

**Pediatric HIV Care Cascade in Southern Mozambique: missed opportunities for early ART and re-engagement in care.**

**Authors:** Sheila Fernández-Luis<sup>1,2§</sup>, Tacilta Nhampossa<sup>1,3</sup>, Laura Fuente-Soro<sup>1,2</sup>, Orvalho Joaquim Augusto<sup>1</sup>, Aina Casellas<sup>2</sup>, Edson Bernardo<sup>1,3</sup>, Maria Ruperez<sup>4</sup>, Raquel Gonzalez<sup>1,2,5</sup>, Sonia Maculuve<sup>1</sup>, Anna Saura<sup>2</sup>, Clara Menendez<sup>1,2,5</sup>, Denise Naniche<sup>1,2,5\*</sup>, Elisa Lopez-Varela<sup>1,2\*</sup>.

1 Centro de Investigação em Saúde de Manhiça (CISM), Rua 12, Cambeve CP 1929 Maputo, Mozambique.

2 ISGlobal, Hospital Clínic - Universitat de Barcelona, Barcelona, Spain.

3 Instituto Nacional de Saúde (INS), Mozambique.

4 London School of Hygiene and Tropical Medicine London, United Kingdom

5 CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain.

§ Corresponding author: Sheila Fernández Luis

Bairro Cambeve, Rua 12,

Distrito da Manhiça, CP 1929, Maputo-Moçambique

Phone: (+258) 21810002

Email: Sheila.fernandez@isglobal.

\*These authors have contributed equally to the work.

E-mail addresses of authors:

SFL: Sheila.fernandez@isglobal.org

TN: Tacilta.Nhampossa@manhica.net

LFS: laura.delafuente@isglobal.org

OJA: orvaquim@gmail.com

AC: aina.casellas@isglobal.org

EB: edsonber852@hotmail.com

MR: Maria.Ruperez@lshtm.ac.uk

RG: raquel.gonzalez@isglobal.org

SM: sonia.maculuve@manhica.net

AS: annasauralazaro@gmail.com

CM: clara.menendez@isglobal.org

DN: denise.naniche@isglobal.org

ELV: [elisa.lopez@isglobal.org](mailto:elisa.lopez@isglobal.org)

Conflicts of Interest and Source of Funding: E.L.V. is supported by a Spanish Pediatrics Association (AEP) fellowship and a Ramon Areces Foundation fellowship. For the remaining authors none were declared.

Keyword: HIV children, HIV care cascade, HIV care continuum, retention in HIV care, lost to follow up, sub-Saharan Africa

## **Abstract**

**Introduction:** There were 170,000 children living with HIV in 2017 in Mozambique.

Scaling-up HIV care requires effective retention along the cascade. We sought to evaluate the cascade in HIV care in children enrolled at the Manhica District Hospital.

**Methods:** A prospective cohort of children <15 years was followed from enrollment in HIV care (January 2013-December 2015) until December 2016. Loss to follow up (LTFU) was defined as not attending the regular HIV hospital visits for  $\geq 90$  days following last visit attended.

**Results:** From the 438 children included (median age at enrollment in care of 3,6 (IQR:1.1-8.6) years), 335 (76%) were ART eligible and among those, 263 (78%) started at enrollment in HIV care. A total of 362 children initiated ART during the study period. Among those who started ART, the LTFU at 12, 24 and 36 months after ART initiation was 30%, 38%, and 40%, respectively. Median time to first LTFU episode was 5.8 (IQR:1.4-12.7) months. Children aged 5-9 years had an Subhazard Ratio of 0.24 (95%CI 0.12; 0.47) for LTFU compared to children <1 year of age. Re-engagement in care (RIC) was observed in 25% of the LTFU children.

**Conclusions:** Early infant diagnosis and frequent testing in HIV negative breastfeeding women could accelerate access to ART for children. Once on ART, attention must be given to the youngest children in the first six months after ART initiation in order to prevent LTFU. Additionally, elucidating the factors associated with RIC could help to fine-tune interventions which promote RIC in LTFU patients.

Keyword: HIV children, HIV care cascade, HIV care continuum, retention in HIV care, lost to follow up, sub-Saharan Africa.

1 There are 2.1 million Mozambicans living with HIV and 170,000 of them are children under  
2 15 years of age(1).

3 The cascade in HIV care describes the sequential stages of medical attention that people living  
4 with HIV experience between diagnosis and achieving sustained viral suppression(2). The  
5 WHO has adopted the UNAIDS 95-95-95 targets to reach 95% of people living with HIV  
6 diagnosed; 95% of diagnosed initiating antiretroviral therapy (ART); and 95% on ART with  
7 viral load suppression in order to end the AIDS epidemic by 2030(3). The pediatric HIV care  
8 cascade has not been studied well and the available reports on the quality of pediatric HIV care  
9 have documented high rates of loss to follow-up (LTFU) and early mortality(4–9).  
10 Additionally, little is reported about the dynamics of re-engagement in care (RIC) in children  
11 living with HIV who were LTFU.

12 This study aims to evaluate the HIV care cascade, factors associated with LTFU and the  
13 dynamics of RIC in a cohort of children enrolled at the Manhiça District Hospital (MDH),  
14 Mozambique.

