HHS Public Access

Author manuscript

J Acquir Immune Defic Syndr. Author manuscript; available in PMC 2019 July 01.

Published in final edited form as:

J Acquir Immune Defic Syndr. 2018 July 01; 78(3): 322–328. doi:10.1097/QAI.0000000000001670.

High Medication Possession Ratios Associated with Greater Risk of Virologic Failure Among Youth Compared to Adults in a Nigerian Cohort

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Abstract Presentations: These data were presented in part at the 11th International Conference on HIV Treatment and Prevention Adherence (IAPAC) 2016, Fort Lauderdale, FL, USA; and at the Society for Adolescent Health and Medicine's annual conference 2017, New Orleans, LA, USA.

Conflicts of Interest: The authors declare no conflicts of interest.

Abstract

Background—Medication possession ratio (MPR) is widely used as a measure of adherence to antiretroviral therapy (ART). Many adolescents and young adults (AYA) experience ART adherence challenges. Our objective was to determine whether the relationship between MPR and virologic failure (VF) is consistent between AYA and older adults in Nigeria.

Methods—We conducted a retrospective study of AYA (15–25 years) and adults (>25 years) who initiated ART between January 2009 and December 2012 at 10 university-affiliated HIV clinics in Nigeria. We used multivariate generalized linear models to assess the relationship between age, MPR (ART doses dispensed)/(days since ART initiation), and risk of VF (HIV RNA >1,000 copies/mL) in the first year on ART.

Results—The cohort included 1,508 AYA and 11,376 older adults. VF was more common in AYA than older adults (30% vs. 24% p<0.01). Overall, 74% of patients had optimal, 16% suboptimal, and 9% poor adherence (MPR >94%, 80–94%, and <80%). AYA attended fewer pharmacy-only visits than older adults (5 vs. 6, p<0.001). Higher MPR was associated with decreased rate of VF (80–94%, aRR 0.57; >94% aRR 0.43, p<0.001 vs. MPR <80%). Among those with optimal adherence by MPR, 26% of AYA had VF, a risk that was 20% higher than for older adults with optimal adherence (p<0.001).

Conclusions—In this Nigerian cohort, MPRs were high overall, and there was a strong association between low MPR and risk of VF. Nonetheless, 26% of AYA with high MPRs still had VF. Understanding the discrepancy between MPR and viral suppression in AYA is an important priority.

Keywords

adherence; medication possession ratio; MPR; youth; adolescent; young adult; virologic failure

Introduction

Scale-up of antiretroviral therapy (ART) has led to unprecedented progress in the global AIDS response, but adolescents and young adults (AYAs, 15–25 years) have not benefitted fully from these gains (1). Marked disparities have been described between the health outcomes of HIV-infected AYA and older adults (2). In fact, in an era from 2005–2012 when AIDS-related deaths declined by 30% for adults, they increased by 50% in this high-risk group (3). Adolescence and young adulthood is a unique time of development often characterized by increased risk-taking and poor abstract thinking, both of which may negatively impact health behaviors (4, 5). Likely in part as a result of these dynamics, HIV-infected youth have been found to have poorer attendance at clinical visits and adherence to life-saving antiretroviral therapy (ART), culminating in greater risk of virologic failure and death (6–9).

Optimal adherence to ART is central to effective HIV treatment for all patients, including AYA (10). Early identification of patients poorly adherent to ART may be an important health system indicator, to guide patient level interventions to improve adherence, to decrease HIV drug resistance in the community, and to reduce viral transmission (11).

Indeed, the WHO has recommended that adherence be routinely monitored at the clinic level, with a target of at least 90% adherence to minimize the risk of HIV drug resistance (11). Nonetheless, there is no gold standard for measuring adherence, and in settings where routine viral load monitoring is not available, utilizing additional markers of adherence is even more important (12, 13). However, there are limited data to determine how existing measures perform in AYA relative to older adults (12, 13).

