at 1 year after enrollment. Among children who initiated ART, cumulative incidence of death and loss to follow-up (LTF) were estimated using survival analysis.

RESULTS—11 695 children 0–14 years were enrolled in HIV care and 6815 (58.3%) initiated ART. At enrollment, 31.2% were WHO stage III and 6.3% stage IV. The majority (87.9%) were enrolled in secondary or tertiary facilities. At 1 year after enrollment, 17.9% of children were LTF prior to ART initiation. Among children initiating ART, cumulative incidence of death was 3.4%, 4.1% and 4.8%, and cumulative incidence of LTF was 7.7%, 11.8% and 16.6% at 6, 12 and 24 months, respectively. Children <2 years had higher risk of LTF and death than older children ($P < 0.0001$). Children with more advanced disease and those enrolled in rural settings were more likely to die. Children enrolled in more recent years were less likely to die but more likely to be LTF.

CONCLUSIONS—Over the last decade large numbers of HIV-infected children have been successfully enrolled in HIV care and initiated on ART in Ethiopia. Retention prior to and after ART initiation remains a major challenge.

Corresponding Author Elaine J. Abrams, ICAP-Columbia University, 722 W168th Street, New York, NY 10032, USA. eja1@cumc.columbia.edu.

Keywords

paediatric HIV; antiretroviral treatment; Ethiopia; ART scale-up; HIV retention

Introduction

Globally, the scale-up of antiretroviral treatment represents one of the greatest successes in the history of global health. By the end of 2014, an estimated 15 million individuals, including more than 800 000 children younger than 15 years, initiated antiretroviral therapy (ART) [1]. While paediatric treatment still lags behind adult successes, many countries, particularly in Southern Africa, have reported high rates of ART initiation, diminishing mortality and markedly improved health outcomes among children with HIV [2, 3].

By comparison, far less is known about efforts to treat children in other parts of sub-Saharan Africa including Ethiopia [4–7]. With an estimated 790 000 individuals living with HIV infection, a seroprevalence of 1.2% in the general population and close to 25 000–30 000 HIV-positive women delivering annually, Ethiopia is one of the 21 global priority countries to eliminate new paediatric infections [8, 9]. In 2014, there were an estimated 4800 new paediatric HIV infections and roughly 110 000 children with HIV infection in the country [1, 9]. Treatment coverage for children is low at 22%, and compares unfavourably with estimates of >50% in the adult population [9].

Over the last decade, there has been a broad and systematic expansion of HIV services in Ethiopia. Free ART became available in 2005, with rapid scale-up of services across the country by decentralising HIV services to urban and rural centres starting 2007. In 2008, provider-initiated HIV testing and counselling (PITC) was promoted as part of standard HIV care in all health facilities. The national early infant diagnosis (EID) programme was initiated in 2006 and scaled up in 2007. Standalone paediatric HIV care and treatment guidelines were issued in 2007 providing a framework for provision of comprehensive services for HIV-exposed and HIV-infected children [10]. Paediatric HIV care and treatment services were subsequently decentralised with an emphasis on infant diagnosis, ART, adherence and psychosocial support.

ICAP at Columbia University has been a major implementing partner for the U.S. President’s Emergency Plan for AIDS Relief (PEPFAR) since September 2005, supporting comprehensive HIV care and treatment programmes in four regions of Ethiopia with a total population of over 35 million people. By the end of 2013, ICAP’s support included technical assistance to 70 health facilities providing comprehensive HIV services including paediatric care and treatment. As part of the Identifying Optimal Models of HIV Care and Treatment, we report on a large cohort of HIV-infected children enrolled in routine HIV care and treatment services in Ethiopia and describe characteristics at enrolment, and outcomes prior to and after initiating ART [11–13].

Methods

Study design and study population

We analysed routinely collected clinical information on HIV-infected children (0–14 years of age) enrolled at 70 health facilities from four regions (Oromia, Dire Dawa, Harari and Somali) in Ethiopia. These health facilities collected longitudinal electronic patient-level clinical information as part of routine care, which was de-identified and included in the Optimal Models of HIV Care study [11–13]. Data on all children enrolled in care between 1 January 2006 and 30 September 2013 with follow-up visits through 30 September 2014 were included. During each clinic visit, healthcare providers documented patient information using the national clinical forms. Trained data clerks at the health facilities entered the forms into an electronic database. Data quality was assessed every 3 months for completeness and accuracy. An anonymised version of onsite electronic databases was created by stripping patient identifying information and replacing patient ID with a unique randomly generated study ID; these databases were then shared with study investigators at ICAP-Columbia University.

During this time, national guidelines recommended ART initiation for all infants aged <1 year of age; children aged 1–4 years with WHO stage III/IV or CD4 cell count <750 cells/mm^3; and children aged 5–14 years WHO stage III/IV or CD4 cell count <350 cells/mm^3 [10]. In 2014, the guidelines were revised to recommend universal ART for all children aged <15 years of age [14].

Statistical methods

We summarised clinical and demographic characteristics of HIV-infected children at enrolment into HIV care and at ART initiation using descriptive statistics stratified by age group (0–4 years and 5–14 years). We further subdivided these categories into groups of <1 year, 1 year, 2–4 years and 5–14 years. CD4 cell counts presented are the closest recorded counts within a window period of 3 months prior to and one month after enrolment into HIV care or ART initiation. Outcomes in the time period up to ART initiation were assessed by categorising outcomes one year after enrolment into mutually exclusive outcomes of retained in pre-ART care, initiating ART, transferring to another health facility before ART initiation, recorded death before ART initiation and loss to follow-up (LTF) before ART initiation. Among those who initiated ART, time from enrolment to ART initiation was calculated and categorised (<1, 1–3, 4–6, 7–12 months). Patients were considered LTF after ART initiation if they did not have a recorded visit for 6 months or more and were not recorded as dead or transferred out.