## 15 **METHODS**

### 16 **Study setting**

17 The study was conducted at the MDH, a public hospital located in a semi-rural area in  
18 southern Mozambique with an estimated overall HIV community prevalence in adults of 39.9%  
19 [95% confidence interval (CI) 35.9-43.8%] in 2012 (10). Since 1996, the Manhiça Health  
20 Research Centre has run a continuous health and demographic surveillance system (HDSS) for  
21 vital events including births, deaths and migrations covering a total population of nearly  
22 174,000 individuals(11). At the time of the study, children under age 18 months were diagnosed  
23 with HIV infection through a DNA polymerase chain reaction (PCR) assay in the reference  
24 laboratory. After age 18 months, serological testing was used for HIV diagnosis. Clinical

25 consultations were monthly but could be spaced to every two months or quarterly in children  
26 with good clinical and immune response. Children  $\geq 5$  years of age were eligible for anti-  
27 retroviral therapy (ART) if based on CD4+ T-lymphocyte (CD4) cell count below 350 cell/mm<sup>3</sup>  
28 or below 500 cell/mm<sup>3</sup>, before and after May 2015 respectively, or WHO stage III-IV.  
29 Universal treatment was recommended for all HIV-infected children <5 years of age(12).  
30 Pharmacy pickup of ART was monthly for all children. First-line treatment was zidovudine  
31 (AZT)+ lamivudine (3TC) + nevirapine (NVP) for children  $\geq 5$  years of age and <35kg and  
32 tenofovir disoproxil fumarate (TDF)+3TC+efavirenz (EFV) for those  $\geq 5$  years of age and  
33  $\geq 35$ kg. Children under 5 years who had previously received prophylaxis for prevention of  
34 mother-to-child transmission (PMTCT) were given AZT+3TC+lopinavir/ritonavir (LPVr) and  
35 those who had not received prophylaxis for PMTCT were given AZT+3TC+NVP according to  
36 national guidelines (12,13).

### 37 **Study design and procedures**

38 This is a descriptive study of a prospective cohort including all children < 15 years newly  
39 enrolled in HIV care at the MDH between January 2013 and December 2015. Children  
40 transferred to MDH from another health facility were excluded from this analysis. Patients  
41 were followed-up from their date of the enrollment in care through to December 2016, for a  
42 maximum study period of four years.

43 Information about the frequency of clinical consultations, ART pharmacy pick-up and referrals  
44 was extracted from the routinely collected data in the electronic MDH HIV pediatric database.  
45 Mortality and sociodemographic data was extracted from HDSS database. Clinical information  
46 was collected in a specific questionnaire in electronic format in Open Data Kit software 1.4  
47 (14) during the clinical visits and uploaded into a database in Research Electronic Data Capture  
48 Software 5.7.3 (14).

## 49 **Study definitions**

50 Care cascade indicators included proportion of children eligible for ART at enrollment in care,  
51 proportion of children initiating ART during the first three months after enrollment in care  
52 among those eligible, and proportion of children retained in HIV care at 12 months post-ART  
53 initiation.

54 Enrollment in care was defined as having a first clinical consultation in the HIV clinic.

55 LTFU was defined for children on ART as not having attended their clinical consultation  
56 appointment or pharmacy pickup for  $\geq 90$  days following last consultation /pharmacy visit  
57 attended among patients considered alive and not transferred to another unit which implies a  
58 delay of at least 60 days in ART pick-up. The date of the last attended visit was considered the  
59 date of LTFU.

60 Among patients considered LTFU, RIC was defined as the date that the patient returned to  
61 clinic or the pharmacy. Those participants who had RIC followed by a new LTFU episode  
62 during the study period were classified as “RIC & LTFU”.

63 Immunosuppression was defined as severe suppression ( $<15\%$ ), moderate suppression (15 to  
64  $<25\%$ ) and no evidence of suppression ( $\geq 25\%$ )(15).

65 Socioeconomic status (SES) was represented by a wealth index generated by an asset-based,  
66 multiple-correspondence analysis to categorize the household SES into five wealth quintiles as  
67 previously described (16). The two lowest quintiles were grouped as ‘low SES’ and the  
68 remaining three quintiles as “higher SES”.

69 Z-scores for nutritional status evaluation were calculated using the WHO Child Growth  
70 Standard 2006(17). Stunting was defined as height-for-age z-score (HAZ)  $<-2$  standard

71 deviations (SD). Underweight was defined as weight-for-age z-score (WAZ) <-2SD for  
72 children <10 years. Wasting was defined as weight-for-height Z-score (WHZ) <-2SD for  
73 children <5 years and body mass index (BMI)-for-age Z-score (BAZ) <-2SD for children 5–19  
74 years.

75 Anemia was defined as  $Hb \leq 8\text{g/dl}$  (12).

76 Health problems were self-reported by the parents/caregivers.

### 77 **Statistical considerations**

78 Data was analyzed using Stata statistical software version 15 (Stata Corp., College Station,  
79 Texas, USA)(18).

80 Medians and interquartile ranges (IQR) were calculated to describe continuous variables and  
81 categorical variables were summarized using frequencies.

82 Cumulative incidence estimation was used to describe LTFU incidence post-ART initiation  
83 among children who started ART at enrollment or during follow-up, excluding those initiating  
84 ART during the last 90 days of the study or those who were transferred before ART initiation.  
85 Censored individuals were included in the denominator.

86 Competing-risks regression for death and migration according to the method of Fine and Gray  
87 (19) was used to assess which variables were related to the first episode of LTFU. A  
88 multivariable model was built performing a stepwise selection of the variables with  
89 significance lower than 0.20 in the bivariable analysis.



90 **Ethics statement**

91 This study was approved by the Mozambican National Bioethics Committee and the Barcelona  
92 Hospital Clinic Institutional Review Board. Written informed consent was obtained from the  
93 parents/caregivers of all children.

94 **RESULTS**

95 **Baseline characteristics of the cohort at enrollment in HIV care**

96 Among 438 children enrolled in HIV care, the proportion of enrollment by year was 0.43  
97 (95%CI:0.39-0.48), 0.31 (95%CI:0.27-0.36) and 0.25 (95%CI:0.22-0.30) in 2013, 2014 and  
98 2015, respectively. Median age at enrollment was 3.6 (IQR:1.1-8.6) years and 209 (48%) were  
99 female (Supplemental Digital Content: baseline characteristics).

100 Advanced WHO stage (III-IV) was present in 39 (9%) children but 134 (31%) did not have a  
101 WHO staging at enrollment. However, when including anemia and wasting as advanced stage,  
102 the number of children considered to have advanced WHO at enrollment was 106 (24%).  
103 Severe immunosuppression was present in 86 (25%) of the 345 with a CD4 result and moderate  
104 immunosuppression in 128 (37%). Although data on immunosuppression and WHO stage was  
105 missing for 21% and 24% children respectively, only 29 (7%) were missing both. Median  
106 values of WAZ, WHZ, BAZ were -1.18 (95%CI: -1.35; -1.01), -0.34 (95%CI: -0.52; -0.16) and  
107 -0.27 (95%CI: -0.41; -0.14), respectively. A health problem during the month before  
108 enrollment in care was reported by 71 (16%) patients, 40 (56%) of them requiring  
109 hospitalization.

