

# Stability of Adherence to Highly Active Antiretroviral Therapy Over Time Among Clients Enrolled in the Treatment Adherence Demonstration Project

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**Summary:** Adherence to antiretroviral medications is essential to therapeutic success. Many published studies have investigated the degree of adherence or nonadherence, but sample sizes have generally been small, and adherence has seldom been viewed as a longitudinal process. This paper investigates the stability of adherence over time among HIV-infected individuals attending adherence support programs in New York State. The study cohort consists of 435 clients who were on HAART at baseline and who completed at least 2 follow-up interviews. Although cross-sectional nonadherence did not exceed 35%, nonadherence reached 54% when considered across all 3 interviews. Analysis of transition matrices revealed moderate stability in adherence over time (e.g., first follow-up adherence was 81.0% for clients adherent at baseline, compared with 58.3% for clients nonadherent at baseline). Second-order transition matrices offered additional predictive utility. Multivariate results indicated that, for some, it was the transition from a desirable to an undesirable state (e.g., from no illicit drug use to illicit drug use) that increased the likelihood of nonadherence, rather than the presence of these characteristics over time. Findings illustrate the importance of multiple, periodic assessments of adherence and the need to consider strategies to increase stability in the factors affecting adherence to HAART. **Key Words:** adherence, HIV, AIDS, highly active antiretroviral therapy (HAART), longitudinal study

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Since its introduction, highly active antiretroviral therapy (HAART) has resulted in decreased morbidity and mortality among individuals infected with HIV.<sup>1,2</sup>

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HAART has been shown to attain durable suppression of plasma HIV-1 RNA,<sup>3–7</sup> improve immunologic function,<sup>3,4,6</sup> and delay progression to AIDS, thereby improving survival among HIV-infected individuals.<sup>1,6,8</sup> Because of its demonstrated effectiveness, HAART has become the standard of care for the treatment of HIV.<sup>9,10</sup> However, the success of these therapies is contingent upon strict adherence to potent antiretroviral medications.<sup>11–19</sup> Research has indicated a minimum of 95% adherence is necessary to maintain adequate suppression of viral replication.<sup>20,21</sup> Nonadherence can also lead to the development of resistance to antiretroviral medications, which may result in treatment failure and limit future therapeutic options for management of HIV.<sup>22–25</sup> Transmission of resistant strains of HIV has also been well documented and can have serious public health consequences.<sup>22,23,26–29</sup>

Adherence to antiretroviral therapy remains a struggle

for many HIV-infected individuals, due to a variety of factors, including complex dosing schedules, heavy pill burden,<sup>30,31</sup> and potentially debilitating side effects.<sup>32-34</sup> Other factors such as active depression,<sup>14,30,32,35</sup> ongoing substance use,<sup>36-38</sup> limited social support,<sup>32,39</sup> unstable housing,<sup>34,40</sup> and the competing demands of work<sup>38</sup> and child care can make adherence to antiretroviral medications an even more difficult challenge.

Many published studies have investigated the level of adherence and the correlates and predictors of adherence to HIV antiretrovirals.<sup>13,19,30,32,35,36,38,39,41-44</sup> Generally, these studies have used cross-sectional or observational designs that assess adherence at one point in time<sup>30,32,35,36</sup> and correlate various independent measures (e.g., depression, social support) with adherence outcomes (e.g., self-report, pill count). A number of longitudinal, prospective studies have also been published that measure adherence to HIV antiretrovirals over time.<sup>5,13,16-18,34,39,45-51</sup> However, the majority of these studies employ cross-sectional statistical techniques that analyze cumulative adherence rates derived from several observation points.<sup>5,16-18,39,45-47</sup> Other methodologic limitations in previous longitudinal studies of adherence to HIV antiretrovirals include small sample sizes<sup>16,45,46</sup> and lack of multivariate analysis to control for potentially confounding variables.<sup>39,47</sup> Few peer-reviewed research articles have focused on the longitudinal patterns of adherence to HIV antiretroviral medications over time using prospective, longitudinal study designs and statistical techniques.<sup>34,48,50,51</sup> We examined the stability of adherence to HAART over time, using data from the Treatment Adherence Demonstration Project, a longitudinal study involving 14 multifaceted adherence support programs in New York State.

