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How late is too late? Timeliness to scheduled visits as an antiretroviral therapy adherence measure in Nairobi, Kenya and Lusaka, Zambia

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Collecting self-reported data on adherence to highly active antiretroviral therapy (HAART) can be complicated by patients' reluctance to report poor adherence. The timeliness with which patients attend visits might be a useful alternative to estimate medication adherence. Among Kenyan and Zambian women receiving twice daily HAART, we examined the relationship between self-reported pill taking and timeliness attending scheduled visits.

We analyzed data from 566 Kenyan and Zambian women enrolled in a prospective 48-week HAART-response study. At each scheduled clinic visit, women reported doses missed over the preceding week. Self-reported adherence was calculated by summing the total number of doses reported taken and dividing by the total number of doses asked about at the visit attended. A participant's adherence to scheduled study visits was defined as "on time" if she arrived early or within three days, "moderately late" if she was four–seven days late, and "extremely late/missed" if she was more than eight days late or missed the visit altogether.

Self-reported adherence was <95% for 29 (10%) of 288 women who were late for at least one study visit vs. 3 (1%) of 278 who were never late for a study visit (odds ratios [OR] 10.3; 95% confidence intervals [95% CI] 2.9, 42.8). Fifty-one (18%) of 285 women who were ever late for a study visit experienced virologic failure vs. 32 (12%) of 278 women who were never late for a study visit (OR 1.7; 95% CI 1.01, 2.8). A multivariate logistic regression model controlling for self-reported adherence found that being extremely late for a visit was associated with virologic failure (OR 2.0; 95% CI 1.2, 3.4).

Timeliness to scheduled visits was associated with self-reported adherence to HAART and with risk for virologic failure. Timeliness to scheduled clinic visits can be used as an objective proxy for self-reported adherence and ultimately for risk of virologic failure.

Keywords: adherence; self-reported adherence; timeliness to visit; virologic failure; antiretroviral; human immunodeficiency virus (HIV); Africa

Introduction

Since the rollout of highly active antiretroviral therapy (HAART) began in sub-Saharan Africa, survival has improved for HIV-infected people who have access to these lifesaving drugs (Jahn et al., 2008; Stringer et al., 2006).[1] Concerns that people living in resource-constrained settings might not be able to adhere to complicated drug regimens have proven largely unwarranted (Attaran, 2007; Carlucci et al., 2008; Laurent et al., 2002; Mills, Nachega, Bangsberg et al., 2006; Orrell, Bangsberg, Badri & Wood, 2003; Weidle et al., 2006). As HAART programs continue to be scaled-up, ensuring that HAART-naïve and HAART-experienced patients remain adherent to treatment is critically important (Mannheimer et al., 2005, 2006; Mills, Nachega, Buchan et al., 2006).

Poor adherence to HAART leads to sub-therapeutic drug levels that increase the risk of developing viral drug resistance (Mannheimer, Friedland, Matts, Child, & Chesney, 2002; Sethi, 2004; Wainberg & Friedland, 1998). There are many methods to measure adherence, but none are perfect, especially within the context of developing countries (Berg & Arnsten, 2006; Colebunders et al., 2006; Gill, Hamer, Simon,

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Thea & Sabin, 2005; Mannheimer et al., 2005; Mills, Nachega, Bangsberg, et al., 2006; Mills, Nachega, Buchan, et al., 2006; Orrell, 2005). High-tech approaches to assess adherence such as cellular phone reminders or techniques that require computer literacy may not be feasible in all resource-constrained settings. Viral-load testing might provide the best measure of drug effect and adherence; however, many resource-constrained countries have neither the resources nor infrastructure to routinely perform this assay (Berg & Arnsten, 2006; Colebunders et al., 2006; Mannheimer et al., 2006; Orrell, 2005). While directly observed therapy has been shown to produce high HAART adherence, it is costly in terms of both monetary and human resources (Liechty & Bangsberg, 2003). Indirect measures, such as self-reported adherence, are used most commonly because they are inexpensive and simple to collect, however, they are subject to social desirability bias (Bangsberg, 2008; Mills, Nachega, Bangsberg, et al., 2006; Mills, Nachega, Buchan, et al., 2006; Nieuwkerk & Oort, 2005; Orrell, 2005). There have been numerous studies to better understand the accuracy of self-reported adherence, but they have not consistently demonstrated that self-reported adherence reliably reflects actual adherence (Bisson, Gross et al., 2008; Gill et al., 2005; Kouanfack et al., 2008; Oyugi et al., 2004).

