

Better Outcomes Among HIV-Infected Rwandan Children 18–60 Months of Age After the Implementation of “Treat All”

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Background: In 2012, Rwanda introduced a Treat All approach for HIV-infected children younger than 5 years. We compared antiretroviral therapy (ART) initiation, outcomes, and retention, before and after this change.

Methods: We conducted a retrospective study of children enrolled into care between June 2009 and December 2011 [Before Treat All (BTA) cohort] and between July 2012 and April 2015 [Treat All (TA) cohort].

Setting: Medical records of a nationally representative sample were abstracted for all eligible aged 18–60 months from 100 Rwandan public health facilities.

Results: We abstracted 374 medical records: 227 in the BTA and 147 in the TA cohorts. Mean (SD) age at enrollment was [3 years (1.1)]. Among BTA, 59% initiated ART within 1 year, vs. 89% in the TA cohort. Median time to ART initiation was 68 days (interquartile range 14–494) for BTA and 9 days (interquartile range 0–28) for TA ($P < 0.0001$), with 9 (5%) undergoing same-day initiation in BTA compared with 50 (37%) in TA ($P < 0.0001$). Before ART initiation, 59% in the BTA reported at least one health condition compared with 35% in the TA cohort ($P < 0.0001$). Although overall loss to follow-up was similar between cohorts (BTA: 13%, TA: 8%, $P = 0.18$), loss to follow-up before ART was significantly higher in the BTA (8%) compared with the TA cohort (2%) ($P = 0.02$).

Conclusions: Nearly 90% of Rwandan children started on ART within 1 year of enrollment, most within 1 month, with greater than 90% retention after implementation of TA. TA was also associated with fewer morbidities.

Key Words: children, antiretroviral therapy, HIV, Treat All

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INTRODUCTION

Evidence for determining optimal timing for starting antiretroviral therapy (ART) for HIV-infected children diagnosed after infancy is limited. As ART is a lifelong commitment, the benefits of ART must be considered against long-term risk of drug resistance and treatment failure as well as toxicity from ART exposure during critical periods of childhood growth and development. Recent guidelines endorse initiating lifelong combination ART for all HIV-infected individuals regardless of clinical or immunologic status or age of diagnosis.¹ Although there is strong evidence that prompt ART initiation provides a substantial survival benefit for children aged 0–12 months, there is less evidence for children diagnosed at older ages. The Children with HIV Early Antiretroviral Therapy (CHER) trial in South Africa found a 76% survival benefit in infants initiated on ART compared with those randomized to defer treatment until immunologically or clinically indicated.² Reduced mortality was also observed among infants randomized to immediate ART treatment compared with those randomized to defer ART until clinical or CD4 criteria were reached.³ Conversely, a multicenter randomized trial conducted in Thailand and Cambodia involving 300 HIV-infected children between 1 and 12 years of age failed to detect differences in AIDS-free survival for children receiving early treatment compared with those initiated based on clinical or CD4 criteria.^{4,5} In addition, a causal modeling analysis using observational data from 2934 Southern African children failed to detect differences in 3-year mortality or outcomes among 2- to 5-year-olds initiated on ART immediately compared with those started at specified CD4% thresholds.⁶

Results from several studies indicate that ART improves childhood growth, which is commonly compromised in children with HIV.^{7–10} Growth recovery occurs more

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rapidly among those treated early in the first 2 years of life.^{10–12} However, the relative effects of immediate ART initiation on preventing or ameliorating growth retardation in older children are less clear.

Apart from any potential clinical benefit, strategies to treat all HIV-infected children after diagnosis may offer programmatic and implementation advantages because of the simplification of treatment decision-making. This approach may also reduce the high loss to follow-up (LTFU) reported during the pre-ART monitoring period.¹³

In 2012, the Rwandan National Pediatric HIV Treatment Guidelines recommended initiation of combination ART for all HIV-infected children 5 years and younger. Before this, only children 0–18 months were eligible for ART independent of CD4% and clinical status. ART for children 18 months to 5 years was limited to those with WHO stage 3 or 4 disease or CD4% <25 or CD4 count <750 per dL. The guidelines change offered an opportunity to assess programmatic and health outcomes among Rwandan children aged 18–60 months enrolled in care before and after 2012. Specifically, this analysis compares measures of growth (weight-for-age Z-scores [WAZs]), frequencies of reported medical conditions (eg, opportunistic infections, hospitalizations, and other illnesses), ART initiation and timing of initiation, and patient outcomes [retention, recorded survival, LTFU, and viral load (VL) suppression] between children enrolling before and after the implementation of Treat All.

METHODS

Sampling Frame and Study Population

We conducted a retrospective chart review of a nationally representative sample of HIV-infected children aged 18 months to 5 years at enrollment receiving HIV care at hospitals and health centers in Rwanda during 2 periods: before the implementation of Treat All (BTA) (between July 2009 and December 2011) and after the implementation of Treat All (TA) (between July 2012 and April 2015). Medical records were abstracted for all children for 12 months after enrollment in HIV care.