## METHODS

### Project Description

In 1999, the Treatment Adherence Demonstration Project was funded by the New York State Department of Health to provide access to innovative models of adherence support to HIV-infected individuals on HAART in New York State. Programs were designed using a network-oriented approach to care and include groups of medical and nonmedical providers who work collaboratively to reduce barriers to adherence and provide ongoing support for maintenance of positive adherence behaviors. Of the 14 adherence support programs, 11 have a hospital as the lead agency, with community-based agencies providing additional services beyond the client's clinical care. Three adherence programs have a community-based organization as their lead agency, with clients receiving clinical care from hospitals, community health clinics, and other health care agencies.

At baseline, adherence staff conducts a thorough assessment as part of the development of an individualized treatment plan. This includes

an assessment of past and present adherence; consideration of the availability of social support; the identification of adherence barriers and risk factors; a thorough review of the client's regimen; and an evaluation of side effects related to the client's medications. Specific services offered by programs include basic HIV and HIV treatment education; referrals to substance use and mental health services; peer education and support; case management and social work services; and pharmacy counseling, education, and home delivery. HIV primary care is also provided to all clients enrolled in the Treatment Adherence Demonstration Project. Programs provide access to a variety of tools intended to further assist clients in taking their medications, including pill boxes, beepers, written instructions, visual aids, and watches equipped with timers.

The type and intensity of program services are generally determined by the needs of the client. Clients with issues that require immediate attention, such as current nonadherence, illicit drug use, untreated mental illness, housing concerns, or side effects from medication, are seen more frequently. This may mean a minimum of once-a-week contact for most programs. Once adherence or the factors that impact adherence have been stabilized, clients may be seen anywhere from once a month to once every 3 months. It is important to note that programs vary in both the availability of certain services and in the ways in which services are rendered. Programs also differ in their staffing configurations and client populations. As a result, the adherence programs in the Treatment Adherence Demonstration Project are diverse and difficult to compare.

### Data Collection

Four of the 14 adherence support programs were ineligible for inclusion in the study. One program enrolled only clients switching regimens or newly initiating HAART. This program had no baseline adherence data, since treatment was withheld at enrollment to address adherence barriers and risk factors prior to prescribing antiretroviral medications. Two programs were excluded because they were part of a separate national adherence study and used a different data collection protocol. Finally, one program was excluded because it exclusively served infants, children, adolescents, and their caregivers.

Data included in the analysis were collected at time of enrollment (baseline), follow-up 1 (F1), and follow-up 2 (F2) using a combination of client interview and chart review. Data that were considered to be accurate and easily accessible in the client's medical records were obtained by chart review, while additional data were obtained by means of a structured client interview that took approximately 30-45 minutes to complete. Programs were instructed to conduct baseline interviews prior to the provision of adherence support services and follow-up interviews every 3 months thereafter. Due to scheduling difficulties and time constraints, interviews did not always take place on a routine 3-month basis but were collected as close as possible to the intended interview date. The median number of days between interviews conducted at baseline and F1, and F1 and F2, was 103 and 99, respectively. Many items, including questions about adherence, were drawn from adherence questionnaires developed for and used in Adult AIDS Clinical Trials Group (AACTG) studies.<sup>52</sup>

Interviews were typically conducted by health educators, case managers, or "treatment adherence specialists" hired specifically for the project. Programs were discouraged from having health care providers conduct client interviews, although this sometimes occurred. Data included in this paper were collected between January 1, 1999 and March 31, 2002.

## Independent Variables

Several independent variables were included in the analysis as correlates or predictors of nonadherence, or as statistical controls in multivariate models. In addition to demographic variables such as gender, age, and race/ethnicity, variables included in the analysis included illicit drug use, stress level, housing status, client's belief in the efficacy of HIV antiretroviral medications, and alcohol use.

Clients were asked whether they had used cocaine, crack, or heroin in the 3 months before the interview, with yes/no response categories. Clients were asked what type of housing they lived in and responses were grouped according to clients who reported they lived in "stable" housing versus clients who lived in other housing categories (e.g., transitional, homeless, institutional). Belief in the efficacy of HIV medications was measured by asking clients, "How sure are you that the antiretroviral medication will help you fight the virus?" Responses were dichotomized according to clients who responded "very sure" and "pretty sure" versus those who reported they were "not sure" about the efficacy of the antiretroviral medications. To measure alcohol consumption, clients were asked if they had regularly drank  $\geq 3$  alcoholic drinks per day in the 3 months before the interview, with yes/no response options.

