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Factors associated with self-reported adherence to antiretroviral therapy in a Tanzanian setting

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Abstract

This study aimed to determine the level of antiretroviral (ART) adherence and factors associated with adherence among patients receiving free ART at one clinic in Tanzania. Adult patients were recruited into the cross-sectional study and completed a survey that included self-reported adherence over four days and over one month. Less than 95% adherence on either measure was considered "poor". Factors associated with adherence in unadjusted analyses (α=0.10) were included in a logistic regression model. 340 patients participated in the study, and 5.9% (20/340) reported poor adherence. The final model found poor adherence associated with: being young (OR=4.03) or old (OR=6.68); having lower perceived quality of patient-provider interaction (OR=2.75); and ever missing a clinic appointment (OR=3.13). Results highlight good adherence, but suggest the importance of addressing: 1) age-specific challenges of adherence through counseling and support; 2) client-focused care and quality of patient-provider interaction; and 3) clinic appointment reminder systems.

Keywords

HIV; adherence; antiretroviral therapy; Tanzania

Introduction

Through an unprecedented international show of financial and political commitment to a health issue, antiretroviral therapy (ART) to manage HIV infection is increasingly available throughout Africa (World Health Organization, 2008). While access to medications is a crucial first step, the success of the broad scale-up of treatment depends on patients' adherence to therapy. Poor adherence can lead to viral resistance, failure of cheaper first-line treatment regimens, and multi-drug resistant forms of the virus (Bangsberg et al., 2000; Paterson et al., 2000). The impact of sub-optimal adherence to ART is particularly concerning in countries that lack capacity for monitoring drug resistance and where second-line regimens are prohibitively expensive or unavailable (Cohen, 2007).

Understanding the prevalence of poor adherence and its correlates are important clinical and public health goals. This information is essential to inform ART programs in developing

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countries and maximize patients' success on therapy. A number of studies have been conducted in African settings to measure ART adherence and explore the factors associated with adherence [for example: (Byakika-Tusiime et al., 2005; Diabate, Alary, & Koffi, 2007; Eholie et al., 2007; Muyingo et al., 2008; Ramadhani et al., 2007; Weiser et al., 2003)]. These studies have demonstrated a broad variation in adherence (between 6% and 76%), largely attributable to the variation in the conditions of the ART programs, in particular regular pharmacy supply and cost of medication. Notwithstanding structural barriers of access, ART adherence in African settings has exceeded that observed in North American settings (a pooled estimate of 77% of participants in African studies achieving adherence vs. 55% of patients in North American studies) (Mills et al., 2006).

Despite an emerging body of evidence about ART adherence in Africa, additional research is needed to explore determinants of poor adherence in a variety of settings and contexts. This study assessed factors associated with ART adherence in a Tanzanian setting in which all patients were receiving free HIV-related services and the large majority were taking single-pill, twice-a-day combinations of ART. We sought to answer two research questions: (1) what proportion of patients achieved at least 95% adherence to ART; and (2) what factors were independently associated with reporting poor adherence. The study was designed to inform existing and new ART programs in Tanzania, and to point to areas where further research on ART adherence is needed.

Methods

The study took place at an urban, faith-based clinic, which provides free ART to patients with a CD4 < 200 or a WHO clinical stage of IV. Clinic patients regularly meet with a clinic counselor and are paired with HIV-positive peer counselors who provide informational and emotional support. At the time of the study in 2006, the clinic had been providing free HIV services for just over two years, with approximately 700 adults receiving ART.

Adult clinic patients were eligible for the study if they were on ART for at least one month and had not participated in the qualitative phase of the study. Over four weeks, the study team approached all adult patients who came to the clinic to pick up their ART. After consent, participants met privately with a Tanzanian interviewer, who administered the questionnaire orally in Kiswahili. Visual aids facilitated responses on scaled questions. The IRBs of the University of North Carolina and the Tanzanian National Institute for Medical Research provided ethical clearance.

Measurements

The survey instrument was developed using measurement scales adapted for this setting based on the formative phase of the study (69 in-depth interviews with patients and other stakeholders). Table 1 lists the factors measured in the survey.

