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Correlates of Adherence and Treatment Failure Among Kenyan Patients on Long-term Highly Active Anti-Retroviral Therapy

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Abstract

Background—Universal access to highly active antiretroviral therapy (HAART) is still elusive in most developing nations. We asked whether peer support influenced adherence and treatment outcome and if a single viral load (VL) could define treatment failure in a resource-limited setting.

Methods—A multi-center longitudinal and cross-sectional survey of VL, CD4 T-cells and adherence in 546 patients receiving HAART for up to 228 months. VL and CD4 counts were determined using *m2000* Abbott RealTime HIV-1 assay and FACS respectively. Adherence was assessed based on pill-count and on self-report.

Results—Respectively, 55.8%, 22.2% and 22% of the patients had good, fair and poor adherence. Adherence, peer support and regimen but not HIV disclosure, age or gender, independently correlated with VL and durability of treatment in a multivariate analysis ($p < 0.001$). Treatment failure was 35.9% using sequential VL but ranged between 27% and 35% using alternate single VL cross-sectional definitions. More patients failed stavudine (41.2%) than zidovudine (37.4%) or tenofovir (28.8%, $P = 0.043$) treatment arms. Peer support correlated positively with adherence (χ^2 , $p < 0.001$), with non-adherence highest in the stavudine arm. VL before the time of regimen switch was comparable between patients switching and those not switching treatment. Moreover, 36% of those switching still failed second-line regimen.

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Conclusion—Weak adherence support and inaccessible VL testing threaten to compromise the success of HAART scale-up in Kenya. To hasten ART monitoring and decision-making, we suggest strengthening patient-focused adherence programs, optimizing and aligning regimen to WHO standards, and a single point-of-care VL testing when multiple tests are unavailable.

Keywords

HIV; adherence; treatment failure; resource-limited; peer support

Introduction

Industrialized countries succeeded at controlling HIV-1 through the years, by efficiently implementing HAART^{1,2}, as the World Health Organization (WHO) proposed treatment scale-up for poor nations to include human and resource capitalization³. Majority of low-income countries now provide integrated HIV-1 management through decentralized and devolved comprehensive services⁴⁻⁷. Despite these concerted efforts to fast-track treatment, universal coverage and realization of UNAIDS' strategy of 'Getting to Zero' remains elusive^{8,9}. Constraints include poor or inefficient healthcare systems to support adherence programs, inaccessible viral load (VL) for treatment monitoring, stringent criteria for ART-eligibility, delayed linkage and retention to care and disproportional mechanisms to cover children¹⁰⁻¹². Adherence in children, adolescents and youths present special challenges, mostly due to variable healthcare seeking behaviors, stigma, substance use, and reliance on adults for treatment decisions among other variables¹³⁻¹⁷. Patients with good adherence show superior virologic and treatment outcomes, including sustained viral suppression and reduced morbidity and mortality¹⁸⁻²⁰. Treatment successes of developed nations cannot therefore, be directly replicated in resource-limited settings⁶. We feared that treatment failure is largely unrecognized in Kenya years after massive HAART rollout began, and sought to provide simplified metrics to assess the effectiveness of the current HAART scale-up campaign. This paper describes the associations among adherence, peer support, VL and regimen in relations to treatment outcomes.

Methods

Participants and data collection

This study was conducted between October 2012 and May 2014. A total of 546 HIV-1 infected HAART patients between ages 5 and 73 years were recruited at six facilities in Coast, Rift valley, Nairobi, Central and Nyanza provinces. Following written consent, trained caregivers and study staff administered questionnaires (supplementary digital content, SDC:- CCC enrolment form) to collect socio-demographic and treatment data. Five milliliters EDTA blood was obtained from each patient and used for VL and CD4 T-cell testing. The patients were then handed the partially filled forms to bring to the attending Clinician, who alongside project personnel, administered the rest of the questionnaires. The clinicians made independent HAART management decisions.

