# Trends and Predictors of Virologic Failure Following Suppression on Antiretroviral Therapy among HIV Infected Children in Kenya

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**Abstract**

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**Background:**

There are limited data on the incidence and predictors of virologic failure among HIV infected children on antiretroviral treatment (ART), particularly among children who have previously suppressed virus. We examined incidence, timing, and correlates of virologic failure following suppression in a longitudinal cohort of children on ART.

**Methods:**

This analysis utilized data from a prospective cohort study among children 15 months to 12 years old, with moderate to severe HIV disease who were initiated on ART and followed for up to 5.5 years with 3-

monthly measurement of plasma HIV RNA levels. Virologic failure was defined as presence of detectable HIV RNA in plasma after achieving viral suppression (<500 copies/ml). A time to event analysis of virologic failure from viral suppression was conducted and predictors of time to virologic failure were determined using Cox proportional hazards regression models.

**Results:**

Overall, 149 children were initiated on ART with a median time of follow-up time of 49 months (IQR 35, 60 months). Ninety-four (63.1%) children achieved plasma viral suppression, among whom 32 (34.4%) experienced virologic rebound after suppression with an incidence rate of 13.8 failures/100 person-years. Children whose caregivers were housewives or unemployed were significantly less likely to fail following suppression (HR: 0.34, 95%CI: 0.16, 0.72; P=0.005). Caregivers who did not know if their spouses had been HIV tested were more likely to fail on treatment [HR: 2.48, 95%CI: 1.02, 5.99 P=0.04). There was a trend towards failure among children who were visibly wasted at baseline and those who were initiated on a stavudine- based regimen [HR: 1.86; 95%CI: 0.93, 3.73; P=0.08] and [HR: 1.97, 95%CI: 0.96, 4.04 P=0.06] respectively.

**Conclusion:**

We found high rates of virologic failure among HIV infected children on ART despite initial suppression. Caregivers play a critical role in ensuring children's success on ART and may need programmatic strategies to support their roles. Recognition of children at risk for failure can complement scale up of virologic testing capacity to ensure better outcomes.

**Key words:** virologic failure; viral suppression; antiretroviral therapy; HIV; children; pediatric

**Background**

Globally, an estimated 1.8 million children under the age of 15 years are HIV infected, with the vast majority (89%) residing in sub Saharan Africa [1]. While global mortality from HIV/AIDS among adults has declined 45% since its peak a decade ago[2], AIDS-related deaths among children have declined less markedly (32% since 2005). The lower rate of decline in mortality among HIV infected children than adults is due to several factors including late diagnosis of HIV, lower rates of ART initiation[3] [1]. and high rates of virologic failure on antiretroviral therapy(ART) among children[4].

Pediatric ART failure has been called the "silent epidemic"[5] ; treatment failure rates among children in Africa are unacceptably high, ranging from 24%[6] to 53%[7]. Treatment failure in children can lead to adverse lifelong consequences as children are experiencing both physical and mental growth and development. HIV infection and inadequate HIV treatment results in stunting, and impaired physical and neurocognitive development in children[8,9].

Viral suppression to undetectable HIV RNA levels in peripheral blood is the hallmark of successful ART. Children who achieve virologic suppression and maintain it have improved rates of growth and development and decreased morbidity and mortality compared to those who never achieve suppression or those who undergo virologic rebound after suppression[10,11]. Importantly, pediatric virologic failure may lead to the development of drug resistance, which limits future options for ART particularly in low resource settings.

Children and adolescents are more likely to fail on ART than adults[12], however little is known about the predictors of virologic failure among children and adolescents. Until 2015, monitoring of children in many sub Saharan ART programs relied on CD4 and clinical markers. Hence, there are limited data on virologic failure rates and the correlates of virologic failure among HIV infected children. These immunologic and clinical criteria of failure on ART[13] correlate poorly with virologic failure in children as these parameters

lag behind changes in HIV viral load in predicting treatment failure[14, 15]. In this longitudinal cohort of children who initiated ART and were followed at 1-3-monthly intervals for up to 5 years, we examined incidence, timing, and correlates of virologic failure following suppression.

## Methods

### *Study site and population*

This study utilized data collected as part of a randomized clinical trial titled "Long-term Efficacy of Pediatric Highly Active Antiretroviral Therapy (PAD study)" (*R01 TW007632*)[16]. Children were enrolled from the Kenyatta National Hospital (KNH) between August 2004 and December 2006. KNH is located in Nairobi - the capital city, and is the largest tertiary teaching and referral hospital in Kenya. As of July, 2016, the KNH HIV Comprehensive Care Clinic had 8500 patients enrolled of whom 620 were children aged 0 to 14 years.

