

# Barriers to Antiretroviral Adherence for Patients Living with HIV Infection and AIDS in Botswana

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**Background:** Botswana has the highest rate of HIV infection in the world, estimated at 36% among the population aged 15–49 years. To improve antiretroviral (ARV) treatment delivery, we conducted a cross-sectional study of the social, cultural, and structural determinants of treatment adherence.

**Methods:** We used both qualitative and quantitative research methodologies, including questionnaires and interviews with patients receiving ARV treatment and their health care providers to elicit principal barriers to adherence. Patient report and provider estimate of adherence ( $\geq 95\%$  doses) were the primary outcomes.

**Results:** One hundred nine patients and 60 health care providers were interviewed between January and July 2000; 54% of patients were adherent by self-report, while 56% were adherent by provider assessment. Observed agreement between patients and providers was 68%. Principal barriers to adherence included financial constraints (44%), stigma (15%), travel/migration (10%), and side effects (9%). On the basis of logistic regression, if cost were removed as a barrier, adherence is predicted to increase from 54% to 74%.

**Conclusions:** ARV adherence rates in this study were comparable with those seen in developed countries. As elsewhere, health care providers in Botswana were often unable to identify which patients ad-

here to their ARV regimens. The cost of ARV therapy was the most significant barrier to adherence.

**Key Words:** adherence, compliance, highly active antiretroviral therapy, Africa, Botswana, treatment barriers

(*J Acquir Immune Defic Syndr* 2003;34:281–288)

AIDS is the leading cause of death in sub-Saharan Africa. According to 2001 estimates, there are 28.5 million people living with AIDS in Africa, comprising >70% of the world's HIV-infected population. Botswana currently has the highest estimated prevalence of HIV infection in the world. According to the 2002 UNAIDS update, >330,000 people of a population of 1.5 million in Botswana have been infected with HIV, and there were 26,000 estimated deaths due to AIDS in 2001 alone. Statistics from 2002 indicate that 38.8% of the economically productive and sexually active adults (aged 15–49 years) have HIV infection/AIDS.<sup>1</sup> In 1997, it was estimated that AIDS patients occupied 60% of hospital beds in medical wards. The large-scale effects of the AIDS epidemic in Botswana transcend the health care sector and impact upon virtually all aspects of society. According to estimations and projections by the US Bureau of the Census, the life expectancy in Botswana in 1996 was down from a projected 61 years in the absence of AIDS to 45 years as a result of the HIV/AIDS epidemic. By 2010, it is estimated that the life expectancy in Botswana will decline further to 33 years.<sup>2</sup> The HIV epidemic has had large macroeconomic repercussions due to the loss of lives of many individuals during their productive years. Households have been facing large financial burdens due to loss of income support from family members who die of the disease as well as increasing costs of treatment of HIV infection/AIDS and associated opportunistic infections.<sup>3</sup>

Lack of strict adherence to highly active antiretroviral (ARV) therapy is considered to be one of the key challenges to AIDS care worldwide. Estimates of average rates of nonadherence with ARV therapy range from 50% to 70% in many different social and cultural settings, and the risks associated with

Received for publication May 10, 2003; accepted August 22, 2003.

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Supported by the Botswana Ministry of Health, the Harvard AIDS Institute and Harvard Medical School (S.W.), NIMH 54907 and The Doris Duke Charitable Foundation (D.B.), and the Secure the Future Foundation (W.W., I.T., P.G., R.M.).

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nonadherence are extensive at both individual and societal levels.<sup>4,5</sup> Treatment adherence has been closely correlated with viral suppression,<sup>6–8</sup> while nonadherence has contributed to progression to AIDS,<sup>9</sup> the development of multidrug resistance, and death.<sup>10–12</sup> Even short-term nonadherence (as little as 1 week) may result in rapid rebound of plasma viremia, leading to treatment failure.<sup>13</sup> Adherence is perceived as a significant barrier to the delivery of ARV therapy in sub-Saharan Africa.<sup>14,15</sup> Little is known about rates of adherence or predictors of adherence in Africa. Therefore, we investigated the level of adherence and the social, cultural, economic, and structural determinants of adherence among HIV-positive patients receiving ARV therapy in Botswana.