During these periods, 492 HIV care and treatment clinics were in operation. After excluding 21 atypical clinics (facilities in refugee camps, prisons, or facilities used for special studies), we categorized the remaining 471 facilities based on number of children receiving ART in the year before study initiation (small: <20, medium: 20–49, and large: ≥50 children). We then randomly sampled 50 clinics for data collection using probability proportional to size methodology. A second round of probability proportional to size sampling, selecting an additional 50 clinics from the remaining 421 health facilities, was taken after it was determined that substantially fewer HIV-positive children were enrolled in ART services than expected. In total, 100 health facilities were selected (Fig. 1). We powered our study at 80% to detect a statistically significant difference in the average change in WAZs after enrollment or ART initiation of approximately 10%, and a difference in the proportion reporting health conditions of 10%–12% between cohorts.

Data Collection and Validation

Across the 100 selected facilities, 374 children met eligibility requirements: 174 in the TA cohort and 227 in the BTA cohort. National pediatric ART clinical medical records were abstracted using a laptop-based OpenMRS database. Data were double-entered from a random sample of 30% of records, with at least one record reabstracted from each clinic. After a systematic review of the double-entered data, a data quality assessment was performed where study staff revisited each clinic to compare key outcome indicators between the abstracted database and the paper-based source documents, and corrections were made to the final study database.

Outcome Measures

Baseline characteristics at enrollment into HIV care and at ART initiation were collected for the 2 study cohorts. Comparisons of the proportion of children initiating ART were conducted using χ^2 tests, and median time to ART initiation was compared using Wilcoxon median tests. WAZ, height-for-age (HAZ), and body mass index-for-age (BMIZ) Z-scores were calculated according to WHO standards.¹⁴

For growth after enrollment into HIV care and ART initiation, 2 analyses were conducted. First, analyses of average Z-scores were estimated at key time points (baseline, 3, 6, 9, and 12 months after enrollment or ART initiation) among those children with a recorded measure within 1 (\pm) month of these time points. Second, repeated-measures analyses were conducted for patients with a baseline measure and at least one follow-up measure. In these analyses, generalized estimating equation linear regression models were used, adjusting for timing of weight measure from enrollment or ART initiation. Multivariable models additionally adjusted for enrollment Z-score, sex, age, and indication of severe illness (based on CD4 count, CD4%, and WHO stage) at enrollment. WAZs were used as the primary measure of growth over time because of the higher proportion of longitudinal nonmissing measures (compared with height and BMI). Children were categorized as having severe illness if (1) they were classified as WHO stage IV, or (2) their CD4% was <20% or CD4 count less than 750 cells/mm³ (18–36 months), CD4% less than 15%, or CD4 count <350 cells/mm³ (37–60 months). For these analyses, regression coefficients represent the average change in Z-score since enrollment, comparing children in the TA with those in the BTA cohort.

For comparisons of frequencies of reported health conditions over time, listings of any reported conditions were presented based on information in each patient's medical record. In addition, a summary measure indicated whether a child had ever had a health condition recorded. Frequencies of reported conditions were compared between cohorts using χ^2 tests.

Outcomes were based on information in the medical record and were stratified into those occurring before or after ART initiation including death, transfer out, initiation of ART, LTFU, and retention. Children were considered LTFU if they were not seen in the clinic for greater than 3 months with no subsequent follow-up date recorded. To compare incidence of outcomes before ART initiation between cohorts, competing-risk cumulative incidence functions were constructed, treating ART initiation as a competing risk according to the method of