One of the challenges with any drug-adherence program is ensuring that patients arrive to their scheduled visit prior to running out of medication. Not attending pill-refill visits has been associated with virologic failure (Berg & Arnsten, 2006; Berg et al., 2005; Carlucci et al., 2008; Krebs et al., 2008; Lucas, Chaisson, & Moore, 1999; Park et al., 2008; Rastegar, Fingerhood & Jasinski, 2003; Sethi, Celentano, Gange, Moore & Gallant, 2003). This effect can be moderated by both the extent of lateness attending a scheduled visit and the absolute number of visits missed (Berg et al., 2005; Park et al., 2008; Sethi et al., 2003).

Within the context of a 48-week observational cohort study, we examined the response to non-nucleoside reverse transcriptase inhibitor (NNRTI)-based HAART among antiretroviral therapy-naïve women presenting for treatment in Kenya and Zambia and analyzed the relationships between self-reported adherence and timeliness to visits, self-reported adherence and virologic failure, and timeliness to visits and virologic failure.

Methods

Study population

This study was a sub-study of larger three-country trial (Kenya, Zambia, and Thailand) to examine the effectiveness of NNRTI-based HAART in women exposed and unexposed to single-dose nevirapine for prevention of mother-to-child HIV transmission. That study found that women with prior exposure to a single intrapartum dose of nevirapine were more likely to experience virologic failure with the highest rate of failure among women exposed to nevirapine within six months of starting HAART; however, women exposed to nevirapine more than one year prior to starting HAART had similar virologic-response rate to unexposed women (Stringer et al., in press). We limited this analysis to women enrolled at the Kenyan and Zambian sites since adequate data were collected to assess visit timeliness only at these sites. All study participants met the Kenyan or Zambian guidelines for starting HAART, which at the time of the study were the same for both countries: (1) $CD4^+$ cell count $<200/\mu L$; (2) World Health Organization (WHO) clinical stage IV; or (3) WHO stage III and $CD4^+$ cell count $<350/\mu L$. The women were HAART-naïve and initiated HAART upon study enrolment at either the Comprehensive Care Centre, Kenyatta National Hospital, in Nairobi, Kenya or at the Matero Reference and Kanyama Clinics in Lusaka, Zambia. Enrolled participants were counseled on how to take their twice daily medications. At each study visit (weeks 2, 4, 8, 16, 24, 36, and 48), an adherence questionnaire was administered and adherence counseling was provided to all women. Drug refills were provided and each study participant was provided an extra three days of HAART at each refill visit, which coincided with the study visits. Women who were late for visits were followed-up with visits by community workers or contacted via cellular phones, when possible, in an effort to improve retention in the cohort. In lieu of a standard operating procedure for following-up women who were late, each clinic site had their own process which typically was to try to contact women after they were three–seven days late.

The Kenyatta National Hospital Ethics and Research Committee, the University of Alabama at Birmingham Institutional Review Board (IRB), the University of Zambia Research Ethics Committee, and the US Centers for Disease Control and Prevention IRB approved the parent study.

Data collection

Nurse counselors administered the adherence questionnaires, which collected self-reported adherence data from study participants at each of seven scheduled study visits (weeks 2, 4, 8, 16, 24, 36, and 48). Participants were requested to provide a one-, three-, and seven-day pill recall from memory. If a

participant indicated that she had missed a dose, the nurse counselor asked the participant to choose up to three reasons for missing the dose from a list of 12 options. Self-reported adherence was calculated by summing the total number of doses reported taken and dividing by the total number of doses asked about at visits attended. If a study participant had attended all scheduled visits, then her total number of doses eligible for query would be 98: seven visits where seven-day recall was probed regarding a twice daily regimen ($7 \times 7 \times 2 = 98$ doses). If she had taken 95 of those doses, her adherence would have been 97%. We calculated the total number of doses queried according to the number of visits attended; if a women missed one visit, her total number of doses queried would be 98–14, or 84, since she would only have contributed data from six visits she attended. We defined a priori self-reported adherence less than 95% as sub-optimal and self-reported adherence greater than or equal to 95% as satisfactory.