Self-reported adherence to ART was measured with two sets of questions: a four-day recall adapted from ACTG (M. A. Chesney et al., 2000) and a modified one-month visual analogue scale (Hardon et al., 2006). For any reported missed pills, the interviewer asked an open-ended question of why they had missed their pills. Adherence was dichotomized to consider whether or not respondents had achieved optimal adherence, defined as achieving 95% self reported adherence on both the 4-day and one-month recalls.

Perceived quality of patient-provider interaction was measured with a 9-item scale adapted from a study in Thailand (Panpanich & Ratana, 2004). Items asked how much patients agreed with statements about their interactions with health care providers (e.g., staff are

willing to listen to your problems or your concerns; staff help you find solutions to health problems) (α =.791).

Social support was measured with a modified version of the Medical Outcomes Study (MOS) social support scale (Sherbourne & Stewart, 1991), including three questions based on HIV-specific support people mentioned during the qualitative interviews as important (how often do you feel you have: someone to remind you to take your pills; someone to give you courage in living with HIV; someone to pick up your pills from the clinic if you're not able) (α =.858).

Perceived HIV stigma was measured by adapting a 10-question scale on experienced stigma developed in a Tanzanian context (Nyblade, Pande, Sanyukta, MacQuarie, & Kid, 2003). Items asked how worried respondents were about particular negative consequences if other people knew their HIV status (e.g., how worried are you that you would be excluded from a social gathering if people knew your HIV status) (α =.899).

Self-efficacy to adhere was measured with a 10-item scale adapted from studies in Thailand and Brazil (Panpanich et al., 2004; Pinheiro, de Carvalho-Leite, Drachler, & Silveira, 2002) and informed by the qualitative data. The scale included 9 items, each assessing respondents' confidence to take their HIV medication given a challenging situation (e.g., when you feel very healthy; when you are away from home) (α =.720).

Depression was measured using the 11 items that make up the psychological sub-scale of the Hopkins Symptoms Checklist that has been validated in the Tanzanian context (Kaaya et al., 2002) (α =.846).

Disclosure was measured with a single question: How many people have you talked with about your HIV status?

Personal beliefs about ART were measured with a set of eight questions, informed by the qualitative phase, each assessing what patients know or believe about ART (e.g., whether ART can completely remove HIV from the body; whether ART are for life).

Normative beliefs about ART were measured with three questions: whether respondents had ever been told that taking ART would make them die sooner; whether they had been told that they should take traditional medicines instead of ART; and whether they had been told that they should pray instead of taking ART.

Strategies used to adhere were measured with a set of six questions about whether respondents had used different strategies to remember to take their ART over the past month (e.g., listening to the radio; setting an alarm).

Perceived side effects were assessed with a single question of whether respondents had experienced any side effects related to their medication over the past month.

Length of time on ART was measured with a single question asking participants when they started taking ART. *ART regimen* was measured with a single question. Interviewers presented respondents with pill bottles to assist in correct identification of the regimen.

We also asked participants about their *sex*, *age*, *religion*, *highest level of education* and *current relationship status. Socio-economic status* (SES) was calculated by a weighted sum of nine ownership items (e.g., radio, bicycle, cows), electricity in the house, indoor plumbing, and food security. To assess *clinic accessibility*, we analyzed separately questions about how much time and money respondents spent traveling from their home to the clinic.

Data management and analysis

SPSS version 15.0 (SPSS Inc. Chicago, IL) was used for all analyses. Logistic regression was used to assess the unadjusted log odds of having less than 95% self-reported adherence. Factors that were significantly associated with adherence at $\alpha = 0.10$ were considered for inclusion in a multiple logistic regression model. The model was built with forward iterations. Adjusted odds ratios and 95% confidence intervals are presented in the final model for the variables. Goodness of fit of the final model was assessed using the Hosmer and Lemeshow test. Non-significance of the chi square statistic from this test supported the model (Kinnear & Gray, 2006). Variables included in the final model were empirically investigated for multicollinearity.

