

Monitoring Adherence and Defaulting for Antiretroviral Therapy in 5 East African Countries: An Urgent Need for Standards

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Objectives: A cross-sectional survey was performed in 24 systems of care providing antiretroviral medications in Ethiopia, Kenya, Rwanda, Tanzania, and Uganda to examine current practices in monitoring rates of treatment adherence and defaulting. **Results:** Only 20 of 48 facilities reported routinely measuring individual patient adherence levels; only 12 measured rates of adherence for the clinic population. The rules for determining which patients were included in the calculation of rates were unclear. Fourteen different definitions of treatment defaulting were in use. Facilities routinely gather potentially useful data, but the frequency of doing so

varied widely. **Conclusions:** Individual and program treatment adherence and defaulting are not routinely monitored; when done, the operational definitions and methods varied widely, making comparisons across programs unreliable. There is a pressing need to determine which measures are the most feasible and reliable to collect, the most useful for clinical counseling, and most informative for program management.

Keywords: adherence; defaulting; antiretroviral medications; East Africa

Introduction

Global health initiatives have responded to the HIV/AIDS pandemic by introducing antiretroviral therapy (ART) to ever-increasing numbers of affected patients. This is a lifelong therapy, and its success relies on continual adherence to the medications. Accepted wisdom is that a 90%¹ to 95%² rate of adherence is necessary to avoid rapid development of drug resistance and treatment failure, although recent analyses have questioned the validity of that standard.³ Whatever the appropriate adherence target, reviews of more than 50 years of research have shown that achieving adherence rates of more than 80% for treating chronic illness has been problematic.^{4,5} Thus far, large-scale African ART programs have reported mixed results on patient adherence to antiretroviral (ARV) medicines⁶ with some programs

reporting high levels^{7,8} and some reporting much lower levels.⁹ With rapidly expanding access to ARV medicines in resource-poor settings, it is vital to monitor adherence and to identify interventions that can encourage sustained adherence.

However, to determine the need for adherence-related interventions, reliable and consistent ways of measuring adherence to therapy at both individual and program levels are needed. Individual measures would help detect patients with poor adherence and guide appropriate personal interventions. Program adherence rates would identify poorly performing programs and target systems improvement interventions and the metrics to evaluate the success of these interventions.

We developed a survey to examine current practices in monitoring treatment adherence and defaulting rates in East African ART programs and

to determine which data on adherence and clinical measures of treatment success are routinely recorded and used to assess program effectiveness.

Methods

We carried out a survey of ART programs and facilities in 5 East African countries (Ethiopia, Kenya, Rwanda, Tanzania, and Uganda). Teams from the International Network for the Rational Use of Drugs (INRUD) together with staff from each country's national AIDS control program administered standardized questionnaires to ART program managers in several of the main systems of care and to clinical practitioners at individual health facilities.

We defined a system of care as a group of health facilities offering ART, which are managed by a single administrative entity, such as the ministry of health, a nongovernmental organization (NGO), a university, or an employer. In principle, AIDS treatment facilities in many countries are overseen by their national AIDS control programs, but policies and procedures often differ in systems of care administered by different organizations. Within each system of care, we surveyed 1 central and 1 satellite health facility providing ART. Field work took place in February and March 2006.

The researchers worked with representatives from the national AIDS control programs to identify the systems of care in each country that were treating the most people with ARV drugs; they also included, if possible, 1 system of care that performed viral load testing. We sought to interview the administrator responsible for program monitoring in each system of care and an individual familiar with

clinical and pharmaceutical information systems and operational procedures in each health facility.

Results

Researchers conducted interviews with ART program managers in 24 systems of care, which represented 663 facilities that provide ART services to more than 200 000 patients in the 5 study countries (Table 1). Of these 24 interviews, 18 were face-to-face, 4 were by telephone, and 2 were self-administered questionnaires. In addition, within these care systems, interviews with facility managers or senior clinicians were carried out in 48 health facilities that provide ART to more than 86 000 patients. Of these 48 interviews, 36 were face-to-face, 7 were by telephone, and 5 were self-administered questionnaires. These health facilities included 13 referral hospitals, 12 provincial or district hospitals, 4 mission hospitals, 3 military or police hospitals, 4 private or public/private hospitals, 4 mission clinics, 5 NGO clinics, 2 health centers, and 1 community-based organization.