Several methods exist to assess adherence to ART (14). Subjective measures such as self-report are easy to operationalize and inexpensive, but tend to overestimate adherence (14). Pill count is also easy to measure and inexpensive, but overestimates adherence (15). Electronic monitoring is expensive and difficult to implement clinically (12). Pharmacy adherence measures are objective, easy to operationalize, and inexpensive when patients utilize one central pharmacy for all drug pick-ups (15). This is often the case in resource-limited settings, and allows for use of pharmacy-based adherence measures as a potential medication adherence screening tool (15). The most popular of these is medication possession ratio (MPR) (15). MPR reflects the proportion of patients' medication doses retrieved from pharmacy. Low MPRs, especially <80%, have been associated with increased risk of virologic failure and death (16–18).

Our objective was to assess the relationship between MPR and virologic failure among AYA (15–25 years) compared to older adults (>25 years) on ART in a multisite, comprehensive HIV treatment program in Nigeria.

Methods

Setting

The study was conducted at the AIDS Prevention Initiative in Nigeria (APIN). APIN is an implementing partner of the President's Emergency Plan for AIDS Relief (PEPFAR) and administers a network of HIV treatment centers in Nigeria. APIN has provided HIV care and treatment services to over 150,000 people living with HIV since 2000. During the study period (2009–2012), APIN oversaw 36 comprehensive treatment centers in 9 of Nigeria's 36 states. APIN supported comprehensive sites provide care for adults and children; prevention of mother-to-child-transmission services; laboratory services including viral load, CD4, and routine safety and monitoring labs; and pharmacy services for ART dispensing. The study was conducted at 10 of these comprehensive clinics with infrastructure to administer on-site viral load testing. First line ART regimens at these sites included two efavirenz (tenofovir/lamivudine/efavirenz; abacavir/lamivudine/efavirenz) and two nevirapine (zidovudine/lamivudine/nevirapine; abacavir/lamivudine/nevirapine) based regimens. HIV RNA samples were processed using Cobas Ampliprep/Cobas TaqMan assays. Both internal (quality control kits to check for outlier samples) and external (twice yearly quality assessment panels from AFRIQUALAB) quality control measures were routinely conducted.

Study Design

We conducted a retrospective cohort study of AYA (15–25 years) and older adults (>25 years) initiated on ART at APIN sites between January 2009 and December 2012. Patients

who defaulted from care (e.g. who had ≥ 6 months between the last clinic encounter and the expected 12-month visit) were excluded from the analysis. We reviewed patient clinic, pharmacy, and laboratory visits in the first 12 months after ART initiation. The exposure of interest was MPR, defined as the number of daily doses of ART dispensed divided by the total number of days on ART, and was measured 12 months after ART initiation. MPR was determined from pharmacy records. MPR was categorized as optimal (>94%), suboptimal (80–94%), and poor (<80%) based on existing literature associating MPR with risk of virologic failure (16). The outcome of interest was virologic failure, defined as HIV RNA >1000 copies/mL. In Nigeria, HIV RNA testing is recommended on a 6-monthly basis. Given that not all sites routinely obtained HIV RNA measurements according to this schedule, we assessed the first HIV RNA at least 6 months, but no more than 18 months, after ART initiation (12 +/− 6 months) for the study outcome.

Analysis

Our aim was to determine the association between MPR category and risk of virologic failure and compare it between AYA and older adults, and potential confounders, of the relationship between MPR and virologic failure, in addition to other covariates significantly associated with virologic failure including sex (M/F), employment status (employed vs. unemployed vs. student), baseline CD4 count (<100/*u*L vs. 101–350/*u*L vs. >350/*u*L vs. missing), and visit pattern (missed visits vs. attended all visits). We used chi-squared tests to compare the proportion of AYA vs. older adults with virologic failure in each MPR category.

In the first year on ART, 13 clinic encounters are recommended by Nigeria's national HIV treatment guidelines: 5 for clinician visits, medication pick-up, and laboratory testing, 1 for clinician visit alone, and 7 for ART pick-up alone. We defined visit attendance based on clinic (and not pharmacy) visits so that the MPR measurement, which relies on pharmacy encounters, was not biased. Patients were defined as most compliant if they attended at least 3 of 5 visits in months 0–3 on ART, and at least 2 of 3 visits in months 3–12 on ART. Patients were defined as least compliant if they attended 0–2 of 5 visits in months 0–3 on ART, or 0–1 of 3 visits required in months 3 to 12 on ART. We summarized the type of clinic encounters (clinician + drug pick-up vs. clinician alone vs. drug pick-up alone) attended by AYA and older adults in the first year on ART. We used t-tests to assess for differences in the mean number of visits attended for each age group.

