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Incomplete adherence among treatment-experienced adults on antiretroviral therapy in Tanzania, Uganda and Zambia

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Abstract

Objectives—To characterize antiretroviral therapy (ART) adherence across different programmes and examine the relationship between individual and programme characteristics and incomplete adherence among ART clients in sub-Saharan Africa.

Design—A cross-sectional study.

Methods—Systematically selected ART clients (≥18 years; on ART ≥6 months) attending 18 facilities in three countries (250 clients/facility) were interviewed. Client self-reports (3-day, 30-day, Case Index ≥48 consecutive hours of missed ART), healthcare provider estimates and the pharmacy medication possession ratio (MPR) were used to estimate ART adherence. Participants from two facilities per country underwent HIV RNA testing. Optimal adherence measures were selected on the basis of degree of association with concurrent HIV RNA dichotomized at less than or greater/equal to 1000 copies/ml. Multivariate regression analysis, adjusted for site-level clustering, assessed associations between incomplete adherence and individual and programme factors.

Results—A total of 4489 participants were included, of whom 1498 underwent HIV RNA testing. Nonadherence ranged from 3.2% missing at least 48 consecutive hours to 40.1% having an MPR of less than 90%. The percentage with HIV RNA at least 1000 copies/ml ranged from 7.2 to 17.2% across study sites (mean = 9.9%). Having at least 48 consecutive hours of missed ART was

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the adherence measure most strongly related to virologic failure. Factors significantly related to incomplete adherence included visiting a traditional healer, screening positive for alcohol abuse, experiencing more HIV symptoms, having an ART regimen without nevirapine and greater levels of internalized stigma.

Conclusion—Results support more in-depth investigations of the role of traditional healers, and the development of interventions to address alcohol abuse and internalized stigma among treatment-experienced adult ART patients.

Keywords

antiretroviral therapy; HIV/AIDS; medication adherence; sub-Saharan Africa; Tanzania; Uganda; Zambia

Introduction

In low-income and middle-income countries, the number of people receiving antiretroviral therapy (ART) grew from 300 000 in 2002 to 9.7 million by the end of 2012, with the greatest increase in coverage occurring in sub-Saharan Africa with 7.5 million ART recipients [1]. This rapid scale-up of ART provision has contributed to a 30% decrease in the global number of HIV-related deaths between 2005 and 2012 [2].

Although these gains are impressive, they also highlight the continued importance of adherence to ART. Delayed initiation of therapy, incomplete adherence and early treatment discontinuation remain among the strongest predictors of incomplete viral suppression, disease progression and mortality among individuals living with HIV [3–8]. Although a 2006 meta-analysis found that adherence levels in sub-Saharan Africa exceeded levels found among patients in developed countries [9], data from both low-income and high-income settings have raised concerns about declining adherence rates over time [10–14]. Factors often associated with incomplete adherence among adults in sub-Saharan Africa include patient-level characteristics (e.g. depression, alcohol use [15]), poor patient–provider interactions [16,17] and structural factors, including the cost of transport and distance to the health facility [18,19]. Less is known about how programme-level characteristics, for example, where ART clinics dispense drugs and if they require treatment support buddies prior to ART initiation, influence ART adherence.

This manuscript presents findings from the adherence component of a two-part study to examine retention in ART services [20] and adherence to ART among treatment-experienced adults in Tanzania, Uganda and Zambia. The objectives of the adherence study were to characterize patient ART adherence levels across multiple programme settings and to examine the relationship between individual and programme-level characteristics and incomplete adherence among ART clients who were on ART for at least 6 months.

Ethical review

The study was reviewed and approved by the ethics review board of the US Centers for Disease Control and Prevention (CDC) and the six partner and national ethical review committees. The Partners Healthcare Institutional Review Board ceded review to FHI 360.

Materials and methods

Design and study setting

A cross-sectional study was conducted among ART patients from 18 facilities from Tanzania, Uganda and Zambia. In each country, six sites with a minimum cohort size of 300 patients at the time of the protocol development (2006) were purposively chosen in order to fulfil the sample size requirement of 250 patients per study site and to explore the impact that different programme characteristics may have on retention and adherence outcomes (see supplemental Table 1, http://links.lww.com/QAD/A616). During study start-up, the study team found that one facility in Tanzania consisted of two adult ART clinics and recruited 125 patients from both the adult-only clinic and the family clinic wherein adults sought care and treatment with their families.