Results

Sample demographics

A total of 340 patients participated in the survey. An additional 17 eligible patients were declined to participate (95% response rate). Table 2 describes the demographic characteristics of the study sample. Patients had been taking ART for an average of 14 months (range 1 to 62). The majority (91.5%) were taking Triomune (manufactured by Cipla in Mumbai, India), a twice-a-day single combination ART pill containing Stavudine, Lamivudine and Nevirapine.

Proportion with poor adherence and reasons for missing doses

Adherence in this setting was high, with 320 of 340 respondents (94.1%) reporting at least 95% adherence on both the four-day and one-month self-report measures (Table 3). Of the 20 respondents who were classified as having poor adherence, 12 reported less than 95% adherence on the four-day measure, five reported less than 95% adherence on the one-month measure, and three reported less than 95% adherence on both measures. When asked in an open ended question why they had missed their pills, the most common response was that they “simply forgot” (45%), followed by “being out of the house or traveling” (20%), “running out of pills because they had not come to the clinic on time for a refill” (9%), “intentionally not taking their pills due to illness or side effects” (8%), or “oversleeping” (5%).

Correlates of adherence

Results from analyses to assess for bivariate associations between our independent (correlate, demographic and treatment) variables and our outcome variable identified six factors that were associated at $p<0.10$: age (being 19–30 years old or older than 51); having less than standard 7 education; having never been married; having lower self efficacy to adhere; reporting lower perceived quality of patient-provider interaction; and reporting having ever missed a clinic appointment (Table 4).

In the final model, age exhibited a U-shaped relationship with adherence. Respondents aged 19–30 years old were four times more likely to report poor adherence, compared with respondents aged 31–40 (OR=4.03, 95%CI 1.21–13.50) and respondents over age 50 were over six times more likely to report poor adherence, compared with respondents aged 31–40 (OR=6.68, 95% CI 1.63–27.31). Perceived quality of patient-provider interaction was also significantly associated with adherence. For each one-point decrease in the four-point scale, respondents were almost three times more likely to report poor adherence (OR=2.75, 95% CI 1.05–7.22). Finally, respondents who reported ever missing a clinic appointment were almost four times more likely to report poor adherence, compared with respondents who said they had never missed a clinic appointment (OR=3.13, 95% CI 1.02–9.66).

Discussion

Adherence was high in this setting, with 94% of patients reporting excellent adherence (defined as taking at least 95% of their pills during both the previous four days and previous one month). While we know that self-report measures tend to overestimate adherence, the high rate of adherence observed in our sample was significantly higher than has been observed in other studies in African settings that also relied upon self report [for example (Byakika-Tusiime et al., 2005; Diabate et al., 2007; Eholie et al., 2007; Nachega et al., 2004)]. The high adherence may be attributable to the fact that this study was conducted in a small faith-based clinic, which offered patients significant personal attention and support that likely was unavailable in other settings. In addition, it is possible that the simple regimen (almost all patients were taking regimens that required just one pill twice a day) facilitated adherence. In previous studies, patients were taking multiple pills at two or more dosing intervals, which has been associated with worse adherence (Ammassari et al., 2002; M. Chesney, 2003; Diabate et al., 2007; Laniece et al., 2003; Orrell, Bangsberg, Badri, & Wood, 2003). Finally, all HIV-related care at this site was offered free of charge to patients, and research has consistently shown that ART adherence is higher when cost is not an obstacle (Byakika-Tusiime et al., 2005; Eholie et al., 2007; Ramadhani et al., 2007; Weiser et al., 2003). The fact that the study participants were all receiving ART at no cost controls for cost as a barrier and allows us to explore other determinants of adherence. Qualitative inquiry into the patient-level factors that facilitated adherence in this sample have been published elsewhere (Watt et al., 2009).