We used generalized linear models with Poisson distribution and log-link function to assess the rate of virologic failure by age and MPR categories. Patient-level variables that were statistically significant in bivariate analysis (P<0.10) were included in the multivariate model. We accounted for potential site-level clustering by adjusting for site-level characteristics including geographic location (urban vs. rural), clinic ownership (public vs. private), and level of care (secondary vs. tertiary facility). Site-level variables remained in the model to adjust for potential site-level clustering. To examine whether the relationship between MPR category and rate of virologic failure was modified by age group, we included an interaction term between age and MPR in the multivariate model. We used the most parsimonious multivariate model, removing covariates that did not exhibit statistically significant association with the outcome (virologic failure) at the level of p<0.05. In

addition, we built separate multivariate models for each MPR category to quantify the rate of virologic failure for AYA compared to adults at optimal, suboptimal, and poor MPR levels.

We conducted sensitivity analysis on the rate of virologic failure by MPR categories utilizing different cut-offs for MPR categories given data showing a relationship between "over-adherence" and virologic failure. For this analysis, we categorized MPR into four categories: superlative MPR (≥ 110%), optimal MPR (95–109%), suboptimal MPR (80–94%) and poor MPR (<80%).

IRB Approval

We obtained IRB approval from Partners HealthCare (Protocol no. 2013P000219) and Harvard T. H. Chan School of Public Health in Boston, MA, USA, the Nigerian Institute for Medical Research (Protocol no. 12/212) in Lagos, Nigeria, and Vanderbilt University Medical Center (Protocol no. 161779).

Results

Cohort Description

There were 27,445 patients who initiated ART at the 10 APIN sites during the study period. Patients who defaulted from care (n=8,495) were excluded from the analysis. An additional 6,066 patients were missing 12-month viral load and were also excluded. We compared patient (sex, education, CD4 count) and site (facility level, facility sector, geographic setting) characteristics between AYA and adults who were excluded from and retained in the analysis. The excluded patient group looked similar to the analysis cohort with regard to sex distribution (88% vs. 88% for AYA, 62% vs. 63% for adults). In both age groups, a higher proportion of patients who were retained in the analysis reported having any education (79% vs. 74% for AYA, 85% vs. 77% for adults). There was no substantial difference in the proportion of patients with the lowest CD4 counts (<100 cells/uL) who were retained in vs. excluded from the analysis for either age category (22% vs. 21% for AYA, 29% vs. 28% for adults); and a higher proportion of those with the highest CD4s (>350 cells/uL) were excluded from the analysis (20% vs 13% for AYA, 16% vs 9% for adults) compared to those retained. There were no substantial differences in the facility types (primary vs. secondary vs. tertiary or faith-based vs. private vs public) or geographic setting (rural vs. semi-urban vs. urban) among patients who were retained in or excluded from the analysis (see Appendix, Table 1). We did not find statistically significant difference between the proportion of AYA (n=725, 32%), and older adults (n=5,341, 32%) with missing viral load data.

Among the 12,884 patients comprising the analysis cohort, there were 1,508 AYA and 11,376 older adults. Twenty one percent of the cohort (n=2,014) had virologic failure at 12 months, but more AYA had virologic failure at 12 months than older adults (30% vs. 24%, p<0.001) [Figure 1]. Overall, 74% of patients had optimal adherence as defined by MPR (MPR >94%), 16% had suboptimal adherence (90–94%), and 9% had poor adherence (MPR <80%). Ninety-seven percent of ART pick-ups were for first-line ART. 62%, p<0.001).

Baseline Characteristics

There were several differences in baseline demographics and clinical characteristics between AYA and older adults. AYA had a greater proportion of females than older adults (88% vs. 63%, p<0.001), and AYA had a greater proportion of unemployed than older adults (31% vs. 15%, p<0.001). Finally, AYA initiated ART with higher baseline CD4 counts (190/uL vs. 160/uL, p<0.001) than older adults. The majority of AYA (88%) and adults (90%) reported heterosexual sex as the transmission risk factor (p=0.003). Perinatal transmission was reported as the risk factor for a small minority of patients (<1% for both AYA and adults, p<0.001) [Table 1].