Study participants and data collection

Patients attending the study sites who were at least 18 years of age at ART initiation, had initiated ART at least 6 months prior to data collection and spoke one of the study languages were eligible. Participants were systematically sampled (see supplemental Table 1, http://links.lww.com/QAD/A616), and if a patient was ineligible, unwilling or unavailable, then the study teams selected the next ART patient attending the clinic. All selected patients underwent a screening and consent process by trained research interviewers and, if they consented, were interviewed. After the interview and clinic visit, the study teams collected adherence estimates from the patient's healthcare providers (doctors, clinicians, nurses, lay workers, pharmacists) and abstracted data from the patient's medical, pharmacy and laboratory records using structured data abstraction forms. Interviews were also held with the ART clinics managers regarding the site-level characteristics. At two sites in each country, the study team collected blood samples from all participants for HIV RNA testing. Data collection took place from May to October 2011.

Measures

Adherence measures—Participant adherence was assessed using self-report, provider report and pharmacy refill data. Participants reported their 3-day adherence using the Adult AIDS Clinical Trials Group (AACTG) measure specifying the numbers of tablets for each drug missed each day [21], followed by an aggregate question of how many ART tablets missed in the previous 30 days. Both of these measures were calculated by dividing the number of missed tablets by the total number of ART pills over the specified time period. The interviewer also asked the three-question CASE Adherence Index Scale [22], with a composite score of more than 10 indicating good adherence, and the 30-day visual analogue scale (VAS) [23], with zero indicating complete nonadherence and 100 indicating perfect adherence. To understand patterns of missed ART, we constructed a missed at least 48 consecutive hours measure from two questions about missed tablets in the past 3 months. Following the participant's clinical visit, the interviewer asked all healthcare providers who interact with patients on adherence to estimate, based on the provider's knowledge of the patient and their medical record, the proportion of time the participant had taken his/her drugs in the past month. In cases wherein multiple providers were interviewed, the lowest adherence estimate was taken for analysis. A Pharmacy Medication Possession Ratio (MPR)

was also constructed from the pharmacy refill data by summarizing the number of pills dispensed to participants in the 6 months prior to the interview divided by the total number of pills the participants should have received during that time.

Independent variables—Basic demographic variables collected included age, sex, marital status and the demographic and health survey's wealth index (see supplemental Table 2, http://links.lww.com/QAD/A616) [24–27].

For psychosocial factors, we assessed stigma using five yes/no questions from the Internalized AIDS Stigma Scale (IA-RSS) [28,29] that resulted in two factors retained with very good fit [with a root mean squared error of approximation (RMSEA) of 0.03, 95% confidence interval (95% CI) 0.02–0.05] and perfect reliability (Tucker and Lewis' reliability coefficient = 1). One factor consisted of three questions on internalized stigma (Chronbach's alpha = 0.78) and the second factor consisted of two questions on disclosure stigma (Chronbach's alpha = 0.72). Country-specific medians were used as the cutoff points to dichotomize responses into high (>median) versus low stigma.

The Hopkins Symptoms Checklist depression subscale (HSCL-15) was used to assess symptoms of depression, using the standard cut-off of 1.75 [30] with good fit (RMSEA 0.055, 95% CI 0.053–0.058), reliability (Tucker and Lewis's reliability coefficient = 0.90) and internal consistency (Chronbach's alpha = 0.84).

Social support was assessed using nine questions from the Duke University, University of North Carolina Functional Social Support Questionnaire [31,32] and an added tenth question on receiving help to remember to take one's ART. Exploratory and confirmatory factor analysis identified a two-factor model with adequate fit (RMSEA 0.097, 95% CI 0.093–0.10) and reliability (Tucker and Lewis's reliability coefficient = 0.83). The first factor, Social Support Care, consisted of seven questions about social support (Chronbach's alpha = 0.76) and the second factor, Social Support Help, consisted of four questions about instrumental help (Chronbach's alpha = 0.78). Scores in the lowest tenth percentile were categorized as having low levels of social support (see supplemental Table 2, http://links.lww.com/QAD/A616).

The four yes/no questions regarding alcohol use [cutting down, annoyance by criticism, guilty feeling and eye-openers (CAGE)] were used to assess alcohol abuse or dependency. Summed scores at least 2 were considered positive for alcohol abuse/dependency [33,34]. Other psychosocial variables assessed included having ever visited a traditional healer/herbalist because of HIV (yes/no), having ever disclosed one's HIV status and the average cost and time it took participants to reach the clinic.

The ART-related variables abstracted from the medical charts included current ART regimen, date of ART initiation and pre-ART initiation WHO stage and $CD4^+$ cell count. In addition, we analysed participants' self-reported daily pill burden and the 20-item HIV Symptom Index (see supplemental Table 2, http://links.lww.com/QAD/A616) [35].

The programme characteristics assessed during the ART clinic manager interviews included background information on the level, type, size and location of the HIV facility; and how the clinic dispensed ART and supported medication adherence (e.g. frequency of ART refills).

