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Antiretroviral Therapy Adherence, Virologic and Immunologic Outcomes in Adolescents Compared With Adults in Southern Africa

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Abstract

Objective—To determine adherence to and effectiveness of ART in adolescents versus adults in southern Africa

Design—Observational cohort study

Setting—Aid for AIDS, a private-sector disease-management program in southern Africa

Subjects—Adolescents (age 11–19 years; n=154) and adults (n=7,622) initiating ART between 1999 and 2006 and having a viral-load measurement within one year after ART initiation

Main Outcome Measures—Primary: virologic suppression (HIV viral load ≤ 400 copies/mL), viral rebound and CD4⁺ T-cell count at 6, 12, 18, 24 months after ART initiation. Secondary:

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Conflict of interest

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adherence assessed by pharmacy refills at 6, 12 and 24 months. Multivariate analyses: log-linear regression and Cox proportional hazards.

Results—A significantly smaller proportion of adolescents achieved 100% adherence at each time point (adolescents: 20.7% at 6 months, 14.3% at 12 months, 6.6% at 24 months; adults: 40.5%, 27.9%, and 20.6% at each time point, respectively; $p < 0.01$). Patients achieving 100% 12-month adherence were significantly more likely to exhibit virologic suppression at 12 months, regardless of age. However, adolescents achieving virologic suppression had significantly shorter time to viral rebound (adjusted hazard ratio 2.03; 95% CI 1.31–3.13; $p < 0.003$). Adolescents were less likely to experience long-term immunologic recovery despite initial CD4+ T-cell counts comparable to adults.

Conclusions—Compared to adults, adolescents in southern Africa are less adherent to ART and have lower rates of virologic suppression and immunologic recovery and a higher rate of virologic rebound after initial suppression. Studies must determine specific barriers to adherence in this population and develop appropriate interventions.

Keywords

HIV; Adolescents; Adults; Adherence; Antiretroviral Therapy; Sub-Saharan Africa

INTRODUCTION

The goal of combination antiretroviral therapy (ART) is to achieve the sustained suppression of human immunodeficiency virus (HIV) replication. Although large studies of efficacy of ART in HIV-infected adults [1–4] and children [5,6] have been conducted, relatively few data have been collected describing the virologic outcomes of ART in adolescents. According to the World Health Organization (WHO), the number of adolescents on ART continues to increase, reflecting successful treatment of perinatally-infected children, infections during early adolescence, and expanding worldwide access to ART [7]. Because of the unique behavioral characteristics of adolescents, they may have worse adherence to ART [8,9], which would increase their risk of both morbidity and drug resistance. As a result, measurement of adherence and virologic outcomes in this population is important.

The level of ART adherence required to achieve optimal virologic response remains controversial. While adherence rates of greater than 95% were traditionally considered to be mandatory for adequate response to non-boosted protease inhibitor-based ART regimens [10], recent findings have shown that Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI)-based ART often leads to viral suppression at moderate levels of adherence (70%–90%). However, individuals with such “moderate” adherence levels are likely to have improved outcomes with higher adherence [11,12]. Mills and colleagues have shown that, on average, 77% of African adults on ART had high levels of antiretroviral therapy adherence (>80%) compared to 55% of North American patients. [13] However, this meta-analysis did not include adolescent populations from Africa. In fact, the existing data on ART adherence and outcomes in adolescents come almost exclusively from the developed world.

Belzer et al. conducted a pilot survey of 31 youth (ages 13–24 years) from a multidisciplinary adolescent HIV clinic and reported that 61% of the subjects self-reported >90% compliance with their medications in the previous 90 days. “Too many pills” was the most common reason youth reported missing medication (46%), especially for the previous 90 days [9]. The first large-scale disease progression study in the U.S. of HIV-positive adolescents infected through sexual behavior or injection drug use, called REACH (Reaching for Excellence in Adolescent Care and Health), found that only 41% of adolescents (ages 12–19 years) on ART reported >95% adherence and that factors associated with poor adherence included depression, pill burden, advanced HIV status, alcohol use, and dropping out of school [14]. In this same cohort,