Despite the potential availability of several types of adherence data, there was little consistency in how the data were used. Less than half of the facilities (20 of 48) reported that they routinely calculated individual patient adherence rates. Of those that did, 2 used a 3-day recall method, asking patients if they had missed any doses in the last 3 days, 6 used pill count data, and the actual method that the other 12 facilities used was unclear.

Only 12 of 48 facilities surveyed calculated adherence rates for the clinic population as a whole, although another 8 were planning to do so. Of these,

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Table 1. Characteristics of the Systems of ART Care and Health Facilities Included in the Study

	Ethiopia	Kenya	Rwanda	Tanzania	Uganda
Systems of care	7 ^a	6 ^b	1 ^c	5 ^d	5 ^e
Earliest ART program	2003	2001	1999	2004	1991
Health facilities in these systems	102	248	84	177	52
ART patients in these systems	24 000	74 535	19 058	42 540	67 438
Adults	22 000	70 035	17 615	38 757	61 332
Children	2000	4500	1443	3783	6106
Health facilities in survey	10	14	5	10	9
ART patients represented in survey	10 051	24 551	6072	21 446	24 892
Adults	9720	22 933	5375	19 779	22 332
Children	331	1618	697	1667	2560

Abbreviations: ART, antiretroviral therapy.

^aEthiopia: Ethiopian North American Health Professionals Association (ENHAPA)/Christian Children's Fund (CCF) Canada; Global Fund for AIDS, Tuberculosis, and Malaria; US President's Emergency Plan for AIDS Relief (PEPFAR); Police; Addis Ababa City Admin Health Bureau: Preventing Mother to Child Transmission; 2 private hospitals.

^bKenya: Academic Model for the Prevention and Treatment of HIV; Catholic Medical Mission Board; Médecins Sans Frontières, Belgium; Médecins Sans Frontières, Spain; Kenyan National AIDS Control Programme (NACP); US President's Emergency Plan for AIDS Relief (PEPFAR).

^cRwanda: Ministry of Health's Treatment and Research AIDS Center (TRAC).

^dTanzania: AIDS Relief; Columbia University; Elizabeth Glaser Pediatric AIDS Foundation; Muhimbili University College of Health Sciences-Dar City-Harvard; Rwandan NACP.

^eUganda: Joint Clinical Research Centre; Mulago-Mbarara Joint AIDS Program; Ugandan NACP; The AIDS Support Organisation; Infectious Disease Institute.

4 facilities used a measure based on appearing for scheduled appointments rather than actual ART adherence; 2 averaged the levels of individual patient adherence across all patients; 1 calculated the percentage of individuals with adherence greater than 95%; for the other 5 facilities, the methods used were, again, unclear. Of 11 facilities that provided an estimate of recent adherence in their patient populations, 9 facilities reported a mean adherence rate of 91.5% (median 95.0%; range 75.0-97.0%), whereas 2 specified the rate as "greater than 85%." In addition, 4 systems of care reported a mean recent adherence of 93.2% (median 94.3%; range 85.0-99.3%). For all facilities and systems of care reporting adherence rates, the rules were unclear for determining which patients they included in the denominator to calculate the rates.

The operational definitions of treatment defaulting were even more variable than the methods used to calculate adherence rates, with 14 different definitions currently in use (Table 2). Depending on the definition, patients could be considered defaulters anywhere from 1 day to 6 months following a missed appointment. This renders any comparison meaningless. However, the use of data on missed appointments to calculate the rates of ART program

Table 2. Frequency of the Use of Varying Definitions of "Treatment Defaulting" in ART Programs in East Africa

	Percentage of Systems of Care (n = 24)	Percentage of Health Facilities (n = 48)
Nonattendance at clinic visits		
For 6 months	4	10
For 4 months	4	0
For 3 months	13	21
For 2 months	4	4
For 1 month	8	15
Missed appointments		
1 appointment	0	13
2 appointments	4	0
3 appointments	8	15
Number of days after missed appointment		
2 days	4	0
3 days	4	0
7 days	8	2
14 days	8	0
One week without drugs	0	2
Patient never classified as defaulting	0	2
Not defined or not clear	29	17

Abbreviations: ART, antiretroviral therapy.