Analysis—Analysis was performed using SAS 9.3 and STATA 11.2. The analysis plan, prepared before the database was locked, included predetermined cut-offs for outcome and predictor variables with a primary focus on perfect (100%) versus incomplete adherence. These predetermined cutoffs were used to summarize the prevalence of adherence across the different measures.

To identify individual modifiable risk factors and programme characteristics associated with incomplete ART adherence, a multiple mixed effects logistic regression model was used for the adherence measure that correlated best with the HIV RNA measurement. The model contained fixed effects for all factors of interest and a random intercept term effect for the mean adherence at each site. Cut-offs for the adherence measures were selected on the basis of receiver operating characteristic (ROC) analysis with HIV RNA at least 1000 copies/ml as the reference standard. The model was constructed using a hierarchical stepwise procedure, with individual-level factors associated at the 0.10 level added first, followed by the programme characteristics significant at the 0.20 level. The model was simplified using step-wise deletion retaining only significant factors and interactions at 0.05. The estimates were corrected for predictor data missing using multiple imputations (see supplemental Table 1, http://links.lww.com/QAD/A616) [36].

Results

A total of 6825 ART clients were screened for eligibility at the participating sites. Of these, 1848 were ineligible (1523 initiated ART <6 months ago, 729 were <18 years of age and 783 did not speak one of the study languages; these categories were not mutually exclusive). Out of the 4977 eligible, 482 (9.7%) declined to participate, leaving 4495 participants who consented and completed the interview. During data cleaning, the team found six participants with ART initiation dates that were less than 6 months prior to the interview, leaving 4489 participants for the final analysis.

Programme characteristics

Nineteen ART clinics from 18 facilities were included in the analysis, seven sites in Tanzania (the facility consisting of two different models of care was considered as two separate sites), six sites in Uganda and six sites in Zambia (see supplemental Table 3, http://links.lww.com/QAD/A616). Slightly more than half of the health facilities were government facilities. Nongovernmental facilities were either faith-based or run by a nonreligious nongovernmental organization (NGO) with more NGO-supported facilities in Uganda compared with Tanzania and Zambia. More than two-thirds of the sites were located in an urban setting and eight sites had less than 2000 ART patients (range: 350–1967), seven sites between 2000 and 4000 patients (range: 2095–3989) and four had more than 4000 patients on ART (range: 4807–7471).

Characteristics of the analysis population

Of the 4489 participants, 68% were female, 56% were married/cohabitating and the average age was 40 years (Table 1). The majority of participants had started ART more than 2.2 years ago (75%), had a pre-ART $CD4^+$ cell count of 250 cells/μl or less (67%) and were currently taking zidovudine (ZDV), lamivudine (3TC) and nevirapine (NVP)/efavirenz (EFV) (49%).

Proportion with incomplete adherence

Results from the self-reported measures of adherence found that 3.2% (141/4425) of participants missed at least 48 consecutive hours of ART in the past three months and 58% (2599/4450) reported taking less than 100% of their ART in the past 30 days using a VAS (Table 2). Providers estimated that 13.5% of participants were less than 80% adherent and 71.3% were less than 100% adherent in the past 30 days. The pharmacy MPR data found that 40% (1634/4070) of participants had less than 90% of their ART during the previous 6 months.

Selection of optimal adherence measures based on association with virologic failure

One thousand, four hundred and ninety-eight participants received HIV RNA testing and were younger, on ART for less time and had different ART regimens, compared with those who had not received testing. The proportion of participants with at least 1000 copies/ml ranged across the testing sites from 7.2 to 17.2% (mean 9.9%). Using the ROC curve analysis cutoff points, only three adherence measures were significantly related to virologic failure (Table 3), with at least 48 consecutive hours of missed ART having the strongest association with an odds ratio (OR) of 2.86 (95% CI 1.56–5.26) followed by the pharmacy MPR less than 90% (OR 1.47, 95% CI 1.02–2.15) and the healthcare provider report less than 98% (OR 1.57, 95% CI 1.02–2.41). On the basis of these results and previous evidence of the importance of treatment interruptions as a predictor of virologic failure and resistance [37,38], combined with provider estimates most likely reflecting a clinical assessment rather than pill-taking behaviours [39–41], the team selected the variable at least 48 consecutive hours of missed ART as the primary outcome variable to examine the factors associated with incomplete adherence.

Factors associated with incomplete adherence

During univariate analysis, significant associations at the 0.10 level between individual demographic and psychosocial characteristics and incomplete adherence were male sex, high levels of internalized stigma, screening positive for depression, low levels of social support care, screening positive for alcohol abuse, having ever consulted a traditional healer/herbalist because of HIV and having a current ART regimen that does not contain NVP (Table 4). In terms of programme characteristics, significant associations at the 0.20 level were having routine ART refills every 2–3 months compared with once a month, the level and type of health facility, urban location and not offering community-based distribution of ART.