Murphy et al. reported that only 28.3% of adolescents reported taking all of their prescribed antiretroviral medications in the previous month, and factor analysis revealed barriers to adherence to be medication-related adverse effects (both physical and psychological) and complications in day-to-day routines [15]. In another U.S. study, the Pediatric AIDS Clinical Trial Group (PACTG) 381, the cohort included 120 adolescents (ages 11–22 years) infected via high-risk behaviors and treated with at least two NRTIs plus either a protease inhibitor or an efavirenz-containing HAART regimen. Of these 120 subjects, 44 (37%) stayed on study treatment for the 3 years of observation. Twenty-nine (24%) subjects reached and maintained undetectable viral loads. Poorer adherence was the main predictor of virologic failure. [16]

In these studies, however, data from adolescents were not directly compared to data from adults, and it is also uncertain whether the data from these adolescents could be generalized to sub-Saharan Africa, currently home to 70% of all people living with AIDS [7]. Therefore, we compared adherence and virologic outcomes in adolescents (not perinatally infected) and in adults enrolled in *Aid for AIDS*, a large private-sector HIV management program in southern Africa.

METHODS

Data source

We evaluated records from HIV-1-infected adults and non-perinatally infected adolescents enrolled in *Aid for AIDS*, a private-sector, employer-subsidized disease-management program that operates in nine countries of southern Africa and that has been described in detail elsewhere. [17] Patients become eligible for ART with either a documented CD4⁺ T-cell count <350 cells/ μ L on two occasions or a medical confirmation of an AIDS-defining illness. *Aid for AIDS* does not manage clinics, but reimburses patients' private medical practitioners. Authorization for ART reimbursement is subject both to the receipt of a physician prescription and to approval by *Aid for AIDS* clinical staff, following pre-specified clinical guidelines. [18] ART is dispensed monthly at a pharmacy of the patient's choice. For reimbursement, patients submit a claim containing the date ART was dispensed, the specific medication regimen followed, and the quantity supplied. Reimbursement requires no patient co-payment.

Adherence in our analysis is estimated by pharmacy refills (the total number of months in which ART medications were claimed, divided by the total number of months during which ART was authorized). Of note, adherence based on pharmacy data has been validated with medication electronic monitor systems (MEMS caps) [19] and therapeutic drug levels [20, 21] and can reliably predict virologic success [22–24], drug resistance [25], and survival [17, 26,27].

This study used data from patients who had initiated ART between January 1999 and August 2006. ART is defined as taking a minimum of two nucleoside reverse transcriptase inhibitors (NRTIs) plus either one non-nucleoside reverse transcriptase inhibitor (NNRTI) or a boosted protease inhibitor (PI). To be included in the study, patients had to meet the following criteria: (1) no known prior exposure to ART; (2) age \geq 11 years old at ART initiation; (3) at least 6 months of follow-up data available; (4) have a baseline (pre-ART) HIV viral load >400 copies/mL; and (5) at least one known viral load measurement after ART initiation. There were no differences in baseline characteristics for patients who did not have at least 6 months of follow-up data compared to patients meeting our eligibility criteria. Follow-up continued from initiation of ART until a) some change in ART regimen; b) loss to follow-up; c) death; or d) study end in February 2007 (six months after the last eligibility date). Patients who left their Medical Insurance Fund (MIF) or whose MIF changed to a different disease-management program were censored as “lost to follow-up” at the date of departure.

Our primary analyses compared adolescents (defined as ages 11 through 19 years, inclusive) to adults (age ≥ 20 years), based on age at ART initiation. The primary outcomes were *virologic suppression* (HIV viral load ≤ 400 copies/mL) and *viral rebound*, defined as virologic failure (viral load > 400 copies/mL) after achieving virologic suppression. The cutoff value of 400 copies/mL was selected because some of the laboratories measuring HIV viral load used assays with a limit of detection of 400 copies/mL. Adherence rates were classified as $\leq 50\%$, 51–67%, 68–84%, 85–99% and 100% of possible pharmacy refills. Other covariates in the analysis included sex, race, CD4⁺ T-cell count and viral load at program enrollment, year of ART initiation, and number of viral-load measurements. In a secondary analysis, we divided the study population into three age group strata: adolescent (11–19 years), young adult (20–29 years), and older adult (30 years or older).