110 Seventy-seven (18%) of children were 10-25 years of age at enrollment in care. Among these,  
111 39% and 23% presented with moderate and severe immunosuppression respectively. Only one  
112 (1%) reported PTV, while 44% reported not receiving PTV and 55% were unknown.

113 **Twelve -month pediatric HIV Care Cascade post-ART initiation.**

114 Of 335 (76%) enrolled children who were ART eligible, 263 (78%) started ART within 3  
115 months of enrollment in care (Figure 1), with a median time between enrollment and ART  
116 initiation of 17 (IQR 6-35) days.

117 At 12 months post-ART initiation, 165 (63%) of the 263 children who initiated ART had been  
118 continuously retained in care (Figure 1), while 51(20%) presented at least one LTFU episode,  
119 10 (4%) had died, and 35 (13%) had transferred to another facility. No differences in mortality  
120 at 12 months post-ART initiation were observed by age group ( $p=0.268$ ).

121 Among the 66 not eligible and the 37 with missing data for ART eligibility at enrollment, 58  
122 (56%) became eligible during the 12-month follow-up period and all of them initiated ART.

### 123 **Incidence of LTFU over 36 months following ART initiation.**

124 We then assessed LTFU in children who initiated ART at any time prior to the last 90 days of  
125 the study period. This population of 362 children included the 263 who initiated ART within 3  
126 months of enrollment, 44 who initiated ART later and 55 children who become eligible and  
127 initiated ART in the above specified time period.

128

129 Figure 2 shows the cumulative incidence of LTFU from ART initiation until the end of the  
130 study period, among the 362 children who initiated ART. The median time of follow-up from  
131 ART initiation to the end of the study period (December 31, 2016) was 32.6 (IQR:20.8-39.9)  
132 months.

133 At 12, 24 and 36 months post-ART initiation, of the 362 children having initiated ART, there  
134 were a total of 107 children [30% (95%CI:25-35)], 136 children [38% (95%CI:33-43)] and 146  
135 children [40% (95%CI:35-46)] respectively, with at least one LTFU episode. The LTFU  
136 incidence rate was 41 (95%CI:34,50), 34 (95%CI:29,41) and 31 (95%CI:27,37) per 100  
137 children years at month 12, 24, and 36 respectively.

138 Among the 146 children who fulfilled the definition for an LTFU episode the median time from  
139 ART initiation until the first LTFU episode was 5.8 (IQR:1.4-12.7) months.

#### 140 **Factors associated with first episode of LTFU post-ART initiation**

141 We then assessed factors associated with first episode of LTFU post-ART initiation including  
142 the 362 children who initiated ART at any time prior to the last 90 days of the study period.

143 Bivariable competing risks proportional sub-hazards regression identified younger age at ART  
144 initiation ( $p < 0.0001$ ), unknown immunosuppression status ( $p = 0.0007$ ), lower/unknown SES  
145 ( $p = 0.0497$ ) and advanced WHO stage ( $p = 0.0837$ ) as significantly associated with increased  
146 incidence of LTFU (Table 1).

147 In the multivariable model, younger age at ART initiation and unknown immunosuppression  
148 status were the independent factors associated with LTFU. Children aged 5-9 years had an  
149 adjusted sub-hazard ratio (aSHR) of 0.36 (95%CI:0.20;0.61) for LTFU compared to children  
150  $< 1$  year of age  $p < 0.0001$  (Table 1). Those with unknown immunosuppression status (no CD4  
151 results) had an aSHR of 2.50 (95%CI: 1.56; 4.01) compared to those with no  
152 immunosuppression even after adjustment for WHO stage. Those with moderate or severe  
153 immunosuppression showed a trend for higher LTFU but did not reach significance. At 2 years  
154 post ART initiation, children aged 5-15 years of age at ART initiation had a 34 % risk of LTFU  
155 whereas children aged  $< 1$  year at ART initiation had close to a 62% risk of LTFU (Figure 2b).

#### 156 **Re-engagement in care after a LTFU episode**

157 We then assessed the dynamics of RIC among the 146 children who had a LTFU episode during  
158 the study period. Longer median times between ART initiation and the end of the study period  
159 allowed demonstration of LTFU-RIC cycles after ascertainment of child status through HDSS

160 and clinical records ( $p=0.0156$ ). The overall median follow up time for the 146 children with  
161 an LTFU episode was 32.4 (IQR:23.6-40.8) months.

162 By the end of the study period, of the 146 children with initial LTFU episodes recorded, 94  
163 (64%) had never come back to the health unit, 5 (3%) had died after becoming LTFU, 10 (7%)  
164 had migrated to another district and 37 (25%) had re-engaged. Median time to RIC was 4.6  
165 (IQR:3.2-6.2) months.

166 Of those 37 children who were LTFU and RIC, 22 (60%) continued RIC at the end of the study  
167 period and 15 (40%) presented another LTFU episode. Median age at ART initiation was 2.3  
168 (IQR:0.5-9.5) years for those who continued RIC and 2.5 (IQR:0.7-11.0) years for those who  
169 RIC and presented another LTFU episode and median follow time was 35.7 (IQR:30.4-40.8)  
170 months and 39.4 (IQR:31.9-43.4) months, respectively.

171 Of the 64% of LTFU who never returned, the median age at ART initiation was 1.7 (IQR:0.9-  
172 4.9) years and follow up time was 30.6 (IQR:20.5-38.7) months.