### *Study procedures*

Parents and caregivers of HIV infected children discharged from the KNH pediatric wards, seen in the pediatric outpatient clinics or in the HIV clinics were invited to participate in the study by nurse counselors. Children 15 months to 12 years old, with moderate to severe HIV disease- WHO clinical stages II to IV, and ART-naïve were eligible to enroll. Additional inclusion criteria were that the caregiver had to be literate and planning to stay in Nairobi for at least one year. Following enrollment, written informed consent was obtained from the child's caregiver and verbal consent was obtained from children 7 to 12 years of age. Swahili, the most widely spoken language in Kenya was used for the consenting process. Child and caregiver enrollment questionnaires were administered to obtain clinical and sociodemographic information, family and medical history. Each child-caregiver pair then underwent a 3-session series of ART adherence counseling over a two week period by trained nurse counselors before ART initiation.

The child-caregiver pair were followed up at 2 weeks and 1 month after initiation of ART, then monthly for the first 9 months and quarterly thereafter. At each visit, a follow-up questionnaire was administered, anthropometric measurements and a clinical examination and assessment of adverse events and adherence was conducted. Every 3 months, 8 mls of blood were drawn from the child for total blood count (TBC), liver function tests (LFTs), urea nitrogen, HIV viral load and CD4 counts. All children were started on ART. The standard WHO regimen during that period was used: zidovudine (ZDV), lamivudine (3TC) and nevirapine (NVP), with efavirenz (EFV) substituted for NVP for children over the age of 3 years. Children with hemoglobin levels of <8g/dl received stavudine (d4T) instead of ZDV.

Children were included in this analysis if they were initiated on ART with a minimum of 3 viral load measurements available. Those who achieved virologic suppression on ART had to have at least one viral load assessment after suppression to be included in the virologic failure analysis

***Covariates of interest***

Child correlates of virologic failure pre-specified for inclusion in the analysis were; age at baseline, gender, visible severe wasting, weight for age z-score (< -2, ≥ 2 standard deviations), baseline CD4 % (<15%, 15-24% and ≥25%) baseline WHO clinical stage (II, III, IV), baseline viral load and ART regimen. The caregiver correlates included were; primary caregiver (mother, father, grandmother, other), gender of primary caregiver, marital status (married, not married), highest achieved education (primary and below, secondary and above), employment (employed, unemployed/housewife), socioeconomic status (number of rooms in house, crowding – number of people per room, flush toilet and sharing of toilet with people outside of home), paternal disclosure of child's HIV status, maternal and paternal deaths, parent tested

for HIV, spouse tested for HIV (yes, no, unknown) and caregiver reported adherence (in the year and 4 months prior to virologic failure date or censoring date).

**Laboratory testing**

HIV testing was conducted in parallel using 2 rapid immunoassays, Determine (Abbott Laboratories, Abbott Park, IL) and Uni-Gold (Trinity Biotech, Dublin, Ireland). Viral load assays for HIV RNA were conducted at the Fred Hutchinson Research Center, Seattle Washington USA using a transcription-mediated amplification (TMA) method (Gen-Probe, San Diego, CA) and CD4 counts were analyzed at the Department of Pediatrics, University of Nairobi, Kenya using the automated FACSCount System (Becton Dickinson, Franklin Lakes, NJ).

**Statistical Analysis**

Description and comparison of the characteristics of participants between the two groups (age <5 years and age 5+ years) were conducted. Means, medians and proportions were compared using t-tests for means, Wilcoxon rank sum tests for medians and chi-square tests for proportions.

Virologic failure was defined the presence of detectable virus in plasma (≥500 copies/ml) after achieving viral suppression (<500copies/ml) any time after initiation of ART up to the end of the follow-up period. A time to event analysis (survival analysis) of time to virologic failure from viral suppression among those who were ever suppressed was conducted. Predictors of time to virologic failure were determined using Cox proportional hazards regression models. Kaplan-Meier curves were used to graphically present the time to virologic failure overall and by relevant variables.

Data were analyzed using Stata (version 14.0, College Station, TX, USA). Power calculations were obtained from power and sample size program v 3.1.2.

The study received ethical approval from the institutional review boards of the University of Washington and the Kenyatta National Hospital. Data were abstracted from a password protected database, all patient identifiers had been de-linked from the data and no attempt was made to contact or follow-up the participants.

**Results**

*Pre-ART Baseline Characteristics*

Overall, 156 children-caregiver pairs were enrolled in the study, 149 initiated ART and 94 (63.1%) achieved plasma viral suppression (<500 copies/ml), of whom, 93 had at least one viral load measurement available after suppression. [Figure 1]

Pre-ART baseline characteristics of the cohort are described in Table 1. Children over 5 years were less likely to have a primary caregiver who was their biological mother (55.6 v. 86.7%, P=0.001), female (81.5 v. 93.1%, P=0.03) and married (53.1 v. 73.3%, P=0.03). Older children (>5 years) were more likely to be orphaned (11.1 v. 1.3%, P= 0.013) or have a deceased parent [mother (34.6 v. 12%, P=0.001), father (22.2 v. 2.7%, P<0.001)] than children <5 years old. They also had lower rates of wasting (23.3 v. 46%, P=0.02) and failure to thrive (2.3 v. 18%, P=0.015). Children over 5 years old had lower median $\log_{10}$ viral loads (5.7 v. 6.1, P=0.007) but lower median CD4% (4.9 v. 9.4, P <0.0001) and more advanced WHO clinical stage pre-treatment at baseline (Stage IV; 24.7 v 6.8%, P=0.01) than children aged under 5 years. Older children were also less likely to have an HIV seropositive (self-reported) biological parent (81.1 v. 95.4%, P=0.04)

and more likely to have a parent who reported that their spouse had undergone HIV testing. (51.7 v. 20.9%, P=0.02). [Table 1]