Among children who started ART, cumulative incidence of recorded death, LTF and total attrition (recorded death and LTF) through 36 months after ART initiation were estimated using Kaplan–Meier methods, overall and then stratified by age group and calendar year. Individual-level factors associated with reported LTF and death after ART initiation were estimated using Cox proportional hazards models with robust sandwich estimates to account for within-clinic correlation, with multivariable models adjusted for age, sex, CD4 cell count

and WHO stage at ART initiation, first ART regimen, facility type (primary *vs.* secondary/tertiary), location (rural *vs.* urban) and the availability of a CD4+ machine onsite.

Ethical approval

Anonymised patient-level data from routine health service delivery settings were used as part of the Identifying Optimal Models of HIV Care and Treatment study. Institutional Review Board (IRB) approval was obtained from the National Research Ethics Review Committee in Ethiopia; the study was also reviewed by the Columbia University Medical Center IRB and the Center for Global Health at the US Centers for Disease Control and Prevention (CDC).

Results

A total of 11 695 HIV-infected children aged 0–14 years of age were enrolled in HIV care at 70 ICAP-supported health facilities between 2006 and 2013. Roughly half (45.8%) of enrolled children were 0–4 years of age (Table 1). Nearly one-third (32.3%) were enrolled from PITC points of testing (inpatient, outpatient, TB and other hospital clinics). Less than one-third (26.8%) of all children were enrolled from voluntary counselling and testing (VCT) venues; among children under 5 years of age, 7.5% were enrolled through prevention of mother-to-child transmission (PMTCT) services. The vast majority of the children (87.9%) received care at secondary- or tertiary-level health facilities in primarily urban (60.1%) and semi-urban settings (34.2%).

Of the 10 009 (85.6%) children with a recorded WHO stage at enrolment, over one-third were WHO stage III (31.2%) or IV (6.3%) [Table 1]. CD4 cell count at enrolment was not documented for 63% of children aged <5 years and was missing for 26.9% of those aged 5–14 years. Based on WHO 2006 classification system, combining available clinical and immunologic data, 20.8% of children aged <5 years and 23.5% of older children were classified with severe immunodeficiency [15].

Overall, 6815 (58.3%) of all children enrolled in HIV care initiated ART through the follow-up period (Table 1). Of these, 27.2% of children aged <5 years and 18.6% of older children were classified as WHO stage I, while 10.3% of the younger and 6.9% of the older children were stage IV. Over half (58.1%) of children aged <5 years were missing CD4 cell count at ART initiation, and among those with recorded CD4 cell count, 8.4% and 12.0% had CD4 < 100 and 100–199 cells/mm^3, respectively. In the older age group, 83.6% had CD4 cell count documented, of whom 24.3% had CD4 < 100 cells/mm^3 and 28.4% had CD4 100–199 cells/mm^3. Roughly one-third (31.5%) of the children aged <5 years and 41.9% of older children had severe immunodeficiency at ART initiation [15].

Trends in patient characteristics over time

New enrolment of children increased from 1336 in 2006 to 2190 in 2008, and then decreased gradually to 1017 in 2012 (Table 1). Median CD4 cell count at enrolment, among children with recorded results, increased over time for both the <5 years and 5–14 year age groups: median CD4 cell count at enrolment among younger children increased from 535 cells/mm^3

in 2006 to 680 cells/mm^3 in 2012, and among older children increased from 255 cells/mm^3 in 2006 to 373 cells/mm^3 in 2012 ($P < 0.0001$, Figure 1).

Between 2006–2007 and 2010–2011, the proportion of paediatric patients initiating ART with WHO stage I increased from 8.9% to 27.4% while the proportion of children initiating ART with WHO stage III and IV decreased from 60.9% to 40.3% (stage III) and 15.0% to 6.9% (stage IV), respectively, $P < 0.0001$. Median CD4+ cell count at ART initiation, among children with recorded results, increased gradually from 260 cells/mm^3 to 419 cells/mm^3 among younger children, and from 135 cells/mm^3 to 205 cells/mm^3 among older children between 2006 and 2012 (Figure 1).

Patient outcomes after enrolment into HIV care and ART initiation

At one year after enrolment into HIV care, 2090 (17.9%) children were lost to follow-up, of whom 412 (3.5% of all children enrolled and 19.7% of all children lost to follow-up) were lost after attending only their initial enrolment visit (Table 2). There were 91 (0.8%) recorded deaths and 426 (3.6%) recorded transfers out of the facility before ART initiation. At one year after enrolment, 45.4% of enrolled children had initiated ART and 32.3% remained in care not yet on ART. While overall recorded deaths were low, children aged <5 years were significantly more likely to die before ART initiation than older children (1.0% *vs.* 0.5%, $P = 0.0001$). Among the 5306 (45.4%) children who initiated ART within the first year of enrolment, 60.6% initiated ART within 30 days and 86.9% started within 6 months of enrolment. A higher proportion of younger children started ART and a slightly higher proportion began treatment within one month after enrolment compared with older children (63.5% *vs.* 57.8%, $P < 0.0001$).

Among the 6815 (58.3%) patients who ever initiated ART before 15 years of age, the cumulative incidence of total attrition (LTF or recorded death) at 6, 12 and 24 months after ART initiation was 10.9% (95% CI: 10.2–11.7%), 15.5% (95% CI: 14.6–16.4%) and 20.6% (95% CI: 19.6–21.6%), respectively (Figure 2a). The cumulative incidence of recorded death was 3.4% (95% CI: 3.0–3.9%), 4.1% (95% CI: 3.6–4.6%) and 4.8% (95% CI: 4.2–5.3%), and the cumulative incidence of LTF was 7.7% (95% CI: 7.1–8.4%), 11.8% (95% CI: 11.1–12.7%) and 16.6% (95% CI: 15.7–17.6%) at 6, 12 and 24 months, respectively. Children with younger age had a higher risk of LTF and recorded death than older children (Figure 2b, c). Children under one year of age had the highest recorded death and LTF rates while children aged 5–9 years had the lowest.