Adherence and Compliance evaluation

Some care facilities in Kenya facilitate community peer support (CPS) program activities. These groups are mainly run by HIV+ peer ‘counselors’, are not monitored or facilitated by the government and participation is voluntary. Peer counselors encourage patients to adhere to ART schedules, and where necessary, use telephones or personal visits. They also verify pill count at refill and pill burden at home visits. These programs are not available at all country facilities. This study was conducted within facilities offering CPS services. Patients were asked if they were actively, partly, or never involved CPS and about their HIV disclosure statuses. Adherence assessment was based on residual pill count and on self-report, focusing on dose-compliance during the 30 days preceding the latest refill. The number of dose pills at refill was counted and reconciled against the dose counts dispensed at last refill. Additional pill count data was extracted from patient cards for the four months preceding the study period. Non-adherence was determined as the percentage of overdue dose at refill, averaged over a four-month period and used to assign adherence as good ($\leq 5\%$ dose skipped), fair (6-15% dose skipped) or poor ($>15\%$ dose skipped)²⁰⁻²².

Criteria for treatment failure definition

The WHO provides three criteria for defining treatment failure, including clinical, immunologic and virologic failure²³. Due to its relative sensitivity, we adopted the virologic failure approach, defining failure as VL persistently above 1000 copies/ml based on two consecutive measurements at least 6 months apart during sustained ART. We also explored alternative approaches to failure diagnosis by applying a single cross-sectional VL (CSVL) framework. Under CSVL strategy, failure was defined alternately as (i) VL >1000 copies plus at least 6 months of uninterrupted HAART, (ii) VL >1000 plus at least 12 months of HAART and (iii) VL >1000 plus at least 24 months of HAART. Second VL (VL2) was used for CSVL criteria. Patients with VL2 >1000 but a duration of HAART less than 6, 12 or 24 months were designated as ‘undetermined virologic responders’ (UDVR) in their respective CSVL categories.

Viral load assays

VL tests were done within two months of sampling using an automated Abbott RealTime HIV-1 assay system following manufacturers protocol (Abbott, USA). Briefly, internal control RNA was added to 200 μ L of plasma and loaded onto the *m2000sp* instrument for RNA extraction. The limits of detection ranged between 40 and 10,000,000 HIV-1 RNA copies. Undetectable VL was reported as 39 copies while 10,000,001 copies served as the reportable upper limit. All VL assays were conducted at the Early Infant Diagnosis laboratory of the Kenya Medical Research Institute (KEMRI), with 50% of the tests done in duplicate for validation.

CD4 T-cell assays

CD4 T-cell counts were determined regularly on-site as part of point-of-care ART management. The Alere Pima™ CD4 Analyser (Alere, South Africa) was used at three of the six facilities while the other 3 facilities used FACS counters (Becton Dickinson).

Statistical and Data analysis—Data were entered into the SPSS platform. Outcome variables were VL, CD4 T-cell counts, duration of treatment and time to regimen switch. Categorical variables were Age, Sex, HAART regimen, CPS, adherence, HIV disclosure and HAART duration. Analysis of variance was used as appropriate. Both univariate and multivariate statistics were used to assess associations. For multivariate analyses, scale and categorical variables were first assessed together exclusive of 32 patients in the Assorted HAART arm, and subsequently without patients under 18 years old. For the univariate tests, the three levels of adherence and three levels of CPS were combined to develop an ACCESS (Adherence and Community Compliance Enhancement Support Systems) matrix of 9 predictors. Patients who were active in CPS (CPS++) and showing good adherence (Ad++) were assigned a variable string of 1. The other components of the matrix were, CPS++/Ad+, CPS++/Ad-, CPS+/Ad++, CPS+/Ad+, CPS+/Ad-, CPS-/Ad++, CPS-/Ad+, CPS-/Ad-, where ‘+’ represented partial CPS or fair adherence and ‘-’ represented no CPS or poor adherence. Tukey’s Post-Hoc test was applied to determine differences in VL between the levels of ACCESS matrix. Chi-Square statistic was used to assess associations between pairs of independent variables. Cox proportional hazard was used to predict the likelihood of treatment failure, applying duration on HAART or months-to-regimen switch as the time variable. For this latter test, only variables that were significant (p value ≤ 0.05) in the multivariate model were fitted into a forward-looking simple logistics regression.

Ethical Considerations

This study was conducted in accordance with the Helsinki Declaration of 1975, (revised in 2000), following official approvals by the Scientific and the Ethical Review Committees of KEMRI (ERC/SSC protocol #2477). Participation was voluntary upon written informed consent and all patient data were anonymized.