Unfortunately, at the present time, most patients in Africa do not have access to subsidized or affordable ARVs. In Botswana, at the time of the study, <1% of HIV-infected patients received subsidized ARV treatment. Of those patients who received medical aid, individuals were typically subsidized from only one quarter to one half of the cost of triple-drug therapy. Consequently, most patients using ARV therapy were receiving suboptimal regimens and underwent forced treatment interruptions due to these financial constraints. As a result of these forced treatment interruptions, we hypothesized that the patterns of adherence would be different in Botswana than in industrialized settings and that “gaps in treatment” would be at least as significant a problem as day-to-day nonadherence.

## METHODS

We conducted a cross-sectional study of barriers to treatment adherence and reported levels of adherence for people receiving ARV therapy in 3 private clinics in Botswana between January and July 2000. The Human Subjects Committee at the Harvard School of Public Health and a review committee at the Botswana Ministry of Health approved the study design and methodology. All aspects of this research (including study design, field research, and data analysis) were conducted in partnership with local health care workers and researchers.

Subjects were identified at 3 private clinics (2 in Gaborone and 1 in Francistown) that served almost all patients treated with ARVs in Botswana during the study period. Patients were eligible for the study if they were older than 18 years of age and if they were treated with ARVs for at least 3 months. We approached every patient or every other patient (only when eligible patients exceeded 5 in a half-day period, which occurred <10% of the time) during each daily interview period. Patients were recruited by their caregivers at the clinic in question. All interviews and surveys were both confidential and anonymous. They were conducted in private by the principal investigator and a locally trained field assistant.

Face-to-face structured interviews with consenting patients that were modeled after the Adult AIDS Clinical Trial Group adherence instrument were carried out to identify

missed doses over a 1-year interval.<sup>16</sup> This approach has been shown to be closely associated with viral load in a number of studies.<sup>17–19</sup> Interviews were conducted in either English or Setswana. In an attempt to minimize recall bias, we asked patients to indicate their adherence over the previous day, previous week, previous month, and previous year successively. Adherence was defined as taking 95% of prescribed doses over the previous year, which corresponded to missing no more than 1 dose in a 10-day period (in a 2 times a day dosing regimen) or 1 dose per week (in a 3 times a day regimen). After all patient interviews, we asked health care providers to indicate their assessment of the patient's adherence over the previous year. For 16 of the 109 patients interviewed, these data were not obtained due to incomplete patient records or provider recall at the time of the interview.

We identified an additional category of medication-taking behavior that we labeled gaps in treatment. This category was created to distinguish those patients who missed their treatment over prolonged intervals ( $\geq 2$  weeks) due to either the inability to procure medications during specified time periods or, less commonly, severe side effects and lack of access to alternative ARV treatment regimens. Patients in this category who were adherent to treatment when they had access to their medications were excluded from the nonadherent group. Patients who were both nonadherent and had gaps in treatment, however, were included in the nonadherent group.

We also gathered the following information from our interviews with patients: demographic characteristics of the patients; patient knowledge, attitudes, and practices; use of traditional medicines and attitudes toward Western medical practitioners and treatment preferences; clinical data concerning HIV-related symptoms and medication side effects; and social stigma and how illness has affected patients' lives, their ability to work, and their relationships. Structured interviews were supplemented by open-ended, qualitative interviews.

In addition, we interviewed and distributed questionnaires to ~60 health care providers to elicit their perspectives on the principal barriers to treatment adherence for ARV therapy as well as their recommendations for improving treatment compliance. This group included 3 of the 4 senior physicians in Botswana who were experienced in the provision of ARV therapy at the time of the study in addition to other physicians, nurses, and public health officers who worked closely with patients receiving highly active ARV therapy.

Initial data were stored and analyzed in a database created with Filemaker Pro 4.1 (Filemaker, Inc., Santa Clara, CA). Statistics were compiled using Microsoft Excel 2001 and the statistical package Splus version 6.0 (MathSoft, Inc., Seattle, WA). Proportions were compared using two-tailed Fisher exact tests of association. Sensitivity and specificity of health care providers' assessment of adherence were determined using self-report of adherence by patients as the “gold standard.” The Cohen  $\kappa$  coefficient was used to assess the



chance-corrected degree of agreement between assessors of adherence.<sup>20</sup> To estimate the independent effects of selected risk factors on adherence, logistic regression modeling was used with maximum likelihood estimation of the regression coefficients and their SEs. All hypotheses tested were two tailed, with significance judged by  $P < 0.05$ .