Risk factors for LTF and death after ART initiation

Among children under 5 years, recorded death was associated with younger age, advanced disease stage and attending a facility in a rural area (Table 3). Compared with children aged 2–4 years, children under one year were 2.3 times more likely to die (adjusted hazard ratio (aHR) 2.3, 95% CI: 1.5–3.5), and children aged 1–2 years were 1.5 times more likely to die (aHR 1.5, 95% CI: 1.0–2.2) (Table 3). Children with WHO stage IV disease were two times more likely to die than children in WHO stage I (aHR 2.0, 95% CI: 1.2–3.5). Children with severe immunodeficiency (aHR 2.5, 95% CI: 1.8–3.6) or with indeterminate immunodeficiency level (aHR 1.7, 95% CI: 1.1–2.8) were at higher risk of death than

children with no severe immunodeficiency. Children enrolled at rural sites were more likely to die than children in urban settings (aHR 2.1, 95% CI: 1.3–3.5). Younger children who initiated ART in more recent years were less likely to die (aHR 0.4, 95% CI: 0.2–0.8, comparing 2012–2013 *vs.* 2006–2007).

Infants were also more likely to be LTF than 2–4 year-olds. Children with WHO stage IV were also at high risk to be lost. Children who initiated ART in more recent years (2008–2009, 2010–2011 and 2012–2013) had significantly higher risk of LTF than children initiated in 2006–2007 (aHR 2.1, 95% CI: 1.3–3.4; aHR 2.8, 95% CI: 1.6–4.9; aHR 3.3, 95% CI: 1.7–6.3, respectively). Those enrolled in rural settings (aHR 0.4, 95% CI: 0.2–0.9) had lower risk of LTF compared with those from urban areas.

Among older children (Table 3), those aged 5–9 years were less likely to be LTF (aHR = 0.8, 95% CI: 0.7–1.0) compared with children aged 10–14 years. Children with CD4 cell counts less than 100 cells/mm^3 had the highest risk of death (aHR 2.2, 95% CI: 1.1–4.9) compared to children with more than 350 CD4 cells/mm^3. The risk of death was lowest in children who started ART in more recent years (aHR 0.2, 95% CI: 0.1–0.3, comparing children who started ART in 2012–2013 to children started in 2006–2007), while LTF was higher in children who started ART in more recent years (aHR 1.9, 95% CI: 0.7–5.1; aHR 1.9, 95% CI: 1.0–3.4; and aHR 1.6, 95% CI: 1.1–2.5 comparing children started ART in 2012–2013, 2010–2011 and 2008–2009 to those started in 2006–2007). Attending a facility located in rural area was associated with a lower risk of LTF (aHR 0.4, 95% CI: 0.2–0.7).

Discussion

Our study provides an unprecedented overview of the scale-up of HIV care and treatment services for children in Ethiopia, a country with one of the largest paediatric HIV epidemics in the world. Among 11 695 HIV-infected children under 15 years of age enrolled in HIV care between 2006 and 2013 in four regions in Ethiopia, we found a high proportion of children enrolling in care with evidence of advanced disease, with over one-third diagnosed with WHO stage III or IV at presentation. Nearly half of all children initiated ART at one year from enrolment, of whom 60% started treatment within a month of enrolment. Overall, rates of attrition, death and LTF were similar to those reported in other countries, with close to 20% of children lost prior to ART initiation and 15% of those on treatment LTF at 1 year. In more recent years, children enrolling in care were healthier, with less advanced clinical disease and higher median CD4 cell count, but also at somewhat higher risk for LTF.

In a systematic review of 45 patient cohorts and 55 904 children on ART in 23 countries, Rosen and Fox estimated retention at 12 and 24 months at 88 and 72%, respectively. There are only a limited number of reports of children on ART from Ethiopia [4–6, 16]. Hagstromer *et al.* compared outcomes among Ethiopian children receiving care at a public hospital with those enrolled at health centres: among 1960 children, 34% were LTF, 2% died, 14% were transferred out and only 46% remained in care [5]. In this cohort, both death and LTF were associated with advanced disease and young age. In our cohort, among children aged <5 years, we also found that the youngest children, particularly those aged <1 year, and those with advanced disease (WHO stage IV) were at highest risk for death and

LTF. Children enrolled in care in more recent years had a lower risk of death, likely a result of better case finding and improved health status at enrolment. Similar to results presented among adult patients in this setting [11], we also found children enrolled in the later years of the scale-up at higher risk for LTF. We have no definitive explanation for this but surmise that with decentralisation and improved access to ART, undocumented transfers to other health facilities may have increased [17, 18]. Our finding that retention was higher for children enrolled in care at rural *vs.* urban sites supports this hypothesis as more treatment options are generally available within urban communities compared to rural settings.

We documented an increase in CD4 cell count at the time of enrolment as well as at ART initiation over the 7 years of observation. Overall, a higher proportion of children were being identified prior to advanced disease progression. After an initial increase in 2007 among children aged 5–14 years with a documented CD4 cell count, the median value at enrolment hovered between 300 and 400 cells/mm^3. Two studies in adults with HIV in Ethiopia identified low socio-economic status, poor HIV knowledge and internalised stigma to be associated with late presentation to HIV care [19, 20]. These factors could be considered relevant to children who are often dependent upon their adult caretakers to engage in care. Despite evidence of some improvement in health status at enrolment, median CD4 at ART initiation among those with recorded tests remained quite low for both age cohorts, below 200 cells/mm^3 for 5- to 14-year-olds and between 400 and 500 cells/mm^3 for <5-year-olds through until 2014. These findings likely reflect fidelity to national guidance – guidelines for paediatric treatment remained unchanged from 2003 to 2014 at which time they were liberalised to recommend universal treatment for all children aged <15 years. Globally, in adults and children there has been a gradual increase in CD4 cell count at ART initiation in parallel with recommendations for higher CD4 thresholds for ART initiation [2, 21–25].

