



The Outcomes of Transition from Pediatrics to Adult Care among Adolescents and Young Adults with HIV at a Tertiary Care Center in Bangkok

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Abstract

Background: Adolescents and young adults with HIV (AYHIV) are at high-risk of loss to follow up and virologic failure, particularly during transition from pediatric to adult clinics. **Methods:** We reviewed the medical records of AYHIV to characterize retention and virologic suppression following their transition. **Results:** 101 AYHIV, 97% perinatally infected, were transferred at the median age of 20 (IQR: 19-21) years. At 1-year post-transition, 92.1% were retained in care and 73.3% had viral suppression and at 2-years the retention and viral suppression were 87.1% and 76.7%, respectively. Factors associated with viral suppression were transition at ≥ 20 years of age (aOR 4.38, 95% CI 1.41-13.65) and receiving first-line ART regimen, compared to second- or third-line regimens, at transition (aOR 6.05, 95% CI 1.55-23.58). **Conclusion:** Transition outcomes of AYHIV in our setting were suboptimal. There is a need for interventions to support AYHIV transition during this vulnerable period.

Keywords

Transition, outcome, HIV, adolescents, Thailand

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Introduction

Over the decades, advancements in pediatric antiretroviral therapy (ART) have improved clinical outcomes and quality of life for children with HIV. However, adolescents and young adults infected with HIV (AYHIV) face ongoing challenges due to physical, mental, and social factors that influence adherence, and the transition from pediatric or adolescent care to adult care represents a vulnerable time for AYHIV. While great strides have been made in achieving World Health Organization's "95-95-95" targets in 2030 (95% of individuals aware of their HIV status, 95% of people diagnosed with HIV receive sustained ART, and 95% of these ART-treated had viral suppression),¹ AYHIV have lower rates of retention and viral suppression relative to adults on ART.^{2, 3} Determining factors involved in improving care for this population is

crucial, yet important knowledge gaps remain in understanding when and how to optimally transition AYHIV from pediatric to adult treatment programs. The success and challenges of clinic

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transition may be different in various settings, due to differences in healthcare systems, socioeconomic differences, or other factors.⁴ Information on transition outcomes for AYHIV in Asia is still limited.^{5,6} The objective of this study was to describe outcomes and identify factors associated with treatment success following transition of AYHIV from pediatric care in Siriraj Hospital to adult clinics in Thailand.

Methods

Study Design

We retrospectively reviewed the medical records of AYHIV who were on ART at the pediatric HIV clinic at Siriraj Hospital, a tertiary care center in Bangkok, Thailand and transitioned to adult clinics within or outside of Siriraj Hospital between December 1, 2011, to November 30, 2017.

Study Setting

Thailand integrated HIV services include ART into its universal health coverage scheme. Thai citizen can access anti-retroviral medicines for free and are available through public health facilities. The pediatric HIV clinic of Siriraj Hospital is a referral center that provide comprehensive HIV care included free ART to children and adolescent as part of universal health coverage scheme. Most of the patients at Siriraj clinic are from the central part of Thailand. There has been no standard protocol for transitioning AYHIV to adult care in Thailand; the process and age of transition vary depending on the accessibility, conveniency, and healthcare settings. Siriraj Hospital has adult HIV clinic in a separate location and accept referral patients from pediatric clinic if their healthcare plan allows.

The Transition Processes

Transfer of AYHIV from pediatric to adult clinics generally occurs between ages 18–20 years. All the AYHIV are educated about their health and conditions and how to manage their wellness and HIV treatment before transition. Some AYHIV participate the “Happy Teen program” which is the education program specific for adolescents living with HIV, prepare for adulthood including the transition training at clinic visit.⁷ At the time of transfer, a medical summary of the AYHIV is sent to the attending physicians at the adult HIV clinic. The linkage to adult HIV clinic was defined by time elapsed between the last pediatric clinic visit and the first adult clinic visit. There was no standard time for linkage of transition, however, almost of AYHIV were successfully linked to adult clinics within 3–4 months of the last pediatric visit according to the routine follow-up interval.