Statistical analysis

Two analytic methods to compare virologic suppression in adolescents versus adults were used. In the first method, four pre-specified time points for viral load assessment were used: 6, 12, 18 and 24 months after ART initiation. Assessments performed within 3 months of each specified time point were deemed valid for that time point. In addition, the following data were also recorded at each pre-specified time point: (a) pharmacy refill adherence to that point, and (b) last available post-ART viral load measurement. We then used virologic suppression at each time point as the dependent variable in a log-linear model, with adolescent status as an independent variable. Both univariate and multivariate models (including all covariates listed above) were analyzed. The imputation by chained equations (ICE) technique was used in $< 4\%$ of adults and $< 10\%$ of adolescents; in this technique, a missing value in a variable is replaced by its predicted value, as determined by multiple regression with the rest of the full model predictors [28]. The Pearson χ^2 Goodness-of-Fit statistic was used to assess model fit. The second analysis employed a Cox proportional hazards model to evaluate the association between adolescent status and time from virologic suppression to virologic rebound. The assumption of proportional hazards was assessed by the model-based test for the time-by-log (t) interaction.

All *p* values reported are 2-tailed, with a value of < 0.05 considered statistically significant. Fisher's exact test and the Wilcoxon rank-sum test were used in two-way comparisons of binary and continuous variables, respectively. Statistical analyses were performed using STATA Release 8.2 (Stata Corporation, College Station, TX, USA).

Ethical Approvals

This study was approved by the University of Cape Town Research Ethics Committee and by the *Aid for AIDS* Clinical Advisory Board, Cape Town, South Africa.

RESULTS

7,776 eligible patients (97% on NNRTI-based ART versus $< 3\%$ on PI-based ART) were included, of whom 154 were adolescents (11–19 years) per our definition, 1,380 were young adults (20–29 years), and 6,242 were adults (30 years and older), for a total adult (20.1–76.7 years) sample size of 7,622. Characteristics of the study cohort are shown in Table 1. Adolescents were more likely than adults to be female (72.7% vs. 62.3%, $P = 0.01$) and to initiate ART in 2003 or later (50.1% vs. 40.3%, $P = 0.02$). The adolescents were less likely to get NNRTI-based ART (92% vs. 97.2%; $P < 0.001$) and more likely to have shorter follow-up duration (median 27 months; inter-quartile range [IQR] of 18.1–43.7 vs. 36.9 [IQR: 23.6–54.5], $P < 0.001$).

In a subset of patients with adherence data available through 6, 12, and 24 months of follow-up, adolescents had consistently and significantly lower adherence than adults. Adolescents claimed medication for a median of 4/6 (IQR 3–5), 8/12 (IQR 5–10), and 15/24 (IQR 8–19) months, versus 5/6 (IQR 3–6), 10/12 (IQR 6–12), and 19/24 (IQR 12–23) months for adults ($p \leq 0.001$ at all time points). Similarly, the percentage of adolescents achieving 100% adherence was 20.7% at 6 months, 14.3% at 12 months, and 6.6% at 24 months, compared to 40.5%, 27.9%, and 20.6% for adults ($p < 0.01$ at all time points, Table 1). For patients started on the NNRTI-based regimen, the proportion of adolescents with 100% adherence at 6, 12, and 24 months was 23.9%, 14.9% and 7.6%, compared to 99.4%, 28.8% and 21.5% for adults ($p < 0.01$ at all time points).

The proportion of adolescents achieving viral suppression was lower than that of adults, although the differences were significant only at 12, 18, and 24 months after ART initiation (Table 1). Patients achieving 100% 12-month adherence were significantly more likely to exhibit virologic suppression at 12 months, whether adolescent (91% of perfect adherers suppressed at 12 months vs. 45% of others, $p = 0.007$) or adult (86% vs. 59%, $p < 0.001$). The association between adolescent status and lower rates of virologic suppression persisted despite adjustment for potential confounders, although adjustment for adherence did weaken the measured association (Table 2).