Using clinical records we measured the timeliness to scheduled visits by comparing the date for which the visit was scheduled to the date that the participant showed up for her visit. A study participant was defined as "on time" if she arrived for her scheduled appointment ahead of, on the scheduled day of, or within three days after the scheduled visit; as "moderately late" if she arrived four–seven days after the scheduled visit; and as "extremely late" if she was eight or more days late or missed the visit altogether.

CD4 cell counts and HIV viral loads were measured at enrollment, 24 weeks and 48 weeks. Per study protocol, women whose HIV viral load was >400 copies/ml at 24 weeks could be changed at the discretion of the provider to a second-line protease-inhibitor (PI)-based regimen. We analyzed virologic failure in two ways. We first performed analyses using the study's on-treatment criteria, by which a woman was defined as having experienced virologic failure if at 24 or 48 weeks and while taking NNRTI-based HAART her plasma HIV-RNA viral load was ≥ 400 copies/ml. In our second set of analyses, we considered only the viral load at 48 weeks regardless of whether or not she had experienced a plasma HIV-RNA viral load ≥ 400 copies/ml at 24 weeks and regardless of whether she had consequently changed to a PI-based regimen. This second on-treatment analysis is a programmatic evaluation of overall virologic response of the cohort without the confines of the study's definition for virologic failure on NNRTI. We used logistic regression to analyze the relationship between timeliness to visit, adherence, and virologic failure. For the categorical data, we used chi-square tests and calculated odds ratios (OR) and 95% confidence intervals (95% CI). For the continuous data we used Wilcoxon rank-sum tests. All analyses were performed using SAS version 9.1 (SAS Institute, Cary, NC, USA).

Results

Participant characteristics

From May 2005 through January 2007, 661 women (509 Zambian and 152 Kenyan) were enrolled in the study. By January 2008, 566 women (438 Zambian and 128 Kenyan) completed the full 48 weeks of the study and were included in the present analysis (Table 1). Compared to women in Zambia, women in Kenya were similar with respect to age, body-mass index, WHO stage of HIV disease, enrolment CD4 cell count, and prior exposure to single-dose nevirapine, but had a higher body weight and higher HIV viral load at enrolment.

Among these 566 women, 32 (6%) had a self-reported adherence below 95% (Table 2). When comparing baseline characteristics between women with self-reported adherence $<95\%$ compared with women with self-reported adherence $\geq 95\%$ there were no differences with regard to median age (32 years vs. 32 years, $p = 0.9$), weight (50.5 kilograms vs. 53 kilograms, $p = 0.2$), CD4 cell count (179 vs. 149.5, $p = 0.8$), HIV viral load (151,968 vs. 107,629, $p = 0.9$), and the proportion exposed to single-dose nevirapine (41% vs. 41%), respectively. Throughout the study 126 (22%) women reported missing at least one antiretroviral dose at 157 (4%) of 3962 adherence visits. The three most common reasons for not taking a dose were "forgetting" (39%), "participant ran out of medication" (27%), and "traveling" (16%).

Two hundred eighty-eight (51%) women were ever late for or missed 453 (11%) of 3962 scheduled visits (Table 2). At 221 (49%) of the 453 ever late and missed visits, the study participant arrived moderately late, at 213 (47%) visits the study participant was extremely late, and 19 (4%) visits were missed. Among the 288 participants who were late or missed a visit, 182 (63%) participants were late for or missed one visit, 68 (24%) were late for or missed two or more visits, and 38 (13%) were late for or missed three or more visits. Women who were extremely late were late a mean of 14 days (range 8–148).

Timeliness to visit by self-reported adherence

Self-reported adherence $<95\%$ was associated with being late for at least one study visit; 29 (10%) of 288 women who were late for at least one study visit reported adherence $<95\%$ compared with 3 (1%) of 278 women who were never late for a study visit

Table 1. Baseline characteristics of study participants who started NNRTI-based HAART between June 2005 and January 2007 in an observational cohort study, Nairobi, Kenya and Lusaka, Zambia.