Results

Patient and treatment characteristics

Out of 546 patients, 4 were aged 5 to 12 years while 6 were 12 to 17 years old. We could not verify the mode of HIV-1 infection for these 10 subjects. Treatment regimens included various combinations of zidovudine (AZT), lamivudine (3TC), stavudine (D4T), nevirapine (NVP), efavirenz (EFV) and tenofovir (TDF). By regimen, 36.1% were on first-line AZT +3TC+NVP/EFV, (AZT+ arm) 35% on D4T+3TC+NVP/EFV (D4T+ arm), 23% on TDF +3TC+NVP/EFV (TDF+ arm) and 5.9% on assorted regimens (Assorted arm). About 46% were active in CPS while, 33% and 21% never or only partly participated (table 1). Median duration of treatment was 48 months, and 92.5% were already treated for over 12 months. Patients in the D4T+ arm had stayed longest in treatment.

Data quality assessment and study limitations

Patient enrolment varied minimally across the 6 study sites. The variations in proportions participating in CPS across sites were insignificant (χ^2 $p=0.269$, SDC table 5). Adherence levels (χ^2 $p=0.205$) and VL ($p=0.204$) were also comparable across sites. Thirty-two of 546 patients were excluded for not receiving a 3-drug HAART regimen. No reasons were on record for this suboptimal ART decision. Loss to VL follow-up at time 1 (VL1) occurred in

96 of the remaining 514 patients. These patients were distributed variously across all sites and were excluded accordingly from relevant section analyses. These strategies for data analysis diminished any bias by assuring inter-site comparability. These data should still be interpreted contextually, since adherence behaviors are unique to different settings.

Longitudinal trajectory of viral load and treatment failure

We assessed treatment failure on the basis of the two sequential VL measurements within the AZT, D4T and TDF treatment arms. Of the 514 patients with second VL data (VL2), 418 also had first VL (VL1) data. Another 96 who lacked VL1 data were excluded from this analysis. Both VLs were comparable across the HAART arms (table 2). The median duration between VL1 and VL2 tests was 19 months, and VL2 was significantly lower than VL1 (T-test, $p < 0.001$). Defining virologic failure (VF) by longitudinal criteria as VL1 and VL2 above 1000 or VL1 below 1000 followed by VL2 above 1000 HIV-1 RNA copies, 35.9% of the patients failed treatment overall. VF was high but comparable across all study sites (SDC table 5), and was significantly higher in the D4T arm (41.2%) than in the TDF (28.8%, $p=0.043$) but not the AZT arm. VF patients treated for less than 12 months maintained comparably higher VL (4.69 Log₁₀ HIV-1 copies), than failures treated for 12-60 months (4.22 Log₁₀ copies) or those treated for longer than 60 months (4.25 Log₁₀ copies) (figure 1A). Thus the higher failure rate in the D4T arm was not due to their longer treatment exposure. VF was higher but not significantly so, among male (40.4%) than female (33.7%) patients. There were significantly fewer patients aged below 18 years to allow rational comparisons.

Predictors of treatment outcome under multivariate and univariate models

Multivariate tests were modeled to assess independent associations between variables among the 514 patients in the 3 HAART arms. Age, Sex, regimen, CPS, Adherence and HIV disclosure were fitted into the step-wise model as predictors while CD4 counts, HAART duration and VL were fitted as outcome variables. CPS, HAART regimen and adherence but not HIV disclosure, age or sex, were independently and strongly associated with outcomes (table 3). Specifically, CPS and adherence influenced VL ($p \leq 0.001$) while regimen was associated with treatment duration. Both CPS and adherence interacted significantly to effect virologic outcome ($p < 0.029$). CD4 T-cell counts had no relationship with the predictors at all levels.

Model estimated marginal means showed that VL declined significantly with increasing participation in CPS at all levels of adherence (fig.1B). Patients actively in CPS had nearly 20-times lower VL (1.87 log₁₀ copies) than those not in CPS (3.13 log₁₀ copies) or those who participated only occasionally ($p < 0.001$). In a univariate analysis, good adherence was separately associated with lower VL (1.93 log₁₀ HIV-1 copies) than fair (2.51 log₁₀) or poor (3.54 log₁₀, $p < 0.001$) adherence whether compared for all patients (data not shown) or for only patients failing treatment (fig.1C).