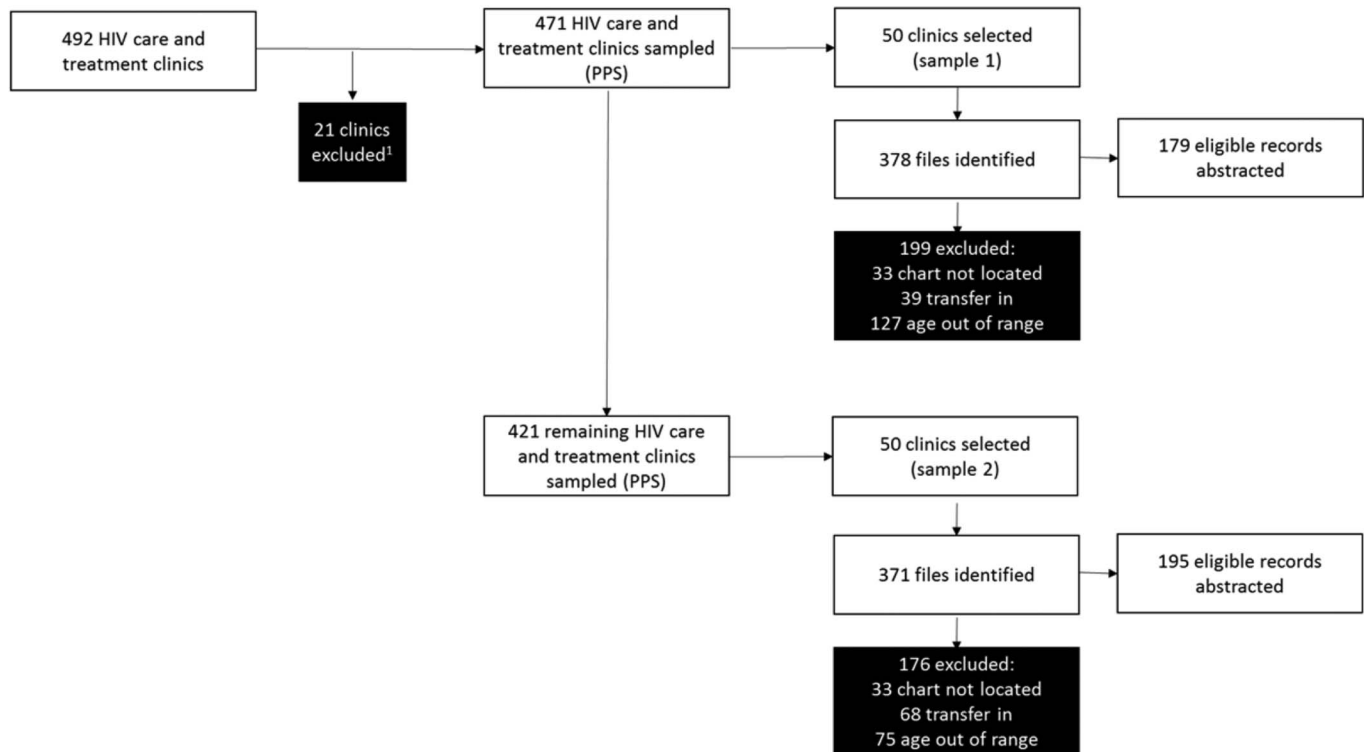


FIGURE 1. Sample selection of Before Treat All and Treat All cohorts.

Fine and Grey.¹⁵ Outcomes assessed in the pre-ART phase included: nonretention (LTFU or death), death, and LTFU. For the outcome of LTFU, death was additionally treated as a competing risk. For outcomes after ART initiation, death was considered a competing risk for LTFU.

Finally, the proportion initiating ART who achieved VL suppression was estimated among the subgroup of children with a VL test result measured at least 6 months after ART initiation. Because an insufficient number of children in the BTA cohort had VL tests performed 6 or more months after ART initiation, we were unable to compare VL suppression between cohorts.

All analyses were performed without consideration of within-clinic clustering because of the small number of children per cluster.

Approval for this study was obtained from Columbia University and US Centers for Disease Control and Prevention Institutional Review Boards and the Rwanda National Ethics Committee.

RESULTS

The study cohort inception is presented in Figure 1. Seven hundred forty-nine medical records of children between 1 and 5 years of age were identified from the on-site registers of 82 of 100 health facilities; no children 1–5 years of age were listed on on-site registers at the remaining 18 selected sites. Clinical medical records were queried for the 749 identified children and were located for 683 (91%).

Of the 683 records, 202 (29.6%) were excluded because they were <18 months or >5 years of age at enrollment based on more determinative information in the clinical medical records. An additional 107 (15.7%) were excluded because they had transferred in from another facility after previously enrolling in HIV care services. Consequently, 374 medical records were abstracted from 82 sites including 147 in the TA and 227 in the BTA cohort (Fig. 1).

Characteristics at Enrollment and ART Initiation

Table 1 presents characteristics of the evaluation population, overall and stratified by cohort. Across both cohorts, 55% were male, with a slightly higher proportion of males in the BTA (58%) compared with the TA cohort (49%). Average age at enrollment was 3 years (SD: 1.05 years). WAZ, HAZ, and BMIZ at enrollment were similar between cohorts [mean (SD) WAZ: -1.74 (1.67), HAZ: -2.66 (2.95), BMIAZ: 0.19 (2.32)]. Of note, 42% of children had an enrollment WAZ < -2 indicative of moderate to severe malnutrition.

Table 1 also presents characteristics at ART initiation, overall and stratified by cohort. Ninety-one percent of all children in the TA cohort initiated ART, compared with 79% in the BTA cohort ($P = 0.003$). Within 1 year of enrollment, 89% in the TA cohort initiated ART, compared with 59% in the BTA cohort ($P < 0.0001$). Among those initiating ART in the TA cohort, 51% would not have been eligible for ART