One rationale for WHO endorsement of treatment for all individuals with HIV infection is the high rates of LTF among individuals in pre-ART care, those not yet qualifying for treatment. Similarly, the WHO decision in 2013 to increase the age threshold for treatment of children from 2 to 5 years of age was influenced by the higher LTF rates among children prior to *vs.* after ART initiation [26]. Findings from this cohort further underscore this rationale. At one year after enrolment into care among the 11 695 children in our cohort, 17.9% were LTF, 91 (0.8%) died, 426 (3.6%) transferred; 45.5% initiated ART and 32.3% remained in pre-ART care. Of the 2090 children LTF after enrolment, close to 20% never returned after the first clinic visit. Treatment for all children with HIV infection may avert these early losses by immediately preparing and/or initiating ART. On the other hand, attrition among children on ART was also high and treating more children could just shift losses from the pre-ART period to ART, further downstream along the treatment cascade. Our findings, along with previous studies in RLS, are evidence that greater efforts are needed to ensure retention of all HIV-infected children enrolled in care. While there is limited information on effective strategies to improve retention, in a study from Botswana, caregivers and children with HIV proposed several facilities changes that could increase retention including weekend clinic hours, reduced clinic wait times, particularly for students to decrease time of school, and providing a library for patients to use while waiting [27]. The use of patient navigators or community health workers to actively follow-up missed

appointments, electronic appointment reminder systems and financial incentives to improve retention among children with HIV infection requires urgent consideration.

Twelve-month recorded mortality after ART initiation of 4.1% documented is lower than what has previously been reported from Addis Ababa, with a mortality rate of 8.8%. However, this study was conducted in a single hospital in Addis Ababa with a relatively modest sample <500 patients, making the comparison difficult but may be a result of differences in the age distribution of children, programme effectiveness and other contextual factors [28]. The mortality rate in our study, however, was similar to findings from studies in Southern Africa and Kenya [29, 30]. We also recognise that our measure of recorded mortality might well be an underestimate of the true mortality as we did not actively ascertain outcomes among children classified as LTF. Of note, nearly half of the patients LTF after ART initiation were lost within in the first six months, likely including unreported deaths among the sickest children who were at highest risk for attrition.

There are both strengths and weaknesses to this study arising primarily from its data source. We used data routinely collected as part of clinical care in Ethiopia. Routinely collected data are often subject to levels of missing data higher than that collected as part of research study. In particular, CD4+ cell counts were missing for more than half of the young paediatric patients less than 5 years of age at enrolment and ART initiation. Consequently, caution is warranted in interpreting the CD4 results, particularly for children less than 5 years of age. Furthermore, we relied on death recorded as part of routine clinical care and did no independent verification of patients' vital status. A large but unknown proportion of patients classified as LTF were likely undocumented deaths, suggesting that our mortality estimates are underestimates. Similarly undocumented transfers are being treated as LTF. However, use of routinely collected data enables us to provide a more comprehensive description of patient characteristics and outcomes at the types of clinics where the majority of HIV-infected children individuals in Ethiopia are seeking HIV care and treatment.

Conclusions

We report on the health outcomes of more than 11 600 HIV-infected children enrolled in HIV care in Ethiopia, one of the 21 global priority countries. Overall, we saw improved identification and enrolment of children into HIV care from 2006 to 2011, likely associated with the introduction and scale-up of paediatric PITC. Over this period, ART initiation also increased among all enrolled children; however, a subset of eligible children never initiated initiate ART. Among those starting treatment, we saw ART initiated an increasingly higher CD4 cell counts and lower WHO stage. High rates of mortality and LTF, particularly among young children, require urgent attention and innovative solutions to ensure that all HIV-infected children accrue lifelong benefits of the ART scale-up.

Acknowledgements

The authors note appreciation to the children and families engaged in HIV care and to the many health workers providing HIV services in Ethiopia. We thank Zachary Peters for his administrative assistance. The findings were first presented at the International Conference on AIDS and Sexually Transmitted Infections in Africa (ICASA), Cape Town, South Africa, 7–11 December 2013. This work was supported by the 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.