## RESULTS AND ANALYSIS

One hundred nineteen people were approached for this study. Of the 112 individuals who consented to participate, 2 were ineligible, and 1 did not complete the interview; therefore, 109 patients were eligible for inclusion in the study.

### Demographic and Treatment Data

Demographic data are summarized in Table 1. Most patients treated with ARVs clustered in the 30- to 50-year age range, consistent with current statistics on the prevalence of HIV infection in Botswana. An equal number of female and male subjects participated in this study. Fifty-three percent of the patients interviewed were married or cohabiting. Education level and occupation were used as markers of socioeconomic status (local collaborators recommended against asking patients directed questions about income level, stating that such questions would be viewed as culturally inappropriate).

Forty-six percent of patients had some form of higher education (many of whom had taken brief training courses after secondary school), and an additional 37% of patients completed at least 3 years of secondary school. A wide range of occupations were represented in this study, including service, administrative, government, custodial, and professional.

Most patients were well informed regarding the modes of transmission and prevention of HIV infection. Ninety-eight percent of patients who responded to the question listed  $\geq 1$  of the following as responsible for HIV transmission: blood transfusion, sexual intercourse, mother-to-infant transmission, needle sharing, exchange of bodily fluids, and traditional remedies (bloodletting and use of razor blades). Almost all patients interviewed (96%) said that transmission could be prevented with condom use, abstinence, monogamy, or universal precautions for health care workers. Forty-seven percent of patients interviewed had used traditional remedies for HIV infection in the past. Nevertheless, most patients (92%) claimed to prefer modern medicines, typically as a result of their conviction that Western medicine had more rigorous diagnostic and treatment modalities. Only 21% of patients anticipated visiting a traditional healer in the future for treatment of HIV infection. Almost all patients interviewed had excellent relationships with their Western practitioners and felt respected and supported by

TABLE 1. Demographic Data (n = 109)

Finding	No. (%)	ARV Treatment Regimen*	
Age (y)			
<30	9 (8)	$\geq 3$ ARVs	34 (31)
30–49	90 (83)	PI regimen	20 (18)
$\geq 50$	10 (9)	NNRTI regimen	14 (13)
Sex		PI/NNRTI	0
Male	54 (50)	NRTI only	0
Female	55 (50)		
Marital status		1 or 2 ARVs	57 (52)
Single, divorced, separated	51 (47)	Dual PIs	9 (8)
Married, cohabiting	58 (53)	Single PI regimen	2 (2)
Level of education		NNRTI regimen	1 (1)
Primary school only	14 (13)	NRTI only	45 (41)
Secondary school	45 (41)		
Some postsecondary education	50 (46)	Regimen unclear	18 (17)
Treatment duration (mo)		1 NNRTI + unknown	1 (1)
3–6	31 (28)	2 RTIs + unknown	2 (2)
7–12	15 (14)	1 NRTI + unknown	5 (5)
13–24	35 (32)	Regimen unknown	10 (9)
25–36	16 (15)		
>36	12 (11)		

\*Fourteen patients were receiving hydroxyurea in addition to ARV agents.

NRTI indicates nucleoside reverse transcriptase inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI = protease inhibitor.

their caretakers. Many patients stated that their health care providers have significantly impacted upon their lives in the medical, social, and psychologic realms. Ninety-five percent of patients claimed that they trusted their doctors, and 96% thought that their providers treated them with respect and dignity. Physicians and nurses were often cited by patients as their primary source of support in coping with the challenges of living with their illness.

Forty-three patients were receiving combination therapy with 2 nucleoside reverse transcriptase inhibitors (NRTIs) and 1 protease inhibitor, 2 NRTIs and 1 non-NRTI, or 2 protease inhibitors. Thirteen patients were receiving regimens that included hydroxyurea in combination with 1 or 2 NRTIs. Thirty patients were receiving 2 NRTIs; 2 were receiving 1 NRTI, 1 was receiving 1 protease inhibitor with 1 NRTI, and 1 was receiving 1 protease inhibitor alone. The substantial portion of patients receiving suboptimal therapy reflects the practice at the time of the study of providing 1 or 2 ARVs for patients who could not afford an optimal 3-drug regimen. (At the time of the study, the cost of triple-drug therapy ranged from 2,000 to 4,000 pula per month, depending on the regimen. Unfortunately, most patients were provided only  $\leq 1,000$  pula per month by medical aid programs.) Dosing schedules were as follows: 30 patients were receiving 3 times a day dosing regimens, and 61 patients were receiving 2 times a day dosing regimens. For 18 patients, full data on their dosing schedules and regimens were not available at the time of the interview. These regimens are summarized in Table 1, along with the duration of treatment at the time of interview.