TABLE 1. Characteristics at Enrollment Into HIV Care and at ART Initiation

N	Total		Treat All Cohort		Before Treat All Cohort		P
	N	%	N	%	N	%	
	374		147		227		
Male	204	55%	72	49	132	58	0.08
Female	170	45%	75	51	95	42	
Age (yrs)							
Age: mean (SD)	3.05 (1.05)		2.95 (1.10)		3.11 (1.01)		0.34
<2 yrs	80	21%	41	28	39	17	
2–3 yrs	112	30%	38	26	74	33	0.09
3–4 yrs	99	26%	36	24	63	28	
4–5 yrs	83	22%	32	22	51	22	
WHO III or IV at enrollment	140	37.4%	41	27.9	99	43.6	0.002
Weight-for-age Z-score at enrollment*							
Mean (SD)	−1.74 (1.67)		−1.77 (1.73)		−1.70 (1.61)		0.70
<−2	157	42%	62	42	95	42	
−1 to −2	89	24%	37	25	52	23	
0 to −1	74	20%	26	18	48	21	0.40
0 to 1	29	8%	16	11	13	6	
>1	13	3%	4	3	9	4	
Missing	12	3%	2	1	10	4	
Height-for-age Z-score at enrollment*							
Mean (SD)	−2.66 (2.95)		−2.74 (3.08)		−2.60 (2.85)		0.68
<−2	224	60%	92	63	132	58	
−1 to −2	50	13%	20	14	30	13	
0 to −1	15	4%	6	4	9	4	0.99
0 to 1	13	3%	6	4	7	3	
>1	20	5%	8	5	12	5	
Missing	52	14%	15	10	37	16	
BMI for age Z-score at enrollment*							
Mean (SD)	0.19 (2.32)		0.22 (2.32)		0.17 (2.31)		0.86
<−2	40	11%	16	11	24	11	
−1 to −2	34	9%	14	10	20	9	
0 to −1	58	16%	22	15	36	16	0.92
0 to 1	84	22%	38	26	46	20	
>1	105	28%	42	29	63	28	
Missing	53	14%	15	10	38	17	
Ever-initiated ART	314	84%	134	91	180	79	0.003
Initiated ART within 1 year of enrollment	265	71%	131	89	134	59	<0.0001
Percent ever initiating ART not eligible under 2009 guidelines			68	51	N/A		
Median (IQR) time to ART initiation, days			9 (0–28)		67.5 (14–493.5)		<0.0001
Severe illness at ART initiation†							
Yes	163	52%	87	65	76	42	
No	77	25%	32	24	45	25	0.09
Missing	74	24%	15	11	59	33	
Weight-for-age Z-score among those initiating ART*							
Mean (SD)	−1.87 (1.50)		−1.80 (1.46)		−1.92 (1.55)		0.21
<−2	107	34%	51	38	56	31	
−1 to −2	68	22%	35	26	33	18	0.74
0 to −1	50	16%	25	19	25	14	
0 to 1	13	4%	8	6	5	3	
>1	4	1%	3	2	1	1	
Missing	72	23%	12	9	60	33	

(continued on next page)

TABLE 1. (Continued) Characteristics at Enrollment Into HIV Care and at ART Initiation

N	Total		Treat All Cohort		Before Treat All Cohort		P
	N	%	N	%	N	%	
	374		147		227		
Height-for-age Z-score among those initiating ART*							
Mean (SD)	-2.91 (2.31)		-2.74 (2.62)		-3.06 (1.95)		0.79
<-2	152	48%	82	61	70	39	
-1 to -2	26	8%	10	7	16	9	
0 to -1	15	5%	8	6	7	4	0.45
0 to 1	5	2%	4	3	1	1	
>1	6	2%	3	2	3	2	
Missing	110	35%	27	20	83	46	
BMI for age Z-score among those initiating ART*							
Mean (SD)	0.17 (2.23)		0.21 (2.21)		0.13 (2.27)		0.77
<-2	22	7%	8	6	14	8	
-1 to -2	27	9%	15	11	12	7	
0 to -1	33	11%	17	13	16	9	0.59
0 to 1	64	20%	36	27	28	16	
>1	58	18%	31	23	27	15	
Missing	110	35%	27	20	83	46	

*Z-scores calculated based on WHO standard population guidelines. Weight and height measures the closest to enrollment within a window of ±2 months were included in this assessment.

†Children were categorized as having severe illness if (1) they were classified as WHO stage IV or (2) their CD4% was less than 20% or CD4 count less than 750 cells/mm³ (18–36 months), CD4% less than 15% or CD4 count <350 cells/mm³ (37–60 months).

IQR, interquartile range.