Data Collection

All AYHIV who age at transfer <25 years and in care at pediatric HIV clinic of Siriraj Hospital for at least 6

months prior to transfer. We abstracted demographic and clinical data including CD4 T-lymphocyte (CD4) cell count, HIV-1 RNA viral load (VL), ART regimen, and available viral genotypes prior to and within 2 years after the transition to an adult clinic. HIV-related post-transition data were obtained from the Thai National AIDS Program database (NAP). NAP obtains the HIV-related data for all Thai citizen that received care under universal coverage scheme which is the National HIV program. The outcomes of interest were drawn from the HIV care continuum with a focus on retention in care and virologic suppression. Retention in care was defined as having presented to the adult clinic for HIV care and ART refills for at least 2 visits separated by at least 3 months within the first 12 months and again at second year after initiating adult care. Those who were not retained in care were classified as dead if there was documented evidence of their death in the NAP database. Virologic suppression was defined as any value below the limit for the hospital-specific assay, which all cutoffs were 50 copies/ml or less, and virological failure was defined as a single VL of > 200 copies/ml.

Statistical Analysis

Results for demographic, clinical data, and retention in care were summarized using descriptive statistics. First line regimens were generally NNRTI-based according to the National Guidelines. The second line (PI-based regimens) or third line regimens (integrase inhibitor-based regimens) were defined as the regimens that were changes to according to the National Guidelines due to drug resistance, not from toxicity. All data was presented using medians, interquartile ranges (IQR) or proportions, as appropriate. Univariate and multivariate logistic regression analyses were performed to identify the factors associated with viral suppression and retention in care. The variables included were sex, age, clinical stage, comorbidity, education level, duration of ART, age at first ART initiation, participation in Happy Teen program, at pre-transition CD4 level and ART regimens, post-transition ART regimens, and the adult clinic transition to. Covariate with p -values <0.05 on univariate analyses was entered into multiple logistic regression analysis using adjusted odd ratios (aOR) with statistical significance defined as p -values <0.05.

Ethical Approval and Informed Consent

The study was approved by the Institutional Review Board (approval no. Si441/2561). Informed consent was waived because the data collected retrospectively and were de-identified for use in this study.

Results

A total of 101 AYHIV transitioned from the Siriraj Hospital pediatric HIV clinic to adult care clinics in Bangkok between

December 1, 2011, and November 30, 2017. Of these, 98 (97.0%) had perinatally acquired HIV, and 55 (54.5%) were female. The median age at diagnosis of HIV was 4.2 years (IQR: 0.8–8.3) while the median age at first ART initiation was 5 years (IQR: 1.5–9.0) and the median duration on ART prior to transition was 14.9 years (IQR: 4.2–20.2). The

median age of transition from pediatric to adult ART care was 20 years (IQR: 19–21). Fifty-one (50.5%) AYHIV transitioned to the adult clinic within the Siriraj Hospital and the remainder to outside clinics. Thirty-two (31.7%) individuals had at least one co-morbidity diagnosed before transition, with the most common being diabetes mellitus and/or

Table 1. Characteristics of AYHIV.

Characteristics	(N = 101)
Female, n (%)	55 (54.5)
Age at transition, median (IQR), year	20 (19–21)
Post-transition follow-up duration, median (IQR), year	2.6 (1.7–3.2)
Age at HIV diagnosis, median (IQR), year	4.2 (0.8–8.3)
Age at first ART initiation, median (IQR), year	5 (1.5–9.0)
Duration on ART prior to transition, median (IQR), year	14.9 (4.2–20.2)
Mode of transmission, n (%)	
Perinatal	98 (97.0)
Sexual transmission	2 (2.0)
Unknown	1 (1.0)
Worst CDC clinical stage, n (%)	
A	27 (26.7)
B	31 (30.7)
C	43 (42.6)
Transitioned to adult clinic within Siriraj Hospital, n (%)	51 (50.5)
Reason for transitioning to adult clinic, n (%)	
Age > 18 years	53 (52.5)
Changed in health insurance coverage	43 (42.6)
Moved houses/logistics	5 (4.9)
Enrolled in transition training program (Happy Teen), n (%)	60 (59.4)
Pre-transitioning	
VL suppression (< 50 copies/mL) prior to transition ^a , n (%)	70 (69.3)
CD4 cell count prior to transition, median (IQR), cell/mm ³	587 (391–767)
CD4 < 200 copies/mL, n/N (%)	12 (11.9)
CD4 < 350 copies/mL, n (%)	20 (19.8)
ART regimens pre-transition, n (%)	
first line ART (NNRTI-based regimens)	44 (43.6)
second line ART (PI-based-based regimens)	52 (51.5)
third line ART (Integrase inhibitor-based regimens)	5 (4.9)
Had ART-resistant virus prior to transition ^b , n (%)	63 (62.4)
NRTI resistant	7/63 (11.1)
NRTI and NNRTI resistant	52/63 (82.5)
PI resistant	4/63 (6.4)
Presence of comorbidity prior to transition, n (%)	32 (31.7%)
Diabetes mellitus and/or dyslipidemia	15 (14.9)
Cognitive impairment	8 (7.9)
AIDS related disease: CMV retinitis	4 (4.0)
Mental health disorders: MDD, bipolar disorder, conduct disorder	5 (5.0)
Highest education prior to transition, n (%)	
Primary school	10 (9.9)
High school	54 (53.5)
Bachelor's degree	33 (32.67)
Post-transitioning	
CD4 cell count at 1-year post-transition, median (IQR), cell/mm ³	565 (367–764)
CD4 < 200 copies/mL, n/N (%)	7/90 (7.8)
CD4 < 350 copies/mL, n/N (%)	17/90 (18.9)
CD 4 cell count at 2-year post-transition, median (IQR), cell/mm ³	536 (297–752)
CD4 < 200 copies/mL, n/N (%)	12/86 (13.9)
CD4 < 350 copies/mL, n/N (%)	22/86 (25.6)