The final multiple regression model found five independent variables associated with incomplete adherence (Table 5): having high levels of internalized stigma, screening

positive for alcohol abuse, ever consulting a traditional healer/herbalist because of HIV and having higher numbers of HIV-related symptoms. The analysis also found that having an ART regimen containing NVP was protective against incomplete adherence and a lack of social support care was marginally associated with incomplete adherence. The final model did not include any of the programme characteristics.

Discussion

This first multicountry study of individual and programme-level factors related to adherence among patients in sub-Saharan Africa on ART for at least 6 months found that social and behavioural factors, including HIV stigma and alcohol abuse, are associated with lower ART adherence. These data support the development of interventions to address high-risk alcohol use and internalized stigma as potential ways to enhance ART adherence and HIV-related health outcomes. The findings also underscore the need to examine how traditional healers may support or hinder ART adherence. Furthermore, these data highlight the variability of existing adherence measures and the need for both accurate research and programme-level methods for assessing pill-taking behaviours in order to inform programme strategies and assess intervention impact.

This research is also the first multicountry study to examine self-reported prevalence of missed antiretroviral drugs for at least 48 consecutive hours, in addition to the more common adherence measures of 3 and 30-day self-reports, pharmacy refill and provider reports. Similar to previous studies, the adherence estimates varied greatly with the 3 and 30-day aggregate questions generating the lowest estimates of missed ART [42] and corresponding poorly with virologic failure. The study results also reaffirm findings that pharmacy MPRs are associated with virologic failure [43], and contrary to other studies [39,41], found that provider estimates were also associated with virologic failure. Providers, including clinicians, pharmacists and adherence counsellors, gave their adherence estimates after a patient visit based on their knowledge of the patient and the patient's medical record. As such, their assessment presumably reflects a combination of factors including knowledge of patient behaviours as well as clinical and laboratory treatment response prior to the assessment. Similarly, the pharmacy MPR takes into account patient's medication refills over a 6-month time period capturing the maximum adherence a patient may achieve rather than actual pill-taking behaviours. Although only able to identify 11% of virological failures in our cross-sectional assessment, the strength of the relationship between the at least 48 consecutive hours measure with virologic failure is consistent with several observations that patterns of adherence, namely interruptions during otherwise good adherence, is an important cause of virologic failure [37,38].

This is also the first study to examine the factors associated with incomplete adherence using at least 48 consecutive hours of missed ART as the main outcome. The factor most strongly related to incomplete adherence was having ever consulted a traditional healer or herbalist because of HIV. About three-quarters of the 253 participants who reported having ever visited a traditional healer or herbalist were from Tanzania. During data collection, a famous healer in the Manyara District of Tanzania was offering a liquid cure for chronic illnesses including HIV/AIDS [44,45]. Although our questionnaire did not investigate

details regarding the healer, this finding does contribute to a growing body of research on the role that traditional healers and alternative medicines may have in delaying HIV testing and care-seeking behaviours [46–48] and influencing sustained HIV ART adherence [49–52].

This research also reinforces findings that alcohol abuse [53,54] and HIV stigma [55] are broad and consistent correlates of ART adherence. The CAGE questionnaire is a concise four-question tool that may be incorporated into clinic assessments to identify ART recipients who may benefit from alcohol counselling interventions. More than one-third of participants reported high levels of internalized stigma defined as feelings of worthlessness, shame and guilt because of one's HIV-positive status, despite the fact that most of the participants in this research had initiated ART more than 2 years earlier. Stigma is associated with lower rates of HIV disclosure, which can compromise adherence due to both concealing the medication and preventing access to social support [56–58]. Several qualitative studies have found social support to be critical for people to overcome barriers, particularly structural and economic barriers, to adherence [16,59–61]. Although this study did not find a significant relationship between structural barriers (e.g. transport costs to the clinic) and adherence, we did find that people with lower levels of social support care were more likely to have missed at least 48 consecutive hours of ART in the past 3 months ($P < 0.054$).

Other factors related to incomplete adherence include having a greater burden of HIV-related symptoms as well as an ART regimen that did not include NVP. Women of childbearing age and/or actively considering pregnancy were given NVP rather than EFV during the study period out of concern for EFV-related teratogenicity. Pregnancy has been shown to positively impact adherence in some but not all studies [62,63]. Although our analysis controlled for age and sex, we did not control for fertility desire or pregnancy intention. Therefore, the association between NVP and adherence may be confounded by preferential prescription of NVP to patients pregnant or considering pregnancy. Alternatively, higher adherence to NVP may be related to differing side effect profiles for NVP versus EFV, which was not fully controlled for in our analysis.