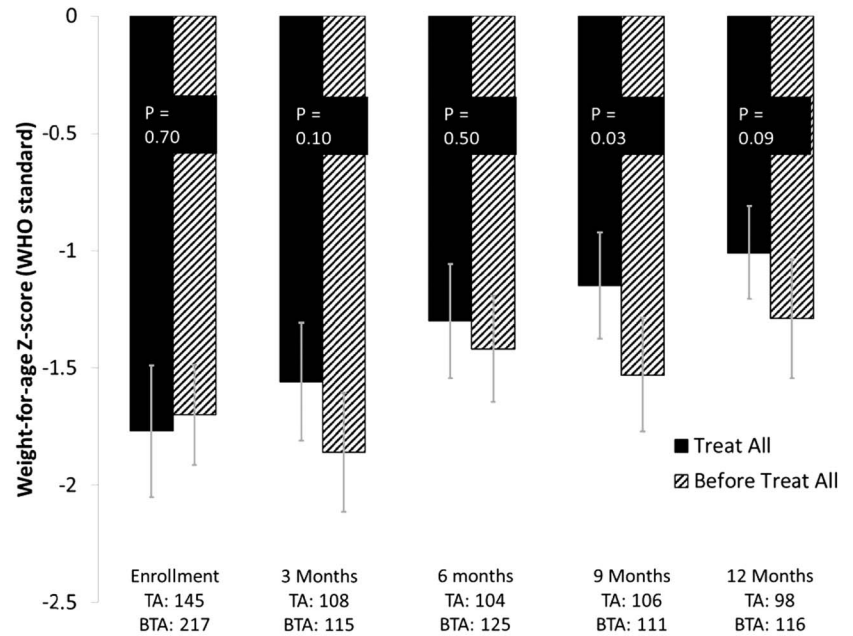
under pre-2012 guidelines. Median (interquartile range) time to ART initiation was 9 days (0–28 days) in the TA compared with 68 days (14–494 days) in the BTA cohort (*P* < 0.0001).

Change in WAZ Over Time

Three hundred sixty-two children (97%) had a weight measure within 2 months of enrollment, 145 (99%) in the TA and 217 (96%) in the BTA cohort. Sixty percent had a weight measure at 3 months, 61% at 6 months, 58% at 9 months, and 57% at 12 months after enrollment, with a significantly higher proportion having these measures in the TA (73% at 3 m, 71% at 6 m, 72% at 9 m, and 67% at 12 m) compared with the BTA cohort (51% at 3 m, 55% at 6 m, 49% at 9 m, and 51% at 12 m). Average WAZ was similar between groups at enrollment (Table 1). After enrollment, mean WAZ was higher in the TA compared with the BTA cohort [3 m mean (SD) WAZ: -1.56 (1.33) TA vs. -1.86 (1.39) BTA, *P* = 0.10; 6 m mean (SD) WAZ: -1.30 (1.27) TA vs. -1.42 (1.29) BTA, *P* = 0.50; 9 m mean (SD) WAZ: -1.15 (1.19) TA vs. -1.53 (1.30) BTA, *P* = 0.03; 12 m mean (SD) WAZ: -1.01 (1.00) TA vs. -1.29 (1.39) BTA, *P* = 0.09] (Fig. 2A). Among the 314 initiating ART, 242 (77%) had a weight measure within 1 month of ART initiation, with a higher proportion having a recorded weight in the TA (91%) compared with the BTA cohort (67%). Sixty-one percent had a weight measure at 3 months, 61% at 6 months, 58% at 9 months, and 55% at 12 months after ART initiation, with a higher proportion having these measures in the TA (75% at

3 m, 75% at 6 m, 73% at 9 m, and 67% at 12 m) compared with the BTA cohort (51% at 3 m, 52% at 6 m, 47% at 9 m, and 46% at 12 m). The average WAZ at ART initiation and follow-up was higher in the TA compared with the BTA cohort [ART initiation mean (SD) WAZ: -1.76 (1.42) TA vs. -1.98 (1.35) BTA, *P* = 0.21; 3 m mean (SD) WAZ: -1.48 (1.15) TA vs. -1.84 (1.43) BTA, *P* = 0.05; 6 m mean (SD) WAZ: -1.36 (1.20) TA vs. -1.52 (1.26) BTA, *P* = 0.38; 9 m mean (SD) WAZ: -1.12 (1.16) TA vs. -1.46 (1.19) BTA, *P* = 0.06; 12 m mean (SD) WAZ: -1.13 (1.10) TA vs. -1.41 (1.22) BTA, *P* = 0.13] (Fig. 2B).