^aPerformed in the 12 months prior to transition to adult clinic

^bBased on any prior genotype

dyslipidemia (14.9%), cognitive impairment (7.9%) and mental health disorder (5.0%). There were 60 (59.4%) AYHIV that participated in the Happy Teen program (Table 1).

At the time of transition, 44 (43.6%) AYHIV were on non-nucleoside reverse transcriptase inhibitor (NNRTI) based first-line ART, 52 (51.5%) were on protease inhibitor (PI) based second-line ART, and 5 (4.9%) were on integrase inhibitor (INSTI) based third-line ART. Seventy AYHIV (69.3%) had a VL < 50 copies/mL and the median CD4 cell count was 587 cells/mm³ (IQR: 391–767), with 11.9% and 19.8% had CD4 cell count <200 and <350 cells/mm³, at the most recent visit in the year prior to transition, respectively (Table 1).

One- and two-Year Outcomes

At one-year post-transition from pediatric to adult care, retention was 92.1%. Of the AYHIV with VL and CD4 data available ($n = 90$), 66 (73.3%) had VL < 50 copies/mL, and the median CD4 count was 565 cells/mm³ (IQR: 367–764), with 7.8% (7/90) and 18.9% (17/90) had CD4 cell count <200 and <350 cells/mm³, respectively (Figure 1, Table 1). Of those with detectable VL, median VL was 5850 copies/mL (IQR: 248–43,605), and 12.5% (3/24) had VL in the range of 200–1000 copies/mL, and 66.7% (16/24) had VL >1000 copies/mL. Of the 31 AYHIV who had viremia before transition, 7 (22.6%) had a suppressed VL in the year following transition. Seven AYHIV who were suppressed pre-transition subsequently developed virologic failure during the first-year post-transition, with a median VL of 10,565 copies/mL (IQR: 369–40,600). There were 3 deaths: 2 due to complications of AIDS, and 1 due to bloodstream infection and arrhythmia (Figure 1).

At 2 years post-transition, retention was 87.1%, and 66 of 86 (76.7%) had viral suppression, and the median CD4 count was 536 cells/mm³ (IQR: 297–752), with 13.9% (12/86) and 25.6% (22/86) had CD4 cell count <200 and <350 cells/mm³, respectively (Figure 1, Table 1). Of the 20 AYHIV with detectable VL, the median was 21,455 copies/mL. (IQR: 1400–49,911), 5.0% (1/20) had VL in the range 200–1000 copies/mL, and 85.0% (17/20) had VL >1000 copies/mL., 12 (60%) had persistent viremia from pre-transition, and 8 (40%) had newly developed virologic failure in the second year after transition. The 7 AYHIV who developed virological failure during their first-year post-transition subsequently suppressed during the second year after transition. There were additional 3 deaths in the second-year post-transition, and all were died at home with unclear causes of death, resulting in 5.9% mortality rate over 2 years (Figure 1) with the median age at death of 22 years (IQR: 20–24). All of the deceased patients had advance HIV stage due to persistently poor ART adherence during pre- and post-transition. There was no statistical difference in viral suppression from pre- and post-transition among the AYHIV who remained in care post-transition (pre-to 1-year post-transition; $p = 1.0$, pre- to 2-year post-transition; $p = 1.0$, 1-year to 2-year post-transition; $p = 0.2$).