*Incidence of virologic failure*

Among 93 children who achieved viral suppression and had at least one follow-up viral load assessment, 32 (34.4%) had virologic failure during 232.4 person years of follow-up. The incidence of virologic failure was 13.8 failures/100 person-years. Fourteen percent of children had virologic failure within 12 months of suppression and 25% (20) children failed by 2 years. The median time to virologic failure among those that failed was 30.9 months (IQR: 11.7, 47.2) [Figure 2]

*Age as a predictor of virologic failure*

There was no association between age at ART initiation and virologic failure in this cohort with similar incidence and time to virologic failure among children under 5 as those greater than 5 years old (HR: 0.83, 95% CI: 0.41, 1.67 P=0.60). [Figure 3].

*Child and caregiver correlates of virologic failure*

Children of primary caregivers who were housewives or unemployed were significantly less likely to fail on ART than children of primary caregivers who were employed or working (HR: 0.34, 95%CI: 0.16, 0.72; P=0.005). The children of caregivers who did not know if their spouses had been HIV tested were more likely to fail on treatment [HR: 2.48, 95%CI: 1.02, 5.99 P=0.04). Children who were visibly wasted at baseline (pre-ART) and those who were initiated on a stavudine- based regimen had a trend to be more likely to experience virologic failure [HR:1.86; 95%CI: 0.93, 3.73; P=0.08] and [HR: 1.97, 95%CI: 0.96, 4.04 P=0.06] respectively. [Table 2]

*Caregiver reported adherence*

Because adherence is critical for success on therapy, at every follow up visit caregivers reported if any medication doses had been missed in the preceding 2 weeks and 3 days prior to the appointment. No association was found between caregiver reported adherence and success or failure on ART in the 1 year or in the 4 months prior to failure. Only 2 caregivers reported any missed doses in the 3 visits prior to failing on therapy. [Table 2].

**Discussion**

We observed a high incidence of virologic failure in this cohort of previously suppressed HIV infected children. Overall, only 63.1% were ever virally suppressed and among those who suppressed virus, 34.4% eventually failed on therapy during a median of 49 months on therapy. Failure within the first 12 months of suppression was 14%, lower than what has been reported in a similar study in rural South Africa, in which 38% of the children experienced virologic failure almost all within 12 months of achieving virologic suppression[15]. It is difficult to contextualize our findings to other cohorts, because there are few studies that distinguish between those who never suppress and those who failed after suppression. A Ugandan study assessed virologic failure after 12 months of therapy irrespective of whether suppression had occurred, 26% of children and adolescents aged 0 to 18 years were not suppressed after an average of 1 year of follow up, almost double the failure rate of adults [12]. Studies among children in high income countries have also found an unacceptably high failure rate, in a HIV clinic in Rhode Island USA, 57% of children had virologic failure and 32% never suppressed after 12 months of therapy[17]. Compared to children, studies conducted in adults have demonstrated a lower rate of long term virologic failure after initial suppression, a multicenter clinical trial of ART among adults in 9 diverse countries found a virologic failure rate of 9% after a median of 3.5 years of follow-up[18], a rate much lower than what was demonstrated in our and other pediatric studies. This high virologic failure rate among children is of

concern due to the increased morbidity and mortality and high likelihood of drug resistance which limits lifelong therapy options for these children.

We found that the children of caregivers who were housewives or unemployed (47.3% of the caregivers), were >60% less likely to fail on ART than those who were employed. This was independent of socioeconomic status and caregiver education and may indicate the ability of the caregiver to dedicate more time to the child and to provide medication in a timely and consistent manner. Initial suppression may indicate waning of early adherence to ART administration and suggests that virus may not have had resistance at baseline. Caregivers play a pivotal role in ensuring adherence to therapy and the child's continued success on ART. Children rely on their caregivers to ensure timely and consistent administration of medication as well as nutritional and psychosocial support, all of which have been found to influence treatment outcomes. Understanding caregiver characteristics that predispose to treatment failure is important so that providers can enhance clinical monitoring or implement interventions to prevent failure. Better outcomes on ART have also been found among institutionalized children which may point to the role of timeliness and consistency of medication administration[19], and among children whose caregivers are grandmothers who, because they tend to be unemployed and live in rural areas, may have more time to dedicate to the child[20]. Our findings suggest that it may be beneficial for HIV care and treatment programs to develop systems or interventions, such as phone reminders, to support working caregivers to remember to regularly provide child medications. Health care workers may need to take time to discuss the daily routines and how medication administration could fit within the schedule.