### Patient Reported Rates of Adherence

Assessments of adherence to ARV therapy are summarized in Table 2. Fifty-four percent of patients in the study were adherent by self-report, based on the definitions of adherence outlined above. Thirty percent of patients claimed never to have missed a single dose over the entire duration of therapy.

**TABLE 2.** Patient and Health Care Provider Reports on Adherence

Finding	No. (%)
Self-assessment of adherence (n = 109)	
Adherent*	59 (54)
Nonadherent	18 (17)
Gaps in treatment†	32 (29)
Physician/nurse assessment of adherence (n = 93)	
Adherent	52 (56)
Nonadherent	41 (44)

\*Defined as completing  $\geq 95\%$  of prescribed doses.

†Defined as stopping all medications for a period of  $\geq 2$  weeks.

For the subjects of this study, gaps in treatment were reported more frequently than day-to-day nonadherence. Seventeen percent of patients were nonadherent, while 29% reported significant gaps in treatment. The most common reason cited for gaps in treatment was inadequate insurance coverage for expensive medication regimens (69%). Other reasons included frequent travel and migration (16%) and lack of access to alternative ARV regimens when side effects proved intolerable (22%).

Using logistic regression models to determine predictors of adherence, the relative rate of adherence among patients who considered cost a barrier to treatment was 0.4 (95% CI, 0.25–0.64;  $P < 0.0001$ ). In addition, the odds ratio of adherence was 0.15 (95% CI, 0.06–0.35;  $P < 0.0001$ ), and when controlling for age, sex, education, disclosure of HIV status, and side effects as barriers in a multivariate logistic regression model, the adjusted odds ratio was similar: 0.11 (95% CI, 0.04–0.30;  $P < 0.0001$ ). By eliminating cost from the equation, the predicted probability of adherence was 74% (95% CI, 61%–83%). It is interesting that lower levels of education were associated with higher adherence. For patients who did not complete secondary school as compared with those with higher levels of education, the odds ratio of adherence was 3.87 ( $P = 0.02$ ). We found that age, socioeconomic status, sex, marital status, knowledge, symptom improvement, dosing schedules, and use of traditional medicines were not significantly associated with adherence to ARV therapy in this study. Predictors of adherence are summarized in Table 3.

### Barriers to ARV Treatment Adherence

In assessing the principal barriers to treatment adherence, we asked both open-ended and structured questions. Patients' narrative responses when asked why they missed their treatment doses are shown in Table 4. Patients who claimed never to have missed treatment were not asked this question. Forty-eight percent of patients asserted that they missed their doses due to finances, while 24% listed forgetting as a primary reason for treatment nonadherence. Other barriers to treatment included running out of medications (17%), travel/migration (13%), side effects (12%), and being too busy (12%).

We selected some key barriers to treatment and asked patients directed questions about whether each factor interfered with their ability to comply with treatment (Table 4). The cost of ARVs was considered to be a problem by 70% of patients; 44% of patients stated that the cost of ARVs directly interfered with their ability to take treatment regularly. Fifty-five percent of patients stated that their overall economic situation interfered with their ability to take treatment. In addition to the cost of ARVs, other economic constraints included additional medical expenses, lack of food, and lack of money for clothes for patients and their children.

Approximately one half of respondents (51%) noted some side effects associated with ARV therapy. Only 9% of



**TABLE 3.** Predictors of Adherence

Predictor	OR* Adherence	95% CI	P Value
Cost a barrier to treatment	0.15	0.06–0.35	<0.001
Cost a problem	0.43	0.18–1.03	0.06
Incomplete secondary education†	3.87	1.21–12.40	0.02
Side effects a barrier to treatment	0.18	0.04–0.88	0.03
Disclosed HIV status to others	3.55	0.91–13.92	0.07

\*Univariate unadjusted OR.