	Zambia ($N=438$)		Kenya ($N=128$)		
	N (%)	Median (IQR)	*N* (%)	Median (IQR)	*p*-Value
Age, median years		32 (28, 37)		32 (28, 36)	0.81
Weight, median kilograms		52 (47, 58)		55 (49.4, 63)	<0.01
Body-mass index, median kg/m^2		19.8 (18.4, 22.1)		20.3 (18.0, 22.7)	0.48
WHO stage of HIV disease					
I/II	189 (43)		57 (45)		
III	216 (49)		59 (46)		
IV	33 (8)		12 (9)		
CD4+ lymphocyte count, median cells/μL		149 (91, 215)		157 (83.5, 216.5)	0.74
Plasma viral load, median log copies/mL – (missing = 4)		90,600 (25,300, 272,000)		212,319.5 (44,459, 750,000)	<0.01
Exposed to single-dose nevirapine for prevention of mother-to-child transmission in the past	173 (39)		60 (47)		0.14

Note: IQR, interquartile range; WHO, World Health Organization.

(unadjusted OR 10.3; 95% CI 2.9, 42.8: Table 3). Using a logistic regression model, when compared with having never been late for a study visit, we found that self-reported adherence <95% was also associated with being moderately late, but never extremely late for a visit (unadjusted OR 9.4; 95% CI 2.6, 34.4) or having ever been extremely late (including missed visits) for a visit (unadjusted OR 10.9; 95% CI 3.1, 37.4). The association with self-reported adherence <95% was similar among women who were moderately late for one visit (unadjusted OR 9.4; 95% CI 2.5, 35.4) and moderately late for two visits (unadjusted OR 12.2; 95% CI 1.9, 78.8).

Timeliness to visits, self-reported adherence, and virologic failure on non-nucleoside reverse transcriptase inhibitor (NNRTI)-based highly active antiretroviral therapy (HAART)

Using the on-treatment analysis criteria, 83 (15%) of 563 women experienced virologic failure at either 24 or 48 weeks on NNRTI-based HAART (three

Table 2. Adherence and timeliness to visit characteristics of study participants in NNRTI-based HAART study between June 2005 and January 2007, Nairobi, Kenya and Lusaka, Zambia.

Variable	Total ($N=566$)	Zambia ($N=438$)	Kenya ($N=128$)	*p*-Value
Adherence				
Number who reported adherence <95%[a]	32 (6%)	21 (5%)	11 (9%)	0.19
Number who reported missing ≥one dose	126 (22%)	80 (18%)	46 (36%)	<0.01
Number of times doses reported missed	157	95	62	–
Timeliness to scheduled visits				
Number who were late >three days or missed a visit ≥one time[b]	288 (51%)	222 (51%)	66 (52%)	0.86
Number who were moderately late (four–seven days late), but never extremely late	118 (21%)	93 (21%)	25 (20%)	0.76
Number ever extremely late (>eight days late) and/or missed scheduled visit	170 (30%)	129 (29%)	41 (32%)	0.58

[a]There were no significant differences between women with self-reported adherence <95% and women with self-reported adherence >95% for the baseline characteristics age, body-mass index, CD4 cell count, viral load, and prior exposure to single-dose nevirapine (as shown in Table 1).

[b]Women who were never late tended to be older, median age was 33 (IQR 29, 37) vs. those who were ever late, median age was 31 (IQR 27, 36; $p=0.001$). There were no other significant differences between women who were ever late for a visit and women who were never late for a visit for the baseline characteristics. Adjusting for age did not alter the *p*-value significantly for any of the "timeliness to scheduled visits" analyses.

Note: HAART, highly active antiretroviral therapy; NNRTI, non-nucleoside reverse transcriptase inhibitor.

Table 3. Univariate and multivariate odds ratios and 95% confidence intervals for self-reported adherence, timeliness to visit, regimen change, and virologic failure in NNRTI-based HAART study between June 2005 and January 2007, Nairobi, Kenya and Lusaka, Zambia.

	Self-reported adherence <95%	Changed regimen to PI-based HAART	Virologic failure, while on NNRTI-based HAART regimen		Virologic failure, regardless of NNRTI- or PI-based regimen	
	Unadjusted OR (95% CI)	Unadjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)
Self-reported adherence						
≥95%	–	Ref	Ref	Ref	Ref	Ref
<95%	–	7.2 (2.5, 20.2)[a]	2.5 (1.1, 5.7)	2.1 (0.9, 4.9)	2.9 (1.3, 6.6)	2.3 (1.0, 5.5)
Ever late to a scheduled visit?						
Never late	Ref	Ref	Ref	–	Ref	–
Ever late	10.3 (2.9, 42.8)	2.4 (0.97, 6.0)	1.7 (1.04, 2.7)	–	2.0 (1.2, 3.3)	–
How late to scheduled visits						
Never late	Ref	Ref	Ref	Ref	Ref	Ref
Moderately late (four–seven days late), but never extremely late	9.4 (2.6, 34.4)	2.1 (0.8, 6.0)	1.06 (0.5, 2.1)	1.0 (0.5, 1.9)	0.9 (0.4, 2.0)	0.9 (0.4, 1.9)
Ever extremely late (>eight days late) and/or missed scheduled visit	10.9 (3.1, 37.4)	2.6 (1.03, 6.4)	2.2 (1.3, 3.6)	2.0 (1.2, 3.4)	2.8 (1.6, 4.9)	2.6 (1.5, 4.5)