Age, MPR, and Risk of Virologic Failure

In bivariate analysis of patient level variables, AYA had an increased rate of virologic failure compared to older adults (RR 1.25; 95% CI 1.13,1.38]. Patients with optimal (MPR>94%, RR 0.42; 95% CI 0.38–0.46) or suboptimal adherence (MPR 80–94%, RR 0.56; 95% CI 0.50–0.63) had a decreased rate of virologic failure compared to patients with poor adherence as defined by MPR (MPR <80%). We found several factors independently associated with the rate of virologic failure. Females had an increased rate of virologic failure at 12 months compared to males (RR 1.13; 95% CI 1.04–1.21), and this cohort notably did not include women who were initiating ART for the prevention of mother-to-child transmission; and educated patients had a decreased rate of virologic failure compared to patients with no education (RR 0.92; 95% CI 0.84–1.01). There was a U-shaped relationship between baseline CD4 count and rate of virologic failure. Compared to patients with baseline CD4<100/*u*L, those with CD4 101–350/*u*L (RR 0.76; 95% CI 0.70–0.82), had a decreased rate of virologic failure but not those with higher or missing CD4 counts. Patients with optimal visit attendance had a decreased rate of virologic failure (RR 0.84; 95% CI 0.78–0.90) compared to patients with poor visit attendance. Finally, patients attending tertiary facilities (RR 0.81; 95% CI 0.70–0.92) and public facilities (RR 0.87; 0.79–0.95) had a decreased risk of virologic failure relative to secondary and faith-based clinics respectively. The former likely had a wider variety of multidisciplinary services to support comprehensive HIV care [Table 2].

In multivariate analysis, AYA status remained an independent risk factor for virologic failure relative to older adults (RR 1.15; 95% CI 1.04–1.27), while suboptimal and optimal MPR remained protective against virologic failure relative to poor MPR (RR 0.57; 95% CI 0.51–0.64 and RR 0.43; 95% CI 0.39–0.49 respectively) even while adjusting for potential confounders and other significant covariates including sex, education, baseline CD4 count, visit attendance, and site level variables [Table 2]. In sensitivity analysis, when MPR was categorized into four groups; poor MPR <80%), suboptimal (MPR 80–94%), optimal (MPR 95–109%), and superlative (MPR ≥ 110%), superlative MPR was associated with a decreased rate of virologic failure relative to poor MPR [RR 0.37;95% CI 0.30–0.45] [Table 2].

Associations Among Age, MPR Category and Virologic Failure

When we added an interaction term between age and MPR categories to the most parsimonious multivariate model, we found that age modified the relationship between MPR

and virologic failure (p<0.05) [Table 2]. We therefore conducted additional stratified analyses, presenting results for AYA and older adults separately. AYA had a greater proportion of patients with virologic failure than older adults in each MPR category, but these differences were only significant in those with optimal adherence as defined by MPR. Among patients with poor adherence (MPR <80%), 51% of AYA and 50% of adults had virologic failure at 12 months (p=0.97). Thirty-three percent of AYA and 28% of adults with suboptimal adherence (MPR 80–94%) had virologic failure at 12 months (p=0.07). Finally, 26% of AYA with optimal adherence (MPR >94%), had virologic failure at 12 months compared to 20% of older adults (p=0.01) [Figure 2]. We quantified these rate differences between age groups with multivariate models built for each of the three MPR categories (adjusted for sex, baseline CD4 count, visit attendance, site level, site ownership, and site setting). Among those with poor and suboptimal MPR (MPR <80% and MPR 80–94%), AYA did not have an increased rate of virologic failure compared to older adults (aRR 1.00; 95% CI 0.80–1.25; aRR 1.13; 95% CI 0.90–1.42). However, among patients with optimal MPR (>94%), AYA had a 20% increased rate of virologic failure compared to adults (aRR 1.20, p<0.005) [Figure 2].

Visit Patterns for AYA and Adults

Consistent with the recommended visit and ART pick-up schedule, more visits overall were for ART pick up alone (mean 6, SD 3.1) than for clinician and ART pick up (mean 4, SD 2.2) or clinician alone (mean 2, SD 1.7). There was no difference in average number of clinician (2 vs. 2, p=0.05) or clinician + ART pick-up visits (4 vs. 4, p=0.93), but AYA had fewer drug pick-up only contacts than older adults overall (5 vs. 6, p<0.001). Within MPR categories the difference in the number of drug pick-ups by age group was significant only for the MPR>94% group (5 for AYA vs 6 for older adults, p<0.0001).