†Patients who did not complete secondary school compared with patients with higher education.

patients considered side effects a significant barrier to treatment adherence. Frequency of clinic visits posed a barrier to treatment for 30% of patients. Some of the reasons cited for the difficulties included problems leaving work to make clinic appointments and the need to travel long distances to the clinic. Some patients said that they lived 800 to 1000 km away from the clinic and had to travel that distance on a monthly basis.

Stigma surrounding HIV infection was pervasive in Botswana at the time of the study. The negative repercussions of stigma for patients included broken marriages and relationships, rejection by family, ostracism by the community, and loss of employment. As a result of the stigma, 69% of patients kept their HIV status a secret from their families, and 94% kept their status a secret from people in their community. When asked about potential discrimination at the workplace, 32% of patients feared that they could lose their job if they divulged their status at work. In spite of the devastating social and psychologic effects of stigma, only 15% of patients claimed that stigma interfered with their ability to take treatment. Stigma usually posed a barrier for patients who thought that they could not take their treatments at home or at work due to fear of detection and for patients who felt uncomfortable going to the clinic for tests and medication refills as a result of confidentiality concerns.

Consistent with the extremely mobile nature of the Botswana population, 54% of patients reported having traveled or lived in >1 place since starting treatment. Ten percent of patients thought that travel had made it difficult for them to adhere to their treatment regimens. Malnutrition was considered a significant barrier to treatment by only 7% of respondents. Thirty percent of patients believed that they had to swallow too many pills every day; nevertheless, only 5% of patients stated that the large quantity of pills interfered with their ability to take treatment. Few patients (8%) said that they stopped treatment as soon as their symptoms disappeared, likely as a result of the strong educational efforts on the part of health care

staff at the private hospitals and clinics. Thirty-one percent of patients found it difficult to cope with the long duration of ARV treatment. Only 4% of patients believed that the long duration of treatment contributed to treatment nonadherence.

### Health Care Provider Estimates of Adherence

According to physician and nurse assessments, 56% of patients in total were considered adherent (Table 2). Although the estimates of adherence rates by patient self-report and physician assessment were very similar (54%–56%), there was disagreement about which patients were able to adhere to treatment. Of the patients who were adherent by self-report, 71% were considered adherent by their health care providers, and 29% were considered nonadherent (Table 5). Similarly, of patients found to be nonadherent by self-report, 37% were considered adherent by their health care providers, and 63% were considered nonadherent. Of the patients who reported gaps in treatment, 34% were considered adherent, and 66% were considered nonadherent by their health care providers. To assess the concordance between physician and patient self-report of adherence, the Cohen  $\kappa$  coefficient was used to measure adjusted agreement between assessors. The observed amount of agreement between patients and doctors was 68% (95% CI, 59%–77%). Using patient self-report as the gold standard, provider assessment was 63% sensitive for the detection of nonadherence (including gaps in treatment) and 71% specific. There was evidence of agreement between patients and physicians after adjusting for chance agreement ( $\kappa = 0.35$ ;  $\chi^2 = 11.13$ ;  $P < 0.001$ ).

Most health care providers claimed that there were significant gaps in patient knowledge that impacted upon treatment adherence. Seventy percent of providers believed that lack of knowledge among patients played a key role in treatment nonadherence for patients treated with ARVs; 78% said that lack of understanding of the importance of chemotherapy regimens sometimes or often contributed to treatment nonadherence. Sixty-two percent of providers stated that patients' traditional etiologic explanations sometimes or often impeded treatment adherence.