## 173 **DISCUSSION**

174 This analysis documents that younger age at ART initiation increases the risk for LTFU, mainly  
175 occurring in the first six months post-ART initiation. Not having a CD4 result was also  
176 associated with a high risk of LTFU. A follow up time of over three years allowed us to estimate  
177 that one quarter of LTFU children re-engaged in care in a median time of 4.6 months after  
178 LTFU.

179 A high rate of LTFU, particularly for younger children, has also been observed in pediatric  
180 cohorts from Kenya, Mozambique, Rwanda and Tanzania in 2005-2011 (20). However, few  
181 studies have explored mothers' reasons for LTFU which may include lack of money for  
182 transportation and/or medication side effects (21). Nearly half of the children had moderate to

183 severe immunosuppression at enrollment in care. Similar levels in other pediatric cohorts from  
184 Mozambique in 2013 (22) and other sub-Saharan African countries in 2004-2012 (23) suggest  
185 little improvement over time. Another 20% were missing a CD4 result, which could indicate a  
186 lower quality of care and it was associated with a 2.3 higher risk of LTFU as compared to non-  
187 immunosuppressed children.

188 The decrease in numbers of children enrolled at the MDH between 2013 and 2014-2015 was  
189 likely related to Mozambique's decentralization of HIV care to lower level health facilities,  
190 since the MTCT rate remained relatively stable in Mozambique (24).

191 The high proportion of children with immunosuppression along with the elevated median age  
192 at enrollment in care points toward a missed opportunity for more timely diagnosis both in  
193 infants with known perinatal HIV exposure and/or in infants whose mothers acquired HIV  
194 infection in pregnancy or during breastfeeding. The implementation of point-of-care infant  
195 HIV diagnosis in 2017 may improve early diagnosis in infants with known perinatal HIV  
196 exposure. However, HIV incidence in postpartum women in Mozambique in 2008-2011 was  
197 3.20/100 women-years (95%CI:2.3;4.5) with an associated MTCT rate of 21% (95%CI:5;36)  
198 (25). Similar incidence (average 4%) in pregnant and breastfeeding women have also been  
199 observed in other Sub-Saharan Africa countries (26). Mozambican guidelines recommends  
200 HIV testing every three months for key populations, sero-discordant couples, blood donors,  
201 pregnant women and her partners (27). Reduction of time between tests as well as self-testing  
202 options for lactating mothers living in areas of high HIV incidence may be promising  
203 interventions to ensure that seroconversions during breastfeeding are diagnosed in a timely  
204 fashion.

205 This analysis revealed that 25% of those LTFU re-engaged in care. However, this number is  
206 likely to be underestimated since we did not have sufficient follow-up time for all of the LTFU

207 in the study. Additionally, further studies are needed in order to evaluate the impact that LTFU-  
208 RIC cycles have on immunosuppression, nutritional status and other clinical parameters. RIC  
209 has been described very little in the literature, especially in children. In a study of adults in  
210 Kenya, the cumulative incidence of re-engaging in care, to either a new clinic or the original  
211 clinic was 14% (95%CI:7;23%) at three months and 60% (95%CI:48;69%) at six months after  
212 the most recent attended clinic appointment (28).

213 Understanding a child's LTFU-RIC cycles is fundamental to having a more global view of  
214 retention, limiting LTFU and accelerating time to RIC in this vulnerable population. Assessing  
215 routinely collected data could contribute to identifying factors associated with RIC and  
216 designing specific interventions. However, paper-based charts, lack of unique identifiers and  
217 high rates of transfer and migration complicate the task. Considering the 5.8-month median  
218 time from ART initiation to the first LTFU episode in the PECA cohort, there is a window of  
219 opportunity for interventions during the first 6 months in all children initiating ART both to  
220 minimize LTFU and to promote timely RIC.

221 The Expanded Programme on Immunization (EPI) programs in sub-Saharan African countries  
222 have a high vaccination coverage and extend to rural areas such as the Manhica district (29).  
223 A systematic review on integration of HIV testing during immunization clinic visits in SSA  
224 reported over 90% acceptability by mothers (30). Such programs could also be used as a  
225 platform to send reminders to mothers and children HIV counselling and visits.

226 Our study has several limitations. First, enrollment in the study happened during the first  
227 consultation. The diagnosis of HIV was not made during the study and we cannot guarantee  
228 the identification of false positives. However, we assume compliance with the Mozambican  
229 guidelines that all children under 18 months should be diagnosed and confirmed by virological  
230 methods, which minimizes the possibility of bias. Second, the high proportion of missing data

231 in CD4 and WHO stage could have resulted in underestimates of ART eligibility. Third, lack  
232 of systematic active tracing of LTFU children results in some children classified as LTFU who  
233 are actually silent. Incomplete identification of deaths, despite HDSS access, could also results  
234 in some deaths being classified as LTFU, further contributing to overestimates of. Fourth, the  
235 median of follow-up from ART initiation to the end of the study was 32 months. Censored data  
236 could have affected the estimation of LTFU at 36 months post-ART initiation and proportion  
237 of the RIC after LTFU.

238

### 239 **Conclusions**

240 The high LTFU found in this study highlights the special attention that should be given to  
241 younger children during the first six months after ART initiation in order to prevent LTFU.  
242 Once LTFU, only a quarter of those children return to the health unit, mostly within the first  
243 months after drop out. Elucidating factors associated with RIC could help to refine  
244 interventions which promote RIC.

245

246 **Competing interests**

247 We declare no competing interests.

248 **Authors' contributions**

249 Conceived and designed the study: ELV, DN, SFL, LDF. Implemented the study: LDF, SFL,  
250 TN, SM, MR, RG, EB, supervised by ELV, DN and CM. Analyzed the data: AC, ELV, OJA,  
251 AS. Wrote the paper: SFL, TN, LDF, ELV, DN. All authors contributed to refinement of the  
252 study protocol and approved the final manuscript.