Associations of peer support activity, adherence and HIV disclosure

We sought to understand how adherence and CPS might associate to influence treatment outcomes. The cross-tabulation table 4 shows adherence by proportions of patients in each

regimen, HIV disclosure and CPS groups. Of the 238 patients active in CPS (CPS++), 82.8% had good adherence, as compared respectively to 39% and 28.7% who only partly (CPS+) or never (CPS-) participated in CPS. Higher proportions of patients reported poor adherence within CPS- than those in CPS+ or CPS++ arms (χ^2 , $p<0.001$). Prevalence of poor adherence was lowest in the TDF arm compared to D4T or AZT arms, but good adherence was comparable across groups. Adherence was not associated with age group (χ^2 $p=0.771$). The reasons for adherence behavior were significantly correlated with adherence outcome (χ^2 $p<0.001$, SDC table 6). Majority (69.9%) of patients with poor adherence cited 'bad' feeling, hopelessness or inconvenience as reason for adherence behavior. Most (74.2%) patients with good adherence believed the drugs would prolong their lives and make them healthy. Eight of 514 patients were children aged 5-17 years, and 5 had good adherence. Longevity and health were the main reason for adherence behavior in 6/8, but these should be interpreted within veracity limits of guardian disclosure. In a Cox proportional Hazard analysis using duration of HAART as time variable and virologic failure as status variable, the risk of treatment failure was low for CPS++ participants but increased comparably in all patients as treatment duration increased (fig 1D). The three CPS and three adherence categories were used to develop a compliance matrix (see methods). Univariate analysis conducted to compare VL among the various levels of the matrix showed that a combination of CPS++ and good or fair adherence also produced the lowest VL (figure 1E, $p<0.001$). The same was true for patients in the CPS+ group who had good adherence.

Some 81.5% of the patients had disclosed their HIV status, including all who were in CPS+ +. More patients had good adherence compared to those with poor or fair adherence ($p=0.012$), although the numbers were comparable across HIV disclosure statuses. Disclosure was associated with peer support (χ^2 $p<0.001$), but this association was biased by the exclusive disclosure in the CPS++ group. The association disappeared when CPS++ patients were excluded from the analysis. VL was comparable for patients disclosing (mean, 2.37) and those not disclosing (mean 2.58) their HIV status (anova, $p=0.55$). Pearson's χ^2 tests showed no association in treatment response between patients disclosing and those not disclosing status ($p=0.41$). Taken together, disclosure had no effect on outcome, and appeared unrelated to peer support in this setting.

Virologic response to second-line HAART

Switching regimen is an important decision when patients fail first-line treatment. Of the initial 546 patients, only 17.4% switched regimen after a median treatment time of 32 months. Duration before regimen switch was 35, 30.5, 36 and 14 months respectively for patients in the AZT, D4T, TDF or assorted arms and 57, 24, 30.5 or 35 months for those aged 12-17, 18-35, 36-45 or 45 years. Majority (76%) of patients switching treatment were in the D4T+ regimen arm, while only 9.5% and 13.7% switched respectively from primary TDF and AZT arms. VL did not differ significantly between age groups (data not shown) or between regimen categories of patients switching ART. Patients who switched were not more likely to have failed respective first-line regimens before the switch than those not switching. Of the patients switching regimen, 36.2% still failed second-line treatment (table 2). Considering VL before the time of switch, no difference was observed between patients

who switched (3.311 Log₁₀ HIV copies) and those not switching regimen ($p=0.969$, SDC table 7). Using a Cox proportional hazards analysis, patients in active peer support were more likely to remain longer on treatment before switching regimen and had lower risk of failure than counterparts in CPS+ or CPS- (fig. 1F). Together, these data suggest that patients are switched to second-line without proper guidelines, while the deserving ones are not promptly linked to care.