Table 1 displays the 4-item scale used to assess levels of stress and coping. Response options, which included "never," "rarely," "sometimes," and "often," were coded 1 through 4, with 1 and 4 representing the least and most stressful responses, respectively. An index of perceived stress was constructed by summing the responses, and a dichotomous variable was created, isolating the highest baseline quartile of responses (higher stress) from the remainder of responses (lower stress). To maintain consistency, the ranges that defined the highest quartile of stress responses at baseline were also used in the computation of a dichotomous stress variable at F1 and F2.

Initial models also controlled for individual adherence programs, regimen complexity (the number of doses and the number of pills per regimen), and the number of adherence-related visits between interviews. These variables were dropped from the analysis since they were not associated with adherence at either the bivariate or multivariate level and since their inclusion did not impact other variables in the analysis.

## Measurement of Adherence

Adherence was measured by 3-day self-report during the client interview. Clients were asked what HIV antiretroviral medications they were taking, the number of pills and doses per day prescribed for each medication, and the number of doses they missed for each antiretroviral in each of the 3 days preceding the interview. Mean adherence was calculated by dividing the number of doses prescribed by the number of doses missed over the 3-day period. Because of the highly skewed distribution of the continuous adherence measure, adherence was dichotomized to 100% adherent versus <100% adherent. Since satisfactory clinical response to HAART requires extremely high adherence

(i.e.,  $\geq 95\%$ ), less than perfect adherence is often tantamount to unsatisfactory adherence. This was true in our sample, since  $\leq 3$  clients had adherence rates between 95% and 100% at any given interview period (the remainder were either 100% adherent or <95% adherent).

## Statistical Analysis

The median test and the independent samples *t* test procedures were used to compare median and mean age of included and excluded clients, respectively. Differences between included and excluded clients for categorical variables were assessed using the  $\chi^2$  test of independence. The stability of nonadherence was examined by tracking the dichotomous measure of nonadherence across 3 interview periods—baseline, F1, and F2. First, overall nonadherence rates were calculated at each interview period. McNemar tests were used to determine whether changes in the aggregate adherence status of clients across time periods were statistically significant. Next, individual states of nonadherence were tracked across the study through the use of "transition matrices," as originally outlined by Goodman.<sup>52</sup> Transition matrices were used to calculate the probability of an individual being adherent at time *N*, given that person's adherence status at previous time points.  $\chi^2$  tests of independence were used to test for differences within and between matrices. Finally, multiple logistic regression was used to investigate the relationship between changes in the variables traditionally associated with adherence (e.g., illicit drug use, stress/coping level, housing status) and changes in adherence status. All data analyses were conducted with SPSS Version 10.0 (SPSS, Chicago, IL).

## RESULTS

### Comparison of Included and Excluded Clients

All clients enrolled in adherence support programs who were on HAART at the time of their baseline interview were eligible for inclusion in these analyses. Of the 1155 clients who were on HAART at baseline, 435 (37.7%) clients completed F1 and F2 interviews and had complete adherence data at all 3 interviews and were therefore included in the analysis. Table 2 displays data comparing included and excluded clients across several client social and demographic characteristics. No significant differences were found between the study cohort and excluded clients according to gender, race/ethnicity, substance use, housing status, medication efficacy, alcohol use, or baseline adherence status. However, there was a statistically significant difference in the median and mean age of clients who were included in the analysis (median: 43.2 years; mean: 43.1 years), compared with

TABLE 1. Stress assessment questions

Assessment questions	Response categories
"In the past month, how often have you felt:	
That you were unable to control the important things in your life?	Never, rarely, sometimes, often
Confident in your ability to handle your personal problems?	Never, rarely, sometimes, often
That things were going your way?	Never, rarely, sometimes, often
Difficulties were piling up so high that you could not handle them?"	Never, rarely, sometimes, often