Discussion

While there is no gold standard for the measurement of medication adherence, pharmacy-based measures are considered to be robust correlates of adherence to ART that consistently predict patient outcomes (12). Our study of MPR among patients initiating ART in Nigeria illustrates the capacity of the APIN network to effectively administer ART to patients who are retained in care, with nearly three-fourths of all patients having MPR values greater than 94%. In addition, we found a strong, dose-dependent correlation between MPR category and risk of virologic failure in the first year on ART. We observed discordance, however, between ART pick-up and virologic control in a subset of AYA patients. Overall, about 1 in 4 patients with optimal adherence (MPR >94%) had virologic failure, and this risk was 20% higher in AYA than older adults.

Despite a strong relationship between MPR category and viral load outcomes in our analysis, the correlation was not perfect. About half of those with poor MPR (<80%), one third of those with suboptimal MPR (80–94%), and one fourth of those with optimal MPR (>94%) still had virologic failure. Higher rates of virologic failure are expected with poor MPR, but we did observe notable rates of virologic failure among those with optimal MPR that were higher than reported in other cohorts in Sub-Saharan Africa. One analysis of adults living with HIV in Abidjan, Côte d'Ivoire reported detectable viremia in 9% of patients with

MPR >94%; another in Tanzania reported detectable viral load in 10% of those with high MPRs (17, 19). This was less than half of the rate of viremia in the adults, and one third the rate of viremia in the AYA in our cohort. These studies are difficult to compare directly given different approaches to categorizing MPR, and different thresholds utilized for viremia. There may be sociocultural factors contributing to these cohort-level difference as well.

Our analysis underscores important age-related differences in MPR and risk of virologic failure in apparently adherent patients. In contrast to other studies that have identified over-adherence (defined by MPR>100%) as a risk factor for virologic failure (due to pill dumping, and social desirability bias), “over-adherence” in our cohort (defined by MPR >109%) was protective against virologic failure (20, 21). Nonetheless, more than 1 in 4 AYA with optimal MPR (>94%) experienced virologic failure in the first year on ART, suggesting a tension between medication pick-up and medication-taking behavior. Such discordance might be explained by the overwhelming role played by both perceived and experienced stigma and the fear of unwanted disclosure in the lives of AYA living with HIV (22–24). Qualitative studies of AYA living with HIV have consistently identified stigma and fear of disclosure as central obstacles to adherence, and have described how HIV is typically managed in isolation, within the immediate family unit, and within the home (22–25). As such, few youth were comfortable taking ART outside of the home, so that not being at home at the time they were expected to take ART was a very common reason for missed doses (22–25).

We also observed interesting differences in the types of clinic encounters (clinic, laboratory, and pharmacy) most common for AYA compared to older adults. Overall, AYA had fewer encounters for ART pick-up alone than adults (5 vs. 6 visits), but there was no difference in attendance at combined visits or clinic visits alone in the first year on ART. While the magnitude of the difference is not large, other studies have found a strong linear correlation between the number of missed visits in the first year on ART and long-term mortality (26, 27). Data from US cohorts also suggest that positive provider relationships are associated with medication adherence and engagement in care (28, 29). Interaction with their providers might have served as an incentive for engagement in care for youth. However, many youth still appeared to have particular challenge with encounters for the pharmacy alone, even among those who otherwise appear to be compliant with their care. There are several factors that might disproportionately impact medication pick-up for youth as they transition from dependence to autonomy, including declining caregiver accompaniment to clinic and transportation barriers (30–32). Lack of healthcare and financial autonomy, coupled with monthly clinic visits required for ART pick up, may combine to create major obstacles to frequent pharmacy encounters for some youth.