In the subset of patients who achieved initial virologic suppression ($N = 5504$ adults and 93 adolescents, of which 3805 adults and 62 adolescents had at least one viral load measurement after initial suppression), the proportion of adolescents with viral rebound was greater than for adults (31.3% vs. 16.6%, $p = 0.02$ at 6 months; 42.4% vs. 20.2% at 12 months, $p = 0.004$; 38.9% vs. 21.5% at 18 months, $p = 0.09$; and 37.5% vs. 24.2%, $p = 0.24$ at 24 months) (Table 1). This association between adolescent status and higher rate of viral rebound was sustained in both unadjusted and adjusted models (Table 3). Furthermore, adolescents were less likely than adults to experience immunologic recovery on ART as evidenced by their median $CD4^+$ T-cell count (IQR): 295 (135–482) vs. 246 (142–377), $p = 0.26$ at 6 months; 281 (154–538) vs. 276 (159–412) at 12 months, $p = 0.96$; 263 (157–439) vs. 308 (177–464) at 18 months, $p = 0.72$; and 172 (44–451) vs. 339 (187–496), $p = 0.02$ at 24 months) (Table 1).

In Cox proportional hazards analysis in the subset of patients who achieved initial virologic suppression, adolescents compared with adults had a significantly shorter time to viral rebound when unadjusted (HR 2.10 [1.43–3.08]; $p < 0.001$) and adjusted for both baseline characteristics and adherence (HR 2.18 [1.41–3.38]; $p < 0.001$) (Fig. 1). In our secondary analyses, we found that young adults have virologic outcomes which are intermediate between those of adolescents and adults ≥ 30 years (Table 1 and Figure 2). In the Cox proportional hazards analysis, adolescents compared to adults age 20–29 years had a significantly shorter time to viral rebound when unadjusted (HR 1.82 [1.22–2.73]; $p = 0.003$) and adjusted for both baseline characteristics and adherence (HR 1.79 [1.12–2.86]; $p = 0.02$). In addition, younger adults compared with adults ≥ 30 years had also a significantly shorter time to viral rebound when unadjusted (HR 1.18 [1.02–1.36]; $p = 0.02$) and adjusted for both baseline characteristics and adherence (HR 1.20 [1.03–1.39]; $p = 0.02$) (Figure 2).

DISCUSSION

Our results suggest that HIV-infected adolescents and young adults on ART in southern Africa have poorer adherence rates and poorer virologic outcomes than their adult counterparts. In this study, adolescents were approximately 50% less likely than adults to maintain perfect adherence at all time points and 70–75% less likely to be virologically suppressed (≤ 400 copies/mL) at 1 and 2 years after ART initiation. At six months, rates of virologic suppression among adolescents and adults were similar; thus, lower rates of long-term suppression among

adolescents were largely explained by more rapid viral rebound. Interestingly, we found that young adults (age 19–20 years) have virologic outcomes which are intermediate between those of adolescents and adults ≥ 30 years (Fig. 2). Furthermore, adolescents were less likely than young adults, adults >30 years and all adults to experience long-term immunologic recovery; despite having nearly identical initial CD4⁺ T-cell counts, adolescents experienced very small increases in CD4⁺ T-cell counts after two years, from a median of 144/mm³ to 172/mm³ vs. increases in young adults, adults >30 years and all adults from a median of 75/mm³ to 348/mm³ ($p = 0.01$), 140/mm³ to 337/mm³ ($p = 0.03$), and 146/mm³ to 339/mm³ ($p = 0.02$), respectively (Table 1). Our data are in agreement with studies from the developed world. Flynn and colleagues also reported that adolescents infected with HIV via high-risk behaviors have less than optimal responses to HAART therapy, with only 24% achieving and maintaining undetectable viral loads over 3 years. [13] Also in this study, CD4⁺ T-cell count measurements improved from entry to the end of follow-up only in the subjects with sustained undetectable viral loads.

We also found in the present study that HIV-infected adolescents were more likely than adults to be female (72.7% vs. 62.3%, $P = 0.01$), a finding consistent with previous epidemiological studies in South Africa which found higher HIV seroprevalence in adolescent females that was explained by greater high-risk sexual behavior, earlier sexual debut, greater likelihood of older sexual partners, and additional sociological issues, such as gender-power imbalance. [29,30]

Low medication adherence in adolescents, the very population most likely to benefit from optimal adherence (i.e., those who would have the longest life expectancy on successful ART), underscores the urgent need to identify risk factors that contribute to poor adherence in HIV-infected adolescents in sub-Saharan Africa. Such knowledge would help guide the design of targeted interventions to achieve or maintain high adherence rates in this population. Given the limited availability of second-line and salvage antiretroviral therapy regimens in this region, preserving long-term success of first-line ART is critical, particularly in adolescents, who would be expected to live longer than HIV-infected adults by virtue of their younger age, if both groups are able to achieve equivalent treatment success.