253

254 **Acknowledgements**

255 The authors wish to sincerely thank all the staff at Manhiça District Hospital and Centro de  
256 Investigação em Saúde de Manhiça who worked to collect and manager data. We are deeply  
257 grateful to the patients participating in the study. We thank Elisabeth Salvo for editing and  
258 review of the manuscript. ISGlobal is a member of the CERCA Programme, Generalitat de  
259 Catalunya. CISM is supported by the Government of Mozambique and the Spanish Agency for  
260 International Development (AECID). S.F.L. receives a pre-doctoral fellowship from the  
261 Secretariat of Universities and Research, Ministry of Enterprise and Knowledge of the  
262 Government of Catalonia and cofounded by European Social Fund. E.L.V. is supported by a  
263 Spanish Pediatrics Association (AEP) fellowship and a Ramon Areces Foundation fellowship.

264

265

266



267 **References**

- 268 1. UNAIDS (Joint United Nations Programme on HIV/AIDS). UNAIDS data 2018  
269 [Internet]. Available from:  
270 [http://www.unaids.org/sites/default/files/media\\_asset/unaids-data-2018\\_en.pdf](http://www.unaids.org/sites/default/files/media_asset/unaids-data-2018_en.pdf)
- 271 2. Medland NA, McMahon JH, Chow EPF, Elliott JH, Hoy JF, Fairley CK. The HIV care  
272 cascade: a systematic review of data sources, methodology and comparability. *J Int*  
273 *AIDS Soc.* 2015;18:20634.
- 274 3. UNAIDS. 90-90-90 An ambitious treatment target to help end the AIDS epidemic.  
275 [Http://WwwUnaidsOrg/Sites/Default/Files/Media\\_Asset/90-90-90\\_En\\_0Pdf](Http://WwwUnaidsOrg/Sites/Default/Files/Media_Asset/90-90-90_En_0Pdf). 2014;40.
- 276 4. Leroy V, Malateste K, Rabie H, Lumbiganon P, Ayaya S, Aupibul L, et al. Outcomes  
277 of antiretroviral therapy in children in Asia and Africa: a comparative analysis of the  
278 IeDEA pediatric multiregional collaboration. 2013;62(2):208–19.
- 279 5. Lamb MR, Fayorsey R, Nuwagaba-Biribonwoha H, Viola V, Mutabazi V, Alwar T, et  
280 al. High attrition before and after ART initiation among youth (15-24 years of age)  
281 enrolled in HIV care. *AIDS.* 2014;28(4):559–68.
- 282 6. George E, Noël F, Bois G, Cassagnol R, Estavien L, De Matteis Rouzier P, et al.  
283 Antiretroviral therapy for HIV-1-infected children in Haiti. *J Infect Dis.*  
284 2007;195(10):1411–8.
- 285 7. Nyandiko W, Vreeman R, Liu H, Shangani S, Sang E, Ayaya S, et al. Nonadherence to  
286 clinic appointments among HIV-infected children in an ambulatory care program in  
287 western Kenya. *J Acquir Immune Defic Syndr.* 2013;63(2):e49-55.
- 288 8. Walker AS, Prendergast AJ, Mugenyi P, Munderi P, Hakim J, Kekitiinwa A, et al.  
289 Mortality in the year following antiretroviral therapy initiation in HIV-infected adults

- 290 and children in Uganda and Zimbabwe. *Clin Infect Dis*. 2012;55(12):1707–18.
- 291 9. Weigel R, Estill J, Egger M, Harries A, Makombe S, Tweya H, et al. Mortality and  
292 loss to follow-up in the first year of ART: Malawi National ART Programm. *AIDS*.  
293 2012;26(3):365–73.
- 294 10. González R, Munguambe K, Aponte J, Bavo C, Nhalungo D, Macete E, et al. High  
295 HIV prevalence in a southern semi-rural area of Mozambique: a community-based  
296 survey. *HIV Med*. 2012;13(10):581–8.
- 297 11. Nhacolo AQ, Nhalungo DA, Sacoor CN, Aponte JJ, Thompson R, Alonso P. Levels  
298 and trends of demographic indices in southern rural Mozambique: evidence from  
299 demographic surveillance in Manhica district. *BMC Public Health*. 2006;6:291.
- 300 12. Ministério da Saúde. Guia de Tratamento Antiretroviral e Infecções Oportunistas no  
301 Adulto, Adolescente, Gravidas e Crianças. 2014. 1–262 p.
- 302 13. Republica de Moçambique. Ministério da Saúde. Tratamento Antiretroviral e  
303 Infecções Oportunistas do Adulto, Adolescente, Grávida e Criança [Internet]. 2016.  
304 Available from: <http://www.misau.gov.mz/index.php/guioes#>
- 305 14. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic  
306 data capture (REDCap)—A metadata-driven methodology and workflow process for  
307 providing translational research informatics support. *J Biomed Inform*.  
308 2009;42(2):377–81.
- 309 15. CDC. 1994 Revised classification system for human immunodeficiency virus infection  
310 in children less than 13 years of age; Official authorized addenda: human  
311 immunodeficiency virus infection codes and official guidelines for coding and  
312 reporting ICD-9-CM. [Internet]. Vol. 43, *MMWR Morb Mortal Wkly Rep*. 1994. p. 1–

- 313 19. Available from: <https://www.cdc.gov/mmwr/PDF/rr/rr4312.pdf>
- 314 16. Pons-Duran C, González R, Quintó L, Munguambe K, Tallada J, Naniche D, et al.  
315 Association between HIV infection and socio-economic status: evidence from a  
316 semirural area of southern Mozambique. *Trop Med Int Health*. 2016;21(12):1513–21.
- 317 17. WHO Multicentre Growth Reference Study Group. WHO Child Growth Standards:  
318 Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body  
319 mass index-for-age: Methods and development. Geneva; 2006.
- 320 18. StataCorp. Stata Statistical Software: Release 15. College Station, TX: StataCorp LP.  
321 2017;
- 322 19. Fine JP, Gray RJ. A Proportional Hazards Model for the Subdistribution of a  
323 Competing Risk. *J Am Stat Assoc*. 1999;94(446):496–509.
- 324 20. McNairy ML, Lamb MR, Carter RJ, Fayorsey R, Tene G, Mutabazi V, et al. Retention  
325 of HIV-infected children on antiretroviral treatment in HIV care and treatment  
326 programs in Kenya, Mozambique, Rwanda, and Tanzania. *J Acquir Immune Defic*  
327 *Syndr*. 2013;62(3):e70-81.
- 328 21. Sariah A, Rugemalila J, Protas J, Aris E, Siril H, Tarimo E, et al. Why did I stop? And  
329 why did I restart? Perspectives of women lost to follow-up in option B+ HIV care in  
330 Dar es Salaam, Tanzania. *BMC Public Health*. 2019;19(1):1172.
- 331 22. Teasdale CA, Yang J, Thome B, Yersin I, Sebastian T, Brusamento S, et al. Outcomes  
332 Among Children Enrolled in HIV Care in Mozambique 2009-2013. *Pediatr Infect Dis*  
333 *J*. 2016;35(10):1117–25.
- 334 23. Makadzange AT, Dougherty L, Birri R, Kupakuwana G, van Dijk J, Bwakura  
335 Dangarembizi M, et al. Temporal Improvements in Long-term Outcome in Care