Virologic treatment failure based on cross-sectional single viral load test

Alternative cost-effective yet reliable VL monitoring strategies are necessary for prompt treatment decisions in settings constrained for resources. Limiting our analysis to 418 patients with complete VL1 and VL2 data, we assessed the effectiveness of a cross-sectional single VL (CSVL) strategy to reliably describe virologic failure, applying only the VL2 for CSVL analysis. Patients who had VL2 of at least 1000 HIV-1 RNA copies but had not been treated for at least 6, 12, or 24 months were assigned 'undefined virologic responder' (UDVR) status in respective CSVL criteria. Using this assessment, 0.7% of the patients were UDVRs under the 6-month CSVL definition while 7.4% and 19.6% were UDVRs under the 12- and 24-month definitions respectively. Respectively, 35.2%, 33% and 27% of the patients failed treatment under the alternate 6-, 12-, and 24-month CSVL strategies. Failure rates under the 6- and 12-month definition compared well with the 35.9% failure rate observed under the longitudinal definition (SDC table 7). Thus, a single VL test after 6 or 12 months of HAART defined treatment failure as efficiently as two sequential VLs under the standard longitudinal criteria.

Discussions

We describe factors that influence adherence and virologic failure, and provide evidence to inform treatment decisions under conditions of limiting resources. Of the 514 patients in the three HAART arms, 35.9% failed first-line regimen by longitudinal strategy and 36% failed second-line after switching regimen. First-line HAART failure was highest among males and in the D4T-arm. Industrialized countries have phased out D4T due to toxicities, and the WHO has recommended its discontinuation globally^{3,24}. Elsewhere, drug resistance was highest among Thai patients initiating D4T-containing regimen²⁵. In our study, 35% of all patients used D4T in first-line regimen and another 10.5% upon switching treatment. Adherence and peer support (CPS) influenced VL in a multivariate analysis, while HAART regimen was associated with length of treatment. Adherence is important to success of HAART²⁶⁻²⁸, and in this study, the proportions of patients with poor adherence were highest in the D4T and AZT arms. Poor adherence was in turn associated with higher VL and increased virologic failure. D4T recipients had stayed longer on treatment than patients on alternative regimens, mostly because D4T is comparably cheaper and readily available locally. We did not conduct toxicity assays, but speculate in concurrence with literature, that toxicity may have influenced adherence and virologic outcome in the D4T arm^{23,29}. D4T should therefore, be eliminated from the current treatment regimens.

A study of South African patients concluded that short-term viral suppression was achievable when adherence was at least 80%³⁰. Our study is uniquely focused on peer

support mechanism, as opposed to non-peer counseling. Good and fair adherence was achieved in 55.6% and 21.6% of our patients respectively. A combination of active CPS and good adherence resulted in lowest VL (see ACCESS matrix). Non-compliance is not uncommon in Kenya where cultural predisposition and family circumstances affect patients' attitudes towards HIV medication³¹, and CPS activity clearly enhanced their compliance. This study included a small number of children, and the accuracy of their adherence profiles was limited to the legitimacy of guardian disclosures. HIV status disclosure positively influences care uptake and is correlated with social support^{32,33}. Disclosure was associated with both adherence and CPS activity in this study, although CPS and adherence but not disclosure, were independently associated with VL. Sampling bias may have influenced the association between CPS and disclosure, as all patients who were active in CPS also had disclosed status. A recent study did not find any association between treatment outcome and HIV disclosure among children³⁴. Thus, peer support influenced adherence independent of HIV disclosure in this study.

Patients who fail first-line HAART must promptly switch to second-line regimen to sustain viral suppression. A staggering 54% of ART switches occurred within 12 months of initiating HAART among predominantly urban Kenyans³⁵. Our study of mostly rural and suburban Kenyans showed only 17% of the patients switched regimen 32 months after initiating treatment. Patients who switched were not more likely to have failed first-line regimen before the switch than those not switching, and both switchers and non-switchers had comparable VL before the time of switch. Thus, patients may be switched unnecessarily to secondary treatment, while others fail to gain timely access to critical treatment decisions.

The standard approach to treatment failure definition relies on sequential VL monitoring, which remains expensive in most developing countries^{5,6,12,36,37}. Less than 3% of all HAART-eligible patients initiate treatment, and virologic failure diagnosis is delayed in majority of those initiating HAART^{12,25,38}. We asked if a single VL measured in a cross-sectional context (CSVL) could effectively define virologic failure and hasten treatment decision. Of all patients failing treatment under longitudinal criteria, 98% and 92% also failed under the 6-month and 12-month CSVL criteria respectively. Hence when resources are limited, prompt and reliable treatment decisions can be made with just one VL taken between 6 and 12 months after HAART initiation. CD4 T-cell levels had no significant association with predictors, an observation that has also been reported elsewhere³⁹. Both clinical and immunological criteria are less sensitive at predicting virologic failure⁴⁰, hence overreliance on CD4 T-cell tests for ART decisions in low-income regions may be obscuring treatment failure.