There may be important threats to the validity of MPR as an adherence measure that are more apparent in different environments or patient subgroups. Adherence is comprised of several discrete behaviors (medication retrieval, medication ingestion according to appropriate dosing intervals, and observation of appropriate dietary requirements) that are difficult to incorporate into one measure (12). This phenomenon, called “construct under-representation,” occurs when a measure fails to assess important elements of the construct at

hand (adherence) (33). As we have described in this cohort, medication possession may not always correlate with medication ingestion, or with virologic control. While MPR measures medication retrieval from the pharmacy, and this is presumed to correlate with medication ingestion, our analysis, highlights that “construct under-representation” may be a more important threat to validity when MPR is applied to youth with apparent optimal adherence. In addition, while MPR in our analysis reflects medication retrieval over several months, adherence behaviors may vary widely within that period and directly impact virologic outcomes. Unstructured treatment interruptions are common after ART initiation, and longer treatment interruptions are associated with a greater risk of virologic failure, especially early after ART initiation (34–37).

Our study has several limitations. First, baseline resistance testing was not available in this cohort, so we could not exclude patients with transmitted resistance who would not have been expected to achieve virologic suppression on routine first-line ART. In this retrospective analysis, the timing between the MPR assessment and HIV RNA was driven by the availability of the HIV RNA value, which may have occurred at the end of the MPR assessment or after the MPR assessment. Additionally, non-trivial rates of loss to follow-up along with missing viral load data could have introduced bias into the analysis. We were reassured that the proportion of patients with missing viral load did not differ between AYA and older adults. We found that patients with higher baseline CD4 and less education were over-represented in the excluded patient population. These factors were not significant predictors of virologic failure in our multivariate model, which is consistent with other data from the region (38–40). Despite these concerns, our study also has important strengths. The data are derived from a multi-site cohort from clinics varying in size, geographic location, and sector affiliation (public vs. private) within Nigeria, thus improving the generalizability of our findings.

In Sub-Saharan Africa, more than half of patients on ART do not have access to routine viral load testing. This number may be further reduced as global HIV support is reduced and programs have cut back on the use of laboratory tests and other services (41, 42). Consistent ART pick-up from the pharmacy, especially in a setting where monthly ART pick-up is routine, may lead clinicians to assume a compliant pattern of health behaviors, with minimal or low risk of virologic failure. Our study of patients initiating ART in Nigeria, however, underscores that more than 1 in 4 AYA with optimal adherence as assessed by MPR still developed virologic failure. This risk was 20% greater in AYA than older adults, supporting disparate performance of MPR as a marker of virologic response across age groups, especially among those with the highest MPRs. Our findings support continued investigation for robust correlates of adherence, especially among youth. The findings also underscore the importance of removing obstacles to care, including a consideration of decreasing the frequency of visits required for ART pick-up), continued efforts to combat HIV-related stigma in communities at large, promoting clinic and home, peer-based social support to support adherence, investing the role of digital solutions to support adherence for youth in resource-limited settings (such as mHealth interventions), testing novel medication formulations such as long-acting ART, and formalizing youth-based models of care (43–48).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Sources of Support: Research reported in this publication was supported by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health under Award Numbers: K23 AI106406, R01 AI058736, R01 MH108427. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. This study was also supported in part by cooperative agreement number NU2GGH000924 from the US Centers for Disease Control and Prevention, and by the President and Fellows of Harvard College.