Factors Associated with Viral Suppression After Transition

In univariate analysis, the factors associated with viral suppression at 1-year post-transition were having pre-transition CD4 >500 cells/mm³, and receiving first-line ART (NNRTI-based regimens) at pre-transition. In multivariate analysis, having a pre-transition CD4 >500 cells/mm³, and receiving first-line

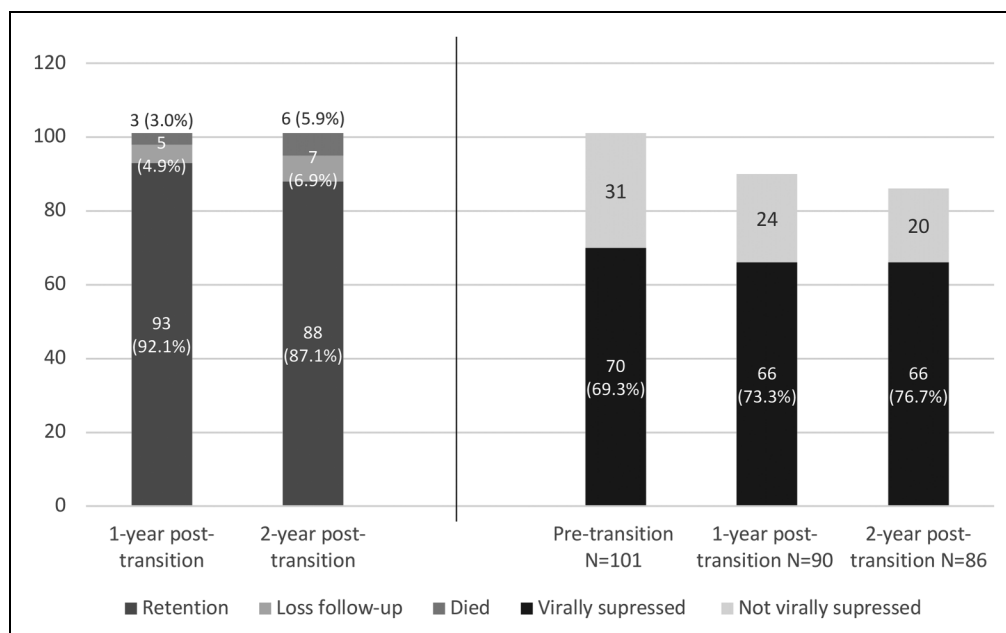


Figure 1. One- and two-year outcomes after transition (left) and the percentage of viral suppression at 1-, and 2-year post-transition (right).

ART pre-transition remained significant (adjusted odd ratio [aOR]: 6.16; 95% Confidential interval [CI]: 1.93–19.62, $p = 0.002$, and aOR: 9.66; 95% CI: 2.34–39.82, $p = 0.002$, respectively). At 2 years post-transition, age at the time of transition of ≥ 20 years, experienced HIV clinical stage C, having a pre-transition CD4 count of >500 cells/mm³, receiving first-line ART regimen at pre- and post-transition were all associated with viral suppression in univariate analysis. In multivariate analysis, transitioning at ≥ 20 years of age (aOR: 4.38; 95% CI: 1.41–13.65, $p = 0.011$) and receiving first-line regimen compared to second- or third-line ART regimen at the time of transition (aOR: 6.05; 95% CI: 1.55–23.58, $p = 0.010$), were the only significant factors (Table 2).

In logistic regression, the AYHIV who receiving first-line ART regimen were less likely to have any of the composite outcome of death, loss to follow-up, or virological failure at 1- and 2-year post-transition (OR: 0.19, $p = 0.001$, and OR: 0.23, $p = 0.005$, respectively, compare with those who were receiving second- or third-line regimens (Figure 2).

Factors Associated with Retention in Care After Transition

There was no factor found to be significantly associated with retention in care after either at 1-or 2-year post-transitions (supplementary).