Several factors were associated with adherence in this sample. Both respondents who were younger (19 to 30 years old) and respondents who were older (50 years or more) were more likely to report poor adherence. Younger age has been associated with poor adherence in other African studies (Diabate et al., 2007; Orrell et al., 2003; Uzochukwu et al., 2009), as well as in North America (Barclay et al., 2007; Murphy, Marelich, Hoffman, & Steers, 2004; Schneider, Kaplan, Greenfield, Li, & Wilson, 2004; Sullivan et al., 2007). The finding that young people were less likely to adhere was possibly related to younger people having less stable social and economic situations than their older counterparts and having less experience interacting with the health care system. The association between older age and poor adherence has not been documented elsewhere. A review of HIV infection among older people points out that scant attention has been given to the impact of the HIV epidemic on the older population (Knodel, Watkins, & VanLandingham, 2003).

Patients with less favorable assessments of their interactions with providers had worse adherence in this sample. Evidence from Africa confirms that patients value personal connections with providers, sometimes prioritizing the interpersonal domain over technical aspects of care (Haddad & Fournier, 1995; Haddad, Fournier, Machouf, & Yatara, 1998; Unger, Van Dormael, Criel, Van der Vennet, & De Munck, 2002). To our knowledge, the association between adherence and patient-provider interaction has not been explored in other African studies, but has been identified in North American settings in both quantitative (Burke-Miller et al., 2006; Heckman, Catz, Heckman, Miller, & Kalichman, 2004; Schneider et al., 2004; Wroth & Pathman, 2006) and qualitative studies (Abel & Painter, 2003; Golin, Isasi, Bontempi, & Eng, 2002; Malcolm, Ng, Rosen, & Stone, 2003; Murphy, Roberts, Hoffman, Molina, & Lu, 2003; Murphy, Roberts, Martin, Marelich, & Hoffman, 2000; Remien et al., 2003; Roberts, 2002; Sankar, Luborsky, Schuman, & Roberts, 2002). Communication between patients and health care providers is recognized as vitally important for good health outcomes (Golin, Thorpe, & DiMatteo, 2008; Lewis, DeVellis, & Sleath, 2002). Adherence is likely to be improved when patients feel they can ask questions and honestly share their experiences with health care providers, when providers listen to their patients and impart relevant information and skills, and when providers exhibit warmth

and empathy (Schneider et al., 2004; Squier, 1990). The quality of patient-provider interactions will be all the more important – and more challenging – as more patients enroll in ART programs, particularly given the shortage of health care workers throughout sub-Saharan Africa (Barnighausen, Bloom, & Humair, 2007; Kumar, 2007). Further research is needed to understand the aspects of patient-provider interactions most valued by patients in the Tanzanian setting, as well as the mechanisms through which patients' assessments of their interactions influence adherence outcomes.

Reporting ever missing a clinic appointment was associated with poor adherence. We do not have information about the reasons that patients missed appointments, but the fact that neither the amount of time nor money spent to reach the clinic were associated with adherence suggests that missing clinic appointments may be a function of personal motivation, rather than structural barriers of access, as have been identified in other studies (Hardon et al., 2007; Rosen, Ketlhapile, Sanne, & DeSilva, 2007; Tuller et al., 2009). Given the evidence of high loss to follow up in African ART programs, understanding and addressing missed appointments is of particular concern in and of itself (Rosen, Fox, & Gill, 2007).

All other variables measured in the survey were not independently associated with adherence. However, this does not mean that these other psychosocial factors are not important to address in ART programs. Factors such as depression, stigma, disclosure and social support play important roles in the lives of people living with HIV whether or not they have an impact on ART adherence, and successful HIV care programs should seek to positively influence these domains to provide optimal care to their patients (Remien & Mellins, 2007). Even though these factors did not distinguish good adherers from poor adherers in this setting, they likely have an impact on the quality of life of people living with HIV and may influence patients' retention in ART programs (Bajunirwe et al., 2009; Rosen, Fox et al., 2007).