- 336 Among HIV-infected Children Enrolled in Public Antiretroviral Treatment Care: An  
337 Analysis of Outcomes From 2004 to 2012 in Zimbabwe. *Pediatr Infect Dis J*.  
338 2018;37(8):794–800.
- 339 24. Encontro Anual de Parceiros do CNCS/MISAU/PEPFAR 2018: Ações Prioritárias do  
340 Governo COP 19 [Internet]. 2018. Available from: [https://mz.usembassy.gov/wp-](https://mz.usembassy.gov/wp-content/uploads/sites/182/Acçoes-Prioritárias-do-Governo-COP-19.pdf)  
341 [content/uploads/sites/182/Acçoes-Prioritárias-do-Governo-COP-19.pdf](https://mz.usembassy.gov/wp-content/uploads/sites/182/Acçoes-Prioritárias-do-Governo-COP-19.pdf)
- 342 25. De Schacht C, Mabunda N, Ferreira OC, Ismael N, Calú N, Santos I, et al. High HIV  
343 incidence in the postpartum period sustains vertical transmission in settings with  
344 generalized epidemics: a cohort study in Southern Mozambique. *J Int AIDS Soc*.  
345 2014;17(1):18808.
- 346 26. D Maman; H Huerga; I Mukui; B Chilima; B Kirubi; G Van Cutsem; C Masiku; E  
347 Szumilin; T Ellman; JF Etard. Most Breastfeeding Women with High Viral Load Are  
348 Still Undiagnosed in Sub-Saharan Africa. In: Conference on Retroviruses and  
349 Opportunistic Infections (CROI). Seattle, Washington; 2015.
- 350 27. MOÇAMBIQUE R DE, SAÚDE M DA. Guião Orientador sobre Modelos  
351 Diferenciados de Serviços em Moçambique. 2018;
- 352 28. Hickey MD, Omollo D, Salmen CR, Mattah B, Blat C, Ouma GB, et al. Movement  
353 between facilities for HIV care among a mobile population in Kenya: transfer, loss to  
354 follow-up, and reengagement. *AIDS Care*. 2016;28(11):1386–93.
- 355 29. Lanaspá M, Balcells R, Sacoora C, Nhama A, Aponte JJ, Bassat Q. The performance of  
356 the expanded programme on immunization in a rural area of Mozambique. *Acta Trop*.  
357 2015;149:262–6.
- 358 30. Chamla D, Luo C, Adjorlolo-Johnson G, Vandelaer J, Young M, Costales MO, et al.

359 Integration of HIV infant testing into immunization programmes: a systematic review.

360 Paediatr Int Child Health. 2015;35(4):298–304.

361

362

## Supplemental digital content

**Table:** Socio-demographic and clinical characteristics of children at enrollment in care

Characteristics at enrollment in care		n (%)*
<b>Gender</b>	Male	229 (52%)
	Female	209 (48%)
<b>Age in years</b> , Median (IQR)		3.6 (IQR:1.1-8.6)
<b>Age in years</b>	<1	93 (21%)
	1-4	165 (38%)
	5-9	103 (24%)
	10-15	77 (18%)
<b>Age (years) at ART initiation</b> (n=365)		2.8 (IQR:1.3-8.1)
<b>Year of enrollment in care</b>	2013	190 (43%)
	2014	136 (31%)
	2015	112 (26%)
<b>Mother and father living with the child</b>	Both present	363 (83%)
	One or both absent	75 (17%)
<b>Socioeconomic index (SES)</b>	Low SES	186 (43%)
	Higher SES	180 (41%)
	Unknown	72 (16%)
<b>WHO stage at first visit</b>	I-II	227 (52%)
	III-IV	106 (24%)
	Unknown	105 (24%)
<b>Immunosuppression</b>	No	131 (30%)
	Moderate	128 (29%)
	Severe	86 (20%)
	Unknown	93 (21%)
<b>Anemia</b>	No	264 (60%)
	Yes	54 (12%)
	Unknown	120 (27%)
<b>HIV diagnosis method among children &lt;18 months</b> (n=136)	Virological	70 (52%)
	Serological	28 (20%)
	Unknown	38 (28%)
<b>HIV diagnosis method among children ≥18 months</b> (n=302)	Virological	12 (4%)
	Serological	208 (69%)
	Unknown	82 (27%)
<b>Health problem during the month before enrollment in care</b>	Yes, without hospitalization	40 (9%)
	Yes, with hospitalization	31 (7%)
	No	309 (71%)
	Unknown	55 (13%)
<b>Stunting</b>	No	209 (48%)
	Yes	205 (47%)
	Unknown	24 (5%)