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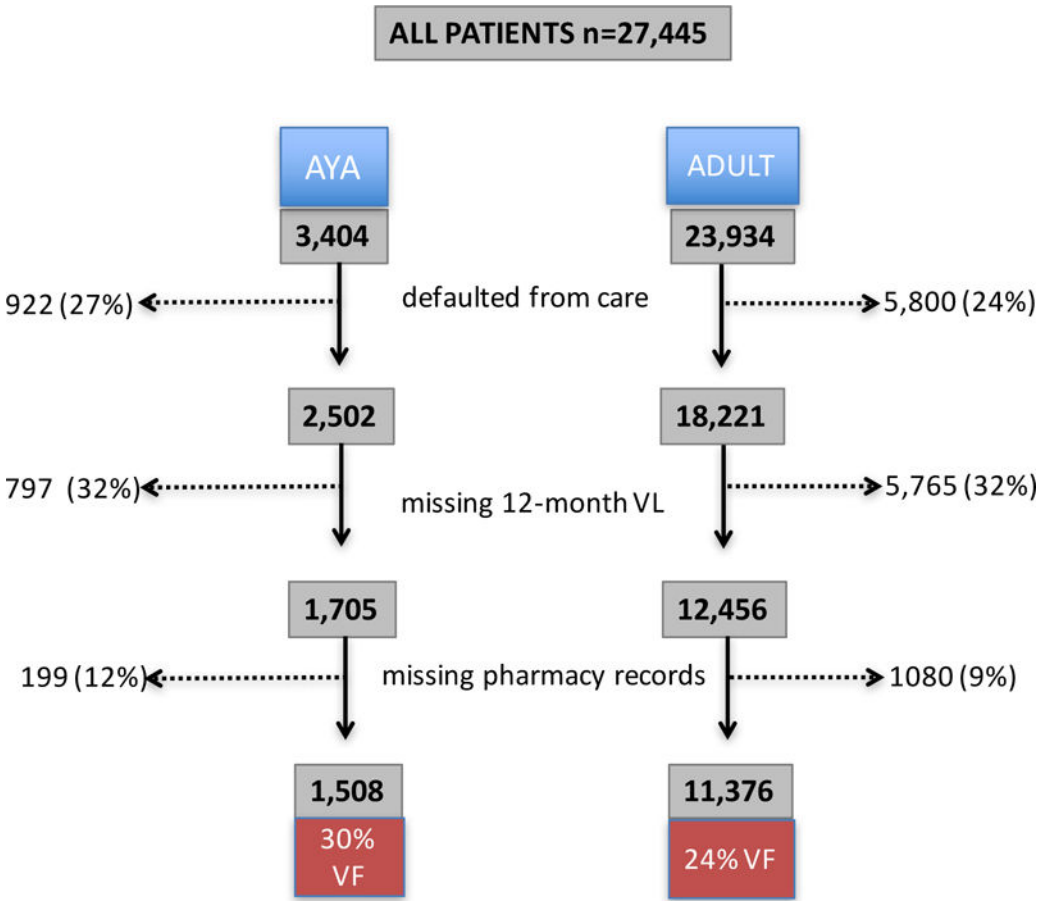

Figure 1. Cohort description of the relationship between medication possession ration (MPR) and virologic outcome in 10 HIV care sites in Nigeria

AYA: Adolescents and Young Adults

VF: Virologic failure after 12 months on antiretroviral therapy (HIV RNA >1000copies/mL)