Table 3. Frequency of Recording Data Useful for Monitoring Adherence at 48 Health Facilities Offering ART in East Africa

	Percentage Always Recorded	Percentage Sometimes Recorded	Percentage Never Recorded
Adherence measures			
Patient self-reported adherence	63	27	10
Provider assessment of patient adherence	56	25	19
Data from patient medication calendar	46	10	44
Pill counts with patient ^a	38	48	15
Reported reasons for nonadherence	44	44	13
ARV regimen and dispensing data			
Prescribed dosing schedule for ARV medications	96	4	0
Number of pills of ARV medications dispensed	98	2	0
Number of days of ARV therapy dispensed	92	0	8
Visit schedule			
Date of next scheduled visit	98	2	0
Dates of actual versus scheduled visit	29	10	60
Clinical measures^b			
Viral load counts	0	31	69
CD4 counts	0	100	0
Lymphocyte counts	0	74	26

Abbreviations: ART, antiretroviral therapy; ARV, antiretroviral.

^aFrequently for patients experiencing adherence problems only.

^bFrequently not measured routinely.

defaulters appears to be well established. Defaulting rates were calculated by 54% of the programs and 40% of the facilities, with reported rates varying from 0% to 26%.

Health facilities gathered several types of data that could be used to monitor adherence rates, but the nature and frequency of the data collected varied widely across systems and health facilities, even among those administered under the same system (Table 3). The most commonly collected type of adherence data was patient self-report, which 63% of facilities “always” recorded and 27% “sometimes” recorded. Respondents reported that 56% of the facilities always recorded clinicians’ assessments of patient adherence. Longitudinal dispensing data can also be used to monitor adherence; nearly all facilities recorded the dosing schedule (96%), number of pills dispensed (98%), and the intended number of days of therapy (92%) in clinic or pharmacy records. More than one third of the facilities conducted pill counts with patients to review adherence, but many appeared to use this method only for patients experiencing problems.

One important way to address ART adherence problems is to follow up with patients who fail to appear for clinic visits and to target them for outreach by telephone or through community case

workers. Virtually all clinics (98%) recorded the date of the next appointment, although less than one third actually monitored and recorded the discrepancy between when patients were expected to appear and when they actually did so.

Most health facilities (94%) had the capability to measure CD4 counts, and about one third (31%) could also measure viral load. Because of the expense, most programs do not use either of these tests routinely.

Discussion

Prior to this study, no survey had assessed practices for calculating rates of adherence to ARV medications and treatment defaulting in a cross-section of programs in Africa, where access to ART is expanding exponentially. With the urgent need to maintain high adherence rates and low defaulter rates to avoid drug resistance, ART programs and health facilities must closely monitor their treatment performance.

Our study results show that rates of treatment adherence and defaulting are often not routinely calculated, but when they are calculated, the operational definitions vary, and the methods lack consistency. This clear lack of agreement on definitions

and methods makes comparison across programs, even within the same country, virtually impossible. Although consistency in adherence measurement has also been lacking in industrialized settings,^{10,11} the implications of failing to agree on standards to monitor adherence in rapidly expanding ART programs in low-resource settings are potentially grave. However, results also show that several types of data may be available to measure rates of treatment adherence and defaulting at the facility level in East Africa.

International donors that are fueling the rapid expansion of ART programs do not yet recommend or provide methods for monitoring adherence rates. None of the current guidelines for monitoring and evaluation of ART programs from the Joint United Nations Programme on HIV/AIDS,¹² the World Health Organization's (WHO's) 3 by 5 Initiative,¹³ the Global Fund to Fight AIDS, Tuberculosis and Malaria,¹⁴ the US Centers for Disease Control and Prevention,¹⁵ the US President's Emergency Plan for AIDS Relief (PEPFAR),¹⁶ Family Health International,¹⁷ or the African Evaluation Association¹⁸ recommend standardized methods for measuring treatment adherence rates. The WHO 3 by 5 Initiative does recommend one program indicator for patient retention, described as "Percentage of people remaining on treatment at 6, 12, and 24 months," but none of the guidelines address the more fundamental concept of treatment adherence.