Conclusions and recommendations

We have demonstrated high rate of virologic treatment failure among Kenyan HAART patients and shown that peer support enhances adherence to improve treatment outcome. To mitigate failure, we recommend the government, through its various HIV/AIDS control agencies to; (i) institutionalize and support patient-focused peer support within provider facilities (ii) train, empower, employ and deploy HIV positive persons as (peer) councilors in community care facilities to facilitate linkage to care and adherence monitoring, (iii)

scale-up point-of-care VL testing with at least one test annually, (iv) synchronize HIV care with the current WHO guidelines, including treatment sequencing, optimization and initiation thresholds and (v) improve overall counseling methodologies and instruments. These steps should be replicable in other low-income settings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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participating in CPS ($p < 0.001$). Patients are grouped according to a 9-factor compliance matrix featuring the 3 adherence and 3 CPS categories and their VL compared between groups (E). † VL is significantly higher than * ($p\text{-value} = < 0.028$). ‡ VL is significantly lower than + ($p = < 0.05$). Finally, a Cox proportional hazard is developed for patients switching regimen, showing time-dependent risk of treatment failure separated by CPS groups (F). C=CPS (community Peer Support Network), Ad, Adherence. ‘++’ Represents active CPS or good adherence; ‘+’, partial CPS or fair adherence; ‘-’ no CPS or poor adherence. Patients in the assorted first-line HAART arm ($n=32$) are excluded.

Table 1
Baseline patient demographic and treatment characteristics

			<u>Males</u>		<u>Females</u>		<u>Total</u>	
			%	Duration*	%	Duration*	%	Duration*
Community peer support <u>Activity</u>	Active (n=251)		14.8	72	31.1	60	46	60
	Occasional (n=113)		7.5	54	13.2	40.5	20.7	48
	Never (n=182)		10.8	36	22.5	36	33.3	36
First-line HAART <u>regimen</u>	AZT+ (n=197)		11.7	43.5	24.4	36	36.1	36
	D4T+ (n=191)		12.3	64	22.7	63	35	64
	TDF+ (n=126)		6.8	36	16.3	28	23.1	36
	Assorted [†] (n=32)		2.4	72	3.5	48	5.9	54
Age group (<u>Years</u>)	5-<12 (n=4)		0.2	72	0.5	41	0.7	44.5
	12-17 (n=6)		0.9	88	0.2	51	1.1	69.5
	18-35 (n=165)		6.2	48	24	36	30.2	39
	36-45 (n=209)		13.4	51	24.9	48	38.3	48
	>45 (n=162)		12.5	60	17.2	60	29.7	60
	Total (N=546)		33.2	54	66.8	48	100	48
Starting first-line and switching regimen	AZT+ (n=13)		4.2	44	9.5	15	13.7	35
	D4T+ (n=72)		28.4	26	47.4	34	75.8	30.5
	TDF+ (n=9)		3.2	37	6.3	35	9.5	36
	Assorted [†] (n=1)		1.1	14	0	-	1.1	14
	Of total, N=95		36.8	30	63.2	34	100	32

* Duration is given in median months since initiating first-line or months before regimen switch for those initiating second-line highly active antiretroviral therapy (HAART);

[†] Patients received one of NVP+TDF, ABC+3TC+NVP, 3TC+TDF or 3TC+NVP drug combinations.