Barriers to risk factors for non-adherence to HIV medication in adults from sub-Saharan Africa have been reported and include non-disclosure to a loved one or fear of being stigmatized [31,32]; substance abuse (mostly alcohol) [31]; cost [33–35] in countries where ART is not free of charge; and the complexity of the drug regimen [31]. While some of these factors may be specific to this setting, others overlap with factors identified in adolescents with HIV-infection or other chronic diseases from industrialized countries. Indeed, as mentioned earlier, factors associated with poor adherence in the REACH cohort included depression, pill burden, advanced HIV status, alcohol use, dropping out of school, side effects and complications of day-today routine [8,9,14,15]. Furthermore, medication non-compliance for other chronic conditions appeared to be associated with a restriction of independence in daily life, lack of harmony in family relations, and low self-esteem in teenage epileptics [36], as well as forgetfulness, busy schedules, and non availability of medication in adolescents with cancer [37]. In a qualitative study in Uganda, Bikaako-Kajural et al. found that structural factors including poverty and stigma were barriers to both ART and cotrimoxazole adherence, even in children who had complete disclosure and a supportive relationship with their parents. [38] If these factors are shared by adolescents, then interventions to encourage voluntary testing and disclosure of HIV status, or to reduce the cost and complexity of antiretroviral therapy, might also improve adherence rates in this age group. Further research on barriers to ART adherence in adolescents is critically needed.

Our study has certain limitations. First, although our study population is among the largest cohorts on ART under observation in sub-Saharan Africa, our sample size for this analysis was

limited by the small proportion of these patients who were adolescents. Adolescents are under-represented in the Aid for AIDS database because many HIV-infected adolescents may be newly-infected and therefore not at a sufficiently advanced disease stage to qualify for ART (CD4⁺ T-cell count <350 cells/ μ L). Furthermore, infected adolescents who are eligible to begin ART are less likely to be previously employed and therefore less likely to qualify for private health insurance -- unless they are children of a qualifying adult, since only adolescent dependents of adult employees in medical insurance schemes participating in the Aid for AIDS program are eligible. Finally, our dataset was not originally designed as a comprehensive research tool and so is limited in certain data elements and is not structured to capture the reasons for non-adherence. As a result of these limitations, further studies on ART adherence in African adolescents are needed to determine whether the results from this study are fully generalizable (e.g., to the public sector), and to describe relationships that could not be measured with the limited data in the current database. Ultimately, studies of interventions to improve adherence in this vulnerable population will be essential to maximize the number of HIV-infected infants who successfully survive into adulthood.

In conclusion, compared with adults, adolescents in southern Africa are less adherent to ART, have lower rates of virologic suppression at all time points after ART initiation, and experience more rapid viral rebound. Studies to determine barriers to adherence in adolescents, as well as to develop interventions to address them are sorely needed in this setting.