These factors —— internalized stigma, alcohol abuse, low levels of social support, visiting traditional healers and burden of HIV symptoms —— all give insights into the challenges treatment-experienced people living with HIV are dealing with on a daily basis even after several years of taking ART. The current biomedical approach to HIV treatment is that you take your ART regularly, you feel better and your life returns to 'normal'. This script, however, does not always play out in people's lives [64]. Tsai *et al*. [65] suggest that stigma in low-resource settings is tied with concepts of disability, economic incapacity and death, and that poverty alleviation strategies may be effective in reducing HIV-related stigma. More innovative research around self-identity and living with HIV as a chronic illness [64], combined with strategies to overcome and reduce stigma through programmes, such as poverty alleviation that can restore one's identity, are needed, as HIV services seek to support life-long ART adherence and healthy outcomes among people living with the virus.

Strengths and limitations

The strengths of this study include representation from 19 ART clinics in 18 different health facilities in three countries using standardized data collection tools, an HIV RNA test among a subsample and a systematic sampling strategy among ART patients who initiated therapy at least 6 months prior to data collection. Although the number of participating sites is one of the study's strengths, 19 ART clinics were too few to fully examine the association of programme characteristics with ART adherence. The cross-sectional design of the study restricts interpretations to associations rather than temporal relationships and causation. For example, virologic failure could have happened prior to the time frame of 3 and 30-days captured by the self-reported adherence measures, potentially explaining the low overall correlations we found between the different measures of adherence and virologic failure. Study sites were also not randomly selected, and this could have introduced selection bias. However, the selection was conducted in consultation with country-specific stake-holders and aimed to balance site characteristics that might influence retention and adherence. Within study sites, we were also unable to assess whether ART clients who declined to participate differed from those who chose to participate.

Conclusion

These data support the importance of social and behavioural factors on impacting adherence in resource-limited settings. Interventions to reduce alcohol abuse and stigma should be paramount and efforts to enhance social support may improve adherence. The findings also support a more in-depth investigation of the role that traditional healers and alternative medicines play in how adults living with HIV in sub-Saharan Africa manage their infection. Although the study did not find evidence that programme characteristics relate to incomplete adherence, there is a need to critically assess programme approaches, as well as develop interventions to address alcohol abuse and internalized stigma, among treatment-experienced adult ART clients.

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Table 1

Participant characteristics among adults in selected antiretroviral treatment programs in Tanzania, Uganda and Zambia, 2011.

Characteristic	Tanzania (*n*=1498)	Uganda (*n*=1495)	Zambia (*n*=1496)	Total number of participants (*N*=4489)	Sample from sites with VL measurements (*n*=1497)
Demographics					
Age (years) median (IQR)	41 (35–47)	39 (34–46)	40 (34–47)	40 (34–47)	39 (33–46)
Age: *n* (%)					
<35 years	350 (23.4)	406 (27.2)	395 (26.4)	1151 (25.6)	443 (29.6)*
≥35 years	1133 (75.6)	1028 (68.8)	1093 (73.1)	3254 (72.5)	1029 (68.7)
Missing	15 (1.0)	61 (4.1)	8 (0.5)	84 (1.9)	25 (1.7)
Sex: *n* (%)					
Female	1096 (73.2)	982 (65.6)	968 (64.7)	3045 (67.8)	999 (66.7)
Male	402 (26.8)	514 (34.4)	528 (35.3)	1444 (32.2)	498 (33.3)
Marital status: *n* (%)					
Single	204 (13.6)	116 (7.8)	122 (8.2)	442 (9.8)	149 (9.95)
Separate/divorced/widowed	425 (28.4)	637 (42.6)	476 (31.8)	1538 (34.3)	496 (33.1)
Married/cohabitating	863 (57.6)	734 (49.1)	898 (60.0)	2495 (55.6)	850 (56.8)
Missing	6 (0.4)	8 (0.5)	0 (0.0)	14 (0.3)	2 (0.1)
ART characteristics					
Length of time on ART: *n* (%)					
<2.2 years	425 (28.4)	373 (24.9)	304 (20.3)	1102 (24.5)	316 (21.1)*
2.2–5.3 years	739 (52.9)	735 (49.2)	721 (48.2)	2249 (50.1)	774 (51.7)
>5.3 years	280 (18.7)	387 (25.9)	471 (31.5)	1138 (25.4)	407 (27.2)
Current ART regimen: *n* (%)					
D4T, 3TC, NVP	561 (37.4)	11 (0.7)	159 (10.6)	731 (16.3)	321 (21.4)*
TDF, 3TC/FTC, EFV	116 (7.7)	86 (5.8)	498 (33.3)	700 (15.6)	263 (17.5)
ZDV, 3TC, EFV	396 (26.4)	300 (20.1)	78 (5.2)	774 (17.2)	271 (18.1)
ZDV, 3TC, NVP	262 (17.5)	909 (60.8)	256 (17.1)	1427 (31.8)	418 (27.9)
Other regimens	70 (4.7)	175 (11.7)	437 (29.2)	682 (15.2)	198 (13.2)
Missing	93 (6.2)	14 (0.9)	68 (4.5)	175 (3.9)	26 (1.7)
$CD4^+$ cell count prior to ART: *n* (%)					
>250 cells/μl	213 (14.2)	111 (7.4)	243 (16.2)	567 (12.6)	198 (13.2)
≤250 cells/μl	995 (66.4)	1087 (72.7)	938 (62.7)	3020 (67.3)	989 (66.1)
Missing	290 (19.4)	297 (19.9)	315 (21.1)	902 (20.1)	310 (20.7)