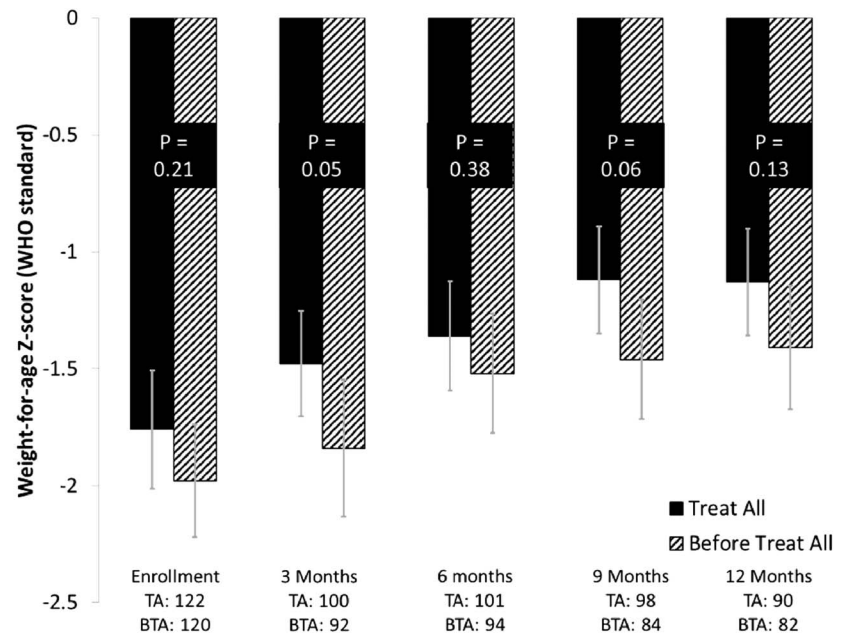
In analyses restricted to the 329 (88%) children with an enrollment and at least one follow-up WAZ, repeated-measures linear regressions were conducted to estimate the average WAZ change after enrollment, adjusting for baseline WAZ and the timing of the follow-up WAZ measures. In these analyses (Table 2), children in the TA cohort experienced, on average, a 0.25-unit increase in WAZ from baseline compared with those in the BTA cohort (95% CI: 0.09 to 0.40, *P* = 0.02). The difference in WAZ persisted after additionally adjusting for sex, age, and severe illness at enrollment into HIV care (average difference in WAZ between cohorts = 0.26, 95% CI: 0.11 to 0.42, *P* = 0.007). Post hoc analysis further stratified this sample into 3 groups: (1) those in the BTA cohort, (2) those in the TA cohort who were ART eligible under 2009 guidelines, and (3) those in the TA cohort who were ART ineligible according to 2009 guidelines. In this analysis, TA cohort members who were ART eligible under 2009 guidelines experienced, on



Notes:

1. Error bars present the 95% CI for the mean WAZ scores.
2. Numbers on x-axis refer to the number of participants with a measure at the given timepoint.

A



Notes:

1. Error bars present the 95% CI for the mean WAZ scores.
2. Numbers on x-axis refer to the number of participants with a measure at the given timepoint.

B

FIGURE 2. A, Mean weight-for-age Z-score (based on WHO standards) after enrollment in HIV care/treatment. B, Mean weight-for-age Z-score (based on WHO standards) after ART initiation.

average, a 0.42-unit increase in WAZ from baseline compared with those in the BTA cohort (95% CI: 0.21 to 0.63, $P < 0.0001$), whereas TA cohort members who were ART ineligible under 2009 guidelines experienced, on average,

a 0.13-unit increase in WAZ from baseline compared with those in the BTA cohort (95% CI: -0.05 to 0.30, $P = 0.15$). Among the 252 initiating ART with a WAZ at ART initiation and at least one during follow-up (80% of those initiating

TABLE 2. Change in Weight-for-Age Z-Score, Since Enrollment and ART Initiation

Population	Model	N	Beta	95% CI	P
All patients since enrolling into HIV care	Average WAZ during follow-up, adjusting for enrollment WAZ and timing of follow-up measures	Treat All: 133 Before Treat All: 196	0.2469	0.09 to 0.40	0.002
	Additionally adjusting for age, sex, and severe illness at enrollment	Treat All: 133 Before Treat All: 196	0.2626	0.11 to 0.42	0.0007
Patients initiating ART	Average WAZ during follow-up, adjusting for enrollment WAZ and timing of follow-up measures	Treat All: 124 Before Treat All: 128	0.2103	0.03 to 0.39	0.023
	Change in WAZ, additionally adjusting for age, sex, and severe illness at ART initiation	Treat All: 124 Before Treat All: 128	0.2525	0.07 to 0.44	0.007

ART), children in the TA cohort experienced an average 0.21-unit increase in WAZ after ART initiation compared with those in the BTA cohort (95% CI: 0.03 to 0.39, $P = 0.02$), which persisted after adjustment for sex, age, and severe illness at ART initiation (average difference in WAZ between cohorts = 0.25, 95% CI: 0.07 to 0.44, $P = 0.007$). Similar post hoc analyses found that TA cohort members ART eligible under 2009 guidelines experienced an average 0.42-unit increase in WAZ from baseline compared with BTA cohort members (95% CI: 0.17 to 0.66, $P = 0.0009$), whereas TA cohort members who were ART ineligible under 2009 guidelines experienced an average 0.10-unit increase in WAZ from baseline compared with BTA cohort members (95% CI: -0.10 to 0.30, $P = 0.33$).

Mortality and LTFU

One child (0.7%) in the TA cohort and 4 (1.8%) in the BTA cohort died before ART initiation. LTFU before ART initiation was also lower in the TA (2.0%) compared with the BTA cohort (7.9%) (Fig. 3A). Among those initiating ART, death and LTFU after ART initiation was similar across cohorts (Fig. 3B).