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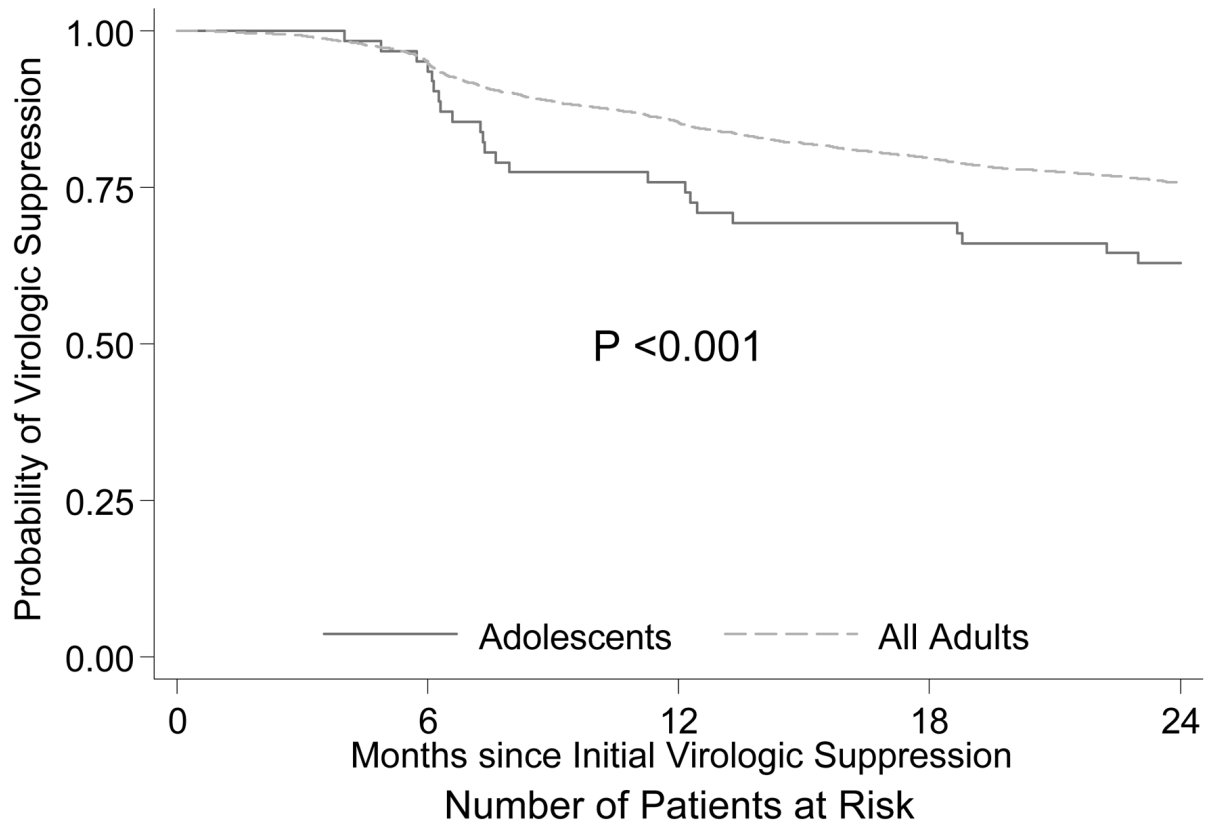
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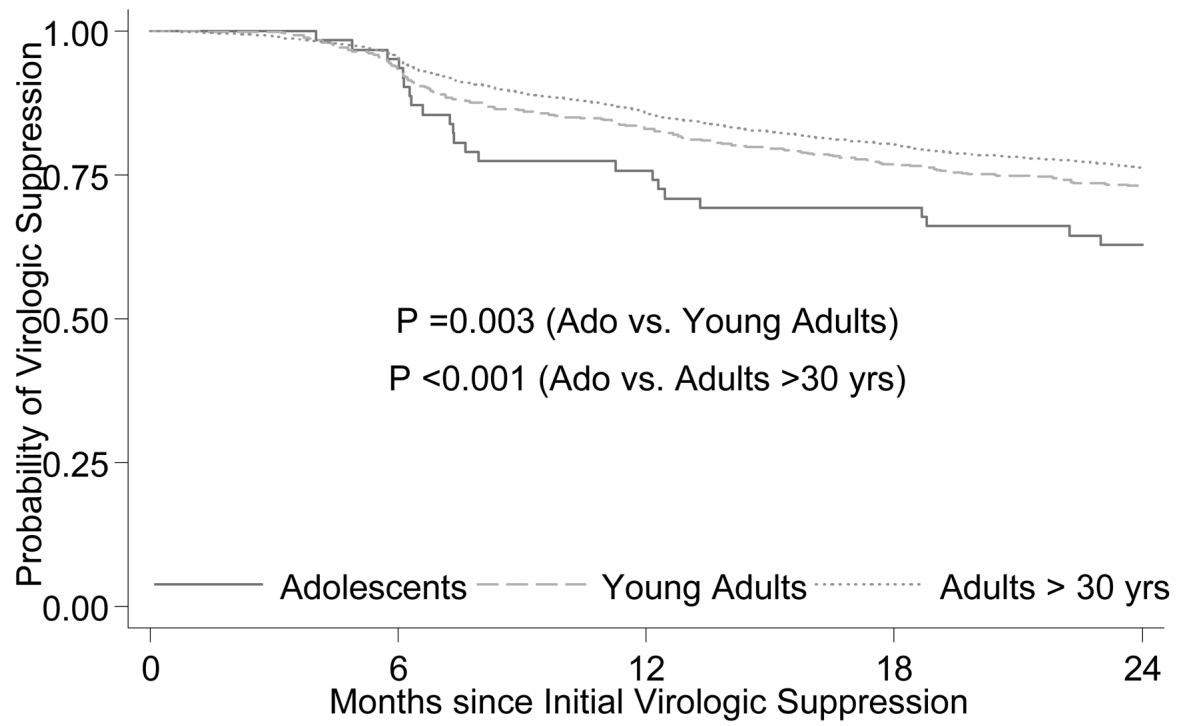
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	0	6	12	18	24
Adolescents	62	52	29	20	12
All Adults	3805	3357	2470	1853	1357