**TABLE 2.** Comparison of included and excluded clients by demographic and other study variables (N = 1155)\*

Characteristic	Included (n = 435)	Excluded (n = 720)	p value
Median age (years)	43.2	41.0	0.006
Mean age (years)	43.1	41.8	0.01
	n (%)	n (%)	p-value
Gender			
Male	261 (61.4)	412 (58.4)	0.17
Female	164 (38.6)	294 (41.6)	
Race/ethnicity			
Black	207 (47.9)	344 (48.6)	0.38
Latino/a	139 (32.2)	247 (34.9)	
White	58 (13.4)	72 (10.2)	
Other	28 (6.5)	45 (6.4)	
Cocaine, crack, or heroin use, past 3 months			
No	306 (79.3)	463 (76.8)	0.20
Yes	80 (20.7)	140 (23.2)	
Stress level			
Lower	336 (79.2)	495 (72.1)	0.004
Highest	88 (20.8)	192 (27.9)	
Housing status			
Stable	336 (77.2)	531 (73.9)	0.11
Other than stable	99 (22.8)	188 (26.1)	
Medication efficacy			
Not sure	114 (26.8)	206 (29.2)	0.21
Very/pretty sure	312 (73.2)	500 (70.8)	
Alcohol use, past 3 months			
No	335 (78.1)	569 (80.6)	0.17
Yes	94 (21.9)	137 (19.4)	
Baseline adherence to HAART			
Missed at least one dose in past 3 days	156 (35.9)	219 (32.2)	0.12
No missed doses in past 3 days	279 (64.1)	461 (67.8)	

\* Totals do not always add to 1155 because of missing values for some variables.

clients excluded (median: 41.0 years; mean: 41.8 years) based on the criteria previously defined (median:  $P < 0.01$ ; mean:  $P < 0.05$ ). Clients with higher stress levels were also more likely to be excluded from the study cohort ( $P < 0.01$ ).

### Characteristics of the Study Cohort

The majority of the study cohort were men (61.4%) and identified themselves as African American (47.9%) or Latino/Latina (32.2%). Almost half of clients (48.5%) received less than a high school education, and about three-quarters (77.2%) reported living in stable housing at the time of their baseline interview. Twenty-one percent of clients reported using cocaine, crack, or heroin in the 3 months prior to enrollment, and 38.2% of clients had been clinically diagnosed with a mental illness at some point in their life. Almost all clients (94.4%) had been on a previous antiretroviral regimen, and 86.1% had tested positive for HIV more than a year before they were enrolled (data not shown).

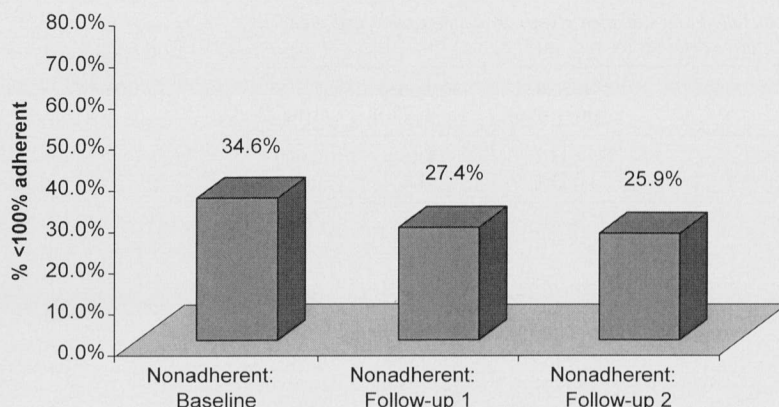
### Cross-Sectional and Longitudinal Nonadherence

Cross-sectional nonadherence in our sample was 34.6% at baseline, 27.4% at F1, and 25.9% at F2 (Fig. 1). A statistically significant decrease in nonadherence was observed between baseline and F1, during which time adherence support services were first provided to clients ( $P < 0.05$ ). The subsequent decrease in nonadherence between F1 and F2 was not statistically significant ( $P = 0.64$ ).

Figure 2 shows the distribution of nonadherence over time according to the number of interviews that clients reported being nonadherent. Overall, 53.6% of clients reported being nonadherent during at least one of these interviews, with 27.5% nonadherent at one time only, 18.0% nonadherent at 2 times, and 8.1% nonadherent at all 3 interviews.