Reported Conditions

Incidence of clinical conditions, including opportunistic infections, hospitalizations, and other illnesses, was compared between cohorts overall and separately for conditions occurring before and after ART initiation. Overall, 65% had at least one clinical condition recorded during the period of observation; 61% in the TA and 68% in the BTA cohort ($P = 0.15$). The most common reported conditions included infections not otherwise specified (41%), diarrhea (21%), hospitalization (14%), malnutrition (9%), and respiratory tract infections (8%). Frequency of reported conditions was similar between cohorts.

Before initiation of ART, reported conditions were lower in the TA compared with the BTA cohort (35% vs. 59% respectively, $P < 0.0001$). All pre-ART reported conditions including noncoded infections (TA: 24%, BTA: 41%, $P = 0.001$), diarrhea (TA: 10%, BTA: 19%, $P = 0.02$), respiratory tract infections (TA: 4%, BTA: 9%, $P = 0.07$), and wasting syndrome (TA: 1%, BTA: 5%, $P = 0.02$) were more frequent in the BTA compared with the TA cohort.

After ART initiation, one or more clinical conditions were reported in 35% with similar proportions in both groups. After ART initiation, the primary reported conditions were noncoded infections (17%) and diarrhea (12%), with similar proportions reporting these in both cohorts.

Viral Load

VL measured at least 6 months after ART initiation was available for 56 of 131 in the TA cohort initiating ART within 1 year of enrollment (43%), and 23 of 134 children in the BTA cohort initiating ART within 1 year of enrollment (17%). Of those with a VL measure, 47 (84%) in the TA and 21 (91%) in the BTA cohort were virally suppressed (ie, VL < 1000 copies/mL (Table 3).

DISCUSSION

In 2012, Rwanda implemented national guidelines recommending a TA policy for children 5 years and younger. This study of a nationally representative sample of public health facilities providing ART for children in Rwanda found that nearly 90% of HIV-infected children started on ART within 1 year of enrollment into care under the new guidelines, including a large portion (34%) who began ART on the day of enrollment. These findings provide support for the TA approach as a means of reaching the WHO goals of treating 90% of all children with HIV infection with ART by 2020.

It is estimated that overall 55% of HIV-infected Rwandan children are receiving treatment with ART, considerably below the estimated 81% ART coverage for Rwandan adults. This differential is seen globally as well, with only 43% of HIV-infected children receiving ART in contrast to 54% of adults.¹⁶ Although it remains to be determined if similar results are achievable in other pediatric age groups and in other settings, the recent experience we report here suggests that inclusion of a TA strategy may be important to include in efforts for improving ART coverage for young children.

We found retention of children in care to be similar to previous reports in Rwanda that use routinely reported data^{17,18} but higher than previously reported for this age group in other countries, both before and after introduction of the TA strategy, with better retention observed among those