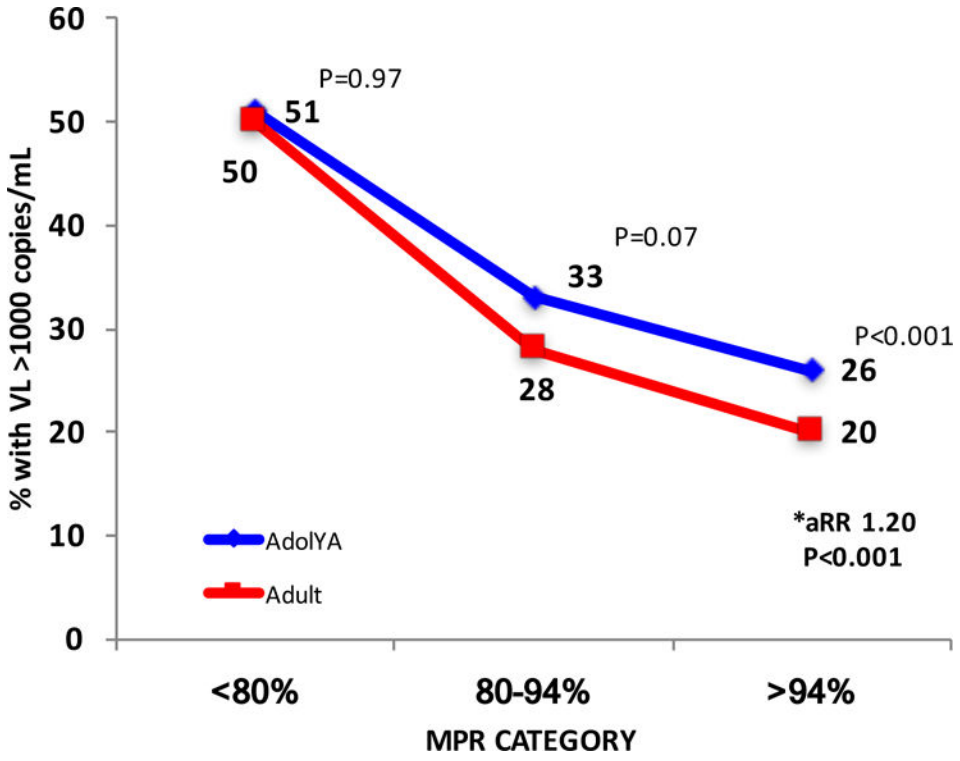

Figure 2. Proportion of Patients with Virologic Failure in each MPR Category

** aRR 1.20 virologic failure among AYA compared to adults with MPR >94% (adjusted for sex, CD4 count at baseline, visit **attendance**, site level (primary vs secondary), private vs. public, and geographic setting: urban vs. semi-urban, vs rural)

AYA: Adolescents and Young Adults

VF: Virologic failure after 12 months on antiretroviral therapy (HIV RNA >1000copies/mL)

Table 1

Baseline Characteristics of a Cohort of Adolescents and Young Adults (15–25yrs), and Adults (>25 years) Initiating ART in Nigeria

	AYA	Adult	p-value
Sex			
Female	1320 (88%)	7203 (63%)	<0.001
Male	188 (12%)	4173 (37%)	
Education			
None	308 (20%)	1724 (15%)	<0.001
Any	1197 (80%)	9625 (85%)	
Marital Status			
Married	645 (43%)	6794 (60%)	<0.001
Unmarried	863 (57%)	4582 (40%)	
Employment Status			
Unemployed	474 (31%)	1690 (15%)	<0.001
Employed or Student	1034 (69%)	9656 (85%)	
Transmission Risk Factor *			
Heterosexual	1321 (88%)	10248 (90%)	0.003
Transfusion	61 (4%)	438 (4%)	0.712
MSM	13 (1%)	25 (<1%)	<0.001
MTC	6 (<1%)	9 (<1%)	<0.001
IVDU	1 (<1%)	4 (<1%)	0.564
Baseline CD4/uL			
median [IQR]	190 [106, 282]	160 [83, 251]	<0.001

AYA: adolescents and young adults; IQR: inter-quartile range; MSM: men who have sex with men, MTCT: mother to child transmission; IVDU: intravenous drug use

* 88%/2%/10% of AYA and 89%/3%/8% of adults had 1/2/unknown transmission risk factors

Table 2

Association Between MPR, Age Category, and Risk of Virologic Failure in the First Year on ART in a Multisite Nigerian Cohort

	Bivariate (RR)			Multivariate (aRR)		
Adult	1			1		
AYA	1.25	<0.001	1.13–1.38	1.15	0.008	1.04–1.27
MPR						
<80%	1			1		
80–94%	0.56	<0.001	0.50–0.63	0.57	<0.001	0.51–0.64
>94%	0.42	<0.001	0.38–0.46	0.43	<0.001	0.39–0.47
Male	1			1		
Female	1.13	0.002	1.04–1.21	1.13	0.001	1.05–1.22
No education	1					
Any education	0.92	0.087	0.84–1.01	1.02	0.647	0.93–1.12
Not married	1					
Married	0.98	0.635	0.92–1.05			
CD4<=100/*u*L	1			1		
CD4 101–350/*u*L	0.76	<0.001	0.70–0.82	0.73	<0.001	0.68–0.79
CD4 >350/*u*L	0.96	0.553	0.85–1.09	0.93	0.257	0.82–1.05
CD4 unknown	0.88	0.132	0.74–1.04	0.83	0.038	0.70–0.99
Missed visits	1			1		
Attended all visits	0.84	<0.001	0.78–0.90	0.86	<0.001	0.80–0.93
Secondary facility	1			1		
Tertiary facility	0.72	<0.001	0.66–0.79	0.81	0.002	0.70–0.92
Faith-based	1			1		
Public	0.80	<0.001	0.75–0.85	0.87	0.002	0.79–0.95
Rural	1			1		
Semi-urban	0.76	0.172	0.51–1.13	1.27	0.276	0.83–1.95
Urban	0.72	0.098	0.49–1.06	1.16	0.486	0.77–1.77

ART: antiretroviral therapy, AYA: adolescents and young adults; MPR: medication possession ratio