The results of this study must be interpreted in the context of its limitations. Although self-reported measures of adherence have been consistently correlated with viral load and have been deemed as robust and appropriate indicators of adherence (Simoni et al., 2006), they are nevertheless subject to social desirability and recall bias, and as such may under-estimate non-adherence compared with more objective measures such as pill counts and the use of electronic pill caps (Arnsten et al., 2001; M. A. Chesney et al., 2000; Liu et al., 2001; Reynolds, 2004; G. Wagner & Miller, 2004; G. J. Wagner & Rabkin, 2000). The 95% cut-off for optimal adherence belies the complex relationship between adherence and resistance, and new evidence that viral suppression is possible with even moderate adherence (Bangsberg, 2006). The recruitment strategy employed introduced the possibility of systematic bias and may have over-estimated adherence. Several eligible patients declined to participate because they were too busy, and we did not interview patients who had someone else pick up their medications for them, or who missed their appointments in the four-week recruitment period.

Despite its limitations, the results of this study documented encouraging high levels of adherence in this setting. The factors associated with adherence highlight the importance of understanding age-related factors that may influence adherence, of providing patient-centered quality services, and of ensuring adequate clinic access and follow-up to eliminate missed appointments.

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Table 1

Factors measured in the cross-sectional survey, with Chronbach's alpha reported for scale measures

Outcome variable
Self-reported adherence to ART
Correlates
Perceived quality of patient-provider interaction (α=.791)
Social support (α=.858)
Perceived HIV stigma (α=.899)
Self-efficacy to adhere (α=.720)
Depression (α=.846)
Extent of HIV disclosure
Personal beliefs about ART
Normative beliefs about ART
Skills used to adhere
Perceived side effects
Treatment-related variables
Time on ART
ART regimen
Demographics
Sex
Age
Religion
Education
Relationship status
Socio-economic status
Clinic accessibility

Table 2

Demographic characteristics of respondents (n=340)

	n	%
Sex		
Male	88	25.9%
Female	252	74.1%
Age		
19–30	54	15.9%
31–40	160	47.1%
41–50	91	26.8%
51 and older	34	10.0%
Education		
Did not complete primary	69	20.3%
Completed primary only	207	60.9%
More than primary	64	18.8%
Religion		
Christian	74	78.0%
Muslim	263	22.0%
Electricity in house		
Yes	110	32.4%
No	230	67.6%
Indoor plumbing		
Yes	56	16.7%
No	283	83.3%
Problems getting food in past month		
Yes	242	71.4%
No	97	28.6%
Time to reach clinic		
< 1 hour	152	44.8%
> 1 hour	187	55.2%

Table 3

Self-reported sub-optimal adherence by 4-day, one-month and cumulative measures (n=340)

	n	%
Respondents with <95% adherence		
4-day recall	15	4.4%
One-month estimate	8	2.4%
Cumulative	20	5.9%

Table 4

Factors associated with reporting <95% adherence.

	n	% <95% adherence	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age						
19–30 years	54	11.1%	**3.80 (1.26 – 11.44)**	**.018**	**4.03 (1.21 – 13.50)**	**.024**
31–50 years	251	3.2%	REF		REF	
51 years and older	34	14.7%	**5.24 (1.61 – 17.08)**	**.006**	**6.68 (1.63 – 27.31)**	**.008**
Education						
Did not complete primary	69	10.1%	**2.24 (.86 – 5.85)**	**.083**	1.96 (.63 – 6.17)	.248
Completed primary	271	4.8%	REF		REF	
Marital status						
Married	128	5.5%	REF		REF	
Single, never married	30	16.7%	**3.46 (1.011 – 11.78)**	**.047**	2.89 (.68 – 12.19)	.150
Divorced or separated	83	3.6%	0.65 (.16 – 2.58)	.539	0.78 (.17 – 3.46)	.739
Widowed	99	5.1%	0.92 (.28 – 2.99)	.889	1.13 (.31 – 4.16)	.854
Missed clinic appointment						
Never missed appointment	280	3.9%	REF		REF	
Ever missed appointment	60	15.0%	**4.32 (1.70 – 10.94)**	**.002**	**3.13 (1.02 – 9.66)**	**.047**
Self efficacy to adhere						
For each 1-point decrease			**3.84 (1.42 – 10.36)**	**.008**	2.24 (.68 – 7.39)	.184
Perceived quality of patient-provider interaction						
For each 1-point decrease			**3.48 (1.56 – 7.78)**	**.002**	**2.75 (1.05 – 7.22)**	**.039**