### DISCUSSION

Our data suggest that adherence rates among patients in Botswana are comparable with adherence rates in most developed countries. Measuring adherence by patient self-report, 54% of patients were adherent with  $\geq 95\%$  of prescribed doses. In comparable studies conducted in developed countries, rates of adherence by self-report ranged from 40% to 70%.<sup>4,21,22</sup> Patients in this study had to overcome great odds to adhere to treatment: they lacked adequate funds, often had to travel great distances (at times up to 1000 km) to the clinics providing ARV therapy, and did not have access to alternative therapeutic regimens when side effects became prohibitive. If cost were eliminated as a barrier, then the adherence rate is predicted to

TABLE 4. Barriers to Treatment (n = 108)

Responses to Directed Questions	Yes	No	Narrative Responses: What Caused You to Miss Dosages of ARV Medications? (n = 75)	
Too many pills?	32 (30)	76 (70)	Finances	36 (48)
Is the quantity of pills a barrier?	5 (5)	103 (95)	Forgetting	18 (24)
Duration of treatment too long?	33 (31)	75 (69)	Ran out of medicine	13 (17)
Duration of treatment a barrier?	4 (4)	104 (96)	Travel	10 (13)
Side effects with ARV medication?	55 (51)	53 (49)	Side effects	9 (12)
Side effects a barrier?	10 (9)	98 (91)	Too busy	9 (12)
ARV cost a problem?	76 (70)	32 (30)	Doctor's orders	6 (8)
ARV cost a barrier?	47 (44)	61 (56)	Distance from clinic	4 (5)
Frequency of required clinic visits a barrier?	32 (30)	76 (70)	Hard to follow instructions	4 (5)
Reason that visit frequency is a barrier (n = 32)			Too sick	3 (4)
Can't leave work	13 (41)		Misunderstood doctor	2 (3)
Live too far away	9 (28)		Pharmacy closed	2 (3)
Can't leave work and live too far	7 (22)		Stigma	2 (3)
Long clinic waits	1 (3)		Alcohol	1 (1)
Too sick to travel	1 (3)		Felt better	1 (1)
Must pay at each visit	1 (3)		Stresses at home/work	1 (1)
Frequent travel or migration?	58 (54)	50 (46)	Too many pills	1 (1)
Travel/migration a barrier?	11 (10)	97 (90)		
Is hunger a barrier to treatment?	8 (7)	100 (93)		
Overall economic situation a barrier?	59 (55)	49 (45)		
Stigma a barrier (n = 106)	16 (15)	90 (83)		
Stop when asymptomatic? (n = 106)	9 (8)	97 (91)		

Data are no. (%) patients.

improve to 74%. This is very encouraging in Botswana, where there is increasing access to ARVs in the public sector. (As of April 14, 2003, >4600 patients had received ARV therapy as part of an HIV treatment program involving 4 sites in Botswana.) Other initiatives planned by the Botswana government may further improve adherence, including improvements in the distribution of ARVs, increased availability of clinical and laboratory monitoring, and strengthened health infrastructures for delivering care.

Few reported studies have investigated the barriers to long-term adherence to ARV therapy in an African setting. Elucidating these barriers is critical if policy makers in Botswana and other African countries are to identify pitfalls in current treatment strategies that should be addressed while devising effective AIDS treatment programs. Clearly, the most significant barrier to treatment in Botswana has been that most individuals have not hitherto had access to ARVs. For subjects in this study who had access, the cost of medications was viewed as the most significant barrier to treatment adherence. Seventy percent of patients claimed that the cost of ARVs posed a problem for them, and 44% of patients believed that

the cost impeded their ability to adhere to treatment. In accordance with patient responses, over one half of health care providers (56%) believed that financial problems often or always impeded adherence to ARV treatment. The extent to which financial difficulties played a key role in nonadherence is consistent with findings reported by Byakika-Tusiime et al<sup>23</sup> for patients receiving nonsubsidized therapy in Uganda.

We found that gaps in treatment were common and related to the financial demands of therapy and an inability to afford medications for varying periods. The patients included in this category were adherent with  $\geq 95\%$  of prescribed doses when medications were available to them. Whereas 17% of patients reported themselves to have difficulties with day-to-day adherence, 29% of patients reported significant gaps in treatment. Consequently, 83% of patients in total were able to adhere to therapy when access to treatment was procured. This bolsters the above-mentioned conclusion that patients in Botswana will achieve much higher adherence rates if structural and economic treatment barriers are minimized.