Because most health facilities collect self-reported adherence data, self-reporting may be the most readily available method for standardizing adherence measurement. Self-reported data are known to overestimate adherence as measured by more objective methods.^{5,19} Nevertheless, meta-analyses have demonstrated that self-reports of short-term adherence to ARV medicines predict viral load and distinguish clinically meaningful patterns of medication adherence.²⁰ Data from Malawi suggest that when asked, the patient's self-reports of missing a tablet either the day before or the week before the clinic visit correlate with subtherapeutic ARV drug levels.²¹ Thus, a standardized question concerning short-term adherence (eg, no doses missed during the previous 4 days) might be a useful clinical tool and provide a meaningful program performance measure.

Because most pharmacies in our survey documented details of the treatment regimen and doses dispensed over time, the potential exists for creating a dispensing-based measure of longer-term ART adherence. In industrialized countries, many pharmacy

systems where patients always collect their medicine from the same pharmacy (closed pharmacy systems) use computerized dispensing data for monitoring adherence or identifying nonadherent patients.⁵ A pharmacy-based adherence measure for ART has shown greater sensitivity than self-reports in distinguishing patients with reduced viral load.²² Some health facilities in our survey had computerized dispensing systems, and some facilities with manual systems organized their dispensing data in a way that allows tracking treatment persistence and therapy gaps for individual patients. The potential feasibility and usefulness of pharmacy-based ART adherence measures in this context deserve further exploration.

One notable finding in our survey is the existence of multiple operational definitions of treatment defaulting. We recommend developing a single definition that has some meaning for action. Failing to appear for a clinic visit or to receive medication provides the first signal that the patient may be at risk of nonadherence, which should ideally trigger a sequence of actions on the part of clinic staff to find the patient and address whatever issues may have caused the missed appointment. If patients do not return to treatment over the following 2 months (typically, a period encompassing 2 visits in many systems), they could be considered adherence failures because their clinical management would usually have to be reassessed. This suggests another useful measurement, which is the rate of recapturing patients at risk—calculated as the percentage of those who miss an appointment who return in fewer than 60 days.

This survey has demonstrated the lack of consistency in adherence monitoring in ART programs in 5 countries in East Africa. We expect that these findings would be replicated in other resource-limited countries. However, we have also shown that most prescribers and dispensers are already recording potentially useful data that could be used to establish a standardized method for calculating and monitoring adherence rates. A method is needed that is feasible for both clinical counseling of individual patients and for program management in resource-limited settings.

The WHO and INRUD collaborated a decade ago on pioneering work to develop internationally recognized indicators for measuring the use of medicines in health facilities in resource-limited settings and applying them to efforts to improve the use of medicines.²³ This work was based on the principles

that meaningful international indicators of medicine use should be (a) relevant to quality improvement in individual facilities and health care systems; (b) easily measured using data found in routine records or with rapid on-site surveys; (c) collectable in any primary care setting; (d) reliable across observers and over time; and (e) able to measure characteristics that were comparable across settings. These same principles should guide efforts to develop standardized measures of adherence in ART programs.

In April 2006, national AIDS control program officers and INRUD members from the 5 study countries met with public health professionals from the WHO, South Africa, Namibia, the United Kingdom, and the United States in Entebbe, Uganda, to discuss the survey results. Together, we have formed the INRUD Initiative on Adherence to Antiretrovirals (INRUD-IAA) to begin a collaborative process of defining adherence indicators and testing their feasibility, reliability, and validity in operational settings in East Africa. Once standard measures are available, a more systematic examination can be made of why some patients and health facilities do well at adherence and why some do poorly, and evidence-based strategies to support adherence can be identified and tested. We welcome collaboration from other groups that recognize this looming problem and wish to move forward to find practical and affordable solutions.

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