Male partner involvement has been found to contribute to HIV-free survival among infants born to HIV infected mothers [21] presumably due to improved uptake and success of PMTCT [22]. It is plausible that male partner involvement may also contribute to improved treatment outcomes among HIV infected children. We found an increased risk of virologic failure among the children of caregivers (95.6% of whom were female) who were unaware if their partner had ever tested for HIV. We believe that this may indicate a

lack of male partner involvement, commitment or a lack of communication. Developing programs in pediatric HIV care that encourage the engagement of the male partner in care and treatment may contribute towards improving treatment outcomes among these children.

Non-disclosure of the child's HIV status to the partner and other relatives who reside within the home has been found in some studies to influence adherence and treatment outcomes [23]. 55 (51%) of the caregivers reported disclosure to the partner and 30 (32%) reported disclosure to other relatives, however this was not associated with virologic outcomes. Furthermore, as our data was limited to disclosure at baseline, we were unable to assess the effect of disclosure in the follow up period on virologic outcomes. We also found no association between caregiver reported adherence and virologic outcomes, as only 2 caregivers reported any missed doses in the period leading up to virologic failure. This is consistent with prior studies that have demonstrated that caregiver reported adherence correlates poorly with virologic outcomes[24,25], it may also indicate challenges with pediatric dosing and drug bioavailability among children which is influenced by various factors,[26] or the development of drug resistance. There is a need for implementation of more robust measures of adherence in routine care so as to better disaggregate the effect of adherence and other factors on treatment outcomes.

Age at initiation of ART has been observed to be a predictor of virologic failure on ART. Although age category varied from study to study, younger children were generally more likely to fail than older children[6,9]. We however, did not find this association in our study, which could have been a consequence of the limited age range of the children in this cohort with 60% of children aged between 3 and 7 years or the exclusion of infants <15 months. In addition, prior studies have evaluated virologic failure in general, including those who never suppressed which examines a different association. We found that children who were visibly wasted were more likely to fail on therapy although this was not statistically significant. Malnutrition as a determinant of virologic failure among children has been demonstrated in other studies - Bartelink et al found that malnutrition decreased the bioavailability of certain ART regimens among

Ugandan children and predisposed them to virologic failure[27]. Children who were initiated on a stavudine-based first line ART regimen had a higher likelihood of virologic failure than children initiated on an zidovudine based regimen, similar to prior studies[12]. It is important to note that at the time of the cohort, stavudine was still in use as first-line therapy, however, it is no longer recommended for use due to its toxicity profile and is not implemented in programs. Some studies have found a high virologic failure rate on NVP-based regimen among children who were exposed to NVP for prevention of mother-to-child transmission (PMTCT) due to the development of drug resistance[9]. Only 4 of the mothers in our study had received any form of PMTCT, and none of the children had received NVP prophylaxis.

Other studies have demonstrated associations between CD4 count, viral load and clinical stage at baseline and virologic failure[6,7,9]. Most of these studies were cross-sectional in nature with majority of the children having never achieved virologic suppression on ART. We did not find these associations in our study, we hypothesize that because we assessed virologic failure after achieving suppression, the baseline immunological, clinical and virologic status of the child may not play a prominent role in failure subsequent to suppression.

Our study had several strengths. Children were followed up for up to 6 years after achieving viral suppression with quarterly viral loads for the duration of follow up. This enabled good precision to estimate time of virologic failure. Our study is thus one of the few studies in SSA that has been able to study virologic failure longitudinally, long-term and with such close virologic monitoring. There were also limitations to our study; we lacked robust adherence data. Change in primary caregiver status (illness or death), and disclosure of HIV status to the child during follow up may have influenced treatment, however, we lacked data on these two parameters.

## Conclusion

Despite the gains made in HIV prevention and treatment, a substantial number of HIV infected children are failing on ART. We demonstrated high virologic failure rates in the long-term follow up of HIV infected children on ART in Kenya with only 41% achieving and maintaining viral suppression. Recognition of children at risk for failure can complement scale up of virologic testing capacity[28] and early recognition of failure may allow more options for second line therapy before the advent of multiple mutations[29]. HIV programs should support working caregivers to regularly provide medication to the children and encourage male partner involvement in care and treatment of HIV infected children. If we are to achieve the UNAIDS 90-90-90[30] goal we must do more to ensure sustained pediatric success on ART.