3TC, lamivudine; D4T, stavudine; EFV, efavirenz; FTC, emtricitabine; IQR, interquartile range; NVP, nevirapine; TDF, tenofovir; VL, viral load; ZDV, zidovudine.

*$P<0.05$ comparing the subset of participants from VL testing sites to the total study sample.

Table 2

Number of individuals with incomplete adherence by the different adherence measures and standardized cut-off points among adults in selected antiretroviral treatment programs in Tanzania, Uganda and Zambia, 2011.

		Complete population		Sample from sites with VL measurements	
	Cut-off	***n/N*** [a]	**% less than the cut-off**	***n/N*** [b]	**%**
Self-reported adherence measures					
% ARV drugs missed – last 3 days	100%	249/4299	5.8	109/1470	7.4
	95%	249/4299	5.8	109/1470	7.4
	90%	235/4299	5.5	106/1470	7.2
	80%	130/4299	3.0	55/1470	3.7
% ARV drugs missed – last 30 days	100%	517/4289	12.1	239/1460	16.4
	95%	113/4289	2.6	43/1460	2.9
	90%	46/4289	1.1	14/1460	1.0
	80%	22/4289	0.5	8/1460	0.5
% ARV drugs missed – visual analogue scale, last 30 days	100%	2599/4450	58.4	682/1484	46.0
	95%	1730/4450	38.9	427/1484	28.8
	90%	1119/4450	25.1	253/1484	17.0
	80%	511/4450	11.5	85/1484	5.7
Case Adherence Index	>10	751/4473	16.8	304/1493	20.4
Missed ≥48 consecutive hours of ARV drugs in last 3 months	Yes	141/4425	3.2	64/1471	4.4
Other adherence measures					
Healthcare provider report	100%	3150/4415	71.3	792/1463	54.1
	95%	1835/4415	41.6	476/1463	32.5
	90%	1236/4415	28.0	302/1463	20.6
	80%	594/4415	13.5	157/1463	10.7
Pharmacy medication possession ratio (MPR)	100%	3261/4070	80.1	1275/1450	87.9
	95%	2131/4070	52.4	837/1450	57.7
	90%	1634/4070	40.1	659/1450	45.4
	80%	979/4070	24.1	429/1450	29.6

[a] Number nonadherent/total number of individuals with data in the population. ARV, antiretroviral.

[b] The denominators for these adherence measures vary due to missing data mainly on the current ART regimen and associated daily pill burden needed to calculate adherence.

Table 3

Association between adherence measures and virologic failure at least 1000 copies/ml among adults in selected antiretroviral treatment programmes in Tanzania, Uganda and Zambia, 2011.

	Patients with virologic failure ≥1000 copies/ml		
	n/N [a]	**OR (95% CI)** [b]	***P*** *
Self-reported adherence measures[c]			
% ARV drugs missed – last 3 days			
<93%	12/107 (11.2%)	1.28 (0.68–2.42)	0.450
≥93%	132/1363 (9.7%)		
% ARV drugs missed – last 30 days			
<99%	22/237 (9.3%)	1.04 (0.63–1.69)	0.888
≥99%	122/1223 (10.0%)		
% ARV drugs missed – visual analogue scale – last 30 days			
<99%	68/633 (10.7%)	0.86 (0.57–1.30)	0.479
≥99%	80/851 (9.4%)		
CASE Adherence Index			
<11	33/304 (10.9%)	1.30 (0.84–2.01)	0.233
≥11	115/1189 (9.7%)		
Missed ≥48 consecutive hours of ARV drugs in past 3 months			
≥48 h	16/64 (25.0%)	2.86 (1.56–5.26)	0.001
<48 h	128/1407 (9.1%)		
Other adherence measures			
Healthcare provider report			
<98%	82/628 (13.1%)	1.57 (1.02–2.41)	0.042
≥98%	60/835 (7.2%)		
Pharmacy medication possession ratio (MPR)			
<90%	72/659 (10.9%)	1.48 (1.02–2.15)	0.037
≥90%	67/791 (8.5%)		

ARV, antiretroviral; CI, confidence interval; OR, odds ratio.