### Adherence Transitions Between Interviews

A series of preliminary analyses were conducted to properly characterize the change processes associated



**FIGURE 1.** Cross-sectional nonadherence rates according to interview at which adherence was measured ( $n = 435$ ).

with nonadherence over time. First, transitional probabilities of adherence between interviews (e.g., baseline–F1 and F1–F2) were created for the total sample and within categories of sex, race/ethnicity, and age. Since there were no statistically significant demographic differences in the transitional probabilities between interviews for either transition, just the probabilities for the entire sample are presented in Table 3.

The data displayed in Table 3 indicate that current adherence status is highly related to previous adherence status at both transitions. For example, 81.0% of clients who were adherent at baseline were also adherent at F1, while just 58.3% of clients who were nonadherent at baseline were adherent at their first follow-up interview. A similar relationship existed for the F1–F2 transition. In fact, additional significance testing (not displayed) indicated that the transitional probabilities associated with the baseline–F1 transition were not significantly different from those characterizing the F1–F2 transition.

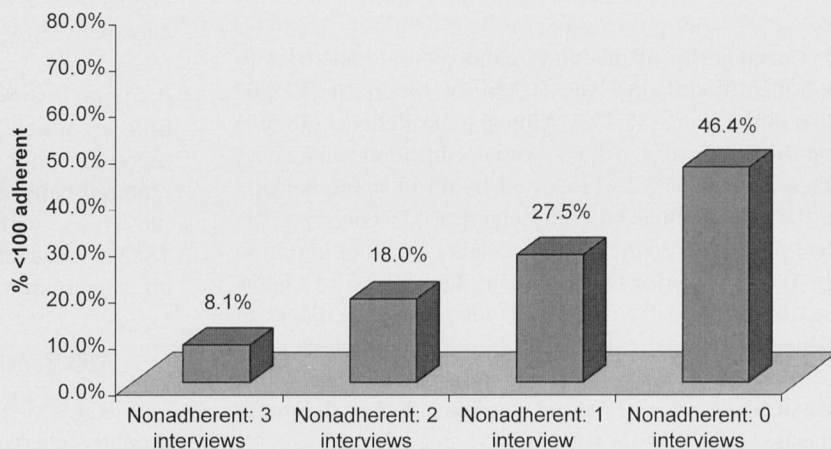
Another result that is less apparent in Table 3 is that more clients transitioned to states of adherence than transitioned to states of nonadherence. This accounts for the

fact that overall adherence rates increased at each follow-up assessment and is most likely related to the receipt of adherence support services at F1 and F2. For example, 91 individuals transitioned from a state of nonadherence to a state of adherence during the baseline–F1 period, while just 53 individuals transitioned from an adherent to a nonadherent state. Differences observed at the F1–F2 transition were smaller, with 59 individuals transitioning from a state of nonadherence to adherence and 54 transitioning from a state of adherence to nonadherence (Table 3).

### Second-Order Processes

Testing for 2nd order change processes was also conducted, to determine whether the use of the 2 preceding adherence measures offered additional predictive utility over simply knowing a person's adherence status during the immediately preceding interview assessment. Results of 2nd order testing revealed significant model enhancements when adherence status from both baseline and F1 was used to predict F2 adherence status (Table 4). Model

**FIGURE 2.** Distribution of nonadherence according to number of interviews at which clients reported being nonadherent ( $n = 435$ ).



**TABLE 3.** Transitional probabilities for adherence status (*n* = 435)\*

Baseline adherence status	Follow-up 1 adherence status	
	Adherent n (%)	Nonadherent n (%)
Adherent (n = 279)	226 (81.0)	53 (19.0)
Nonadherent (n = 156)	91 (58.3)	65 (41.7)

Follow-up 1 adherence status	Follow-up 2 adherence status	
	Adherent n (%)	Nonadherent n (%)
Adherent (n = 317)	263 (83.0)	54 (17.0)
Nonadherent (n = 118)	59 (50.0)	59 (50.0)

$\chi^2$  test for top portion of table (baseline–F1): 24.8, *df* = 1, *P* < 0.001;  $\chi^2$  test for bottom portion of table (F1–F2): 46.9, *df* = 1, *P* < 0.001.