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**TABLES AND FIGURES**

**Figure 1: Flow Chart of Viral Suppression and Failure on ART**

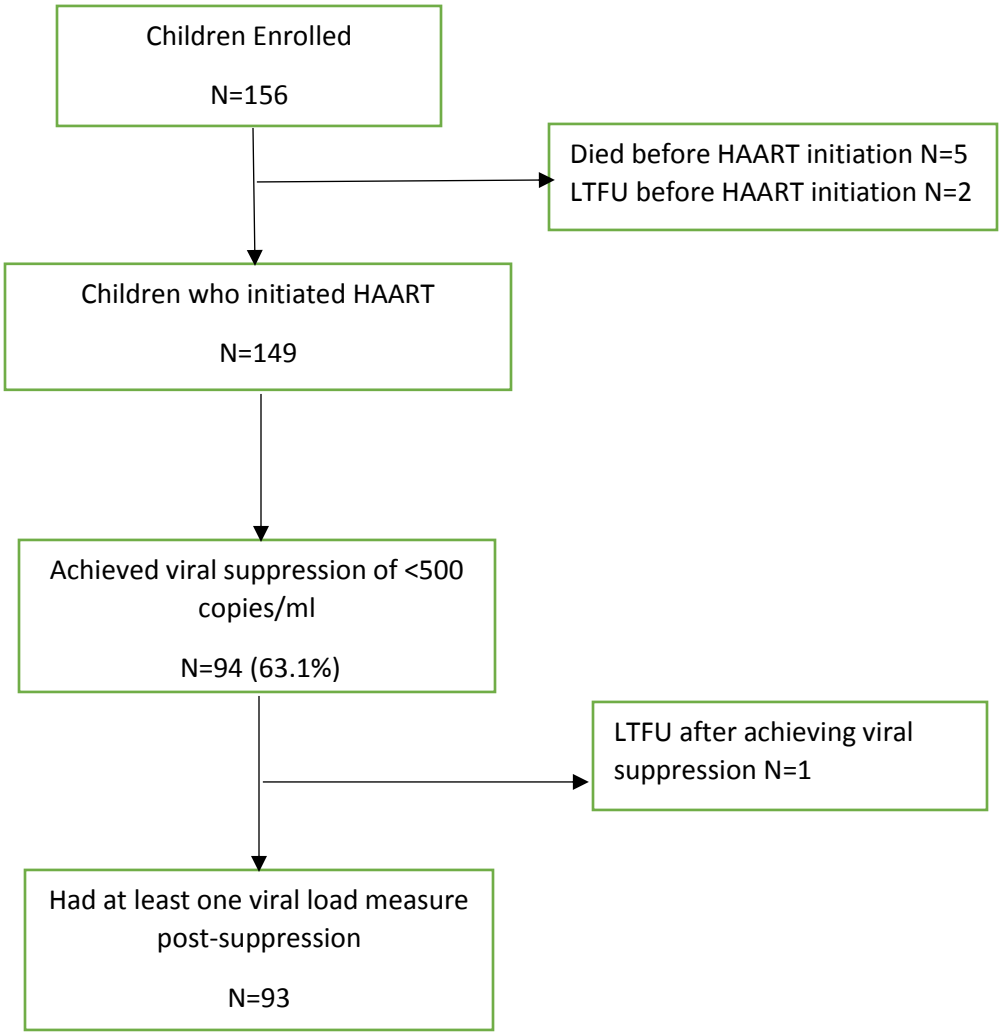


**Figure 2: Kaplan Meier curve of virologic failure among those who were ever suppressed**

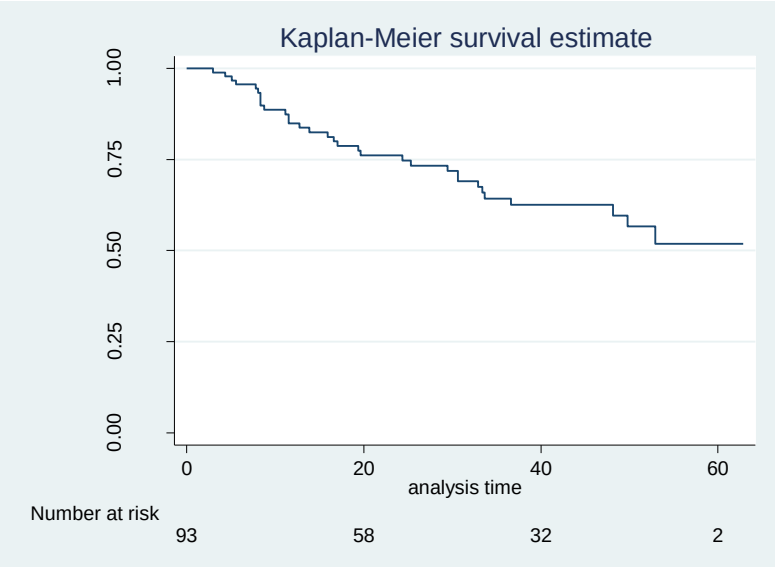
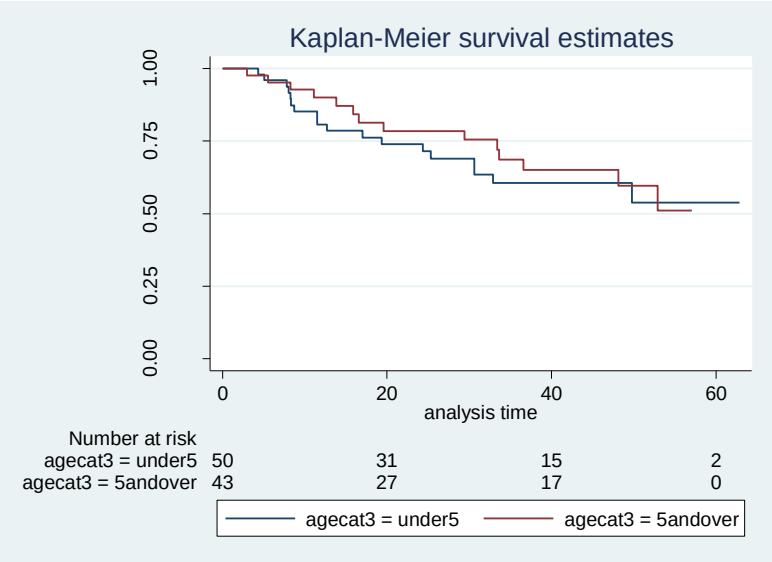