[a] *N*, number of patients in subgroup; *n*, number of failures in subgroup.

[b] OR of failure among incomplete-adherent versus adherent patients from logistic regression.

[c] Cut-off points determined by receiver operator curve (ROC) analysis.

* *P* for association between adherence measure and failure, adjusted for ART study site.

Table 4

Bivariate analysis of missed at least 48 consecutive hours of antiretroviral therapy in the past 3 months among adults in selected antiretroviral treatment programmes in Tanzania, Uganda and Zambia, 2011.

	N=4425	Total %	<48 h (*n*=4284) %	≥48 h (*n*=141) %	Odds ratio (95% CI)	*P*
Demographics						
Age (in years)						
<35	1128	26.0	26.0	26.2	0.97 (0.66–1.43)	0.867
≥35 years	3215	74.0	74.0	73.8	1	
Missing	82		82	0		
Female sex	3006	67.9	68.2	61.0	0.72 (0.51–1.02)	0.065
Marital status						
Single	434	9.8	9.7	12.8	1.54 (0.90–2.63)	0.227
Separated/divorced/widowed	1523	34.5	34.4	37.6	1.24 (0.86–1.80)	
Married or cohabiting	2456	55.7	55.9	49.6	1	
Missing	12		12	0		
DHS Wealth Index						
Low	1473	33.3	33.4	31.2	0.79 (0.50–1.25)	0.579
Middle	1476	33.4	33.4	31.9	0.86 (0.56–1.31)	
High	1476	33.4	33.2	36.9	1	
Psychosocial factors						
Stigma internalized						
High (>median)	1540	34.8	34.3	49.6	1.63 (1.15–2.32)	<0.006
Low	2883	65.2	65.7	50.4	1	
Missing	2		2	0		
Stigma disclosure						
High (>median)	1212	27.4	27.5	25.5	0.92 (0.59–1.44)	<0.728
Low	3211	72.6	72.5	74.5	1	
Missing	2		2	0		
Potential depression						
Positive screen	574	13.0	12.6	23.4	1.89 (1.25–2.87)	0.003
Negative screen	3847	87.0	87.4	76.6	1	
Missing	4		4	0		
Ever-disclosed HIV status						
Yes	4154	94.0	94.0	92.9	0.90 (0.45–1.79)	0.771
No	267	6.00	6.00	7.10	1	
Missing	4		4	0		
Social support care						
Lower 10th percentile	513	11.7	11.4	20.0	1.71 (1.10–2.67)	0.017
Higher	3865	88.3	88.6	80.0	1	
Missing	48		47	1		
Social support help						
Lower 10th percentile	595	13.6	13.5	17.1	1.23 (0.77–1.95)	0.387

	N=4425	Total %	<48 h (*n*=4284) %	≥48 h (*n*=141) %	Odds ratio (95% CI)	*P*
Higher	3782	86.4	86.5	82.9	1	
Missing	48		47	1		
CAGE alcohol abuse						
Positive ≥2	930	21.2	20.8	34.3	1.87 (1.29–2.70)	<0.001
Negative<2	3448	78.8	79.2	65.7	1	
Missing	47		46	1		
Traditional healer						
Ever consulted	253	5.8	5.4	15.6	2.67 (1.55–4.60)	<0.001
Never consulted	4136	94.2	94.6	84.4	1	
Missing	36		36	0		
Cost to clinic						
≥1 USD	1924	45.9	46.0	41.5	0.82 (0.56–1.20)	0.310
<1 USD	2269	54.1	54.0	58.5	1	
Missing	232		226	6		
Time to clinic						
≥30 min	2298	52.0	51.9	52.5	0.93 (0.65,1.34)	0.694
<30 min	2215	48.0	48.1	47.5	1	
Missing	2		2	0		
ART and clinical factors						
ART regimens containing						
EVF	1540	34.8	34.7	38.3	1.35 (0.94–1.95)	0.103
NVP	2567	58.0	58.3	48.9	0.57 (0.40–0.81)	0.002
ZDV	2224	50.3	50.2	51.8	0.85 (0.58–1.25)	0.410
TDF	1131	25.6	25.7	20.6	0.95 (0.60–1.50)	0.823
D4T	805	18.2	18.2	17.0	0.84 (0.50–1.39)	0.490
FTC	1020	23.1	23.2	17.7	0.92 (0.56–1.51)	0.752
3TC	3191	72.1	72.1	72.3	0.72 (0.47–1.11)	0.141
PI	136	3.10	3.10	3.50	1.13 (0.45–2.86)	0.798
Time on ART						
<2.2	1089	24.6	24.5	27.7	1.18 (0.73–1.90)	0.597
2.2–5.3	2213	50.0	50.1	46.8	0.96 (0.62–1.46)	
>5.3	1123	25.4	25.4	25.5		
Pill burden (self-report)						
<4	3510	81.3	81.2	84.7	1.15 (0.70–1.90)	0.578
≥4	809	18.7	18.8	15.3	1	
Missing	106		96	10		
HIV symptom index (≥ median)	2458	55.5	55.0	73.0	1.98 (1.34–2.94)	<0.001
Pre-ART WHO stage						
Missing	381	8.6	8.7	7.1	0.95 (0.47–1.95)	0.144
Stage IV	517	11.7	11.4	19.1	1.74 (1.02–2.96)	
Stage III	1842	41.6	41.6	42.6	1.38 (0.92–2.09)	