\* Probabilities converted to percentages for ease of interpretation.

improvements were observed overall and within categories of sex, race/ethnicity, and age, strongly suggesting that changes in adherence among this cohort are more appropriately modeled as a 2nd order process. Additional testing revealed no statistically significant differences in 2nd order transitional probabilities by sex, race/ethnicity, or age. As a result, just the overall transitional probabilities are displayed in Table 4.

Results in Table 4 demonstrate that adherence information from both baseline and F1 is important to understanding adherence status at F2 and that information from the immediately preceding interview is the more important delineator of the two. Although all clients represented in the first 2 rows of data in Table 4 were adherent at F1, those nonadherent at baseline exhibited an F2 nonadherence rate (25.3%) that was approximately double that of those adherent at both preceding interviews (12.6%). The second point is demonstrated by the fact that rates of nonadherence at F2 were much higher among individuals nonadherent at F1, regardless of their adherence status at baseline. For example, rates of F2 nonadherence were extremely high among those nonadherent at F1, regardless of whether those individuals were adherent (50.0%) or nonadherent (54.1%) at baseline (Table 4).

### Multivariate Results

We also constructed a multiple logistic regression model that took advantage of the longitudinal nature of our study design. A series of 4-category variables were constructed for each adherence correlate, to capture all possible baseline–F1 transitions (e.g., no illicit drug use at baseline–no drug use at F1; no drug use at baseline–

drug use at F1; drug use at baseline–no drug use at F1; and drug use at baseline–drug use at F1). Variables that were significantly associated with nonadherence in bivariate analysis were utilized in the multivariate model and included substance use, stress level, housing status, medication efficacy, and alcohol use. These variables were included in a multiple logistic regression model predicting F1 nonadherence, while controlling for gender, age, race/ethnicity, number of days between interviews, and adherence status at baseline. Controlling for baseline nonadherence creates a “change model,” meaning that rather than predicting F1 nonadherence, the model predicts the change in nonadherence from baseline to F1.

Although transitional probability testing suggested that utilizing data from all 3 interviews simultaneously might be beneficial, too many cells were required to account for all possibilities of transitions from baseline to F1 to F2. Therefore, a multiple logistic regression model was constructed based on baseline–F1 transitional relationship, the results of which are presented in Table 5. The reference group for each adherence correlate represents the most desirable transition. For example, no drug use at both interviews is the reference group to the other 3 transitional categories (see above). Results from Table 5 indicate, as expected, that prior nonadherence status is a strong and statistically significant predictor of current nonadherence status. Individuals who reported being nonadherent at baseline were approximately 3 times more likely than those with perfect baseline adherence to be nonadherent at F1, controlling for the other variables in the model.

Results also demonstrate that all 5 variables that were correlated with nonadherence at the bivariate level were significant predictors of F1 nonadherence in the multivariate model. However, multivariate results also indicate that predicting nonadherence at F1 is more complicated than simply knowing whether individuals report

**TABLE 4.** Second-order transitional probabilities for adherence status (*n* = 435)\*

Adherence status at baseline	Adherence status at follow-up 1	Adherence status at follow-up 2		
		n	% adherent	% nonadherent
Adherent	Adherent	215	87.4	12.6
Nonadherent	Adherent	79	75.7	25.3
Adherent	Nonadherent	50	50.0	50.0
Nonadherent	Nonadherent	61	45.9	54.1

\* Includes clients with matching baseline, F1, and F2 interviews and with valid adherence data at all time periods (*n* = 435).  $\chi^2$  significant at *P* < 0.05.

\* Probabilities converted to percentages for ease of interpretation.

TABLE 5. Multiple logistic regression predicting nonadherence at follow-up 1 (*n* = 435)\*