Table 2
Viral load and treatment failure compared between age and HAART groups

Age in years	Baseline viral load (VL1)			Repeat viral load (VL2)			Virologic failure
	Mean [*]	N	%	Mean [*]	N	%	
5-11	3.67	3	0.7	2.7	3	0.6	33.3
12-17 [†]	3.3	4	1	2.3	5	1	50
18-35	3.3	133	31.8	2.5	157	30.5	36.8
36-45	3.27	155	37.1	2.56	199	38.7	35.5
>45	3.29	123	29.4	2.36	150	29.2	35
Anova <i>p-value</i> [*]	<u>0.966</u>			<u>0.758</u>			
First-line regimen							
AZT+	3.17	174	41.6	2.5	197	38.3	37.4
D4T+	3.02	119	28.5	2.3	191	37.2	41.2 _‡
TDF+	3.74	125	29.9	2.44	126	24.5	28.8 _‡
Total	3.3	418	100	2.4	514	100	35.9
First-line switching regimen							
AZT+	3.22	13	18.8	2.48	13	13.8	38.5
D4T+	2.94	47	68.1	2.2	72	76.6	34
TDF+	3.56	9	13	2.69	9	9.6	44.4
Total	3.08	69	100	2.29	94	100	36.2
Anova, <i>p-value</i> [*]	0.258			0.432			

Virologic failure is based on two VL measurements for patients with completed VL1 and VL2.

^{*} *p-value* is not significant comparing VL between age or regimen. '+' Symbol next to each drug represent 3TC+NVP/EFV in the regimen arm. Patients in the assorted arm are excluded (n=32). AZT, zidovudine; D4T, stavudine; TDF, tenofovir.

[†] Number too small for rational comparison.

Table 3
Multivariate test of associations between predictor and outcome variables

Multivariate Tests ^a					
Independent factor/predictor	Value	F	df	Error df	p-value
CPS	.048	11.37	2	471	<0.001
HIV Disclosure	.002	.377	2	470	0.686
Adherence	.032	7.65	2	471	0.001
HAART regimen	.060	14.24	2	471	<0.001
CPS * Adherence	.025	2.97	4	471	0.019
CPS * Disclosure	.003	.725	2	471	0.485

Tests of Between-Subjects Effects					
	Type III Sum of Squares	df	Mean Square	F	p-value
Factors association with viral load					
CPS	20.898	2	10.449	9.727	<0.001
Adherence	16.137	2	8.069	7.511	.001
HIV Disclosure	.240	1	.240	.223	.637
HAART regimen	1.826	2	.913	.850	.428
CPS * Adherence	11.701	4	2.925	2.723	.029
Factor affecting HAART duration					
HAART regimen	17442.192	2	8721.096	13.824	<0.001

Multivariate tests are shown with viral load (VL) and HAART duration as scale variables and with CPS, Adherence, HAART regimen and HIV disclosure as predictors. Effect of the four independent predictors on either VL or treatment duration is shown at the bottom of the table.

Abbreviations: CPS, community peer support network. HAART, highly active antiretroviral therapy.

Table 4
Adherence characteristics and viral load of various groups of patients

		Adherence index			
		Good	Fair	Poor	Total
HAART regimen					
AZT+ (N=197)	VL % N	1.93 54.8	2.62 20.3	3.68 29.4	2.5 100
D4T+ (N=191)	VL % N	1.88 57.6	2.17 18.3	3.38 24.1	2.3 100
TDF+ (N=126)	VL % N	2.0 54.8	2.71 31	3.56 14.3	2.44 100
Chi-Square p value					0.03
Peer support (CPS) activity					
CPS++ (N=238)	VL % N	1.81 82.8	2.04 14.3	2.45 2.9	1.87 100
CPS+ (N=105)	VL % N	1.99 39	2.5 32.4	3.1 28.6	2.49 100
CPS- (N=171)	VL % N	2.33 28.7	2.86 26.9	3.8 44.4	3.13 100
Chi-Square p value					<0.001
HIV status disclosed					
YES (N=419)	VL % N	1.85 58.9	2.58 20.5	3.66 20.5	2.37 100
NO (N=95)	VL % N	2.4 42.1	2.3 29.5	3.15 28.4	2.58 100
Chi-Square p value					0.012
Total	VL % N	1.93 55.8	2.51 22.2	3.54 22	2.41 100

Chi-square statistics test the associations by proportions, of variables between column cells (adherence) and rows. HAART, highly active antiretroviral therapy. CPS, community peer support. CPS++, actively involved; CPS+, partly involved; CPS-, never involved in CPS programs. AZT, zidovudine; D4T, stavudine; TDF, tenofovir. '+' symbol next to each drug represent 3TC+NVP/EFV in the regimen arm.