	N=4425	Total %	<48 h (*n*=4284) %	≥48 h (*n*=141) %	Odds ratio (95% CI)	*P*
Stage I and II	1685	38.1	38.3	31.2		
Pre-ART $CD4^+$ cell count (cells/μl)						
Missing	889	20.1	20.0	22.0	1.11 (0.73–1.69)	.038
>250	558	12.6	12.7	9.2	0.69 (0.38–1.26)	
≤250	2978	67.3	67.3	68.8	1	
Site-level factors						
Buddy required to start ART (yes)	3440	77.7	77.5	85.1	1.51 (0.54–4.21)	0.4051
Community ART dispensing (yes)	1228	27.8	28.0	19.9	0.53 (0.20–1.39)	0.182
ART dispensing in clinic	2823	63.8	63.4	74.5	1.54 (0.66–3.60)	0.301
ART refill frequency						
Every 3 months	1224	27.7	27.3	39.0	3.15 (0.41–4.11)	0.152
Every 2 months	2217	50.1	50.1	49.6	2.35 (0.77–7.19)	
Every month	984	22.2	22.6	11.3	1	
Level of health facility						
National	732	16.5	16.4	21.3	1.30 (0.41–4.11)	0.174
Provincial/regional	983	22.2	21.9	30.5	1.22 (0.39–3.79)	
District	1480	33.4	34.0	17.7	0.42 (0.14–1.26)	
Primary/community	1230	27.8	27.7	30.5	1	
Type of health facility						
Government	2467	55.8	56.4	36.2	0.40 (0.16–1.00)	0.086
Mission	976	22.1	21.8	31.2	0.84 (0.30–2.39)	
NGO	982	22.2	21.8	32.6	1	
Health facility size						
<1000 on ART	1344	30.4	30.3	31.9	1.05 (0.28–3.95)	0.955
1000–2000	370	8.4	8.4	7.1	1.20 (0.20–7.07)	
2000–4000	1723	38.9	38.8	41.8	1.34 (0.38–4.72)	
>4000	988	22.3	22.4	19.1	1	
Locale						
Nonurban	1470	33.2	33.5	26.2	0.49 (0.19–1.22)	0.118
Urban	2955	66.8	66.5	73.8	1	
Lay person provides adherence counselling	3566	80.6	80.6	80.1	0.86 (0.30–2.42)	0.758
ART stock out past 6 months	497	11.2	11.4	5.0	0.41 (0.10–1.72)	0.209

3TC, lamivudine; ART, antiretroviral therapy; CI, confidence interval; D4T, stavudine; DHS, demographic and health survey; EFV, efavirenz; FTC, emtricitabine; NGO, nongovernmental organization; NVP, nevirapine; PI, protease inhibitors; TDF, tenofovir; USD, United States dollar; ZDV, zidovudine.

Table 5

Final multivariable model for factors associated with incomplete adherence: missed at least 48 consecutive hours of antiretroviral drugs among adults in selected antiretroviral treatment programmes in Tanzania, Uganda and Zambia, 2011.

	Adjusted odds ratio (95% CI)	*P*
Internalized stigma: high	1.50 (1.05–2.13)	0.025
Social support care: low	1.55 (0.99–2.43)	0.054
Alcohol abuse: positive	1.68 (1.16–2.44)	0.006
HIV symptoms: high	1.79 (1.20–2.67)	0.004
Traditional medicine: ever visited	2.41 (1.39–4.18)	0.002
ART regimen includes NVP: Yes	0.60 (0.42–0.85)	0.005

ART, antiretroviral treatment; CI, confidence interval; NVP, nevirapine.