References

1. UNAIDS. How AIDS Changed Everything – MDG6: 15 Years, 15 Lessons of Hope from the AIDS Response. UNAIDS: Geneva, Switzerland, 2015.
2. Davies MA, Phiri S, Wood R et al. Temporal trends in the characteristics of children at antiretroviral therapy initiation in southern Africa: the IeDEA-SA Collaboration. PLoS One 2013: 8: e81037. [PubMed: 24363808]
3. UNAIDS. Global Statistics 2015: World AIDS Day Fact Sheet 2015. UNAIDS: Geneva, Switzerland, 2015.
4. Asfawesen GY, Solomie J, Bisirat T, Berhanu GM, Mebratu B, Rahlenbeck S. Outcome in a paediatric cohort receiving ART in Addis Abeba, Ethiopia. Acta Paediatrica (Oslo, Norway: 1992) 2011: 100: 1164–1167. [PubMed: 21352366]
5. Hagstromer O, Lundstedt L, Balcha TT, Bjorkman P. Decentralised paediatric HIV care in Ethiopia: a comparison between outcomes of patients managed in health centres and in a hospital clinic. Global Health Action 2013: 6: 22274. [PubMed: 24219898]
6. Koye DN, Ayele TA, Zeleke BM. Predictors of mortality among children on Antiretroviral Therapy at a referral hospital, Northwest Ethiopia: a retrospective follow up study. BMC Pediatr 2012: 12: 161. [PubMed: 23043325]
7. Mulu A, Liebert UG, Maier M. Virological efficacy and immunological recovery among Ethiopian HIV-1 infected adults and children. BMC Infect Dis 2014: 14: 28. [PubMed: 24422906]
8. UNAIDS. The Gap Report. UNAIDS: Geneva, Switzerland, 2014.
9. UNAIDS. 2015 Progress Report on the Global Plan. UNAIDS: Geneva, Switzerland, 2015.
10. Federal Ministry of Health E. Guidelines for Paediatric HIV/AIDS Care and Treatment in Ethiopia – 2007. In: Office FHAPaC. Federal Ministry of Health, Ethiopia: Addis Ababa, Ethiopia, 2007.
11. Melaku Z, Lamb MR, Wang C et al. Characteristics and outcomes of adult Ethiopian patients enrolled in HIV care and treatment: a multi-clinic observational study. BMC Public Health 2015: 15: 462. [PubMed: 25934178]
12. McNairy ML, Lamb MR, Carter RJ et al. Retention of HIV-infected children on antiretroviral treatment in HIV care and treatment programs in Kenya, Mozambique, Rwanda, and Tanzania. J Acquir Immune Defic Syndr 2013:62:e70–e81. [PubMed: 23111575]
13. Lahuerta M, Lima J, Elul B et al. Patients enrolled in HIV care in Mozambique: baseline characteristics and follow-up outcomes. J Acquir Immune Defic Syndr 2011: 58: e75–e86. [PubMed: 21725246]
14. Federal Ministry of Health E. Guidelines for Paediatric HIV/AIDS Care and Treatment in Ethiopia – 2014. In: Office FHAPaC. Federal Ministry of Health, Ethiopia: Addis Ababa, Ethiopia, 2014.
15. World Health Organization. WHO Case Definitions of HIV for Surveillance and Revised Clinical Staging and Immunological Classification of HIV-Related Disease in Adults and Children. World Health Organization: Geneva, Switzerland, 2007.
16. Fox MP, Rosen S. Systematic review of retention of pediatric patients on HIV treatment in low and middle-income countries 2008-2013. AIDS (London, England) 2015:29:493–502. [PubMed: 25565496]
17. Reidy WJ, Sheriff M, Wang C et al. Decentralization of HIV care and treatment services in Central Province, Kenya. J Acquir Immune Defic Syndr 2014: 67: e34–e40. [PubMed: 24977728]
18. Fayorsey RN, Saito S, Carter RJ et al. Decentralization of pediatric HIV care and treatment in five sub-Saharan African countries. J Acquir Immune Defic Syndr 2013: 62: e124–e130. [PubMed: 23337367]
19. Beyene MB, Beyene HB. Predictors of late HIV diagnosis among adult people living with HIV/AIDS who undertake an initial CD4 T cell evaluation, Northern Ethiopia: a case-control study. PLoS One 2015: 10: e0140004. [PubMed: 26448332]

20. Gelaw YA, Senbete GH, Adane AA, Alene KA. Determinants of late presentation to HIV/AIDS care in Southern Tigray Zone, Northern Ethiopia: an institution based case-control study. AIDS Res Therapy 2015: 12: 40.

21. Hoffman S, Wu Y, Laheurta M et al. Advanced disease at enrollment in HIV care in four sub-Saharan African countries: change from 2006 to 2011 and multilevel predictors in 2011. AIDS (London, England) 2014: 28: 2429–2438. [PubMed: 25136842]

22. Lahuerta M, Wu Y, Hoffman S et al. Advanced HIV disease at entry into HIV care and initiation of antiretroviral therapy during 2006-2011: findings from four sub-Saharan African countries. Clin Infect Dis 2014: 58: 432–441. [PubMed: 24198226]

23. Mutimura E, Addison D, Anastos K et al. Trends in and correlates of CD4+ cell count at antiretroviral therapy initiation after changes in national ART guidelines in Rwanda. AIDS (London, England) 2015: 29: 67–76. [PubMed: 25562492]

24. Avila D, Althoff KN, Mugglin C et al. Immunodeficiency at the start of combination antiretroviral therapy in low-, middle-, and high-income countries. J Acquir Immune Defic Syndr 2014: 65: e8–e16. [PubMed: 24419071]

25. Koller M, Patel K, Chi BH et al. Immunodeficiency in children starting antiretroviral therapy in low-, middle-, and high-income countries. J Acquir Immune Defic Syndr 2015: 68: 62–72. [PubMed: 25501345]

26. World Health Organization (WHO). Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection. WHO: Geneva, Switzerland, 2013.

27. Machine EM, Gillespie SL, Homedes N et al. Lost to follow-up: failure to engage children in care in the first three months of diagnosis. AIDS Care 2016: 28: 1402–1410. [PubMed: 27160542]

28. Taye B, Shiferaw S, Enquselassie F. The impact of malnutrition in survival of HIV infected children after initiation of antiretroviral treatment (ART). Ethiop Med J 2010: 48: 1–10.

29. Fenner L, Brinkhof MW, Keiser O et al. Early mortality and loss to follow-up in HIV-infected children starting antiretroviral therapy in Southern Africa. J Acquir Immune Defic Syndr 2010: 54: 524–532. [PubMed: 20588185]

30. Nyandiko WM, Mwangi A, Ayaya SO et al. Characteristics of HIV-infected children seen in Western Kenya. East Afr Med J 2009: 86: 364–373. [PubMed: 20575310]