**Figure 3: Kaplan Meier curve of virologic failure after suppression comparing children aged over and under 5 years**



**Tables 1: Baseline Characteristics of <5 year old and >5 year old children**

| Characteristics | | <5 years N=75 | | 5+ years N=81 | |
|---|---|---|---|---|---|
| **Primary Caregiver Characteristics** | **n** | **% or median(IQR)** | **n** | **% or median(IQR)** | **P-value** |
| Biological Mother | 65 | 86.7 | 45 | 55.6 | 0.001 |
| Female | 67 | 93.1 | 66 | 81.5 | 0.03 |
| Married | 55 | 73.3 | 43 | 53.1 | 0.03 |
| Highest education attained is primary school | 33 | 45.2 | 33 | 40.7 | 0.71 |
| Education (years) | 49 | 9.8 | 54 | 9.3 | 0.47 |
| Employment | | | | | |
| Professional | 6 | 8.0 | 8 | 9.9 | |
| Self employed | 11 | 14.7 | 14 | 17.3 | |
| Casual | 14 | 18.7 | 11 | 13.6 | 0.76 |
| Housewife | 30 | 40.0 | 27 | 33.3 | |
| Unemployed | 8 | 10.7 | 10 | 12.4 | |
| Other | 6 | 8.0 | 11 | 13.6 | |
| Socio-economic status | | | | | |
| One roomed house | 45 | 61.6 | 44 | 55.0 | 0.69 |
| # of people in the house | **47** | 4.2 | **43** | 4.4 | 0.57 |
| Density: # of people per room | 47 | 3.1 | 43 | 2.9 | 0.49 |
| Flush toilet | 30 | 41.1 | 40 | 50.0 | 0.27 |
| Shared toilet with people outside of household | 55 | 76.4 | 61 | 78.2 | 0.79 |
| Disclosure of child's HIV status | | | | | |
| Mother knows | 31 | 62.0 | 24 | 55.8 | 0.55 |
| Father knows | 29 | 58.0 | 22 | 51.2 | 0.51 |
| Siblings know | 3 | 6.0 | 2 | 4.7 | 0.78 |
| Other relatives know | 14 | 28.0 | 16 | 37.2 | 0.34 |
| **Parental Characteristics** | | | | | |
| Mother deceased | 9 | 12.0 | 28 | 34.6 | 0.001 |
| Father deceased | 2 | 2.7 | 18 | 22.2 | <0.001 |
| Parent tested for HIV | 44 | 62.9 | 37 | 59.7 | 0.71 |
| HIV test result positive [among tested n=44, 37] | 41 | 95.4 | 30 | 81.1 | 0.04 |
| Spouse tested for HIV | 9 | 20.9 | 15 | 51.7 | 0.02 |
| Spouse test result positive | 5 | 55.6 | 11 | 73.3 | 0.37 |
| Any siblings tested for HIV | 8 | 22.2 | 3 | 12.0 | 0.31 |
| Sibling test result positive | 3 | 37.5 | 2 | 66.7 | 0.39 |
| Mother received PMTCT | 4 | 8.3 | 0 | 0.0 | 0.06 |
| Parent on ART | 10 | 14.5 | 6 | 10.2 | 0.46 |
| **Child Characteristics** | | | | | |
| Female | 39 | 52.0 | 38 | 46.9 | 0.53 |
| Orphan | 1 | 1.3 | 9 | 11.1 | 0.013 |

| | <5 years N=75 | | 5+ years N=81 | | |
|---|---|---|---|---|---|
| | **n** | **% or median(IQR)** | **n** | **% or median(IQR)** | **P-value** |
| Failure to thrive | 9 | 18.0 | 1 | 2.3 | 0.015 |
| Visibly wasted | 23 | 46.0 | 10 | 23.3 | 0.02 |
| Median weight for height Z-score | 72 | -1.1 | 76 | -0.9 | 0.17 |
| Child hospitalized in prior 6 months | 52 | 71.2 | 66 | 81.5 | 0.13 |
| Hospitalized more than once among hospitalized [n=52, 66] | 7 | 24.1 | 6 | 22.2 | 0.87 |
| Received Cotrimoxazole prophylaxis | 39 | 53.4 | 46 | 62.2 | 0.28 |
| Median CD4 count at baseline | 73 | 507 | 80 | 164.5 | <0.0001 |
| Median CD4% at baseline | 69 | 9.4(6.0, 16.2) | 76 | 4.9(2.0, 7.9) | <0.0001 |
| Median viral load at baseline | 66 | 1390450 | 72 | 484850 | 0.003 |
| Median log 10 viral load at baseline | 66 | 6.1(5.8, 6.5) | 72 | 5.7(5.3, 6.4) | 0.007 |
| WHO Clinical Stage | | | | | |
| Stage II | 10 | 13.5 | 8 | 9.9 | |
| Stage III | 59 | 79.7 | 53 | 65.4 | |
| Stage IV | 5 | 6.8 | 20 | 24.7 | 0.01 |