Characteristic	Significant	Adjusted odds ratio	95% CI
Illicit drug use			
No drug use B–drug use F1	<0.05	3.18	(1.05, 9.67)
Drug use B–no drug use F1	0.91	1.05	(0.44, 2.50)
Drug use B–drug use F1	0.24	1.61	(0.73, 3.58)
No drug use B–no drug use F1 (Reference group)			
Stress level			
Lower stress B–high stress F1	<0.05	2.93	(1.22, 7.04)
High stress B–lower stress F1	0.38	1.41	(0.66, 3.01)
High stress B–high stress F1	0.13	1.98	(0.82, 4.73)
Lower stress B–lower stress F1 (Reference group)			
Housing status			
Stable housing B–no stable housing F1	<0.05	2.97	(1.25, 7.08)
No stable housing B–stable housing F1	0.73	1.17	(0.48, 2.81)
No stable housing B–no stable housing F1	0.41	1.37	(0.64, 2.94)
Stable housing B–stable housing F1 (Reference group)			
Medication efficacy			
Very/pretty sure B–not sure F1	0.67	1.24	(0.46, 3.33)
Not sure B–very/pretty sure F1	0.22	0.62	(0.29, 1.33)
Not sure B–not sure F1	<0.01	3.20	(1.44, 7.12)
Very/pretty sure B–very/pretty sure F1 (Reference group)			
Alcohol use			
No frequent drinking B–frequent drinking F1	<0.05	2.92	(1.18, 7.25)
Frequent drinking B–no frequent drinking F1	0.88	0.93	(0.38, 2.26)
Frequent drinking B–frequent drinking F1	0.19	1.66	(0.77, 3.58)
No frequent drinking B–no frequent drinking F1 (Reference group)			
Baseline nonadherence to HAART			
Missed at least 1 dose in the past 3 days	<0.001	3.22	(1.92, 5.38)
No missed doses in past 3 days (Reference group)			

\* Controlling for gender, age, ethnicity, and time between interviews.

Equation included separate categories for missing values for all appropriate variables.

Demographics, time between interviews, and missing value categories were not statistically significant and are therefore not included in the table.

B, baseline; F1, follow-up 1.

behaviors or risk factors associated with nonadherence. In fact, in the case of illicit drug use, alcohol use, housing status, and stress/coping level, it was the transition from a desirable to an undesirable state that increased the likelihood of being nonadherent at F1. Individuals transitioning from no illicit drug use to drug use (OR = 3.18), from lower stress to higher stress (OR = 2.93), from stable housing to other housing situations (OR = 2.97), and from non-frequent alcohol use to frequent alcohol use (OR = 2.92) were significantly more likely to be nonadherent at F1. In contrast, F1 adherence among clients who reported risk factors such as drug and frequent alcohol use, higher stress, and nonstable housing at both interviews was not significantly different from adherence among clients who reported none of these barriers to adherence at baseline and F1 (Table 5).

Only the variable related to belief in the efficacy of HIV medications behaved as we originally hypothesized: Individuals who were “not sure” about the efficacy of their antiretroviral medications at both interviews were significantly more likely to be nonadherent than those who were “very sure” or “pretty sure” at both of these

times (OR = 3.20). The other transitional categories of medication efficacy were not significantly different from the reference group.

Finally, client demographic variables and the number of days between interviews were not significant predictors of F1 nonadherence (data not shown).

## DISCUSSION

Our findings have important implications for both research and clinical practice regarding treatment adherence in the era of HAART. Adherence is clearly a dynamic process that varies over time among individuals. Although no more than 35% of clients in this sample were nonadherent at any given interview, 54% of clients missed  $\geq 1$  dose in at least 1 of 3 interviews. In this cohort, this meant that between 19–28% of clients identified as adherent at each assessment were actually nonadherent when their adherence was measured longitudinally. Repeated measures of adherence may be necessary to more adequately identify nonadherent clients and pro-

vide them with adherence support services. Multiple assessments would also help to identify the subset of individuals who are repeatedly nonadherent over time, aiding in patient management and care.

Results of transitional probability testing suggest that in this cohort, baseline and F1 adherence information is important to understanding adherence behavior at F2. For example, F2 nonadherence rates were twice as high among clients nonadherent at baseline but adherent at F1 (25.3%) than they were among clients adherent at both baseline and F1 (12.6%).