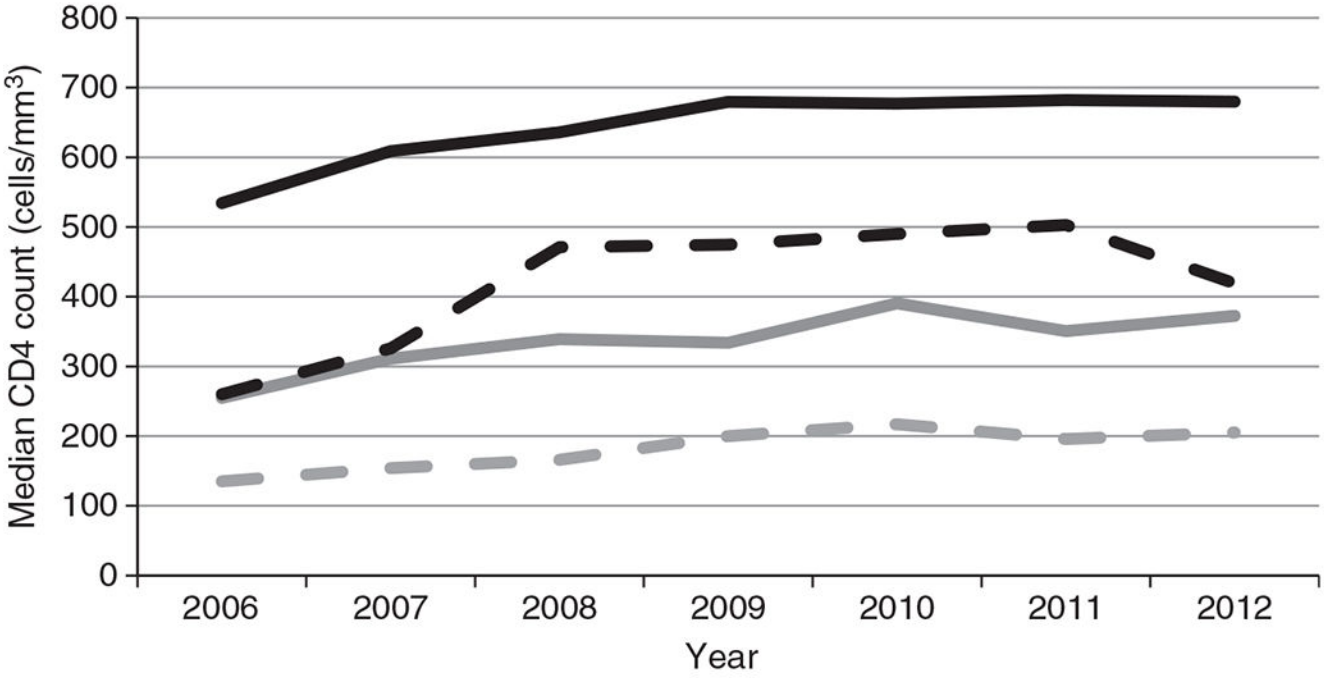

Figure 1.

Median CD4+ cell count (cells/mm^3) at enrolment and ART initiation among paediatric patients in Ethiopia between 2006 and 2012. Key: Black lines refer to patients aged 0–4 years and grey lines to patients aged 5–14 years. Solid lines represent median CD4+ cell count at enrolment into HIV care and dotted lines represent median CD4+ cell count at ART initiation.