**Table 2: Predictors of virologic failure among children who were initially suppressed on ART**

| | N (%) | Hazard Ratio | 95% CI | P-value |
|---|---|---|---|---|
| **Child correlates** | | | | |
| Age | 93 (100%) | 1.00 | (1.00, 1.00) | 0.27 |
| Age: 5 years and over | 43 (46%) | 0.83 | (0.41, 1.67) | 0.60 |
| Female | 49 (53%) | 0.89 | (0.44, 1.78) | 0.74 |
| Orphan | 5 (5%) | 1.59 | (0.38, 6.70) | 0.53 |
| Failure to thrive | 10 (11%) | 1.46 | (0.51, 4.16) | 0.48 |
| Visibly wasted at baseline | 33 (35%) | 1.86 | (0.93, 3.73) | 0.08 |
| Weight for height Z-score (<-2SD) | 24 (27%) | 1.24 | (0.38, 3.76) | 0.42 |
| Cotrimoxazole prophylaxis at baseline | 55 (62%) | 0.71 | (0.35, 1.44) | 0.34 |
| Baseline CD4 | 92 (99%) | 1.00 | (1.00, 1.00) | 0.47 |
| Baseline CD4 WHO categories | | | | |
| <200 (ref) | 32 (35%) | 1 | | |
| 200 -349 | 15 (16%) | 1.89 | (0.69, 5.17) | 0.22 |
| 350-499 | 13 (14%) | 0.81 | (0.26, 2.53) | 0.71 |
| 500+ | 32 (35%) | 0.99 | (0.43, 2.29) | 0.99 |
| Baseline CD4% | 88 (95%) | 0.99 | (0.95, 1.03) | 0.56 |
| Baseline CD4% WHO categories | | | | |
| <15% | 71 (81%) | 1 | | |
| 15 – 24% | 12 (14%) | 1.70 | (0.73, 3.96) | 0.22 |
| 25+% | 5 (6%) | 0.45 | (0.06, 3.30) | 0.43 |
| Baseline WHO clinical stage | 93 (100%) | 0.84 | (0.41, 1.71) | 0.63 |
| Baseline WHO clinical stage | | | | |
| Stage II | 13 (14%) | 1 | | |
| Stage III | 70 (75%) | 1.09 | (0.38, 3.12) | 0.88 |
| Stage IV | 10 (11%) | 0.59 | (0.11, 3.26) | 0.55 |
| Baseline viral load (copies/ml) | 84 (90%) | 1 | (1.00, 1.00) | 0.31 |
| Baseline viral load (copies/ml) | | | | |
| <500 copies | 1 (1%) | 1 | | |
| 500 – 100,000 copies | 9 (11%) | 0.69 | (0.08, 6.21) | 0.74 |
| 100,001 -1,000,000 copies | 33 (39%) | 0.54 | (0.07, 4.20) | 0.56 |
| >1,000,000 copies | 41 (49%) | 0.57 | (0.07, 4.36) | 0.59 |
| Baseline log viral load | 84 (90%) | 0.90 | (0.61, 1.33) | 0.59 |
| Baseline log viral load | | | | |
| <5.0 | 10 (12%) | 1 | | |
| 5.0 -5.9 | 33 (39%) | 0.74 | (0.26, 2.10) | 0.57 |
| 6.0+ | 41 (49%) | 0.78 | (0.28, 2.15) | 0.63 |
| ART regimen | 93 (100%) | | | |
| AZT+3TC+NVP | 45 (48%) | 1 | | |
| AZT+3TC+EFV | 25 (27%) | 0.87 | (0.33, 2.26) | 0.77 |
| D4T+3TC+NVP | 11 (12%) | 1.47 | (0.52, 4.09) | 0.46 |
| D4T+3TC+EFV | 9 (10%) | 2.15 | (0.77, 5.98) | 0.14 |
| AZT+3TC+ABC | 2 (2%) | 18.0 | (3.61, 89.77) | 0.00 |