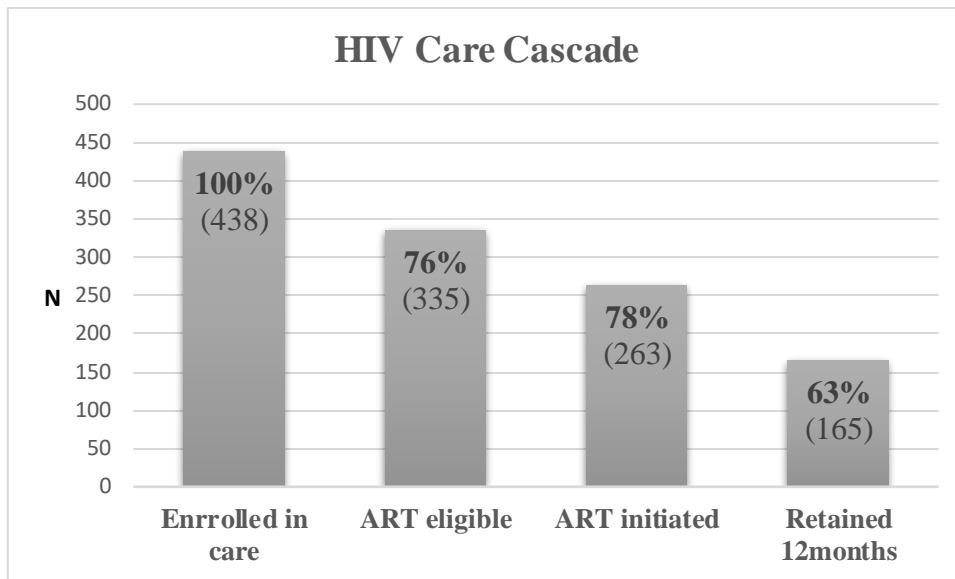
<b>Underweight</b> (in children between 0 and 10yrs) (n=361)	No	252 (70%)
	Yes	93 (26%)
	Unknown	16 (4%)
<b>Wasting</b>	No	331 (76%)
	Yes	46 (11%)
	Unknown	61 (14%)

\*Results expressed as n (%) unless otherwise specified.

N=438 unless otherwise specified.

IQR: Interquartile Range

Severe suppression was defined as CD4 percentage <15%, moderate suppression as CD4 percentage 15 to <25% and no evidence of suppression as CD4 percentage  $\geq$ 25%. Stunting was defined as Height-for-age z-score (HAZ) < -2SD. Underweight was defined as Weight-for-age z-score (WAZ) < -2 SD for children <10 years. Wasting was defined as Weight-for-Height Z-score (WHZ) < -2 SD for children <5 years and body mass index (BMI)-for-Age Z-score (BAZ) < -2 SD for children 5–19 years. Anemia was defined as hemoglobin concentrations of  $\leq$ 8 g/dL. Socioeconomic Index (SES) was represented by a wealth index generated by an asset-based multiple correspondence analysis to categorize the household SES into five wealth quintiles. The two lowest quintiles were grouped as ‘low SES’ and the remaining three quintiles as ‘higher SES’.



**Figure 1: HIV Care Cascade from enrollment to 12-month retention conditioned on the previous step of the cascade.**

The percentage in each column was calculated using as denominator the number of children in the previous column.

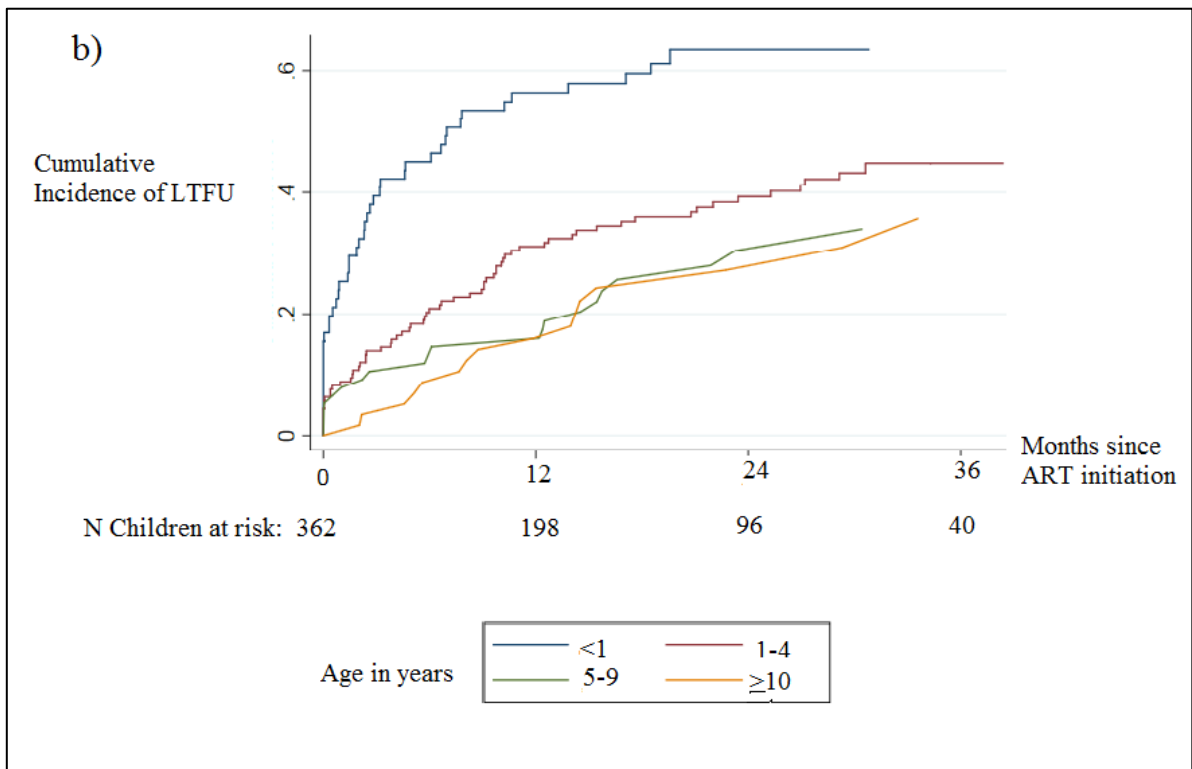
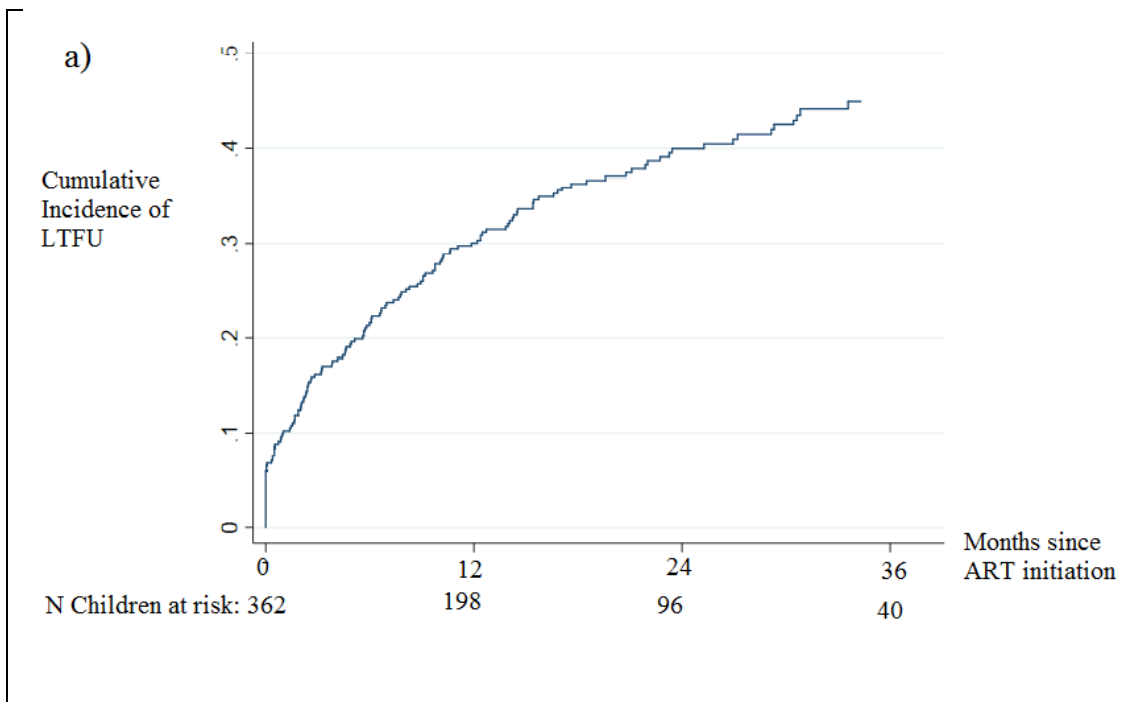
Enrolled in care: with a first clinical visit.