Discussion

Progress in the treatment and care of people living with HIV over the last 30 years has allowed infants with HIV to live into adolescence, creating a need for transitions from pediatric to adult clinics. Data from our cohort of AYHIV transitioning to adult care show low rates of viral suppression at pre-transition and over two years of follow-up: 69.3%, 73.3% and 76.7%, respectively. These rates were lower than that Thailand's HIV care cascade reported in 2020 which revealed 84% of HIV-treated were virally suppressed.⁸ Additionally, we found suboptimal rates of retention in care over two years of follow-up and will lead to below 95–95–95 treatment target, the retention in care rate at 1- and 2-years post-transition to an adult clinic was 92.1% and 87.1%, respectively. However, these rates exceed retention rate reported previously from Thailand in which only 73% of AYHIV were retained in care at 2–5 years post-transition.⁵ The longer period of follow-up may explain the lower rate in that study as retention may decline over the time. The retention rate following transition AYHIV across studies from wealthy countries varies from 76–94.7% at 1–2 years post-transition.^{9–13} Our findings are similar to a South African study in which 90% of 460 AYHIV who transitioned to adult care were retained at 1 year and 84% at 3 years post-transition.¹⁴ It is noteworthy, the proportion of AYHIV who were retained in care post-transition in both high- and low-middle income countries appeared to be highest within the first two years of transition and decrease over time.^{10,14,15} In many

settings including Thailand, adult clinics often provide less support than that provided in the pediatric setting, and, along with challenges associated with adjusting to the adult clinic environment, this could be make it more difficult for AYHIV to remain in HIV care.³ One US-based qualitative studies identified that AYHIV who prepared for readiness in transition program as a key factor in successful of transition, however, we did not find that AYHIV who participated in Happy Teen Program had a better outcome.¹⁶

Our study suggests that virologically suppressed adolescents are likely to remain suppressed after transition to adult care, while those with virologic failure at the pediatric clinic were unlikely to suppress after transition. In contrast, we did find a small number of AYHIV developed virologic failure after transition despite a history of remaining suppressed in pediatric clinic. A study in Netherlands reported that AYHIV between 18–19 years were more likely to have virologic failure around the time of transition compared with the children aged 12–13 years, with low educational attainment and lack of autonomy regarding medication adherence at transition factors associated with virologic failure,¹³ however, we did not find such association in our study. Our study found age 20 or older and use of a first-line ART (NNRTI regimen) were factors associated with viral suppression after transition. The latter factor reflects better adherence rather than anything intrinsic to the NNRTI class. However, the interpretation of this result should be with caution as the confidential intervals are wide. Those AYHIV who were receiving second line or salvage regimens should receive extra support throughout the transition or be continued in pediatric care for a longer duration. A study in Canada found 92% of AYHIV reported that 18 was too young for transition to adult care due to issues with being unable to fully comprehend how to set up their own appointments and as a result of the limited support provided by clinicians in adult clinic settings.⁹ Likewise, in a study of 951 ALWH in South Africa, 64.7% chose to remain in pediatric care rather than transition to adult care.¹⁷

The recommended age for transition to adult care set by the Association of American Physicians (AAP) is 18–25 years.⁴ The adolescent brain continues to develop into early adulthood, affecting learning and memory reinforcement and complex processing, and deficits in these areas appear to correlate with nadir of immune suppression, exposure to certain ART regimens, and early childhood encephalopathy.^{18,19} Lack of developmental readiness has been associated with poor ART adherence and viremia.²⁰ Perhaps delayed transition to adult care may improve overall treatment outcomes particularly across a variety of settings, including in Thailand.

Mortality of AYHIV ranges from 4–9%,^{5,9,12,17,21,22} and most of youth who die have poor ART adherence with causes of death linked to advanced HIV disease, though it is notable that some studies could not determine cause of death. Our findings are similar to these studies, with a mortality rate of 5.9% and half of these deaths from complications of advanced HIV and half from unknown causes.

Our study has several limitations. First, this was a retrospective review of medical records, and we had some

Table 2. Factors Associated to Viral Suppression at 1- and 2-Year Post-Transition.