| | N (%) | Hazard Ratio | 95% CI | P-value |
|---|---|---|---|---|
| AZT+3TC+NFV | 1 (1%) | 1.40 | (0, .)* | 1.00 |
| ART regimen 2 | 93 (100%) | | | |
| AZT+3TC+EFV/NVP | 70 (75%) | 1 | | |
| Other | 23 (25%) | 1.97 | (0.96, 4.04) | 0.064 |
| **Primary Caregiver correlates** | | | | |
| Primary caregiver | 93 (100%) | | | |
| Mother | 64 (69%) | 1.00 | | |
| Father | 10 (9%) | 1.56 | (0.59, 4.13) | 0.37 |
| Grandmother | 14 (15%) | 0.81 | (0.28, 2.35) | 0.70 |
| Other | 5 (5%) | 0.80 | (0.11, 5.95) | 0.83 |
| Female | 76 (82%) | 0.78 | (0.32, 1.90) | 0.58 |
| Married | 62 (67%) | 0.65 | (0.32, 1.33) | 0.24 |
| Marital status | 93 (100%) | | | |
| Married monogamous | 57 (61%) | 1.00 | | |
| Married polygamous | 5 (5%) | 3.71 | (1.06, 12.96 | 0.04 |
| Steady boyfriend | 2 (2%) | 2.87 | (0.38, 21.74) | 0.31 |
| Separated | 8 (9%) | 2.74 | (0.91, 8.31) | 0.07 |
| Widowed | 8 (9%) | 1.45 | (0.33, 6.32) | 0.62 |
| Single | 13 (14%) | 1.35 | (0.50, 3.66) | 0.55 |
| Highest achieved education | 91 (98%) | | | |
| None | 2 (2%) | 1 | | |
| Primary | 37 (41%) | 0.19 | (0.02, 1.58) | 0.13 |
| Secondary | 39 (43%) | 0.39 | (0.05, 3.02) | 0.37 |
| College | 13 (14%) | 0.39 | (0.04, 3.42) | 0.40 |
| Highest achieved education | | | | |
| Primary and below | 39 (43%) | 1 | | |
| Secondary and above | 52 (57%) | 1.85 | (0.87, 3.92) | 0.11 |
| Employment | 93 (100%) | | | |
| Professional | 9 (10%) | 1 | | |
| Self employed | 17 (18%) | 0.50 | (0.17, 1.47) | 0.21 |
| Casual | 11 (12%) | 0.39 | (0.11, 1.39) | 0.15 |
| House wife | 36 (39%) | 0.18 | (0.06, 0.52) | 0.002 |
| Unemployed | 8 (9%) | 0.17 | (0.03, 0.87) | 0.03 |
| Other | 12 (13%) | 0.41 | (0.11, 1.47) | 0.17 |
| Employment | | | | |
| Employed | 49 (44%) | 1 | | |
| Housewife/Unemployed | 44 (46%) | 0.34 | (0.16, 0.72) | 0.005 |
| Socio-economic status | | | | |
| >1 room in house | 40 (44%) | 0.76 | (0.37, 1.56) | 0.46 |
| 4 or more people living in the house | 62 (69%) | 1.31 | (0.57, 3.06) | 0.53 |
| Density (4 or more/room) | 30 (33%) | 1.38 | (0.67, 2.84) | 0.39 |
| Flush toilet | 42 (46%) | 1.48 | (0.73, 3.01) | 0.28 |
| Share a toilet | 69 (77%) | 1.28 | (0.55, 2.97) | 0.57 |
| Disclosure of child's HIV status | | | | |

| | | | | |
|---|---|---|---|---|
| Father disclosed | 51 (55%) | 0.71 | (0.35, 1.41) | 0.33 |
| Siblings disclosed | 5 (5%) | 1.53 | (0.36, 6.45) | 0.56 |
| Other relatives disclosed | 30 (32%) | 1.18 | (0.57, 2.46) | 0.65 |
| **Parental correlates** | | | | |
| Mother deceased | 24 (26%) | 1.26 | (0.57, 2.82) | 0.57 |
| Father deceased | 8 (9%) | 1.65 | (0.50, 5.47) | 0.41 |
| Mother received PMTCT | 4 (5%) | 0.57 | (0.08, 4.17) | 0.58 |
| Parent tested for HIV | 49 (64%) | 0.70 | (0.34, 1.46) | 0.35 |
| HIV test result reported positive | 44 (92%) | 0.57 | (0.13, 2.56) | 0.47 |
| Spouse tested for HIV | 72 (77%) | | | |
| No | 25 (35%) | 1 | | |
| Yes | 24 (33%) | 0.90 | (0.32, 2.47) | 0.83 |
| Not known | 23 (32%) | 2.48 | (1.02, 5.99) | 0.04 |
| Parent on ART | 12 (16%) | 0.33 | (0.08, 1.40) | 0.13 |
| Caregiver reported adherence in 1st year | 92 (99%) | | | |
| < 100% adherence (3 day recall) | 57 (62%) | 0.72 | (0.35, 1.47) | 0.37 |
| < 100% adherence (2 week recall) | 55 (60%) | 0.87 | (0.42, 1.79) | 0.71 |
| Caregiver reported adherence in 120 days leading to failure/censoring | 92 (99%) | | | |
| < 100% adherence (3 day recall) | 1 (1%) | 1.00 | (0.14, 7.33) | 1.00 |
| < 100% adherence (2 week recall) | 1 (1%) | 1.00 | (0.14, 7.33) | 1.00 |

*model did not converge