[a]Adjusted logistic regression models included "self-reported adherence" and "How late to scheduled visits." Models that also adjusted for prior exposure to single-dose nevirapine did not change the adjusted odds ratios presented in the table.

Note: HAART, highly active antiretroviral therapy; PI, protease inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; OR, odds ratios; 95% CI, 95% confidence intervals.

women were switched to PI-based HAART before 24 weeks due to drug intolerance). Nine (29%) of 31 women with self-reported adherence <95% experienced virologic failure compared with 74 (14%) of 532 women with self-reported adherence ≥95% (unadjusted OR 2.5; 95% CI 1.04, 6.1: Table 3). Similarly, 51 (18%) of 285 women who were ever late for a study visit experienced virologic failure compared with 32 (12%) of 278 women who were never late for a study visit (unadjusted OR 1.7; 95% CI 1.01, 2.8). Further analysis demonstrated that, compared with women who were never late, women who were only moderately late were at similar risk for virologic failure (unadjusted OR 1.1; 95% CI 0.5, 2.1), but women who were ever extremely late or missed a visit were at greater risk for virologic failure (unadjusted OR 2.2; 95% CI 1.3, 3.6). A logistic regression model controlling for self-reported adherence found that being extremely late or missing a visit was associated with experiencing virologic failure, (adjusted OR 2.0; 95% CI 1.2, 3.4). Models that also adjusted for prior exposure to single-dose nevirapine did not change the adjusted OR.

Change to a second-line protease-inhibitor (PI)-based therapy by self-reported adherence and timeliness to visit

Women with self-reported adherence <95% were more likely than women with self-reported adherence ≥95% to have switched to a PI-based regimen (7/32 [22%] vs. 20/534 [4%], respectively; unadjusted OR 7.2; 95% CI 2.5, 20.2). Women who were late for or missed any visits were more likely to have switched to a PI-based HAART regimen compared with women who were never late (OR 2.4; 95% CI 0.97, 6.0). When the comparison was limited to women who were extremely late compared with women who were never late, we found that women who had been extremely late were more likely to have switched to PI-based HAART (OR 2.6, 95% CI 1.03, 6.4).

Virologic suppression regardless of the type of HAART regimen

Using our second definition for virologic failure, there were 72 women who were not virologically suppressed at 48 weeks (i.e., study completion), regardless of HAART regimen. We found that compared to women with self-reported adherence ≥95%, women with self-reported adherence <95% were more likely to have experienced virologic failure (unadjusted OR 2.9; 95% CI 1.3, 6.6). Compared with women who were never late for a study visit, virologic failure was more common among women who were ever late for at least one study visit (unadjusted OR 2.0; 95% CI 1.2, 3.3) and women who were ever extremely late (unadjusted OR 2.8; 95% CI 1.6, 4.9).

Discussion

This analysis among women initiating HAART in Zambia and Kenya demonstrated an association between being late for scheduled clinic visits and poor self-reported adherence. Women who reported non-adherence to antiretroviral drugs were more likely to have been late for clinic visits. This association was found whether the women were moderately late (four–seven days late) or extremely late (≥eight days late) for their scheduled visit. We also found being extremely late for a scheduled study visit was associated with (1) virologic failure, whether defined as failure while on NNRTI-based HAART or failure at 48 weeks regardless of regimen, and (2) having switched to a PI-based regimen. Our data suggest that in resource-constrained settings with few antiretroviral options, identifying and removing obstacles to being extremely late for clinic visits would improve response to HAART and reduce the need to switch to second-line therapy.