ART eligible at enrollment in care according to national criteria explained in methods.

ART initiated: those who initiated ART within 3 months of enrollment in care.

Retained 12months: retention 12 months after ART initiation with no episode of LTFU.





**Figure 2: Cumulative Incidence of LTFU after ART initiation** among children who initiated ART at any time before the final 90 days of the study period (N=362) for the

overall population (a) and according to age group (b) Cumulative incidence is expressed as the proportion of LTFU in a given time period. LTFU: lost to follow-up.

1 **Table 1: Cox regression of factors associated with first episode of LTFU after ART**  
 2 **initiation with competing-risks for death and migration.**

Factors		Univariable Model			Multivariable Model*		
		SHR	(95% Conf. Interval)	p-value	SHR	(95% Conf. Interval)	p-value
Gender ( <i>n</i> = 362)	male	1		0.6511	1		0.8697
	female	1.08	(0.78; 1.49)		0.97	(0.64; 1.47)	
Age at ART initiation ( <i>n</i> = 362)	<1	1		< 0.0001	1		< 0.0001
	1-4	0.50	(0.33; 0.74)		0.41	(0.25; 0.68)	
	5-9	0.32	(0.19; 0.55)		0.24	(0.12; 0.47)	
	10-15	0.31	(0.18; 0.54)		0.26	(0.13; 0.53)	
Year of enrollment in care ( <i>n</i> = 362)	2013	1		0.3053			
	2014	1.33	(0.92; 1.93)				
	2015	1.12	(0.73; 1.71)				
Time from enrollment in care to ART initiation		1	(1-1)	0.046			
Mother & father status ( <i>n</i> = 362)	Both present	1		0.3164			
	One or both absent	0.80	(0.51; 1.24)				
Socioeconomic index (SES) ( <i>n</i> = 304)	Low SES	1		0.0839			
	Higher SES	0.72	(0.50; 1.04)				
Immunosuppression ( <i>n</i> = 296)	No	1		0.4609			
	Moderate	1.33	(0.84; 2.11)				
	Severe	1.22	(0.76; 1.96)				
Anemia ( <i>n</i> = 275)	no	1		0.0290			
	yes	1.67	(1.05; 2.65)				

WHO stage at enrollment in care ( <i>n</i> = 243)	I-II	1	0.0431	1	0.0554
	III-IV	1.70	(1.02; 2.84)	1.66	(0.99; 2.78)
Health problem during the month before enrollment in care1 ( <i>n</i> = 312)	Yes	1	0.4699		
	No	0.84	(0.53; 1.34)		
Stunting ( <i>n</i> = 343)	no	1	0.5108		
	yes	0.89	(0.64; 1.25)		
Wasting ( <i>n</i> = 309)	no	1	0.0395		
	yes	1.67	(1.03; 2.73)		

\*Number of observations = 243

SHR: Subhazard Ratio

Severe suppression was defined as CD4 percentage <15%, moderate suppression as CD4 percentage 15 to <25% and no evidence of suppression as CD4 percentage ≥25%. Stunting was defined as Height-for-age z-score (HAZ) < -2SD.

Underweight was defined as Weight-for-age z-score (WAZ) < -2 SD for children <10 years. Wasting was defined as Weight-for-Height Z-score (WHZ) < -2 SD for children <5 years and body mass index (BMI)-for-Age Z-score (BAZ) < -2 SD for children 5–19 years. Anemia was defined as hemoglobin concentrations of ≤8 g/dL,

3

4