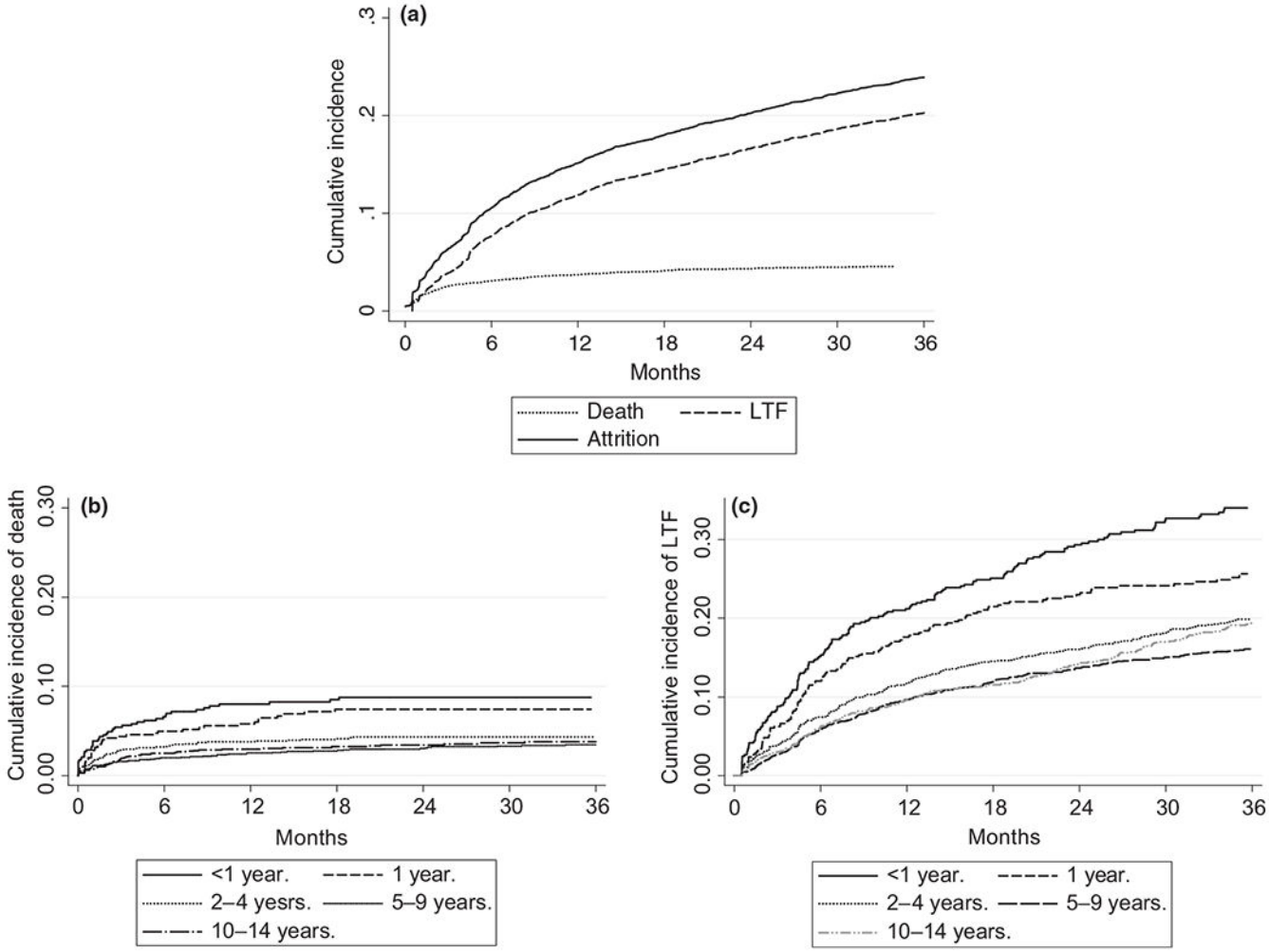

Figure 2.

Cumulative incidence of recorded death and loss to follow-up after ART initiation. (a) Cumulative incidence of recorded death, LTF and attrition (all age groups). (b) Cumulative incidence of recorded death. (c) Cumulative incidence of LTF.

Table 1

Characteristics of HIV-infected children enrolled in ICAP-supported HIV care and treatment facilities at enrolment and ART initiation (70 sites, between 2006 and 2013)

	Total		0–4 years		5–14 years	
	n = 11 695	%*	*n* = 5362	%*	*n* = 6333	%*
Age category						
<1 year (0–12 months)	890	7.6	890	16.6		
1 year (13–24 months)	1235	10.6	1235	23.0		
2–4 years (25–60 months)	3237	27.7	3237	60.4		
5–9 years	4108	35.1			4108	64.9
10–14 years	2225	19.0			2225	35.1
Sex						
Male	5855	50.1	2774	51.7	3081	48.6
Female	5833	49.9	2584	48.2	3249	51.3
Point of entry into care						
VCT	3133	26.8	1258	23.5	1875	29.6
PMTCT/HEI	960	8.2	404	7.5	556	8.8
PITC	3774	32.3	1659	30.9	2115	33.4
Other/Unknown/missing	3828	32.7	2041	38.1	1787	28.2
WHO stage						
Missing	1686	14.4	919	17.1	767	12.1
Stage 1	3802	38.0	1857	41.8	1945	34.9
Stage II	2456	24.5	962	21.6	1494	26.8
Stage III	3119	31.2	1279	28.8	1840	33.1
Stage IV	632	6.3	345	7.8	287	5.2
CD4 count (cells/mm^3)						
Missing	5086	43.5	3380	63.0	1706	26.9
<100	900	13.6	138	7.0	762	16.5
100–199	817	12.4	116	5.9	701	15.2
200–350	1161	17.6	228	11.5	933	20.2
350+	3731	56.5	1500	75.7	2231	48.2

	Total		0–4 years		5–14 years	
	n = 11 695	%*	*n* = 5362	%*	*n* = 6333	%*
Severe immunodeficiency†						
Yes	2600	22.2	1113	20.8	1487	23.5
No	3884	33.2	1016	18.9	2868	45.3
Indeterminate (missing WHO/CD4)	5211	44.6	3233	60.3	1978	31.2
Enrolment Year						
2006	1336	11.4	542	10.1	794	12.5
2007	1864	15.9	872	16.3	992	15.7
2008	2190	18.7	981	18.3	1209	19.1
2009	2090	17.9	1016	19.0	1074	17.0
2010	1617	13.8	735	13.7	882	13.9
2011	1241	10.6	586	10.9	655	10.3
2012	1017	8.7	478	8.9	539	8.5
2013 (Jan–Sept)	340	2.9	152	2.8	188	3.0
Facility type						
Primary (23 sites)	1417	12.1	631	11.8	786	12.4
Secondary/tertiary/other (47 sites)	10 278	87.9	4731	88.2	5547	87.6
Setting						
Urban city (33 sites)	7029	60.1	3236	60.4	3793	59.9
Semi-urban (26 sites)	4002	34.2	1818	33.9	2184	34.5
Rural (11 sites)	664	5.7	308	5.7	356	5.6
Children initiating ART before 15 years of age through follow-up period	6815	58.3	3099	57.8	3716	58.7
WHO stage at ART initiation						
Missing	150	2.2	76	2.5	74	2.0
Stage I	1501	22.5	822	27.2	679	18.6
Stage II	1567	23.5	649	21.5	918	25.2
Stage III	3034	45.5	1241	41.0	1793	49.2
Stage IV	563	8.4	311	10.3	252	6.9
CD4 count at ART initiation						
Missing	2408	35.3	1799	58.1	609	16.4
<100	862	19.6	109	8.4	753	24.2

	Total		0–4 years		5–14 years	
	n **= 11 695**	**%***	***n*** **= 5362**	**%***	***n*** **= 6333**	**%***
100–199	1039	23.6	156	12.0	883	28.4
200–350	1266	28.7	293	22.5	973	31.3
350+	1240	28.1	742	57.1	498	16.0
Severe immunodeficiency at ART initiation						
Yes	2539	37.3	981	31.5	1558	41.9
No	1931	28.3	489	15.8	1442	38.8
Indeterminate (missing WHO/CD4)	2345	34.4	1629	52.6	716	19.3
CD4 testing on site (35 sites)	5287	83.5	2419	83.5	2868	83.5

VCT, Voluntary counselling and testing; PMTCT, prevention of mother-to-child transmission; HEI, HIV-exposed infant; PITC, provider-initiated counselling and testing.

*Category percentages may not add up to 100% in table due to rounding off.