Note: P-value is from Log-rank test for equality of survivor functions

Figure 1. Times to rebound, adolescents versus adults. P for log-rank test <math>< 0.001</math>



	Number of Patients at Risk				
	0	6	12	18	24
Adolescents	62	52	29	20	12
Young Adults	653	569	410	303	226
Adults >30yrs	3152	2790	2061	1552	1132

Note: P-values are from Log-rank test for equality of survivor functions

Figure 2. Times to rebound, comparing adolescents to young adults (20–29 years old) and adults (≥30 years old).

Table 1
Demographic and clinical characteristics of study population. (Adolescent: 10–19 yrs of age; Young adult: 20–30 yrs of age; and Adult: 30 and up yrs of age)

Variable	Adolescent (n = 154)	Young Adult (n = 1,380)	Adult (n = 6,242)	P [†]	All Adult (n = 7,622)	P [†]
Age, yrs [*]	16.4 (11.9–18.8)	27.7 (25.6–29.1)	37.9 (34.0–43.3)	<0.001	36.1 (31.5–42.0)	<0.001
Female, n (%)	112 (72.7)	1,099 (79.6)	3,650 (58.5)	0.05	4,749 (62.3)	0.01
Black, n (%)	125 (94.0)	1,315 (95.3)	5,986 (95.9)	0.52	7,301 (95.8)	0.28
Crude Mortality, n (%)	5 (3.3)	72 (5.2)	470 (7.5)	0.43	542 (7.1)	0.08
Baseline [‡] CD4 ⁺ T-cell count, cells/ μ L [*]	144 (27–246)	175 (78–278)	140 (62–234)	0.003	146 (64–242)	0.24
Baseline [‡] viral load, log ₁₀ -copies/mL, n (%)	5.1 (4.5–5.6)	4.9 (4.4–5.4)	5.1 (4.6–5.6)	0.01	5.1 (4.6–5.5)	0.59
Follow-up time, mos. [*]	27.0 (18.1–43.7)	38.1 (24.3–55.8)	36.6 (23.5–54.1)	<0.001	36.9 (23.6–54.4)	<0.001
NNRTI-based regimen, n (%)	137 (92.0)	1,225 (94.7)	5,858 (97.7)	0.18	7,083 (97.2)	0.001
# of viral loads per patient, n [*]	2 (1–3)	2 (1–4)	2 (1–4)	0.005	2 (1–4)	0.01
CD4 ⁺ T-cell count, cell/ μ L [*]						
6 months	295 (135–482)	281 (167–402)	238 (138–369)	0.69	246 (142–377)	0.28
12 months	281 (154–538)	316 (173–444)	268 (157–402)	0.59	276 (159–412)	0.96
18 months	263 (157–439)	339 (189–486)	305 (172–459)	0.42	308 (177–464)	0.72
24 months	172 (44–451)	348 (195–506)	337 (186–494)	0.01	339 (187–496)	0.02