Variables	1-year post-transition			2-year post-transition		
	Univariate analysis		Multivariate analysis	Univariate analysis		Multivariate analysis
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Female	1.60 (0.64–4.00)	0.316			2.17 (0.78–6.01)	0.137
Age at transition ≥ 20 years	1.94 (0.77–4.89)	0.158	1.04 (0.26–4.17)	0.952	4.36 (1.48–12.87)	0.008
Worst CDC clinical stage					4.38 (1.41–13.65)	0.011
A	1					
B	1.36(0.40–4.56)	0.622			2.00 (0.58–6.85)	0.270
C	1.32 (0.44–3.95)	0.621			3.72 (1.06–13.05)	0.040
Presence of comorbidity prior to transition	2.20 (0.87–5.59)	0.098			2.14 (0.77–5.93)	0.142
Highest education prior to transition						
Primary school	1					
High school	0.45 (0.11–1.84)	0.267			1.03 (0.27–3.94)	0.962
Bachelor's degree	1.14 (0.24–5.39)	0.872			2.50 (0.52–11.99)	0.252
Duration on ART prior to transition (years)	0.92 (0.82–1.04)	0.186			0.94 (0.83–1.08)	0.386
Age at first ART initiation (years)						
<1	1					
1–5	1.10 (0.33–3.66)	0.878			0.69 (0.19–2.51)	0.576
5–10	2.33 (0.63–8.64)	0.205			3.08 (0.63–14.98)	0.164
>10	7.00 (0.73–66.8)	0.091			3.85 (0.39–38.36)	0.251
Enrolled in transition training program (Happy Teen)	1.22 (0.48–3.09)	0.672			0.90 (0.33–2.51)	0.847
Pre-transitioning						
CD4 > 500 cell/mm³ at pre-transition	5.23 (1.96–13.91)	0.001	6.16 (1.93–19.62)	0.002	7.69 (2.40–24.66)	0.001
ART regimens at pre-transition						
second or third line ART (PI-based or other regimens)	1					
first line ART (PI-based or other regimens)	9.25 (2.52–33.95)	0.001	9.66 (2.34–39.82)	0.002	6.02 (1.61–22.51)	0.008
first line ART (NNRTI-based regimen)						
Post-transitioning						
Internal transition (to adult clinic in the study hospital)	1.03 (0.41–2.58)	0.942			2.37 (0.84–6.70)	0.104
ART regimens at post-transition						
second or third line ART (PI-based or other regimens)	1					
first line ART (NNRTI-based regimen)	3.75 (1.13–12.5)	0.031				

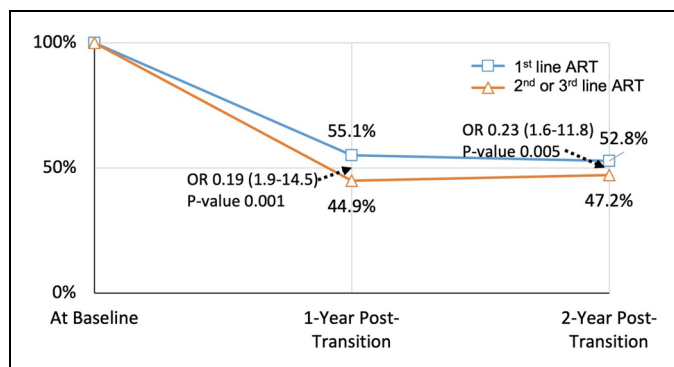


Figure 2. The percentage of patients without any of the three composite outcomes (death, loss to follow up, or virological failure) compared with ART regimens.

incomplete data on CD4 and VL. Secondly, this was a single tertiary care cohort in which half of AYHIV transitioned to adult care within the same institution, which may not be representative of other settings, particularly the primary care-based health system in Thailand where most adults receive care. Thirdly, some of the patients who lost to follow up may be the case of silent transfers to other HIV clinics outside the universal coverage scheme; however, the chance will be very unlikely as all the free ART clinics in the country are included in the NAP database that we retrieve the data from. Future multicenter studies with a larger sample size and prospective, longitudinal follow-up are warranted to better identify outcomes and predictors of success in this vulnerable population.

Conclusion

In this study, we found retention of AYHIV post-transition to adult clinics declined over two years of follow-up and fell short of the UNAIDS 95–95–95 targets. Viral suppression rates were low prior to transition and did not substantially change after transition. Transitioning to adult care at the age of 20 or older and being a first-line ART regimen were associated with viral suppression up to 2 years post-transition, and this important finding can be applied in practice more systematically to improve outcomes. Further studies are needed to develop evidence-based interventions that allow for the successful transition from pediatric to adult clinics and facilitate long-term retention and viral suppression.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Supplemental Material

Supplemental material for this article is available online.

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