†Severe immunodeficiency includes any child with the WHO stage IV or severe immunodeficiency, defined as CD4 < 25% or <1500 cells/mm^3 per for children aged ≤12 months, CD4 < 20% or <750 cells/mm^3 in children aged 12–35 months, CD4 < 15% or <350 cells/mm^3 in children aged 36–59 months and CD4 < 15% or <200 cells/mm^3 in children aged ≥ 5 years [15].

Table 2

Paediatric patient status at one year after enrolment into HIV care, by age group

	Total		0–4 years		5–14 years		
	***n* = 11 695**	**%**	***n* = 5362**	**%**	***n* = 6333**	**%**	***P*-value**
LTF before ART initiation	2090	17.9	971	18.1	1119	17.7	0.57
LTF after initial visit (among all)	412	3.5	181	3.4	231	3.6	0.38
Dead before ART initiation	91	0.8	57	1.1	34	0.5	0.0001
Transferred out before ART initiation	426	3.6	180	3.4	246	3.9	0.15
Retained in pre-ART care	3782	32.3	1587	29.6	2195	34.7	<0.0001
ART initiation within one year from enrolment	5306	45.4	2567	47.9	2739	43.2	<0.0001
Time from enrolment to ART initiation (among ART patients)							
<1 month	3215	60.6	1631	63.5	1584	57.8	<0.0001
1–3 months	877	16.5	391	15.2	486	17.7	0.01
4–6 months	518	9.8	242	9.4	276	10.1	0.39
7–12 months	696	13.1	303	11.8	393	14.4	0.005

LTF, loss to follow-up.

Table 3

Adjusted Hazard Ratio associated with recorded death and loss to follow-up (LTF) among children initiating ART

	Death				LTF			
	<5 years		5 years +		<5 years		5 years +	
	aHR*	95% CI	aHR*	95% CI	aHR*	95% CI	aHR*	95% CI
Age category								
<1 year	2.3	1.5–3.5	N/A		1.7	1.3–2.2	N/A	
1 year	1.5	1.0–2.2	N/A		1.3	1.1–1.5	N/A	
2–4 years	1	Reference	N/A		1	Reference	N/A	
5–9 years	N/A		0.9	0.6–1.2	N/A		0.8	0.7–1.0
10–14 years	N/A		1	Reference	N/A		1	Reference
Sex								
Male	1	Reference	1	Reference	1	Reference	1	Reference
Female	0.9	0.6–1.1	1.2	0.9–1.8	1.1	0.9–1.2	1.0	0.8–1.1
WHO stage at ART initiation								
Missing	0.5	0.1–2.2	0.2	0.0–1.7	1.3	0.8–2.1	1.1	0.7–1.7
Stage 1	1	Reference	1	Reference	1	Reference	1	Reference
Stage II	0.9	0.5–1.6	0.5	0.3–1.1	0.9	0.7–1.2	0.9	0.7–1.3
Stage III	1.3	0.8–2.2	0.8	0.5–1.4	1.3	0.9–1.7	1.3	1.0–1.6
Stage IV	2.0	1.2–3.5	1.4	0.8–2.6	2.2	1.6–3.0	1.2	0.9–1.6
Severe immunodeficiency†								
Yes	2.5	1.8–3.6	N/A		1.0	0.9–1.3	N/A	
No	1	Reference	N/A		1	Reference	N/A	
Indeterminate (missing WHO/CD4)	1.7	1.1–2.8	N/A		1.1	0.7–1.5	N/A	
CD4 count at ART initiation‡								
Missing	N/A		1.6	0.7–3.8	N/A		0.7	0.4–1.2
<100	N/A		2.2	1.0–4.9	N/A		1.2	0.7–1.9
100–199	N/A		1.2	0.6–2.4	N/A		0.8	0.5–1.2
200–350	N/A		0.8	0.4–1.6	N/A		0.8	0.5–1.1
350+	N/A		1	Reference	N/A		1	Reference
ART initiation year								

	Death				LTF			
	<5 years		5 years +		<5 years		5 years +	
	aHR*	95% CI	aHR*	95% CI	aHR*	95% CI	aHR*	95% CI
2006–2007	1	Reference	1	Reference	1	Reference	1	Reference
2008–2009	0.9	0.7–1.3	0.6	0.4–0.8	2.1	1.3–3.4	1.6	1.1–2.5
2010–2011	0.7	0.4–1.0	0.3	0.2–0.5	2.8	1.6–4.9	1.9	1.0–3.4
2012–2013	0.4	0.2–0.8	0.2	0.1–0.3	3.3	1.7–6.3	1.9	0.7–5.1
Facility type								
Primary	0.4	0.1–1.6	N/A§		0.9	0.6–1.3	1.8	1.3–2.6
Secondary/tertiary	1	Reference	1	Reference	1	Reference	1	Reference
Setting								
Urban city	1	Reference	1	Reference	1	Reference	1	Reference
Semi-urban	1.2	0.7–2.2	1.1	0.6–2.1	0.8	0.6–1.1	0.8	0.5–1.2
Rural	2.1	1.3–3.5	1.3	0.7–2.4	0.4	0.2–0.9	0.4	0.2–0.7

*Adjusted models included for all other variables in the table, accounting for within-clinic correlation using robust sandwich variance estimate.

†Severe immunodeficiency was used in the model for children under 5 years, which includes any child with the WHO stage IV or severe immunodeficiency, defined as CD4 < 25% or <1500 cells/mm^3 for children aged ≤12 months, CD4 < 20% or <750 cells/mm^3 in children aged 12–35 months, CD4 < 15% or <350 cells/mm^3 in children aged 36–59 months and CD4 < 15% or <200 cells/mm^3 in children aged ≥5 years (WHO 2006 guidelines).

‡CD4 count was used in the model for children aged 5 years or older, to replace the severe immunodeficiency in the under 5-year children model.

§N/A: No reported deaths in the primary settings.