Pharmacy-claim adherence at specified times post-ART, %^{*}

Variable	Adolescent (n = 154)	Young Adult (n = 1,380)	Adult (n = 6,242)	All Adult (n = 7,622)	P†	P‡
6 months	66.7 (50.0–83.3)	83.3 (50.0–100)	83.3 (66.7–100)	83.3 (50.0–100)	<0.001	<0.001
12 months	66.7 (41.7–83.3)	83.3 (50.0–100)	83.3 (50.0–100)	83.3 (50.0–100)	<0.001	0.001
24 months	62.5 (33.3–80.0)	79.2 (45.8–95.8)	83.3 (53.1–95.8)	80.0 (50.0–95.8)	<0.001	<0.001
Total	72.7 (36.5–95.8)	76.5 (46.7–94.6)	81.8 (51.5–96.2)	81.0 (50.0–95.8)	0.10	0.15
100% Adherence, n (%)						
6 months	17 (20.7)	476 (39.2)	2,359 (40.7)	2,835 (40.5)	<0.001	<0.001
12 months	11 (14.3)	316 (27.0)	1,552 (28.1)	1,868 (27.9)	0.01	0.01
24 months	4 (6.6)	200 (19.3)	973 (20.9)	1,173 (20.6)	0.004	0.004
Viral suppression, n (%)						
6 months	58 (63.0)	444 (63.7)	2,267 (70.5)	2,711 (69.3)	0.13	0.21
12 months	32 (45.7)	323 (56.0)	1,659 (63.5)	1,982 (62.1)	0.01	0.01
18 months	24 (45.3)	276 (54.2)	1,375 (61.6)	1,651 (60.2)	0.02	0.03
24 months	17 (43.6)	246 (55.8)	1,210 (63.8)	1,456 (62.3)	0.01	0.02
Viral rebound, n (%)§						
6 months	14 (31.1)	84 (19.9)	312 (15.9)	396 (16.6)	0.01	0.02
12 months	14 (42.4)	72 (21.2)	312 (19.9)	384 (20.2)	0.004	0.004
18 months	7 (38.9)	67 (24.4)	268 (20.9)	335 (21.5)	0.08	0.09
24 months	6 (37.5)	53 (25.0)	244 (24.0)	297 (24.2)	0.24	0.24
Ever-suppressed, n (%)	90 (58.4)	922 (66.8)	4,557 (73.0)	5,479 (71.9)	<0.001	<0.001

* Data are given as median (inter-quartile range).

† P-values are all compared to adolescents and calculated using Wilcoxon rank-sum test for continuous variables and Fisher's exact test for binary variables.

‡ Data collected at program enrollment.

§ The denominator consists only of patients who had initially suppressed viral load.

Table 2
Relative risks for virologic suppression in adolescents compared to adults

Time of follow-up	Unadjusted		Adjusted for all variables other than adherence [†]		Completely adjusted [‡]	
	RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P
At 6 months*	0.91 (0.78–1.07)	0.24	0.88 (0.74–1.05)	0.16	0.96 (0.79–1.16)	0.65
At 12 months*	0.74 (0.57–0.95)	0.02	0.65 (0.48–0.90)	0.01	0.74 (0.53–1.03)	0.08
At 18 months*	0.75 (0.56–1.01)	0.06	0.84 (0.60–1.17)	0.31	-	-
At 24 months*	0.70 (0.49–1)	0.05	0.72 (0.49–1.06)	0.10	0.78 (0.53–1.15)	0.22

* Time is measured in months after HAART initiation.

[†] Includes gender, race, baseline CD4, baseline viral load, ART regimen (NNRTI- vs. PI-based), ART initiation before 2003, and number of viral load measurement per patient-months.

[‡] Adherence categorized in strata of ≤50%, 51–67%, 67–84%, 85–99% and 100% and baseline variables as described in (†). No adherence data at 18 months.

Table 3
Relative risks for viral rebound in adolescents compared to adults

Model	Unadjusted		Adjusted for all variables other than adherence [†]		Completely adjusted [‡]	
	RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P
At 6 months*	1.88 (1.20–2.93)	0.005	2.04 (1.25–3.33)	0.004	2.33 (1.71–3.17)	<0.001
At 12 months*	2.10 (1.40–3.16)	<0.001	1.84 (1.11–3.07)	0.02	1.77 (1.23–2.54)	0.002
At 18 months*	1.81 (1.01–3.26)	0.05	2.16 (1.27–3.66)	0.004	-	-
At 24 months*	1.55 (0.82–2.94)	0.18	1.72 (0.96–3.06)	0.07	1.65 (1.03–2.63)	0.04

* Time is measured in months after HAART initiation.

[†] Includes gender, race, baseline CD4, baseline viral load, ART regimen (NNRTI- vs. PI-based), ART initiation before 2003, and number of viral load measurement per patient-months.

[‡] Adherence categorized in strata of ≤50%, 51–67%, 67–84%, 85–99% and 100% and baseline variables as described in (†). No adherence data up at 18 months.