Data from studies in other African settings suggest that patients of lower socioeconomic status are able to achieve ex-

**TABLE 5.** Provider Detection of Nonadherence (n = 93)

Provider Assessment	Self-report, no.		Total
	Nonadherent	Adherent	
Nonadherent	26	15	41
Adherent	15	37	52
Total	41	52	93

Provider detection of nonadherence using patient self-report as the gold standard (patients who reported gaps in treatment were considered nonadherent for this analysis). Provider assessment of ARV adherence was available for only 93 of the 109 study participants. Sensitivity, 63%; specificity, 71%;  $\chi^2 = 11.13$ ;  $P = 0.0008$ .

cellent rates of adherence with access to routine medical care, subsidized ARV therapy, and free laboratory monitoring. In a recent cohort study of ARV adherence among semiurban South Africans living in extreme poverty, Orrell et al<sup>24</sup> found that lower socioeconomic status was not a predictor of adherence for patients with fully subsidized therapy. In fact, adherence levels were similar to or better than those found in industrialized countries. Similarly, high levels of adherence (78%) were reported by Laurent et al<sup>25,26</sup> in a resource-poor setting in Senegal and by Byakika-Tusiime et al<sup>23</sup> (66%) in 3 treatment centers in Kampala, Uganda. Adherence in our study was lower than the levels reported by Orrell et al<sup>24</sup> and Laurent et al,<sup>26</sup> possibly due to the impact of financial demands on adherence for the patients in our study.

Side effects did not pose a large barrier to adherence in this study group. Whereas 51% of patients noted some side effects associated with the use of ARVs, <10% of patients reported side effects as a significant barrier to treatment. This finding is in contrast to recent results from resource-rich settings, where medication side effects have been shown to be a significant predictor of adherence.<sup>27</sup> Patients may have been more accepting of side effects than their counterparts in resource-rich settings due to the financial sacrifice required to secure therapy combined with the well-known physical, social, and emotional morbidity associated with untreated AIDS in Botswana.

Although most patients agreed that HIV infection and AIDS are associated with powerful social stigma in Botswana, perceived HIV stigma was not significantly associated with adherence. Only 15% of patients interviewed believed that stigma impeded their ability to take treatment. In addition, there was not a significant correlation between medication adherence and patient knowledge, traditional medical beliefs, and alternative health practices. Although in this study adherence levels were inadequate (54%), patients had excellent knowledge of HIV/AIDS, subscribed to Western disease constructs, and had strong relationships with their medical practitioners. Other factors that were not predictive of adherence to

ARV therapy included age, educational status, sex, marital status, dosing schedules, symptom improvement, and use of traditional medicines.

Seventy-one percent of patients self-reported as adherent were believed to be adherent by their health care providers. Of those patients self-labeled as nonadherent (including gaps in treatment), only 63% were believed to be nonadherent by their providers. The observed level of agreement between physician assessment and patient self-report of adherence was 68%, which was statistically significant but only modestly higher than the rate of agreement expected from chance alone. This result is consistent with reports in the literature that health care providers typically are unable to estimate accurately which patients comply with their recommendations.<sup>8,28</sup>

There were a number of methodological limitations in this study. First, we measured adherence by patient self-report, and the literature suggests that patients tend to overestimate adherence.<sup>4</sup> Nevertheless, structured self-report has been reliably associated with both objective measures of adherence and viral load in resource-rich and resource-poor settings.<sup>17–19,24,29–31</sup> Another limitation of our study is that we were unable to corroborate patient self-report of adherence with viral loads and CD4 cell responses because of financial and logistical barriers to frequent laboratory monitoring in this setting. Only patients who had medical insurance (which constitutes a small percentage of the Botswana population) had access to ARVs at the time of this study. Consequently, the patients in our study may not be representative of the broader population of HIV-positive individuals.

## CONCLUSIONS

Adherence rates in Botswana appear to be comparable with those in many developed countries, despite the fact that patients in Botswana face large structural and economic barriers to treatment. The cost of ARVs was the most significant treatment barrier in this study. The pattern of nonadherence in Botswana—characterized by large gaps in treatment rather than day-to-day nonadherence—reflects the lack of consistent access to affordable and efficacious medication regimens. Expanded access to subsidized ARV therapy should improve adherence and, consequently, treatment outcomes for patients receiving therapy in resource-poor settings.

## ACKNOWLEDGMENTS

The authors thank the following individuals for their valuable contributions to this research: Kimberly Hensle, Shahin Lockman, Ria Madison, Leonard Manthe, Howard Moffat, Alexander Mushi, Churchill Onen, Roger Shapiro, Mohamed Kamil Sherif, and Sheila Tlou.

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