The high level of self-reported adherence for taking antiretrovirals that we measured in this study is similar to self-reported adherence levels reported in other studies from sub-Saharan Africa (Carlucci et al., 2008; Jahn et al., 2008; Kouanfack et al., 2008; Mills, Nachega, Bangsberg et al., 2006; Weidle et al., 2006). However, we found many persons were occasionally, moderately, or even extremely late to one or more visits despite reporting high levels of adherence. Others have reported that missing visits was correlated with poor clinical outcomes for persons infected with HIV (Berg et al., 2005; Lucas, Chaisson & Moore, 1999; Park et al., 2008; Rastegar, Fingerhood & Jasinski, 2003). The Berg, Lucas, and Rastegar studies show that non-adherence to scheduled appointments was associated with poor clinical outcomes, specifically failure to suppress viral load; while the Park study collected self-reported reasons for visit non-adherence. None of the above-mentioned studies, however, considered lateness to appointments as a variable. Recent analyses of adherence to HAART in central and southern Africa have used measures such as drug possession ratio or pharmacy refill patterns that incorporate timeliness to visit into the adherence measure, but not lateness to the visit as a stand-alone measure (Bisson, Rowh et al., 2008; Muyingo et al., 2008).

We found that being four–seven days late for a scheduled visit once or twice during a 48-week time frame was not associated with virologic failure.

However, being ≥eight days late for one or more visits or missing a visit entirely was associated with virologic failure and an increased likelihood of having switched to second-line HAART. Likewise, being late for a scheduled visit is positively associated with self-reported adherence <95%, suggesting that timeliness to attending scheduled clinical visits is an effective means of identifying people at risk of or who are experiencing sub-optimal self-reported adherence. Self-report of poor adherence among women who are ≥eight days late for one or more visits or missed a visit entirely suggests that women are forthcoming about their adherence, likely related to running out of medication. Importantly, women who are never late for a scheduled visit are very unlikely to self-report adherence <95%. Regardless, self-reported adherence likely plays an important role within ARV programs because the regular attention given to adherence by making it a standard component of clinic visits reinforces lessons taught during initial counseling about adherence.

Our analysis was subject to several limitations. The study only included women and may not be generalizable to men. We calculated self-reported adherence values based on visits attended. If a woman did not attend a visit at all, the denominator changed to reflect the total number of visits attended (and doses that could have been taken). Women who had missed visits over the course of the study might have received higher overall adherence values despite lower actual adherence, which may have weakened that association between adherence and virologic failure. Additionally, this analysis did not include those participants who were lost to follow-up during the study (approximately 15% of the enrolled study cohort). We did not collect the reasons why study participants were late for their scheduled visits in this study; these data might have provided valuable insight to the barriers preventing women from attending scheduled visits. Women participating in this study were enrolled in an observational cohort study and received a level of care, counseling, monitoring, and follow-up that may not be feasible in all programs in resource-constrained settings. Some women in this cohort had prior exposure to single-dose nevirapine for prevention of mother to child transmission (PMTCT) which might have affected virologic outcome; however, similar numbers of single-dose nevirapine exposed women were in the group with adherence <95% and ≥95% and adjustment for this in multivariate models did not change the magnitude of the findings presented in Table 3.

We found that being late for a study visit was associated with sub-optimal self-reported adherence. We also found that being extremely late to or missing a visit was associated with virologic failure and the need to switch to second-line therapy. Data on timeliness to scheduled visits might help clinicians identify patients who need support to attend clinic visits on time. This in turn could improve adherence to HAART by preventing patients from running out of their medication supply. Our data suggest that staff administering antiretroviral programs could use timeliness to scheduled visits as a means of identifying patients at risk of poor adherence and ultimately virologic failure. If so used, programs would need to include a means for rapidly locating individuals who are late for clinic visits to reduce periods of time where the patient is not on his or her regimen. Many programs use tools such as cell phones for calling or SMS and community liaisons to contact study participants already and these systems can be adapted to contact patients who are late for their HAART-refill visits. Identifying HIV-infected persons on HAART who are late for visits might overcome a barrier to HAART adherence, improve virologic response, and delay the change to second-line HAART regimens.

Conflict of interest

None of the authors report conflict of interests.

Human subjects protections

The Kenyatta National Hospital Ethics and Research Committee, the University of Alabama at Birmingham Institutional Review Board (IRB) and the University of Zambia Research Ethics Committee, and the US Centers for Disease Control and Prevention IRB approved the study.

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Note

1. Preliminary data from this paper were presented at the 17th International AIDS Society Conference, Mexico City, Mexico, August 2008.

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