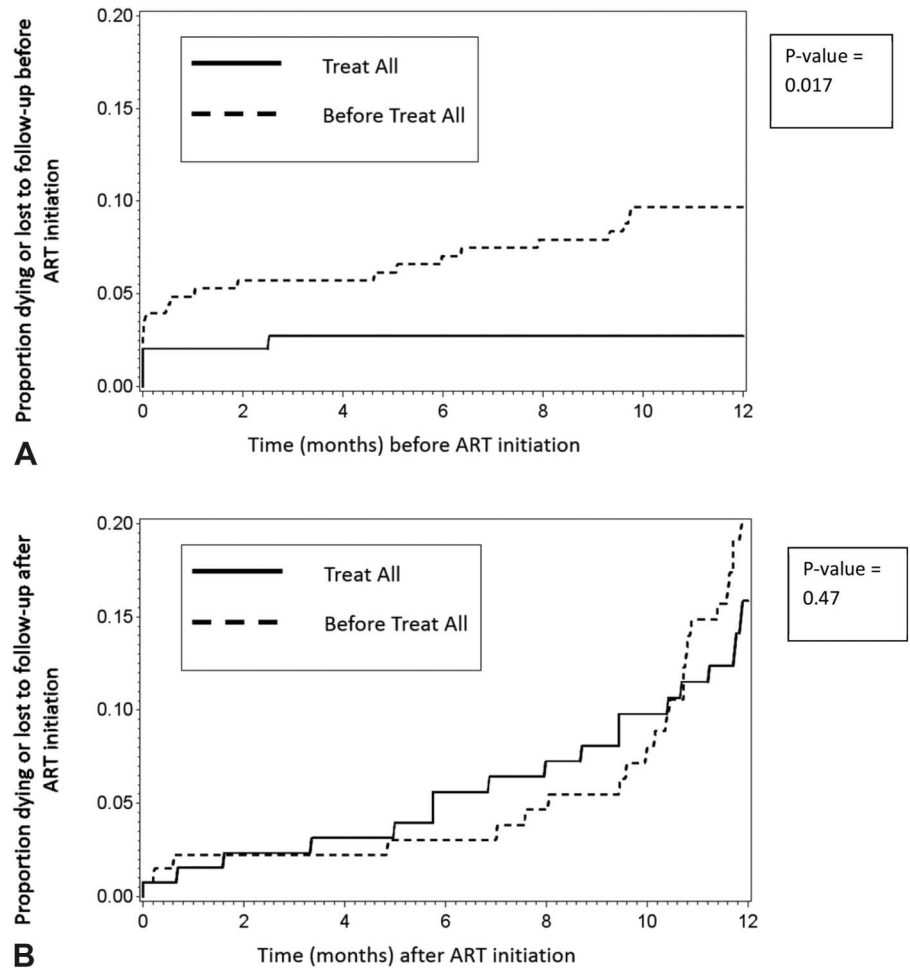


FIGURE 3. A, Cumulative incidence of death or LTFU before ART initiation. *P*-value = 0.017. *Competing-risk cumulative incidence function treating ART initiation as a competing risk. B, Cumulative incidence of death or LTFU after ART initiation. *P*-value = 0.47.

enrolled in care after transitioning to a TA approach.¹³ Our results indicate that practices under TA, which by design greatly reduced the time from enrollment to ART start, were associated with statistically significantly fewer dropouts from care before starting ART, a finding demonstrated among adult patients in Haiti^{19,20} but to our knowledge not yet assessed among children.

Although mortality was lower among children in the TA when compared with children in the BTA cohort before start of ART, given the small numbers of events in both groups, this was not statistically significant, and caution is warranted in drawing conclusions. There were fewer reported conditions in the TA cohort before ART initiation, suggesting that earlier initiation on ART might reduce vulnerability to comorbidities. Because of nonspecific and nonstandardized reporting and limited access to diagnostic testing, it is not possible to ascertain more specifically which conditions were most affected nor were we able to distinguish illnesses from ART-associated adverse events.

Improvements in growth were observed in both groups after ART treatment consistent with previous reports.^{7–12} Although not statistically significant at all time points, overall

a more favorable pattern of growth was observed among the children in the TA cohort compared with those treated under older guidelines. More rapid growth recovery with early ART initiation is also reported in infants with perinatally acquired HIV.²¹ However, despite improvements in WAZ after initiation of ART, children in this study maintained average WAZ scores well below acceptable standards, consistent with other observations among children in Rwanda²² and suggesting that HIV is one of many determinants of poor growth in this setting. Poor growth in childhood has both short- and long-term consequences. Children with poor postnatal growth and malnutrition are at greater risk of common childhood illnesses including malaria, diarrhea, and pneumonia as well as elevated risk of death.²³ Early-life growth faltering often results in irreversible stunting, which in addition to being stigmatizing in many societies, adversely affects outcomes later in life, including pregnancy and birth outcomes as well as reduced work capacity.²⁴ Postnatal growth in early childhood also supports later cognitive development and later educational achievement.²⁵

Although caution is warranted with respect to interpreting VL because of limited availability of VL test results,

TABLE 3. VL Suppression 6 Months After ART Initiation

	Total		Treat All Cohort		Before Treat All Cohort	
	N	%	N	%	N	%
	Initiated ART within 1 yr	265	71	131	89	134
VL measure at least 6 mo after ART initiation	79	30	56	43	23	17
Suppressed (<1000 copies/mL)	68	86	47	84	21	91
At detection limit (20 copies/mL)	48	61	35	63	13	57
21–50 copies/mL	11	14	6	11	5	22
51–100 copies/mL	4	5	1	2	3	13
101–1000 copies/mL	5	6	5	9	0	0
Detectable (≥1000 copies/mL)	11	14	9	16	2	9

especially in the BTA cohort, the limited results are encouraging. This study was conducted while Rwanda and other sub-Saharan African nations began to introduce routine VL testing for all individuals receiving ART. Nonetheless, the high level of viral suppression (84%) is encouraging and exceeds recently available results for children in this age group,^{26–31} however, still falling short of the 2020 WHO goal of achieving viral suppression in 90% of all children receiving ART.

A key limitation of our findings is the noncontemporaneous nature of the treatment groups. Because our cohorts were noncontemporaneous, any differences observed may be due to factors other than changes in ART initiation strategies. Our findings are also vulnerable to a number of biases given the observational nature of the study. Particularly, incomplete data on immune status (CD4⁺ cell count, CD4%, and WHO staging) prevented us from definitively assessing the impact of these measures on outcomes. To maximize data, we created a combined variable of severe illness at enrollment and ART initiation combining available data on CD4 and WHO status. Finally, the lack of specificity in reporting on clinical conditions precluded us from isolating out the impact of the TA strategy on incidence and prevalence of opportunistic infections because these were often nonspecifically coded and difficult to distinguish from other nonopportunistic childhood illnesses.

This nationally representative sample of children attending HIV care and treatment clinics in Rwanda reveals great success in promptly starting children 18 months to 5 years of age on ART after the implementation of TA strategy in Rwanda, concurrent with improved growth trajectories, high retention, and high VL suppression. This assessment suggests that a universal treatment strategy for children is implementable and can be effective in resource-limited settings.

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