Multivariate modeling suggests that the instability in the variables associated with nonadherence may be more important to understanding problems with adherence, rather than simply knowing whether a person exhibits a particular risk factor associated with adherence at any given point in time. For example, changing from a state of no illicit drug use to drug use was significantly associated with increased nonadherence. In contrast, adherence among stable drug users (those reporting drug use at baseline and F1) was not significantly different than clients who reported no drug use at both interviews. This particular finding may help clarify the discordant findings from studies investigating the relationship between drug use and the ability to adhere to HIV medications.<sup>53</sup> A recent article examining these relationships using similar methodology found comparable results among substance-using clients attending an inner city clinic in Baltimore, Maryland. In this study, switching from non-use to use of drugs or alcohol was associated with declining adherence.<sup>51</sup>

It is important to emphasize that clients in this study cohort were receiving adherence support services at the time of their F1 and F2 interviews, which likely influenced adherence behavior at the time these assessments were done. Assuming that adherence programs had a positive impact on adherence behavior, this would result in lower cross-sectional nonadherence at F1 and F2 and reduced overall longitudinal nonadherence over time. Results indicating a statistically significant decrease in nonadherence from baseline to F1 are encouraging, and more research is currently in progress to evaluate specific elements of these programs and their impact on adherence to HAART.

### Limitations

Several limitations of this research require further explanation. Data were drawn from a project primarily focusing on service delivery. In general, clients were selected by programs because they were nonadherent, were at risk for nonadherence, or were starting a new HAART

regimen. In addition, younger clients and clients with higher stress levels were significantly more likely to be excluded from the analysis. This precludes generalizability of study results to the wider HIV-infected population in New York State and elsewhere.

Although analysis of transition matrices uncovered a 2nd order change process, more data could reveal more complex change processes. In addition, concerns over small cell sizes limited our multivariate modeling to 2 rather than 3 waves of interview data.

Due to concerns regarding the length of client interviews, complex issues were measured using 1 question or simplified scales (i.e., illicit drug use, alcohol use, belief in the efficacy of antiretroviral medications, and stress/coping). These dimensions may have been better assessed with more comprehensive measures.

Our research was based on 3-day self-report of adherence to HAART, which has been shown to overestimate adherence compared with other objective measures.<sup>54</sup> This method of 3-day self-report was the only validated measure of adherence to HIV antiretrovirals in the published literature at the time of this study, and overestimating adherence likely served to attenuate rather than increase the strength of our research findings. Despite overestimating adherence in other studies, self-reported adherence to HIV antiretrovirals has been independently correlated with virologic success.<sup>12,13,54,55</sup>

There were insufficient clinical data to investigate associations between nonadherence and viral load and CD4 cell count. However, since these biologic markers are most appropriately viewed as dependent variables impacted by client nonadherence, or as alternative indicators of client nonadherence, their exclusion from this study has only minimal impact given the study objectives defined here.

Finally, although our sample represents one of the largest cohorts of HIV-infected individuals on HAART followed longitudinally in the published literature, some clients were excluded for not completing follow-up interviews or due to incomplete adherence data. However, few differences were observed between the study sample and excluded clients based on demographic, psychosocial, and risk-related variables.

### CONCLUSION

Adherence to HAART is inherently a long-term commitment, and maintaining adequate adherence is essential to achieve the potential benefits of HAART. This research indicates that tracking adherence over time

is necessary to more accurately assess the adherence-related behaviors of HIV-infected individuals. Multiple, periodic assessments of adherence should be performed among clients taking antiretroviral medications to identify lapses in adherence that may lead to treatment failure, poor health outcomes, and reduced quality of life for HIV-infected individuals.

The periodic assessment of potential barriers to adherence (e.g., housing status, stress, drug and alcohol use) also appears important based on our research findings. For at least some clients, it may be the instability in these factors, rather than simply their presence or absence, that contributes to nonadherence. If this is true, more detailed investigation into the factors affecting or producing instability in adherence barriers is needed; as the pathway to increasing client adherence may ultimately be an indirect one, requiring interventions aimed at increasing stability in the life factors that correlate with adherence. For example, it is possible that in some cases, efforts aimed at helping clients cope with and manage their drug use may be an effective way to achieve and maintain high levels of adherence to HIV medications over time.

An important implication of this research is that programs that identify and address adherence and the clinical, psychosocial, and behavioral impediments to adherence should be closely aligned with health care professionals who provide HIV clinical care for individuals on HAART. Regular communication between providers from a variety of disciplines will help ensure that the multiple and complex needs of HIV-infected individuals on HAART are thoroughly addressed.

Finally, overall adherence rates among clients attending these support programs targeted to high-risk individuals increased at each interview period, demonstrating that program clients effectively maintained, and even increased, their adherence to HAART over time. Although this study did not attempt to establish a causal relationship between program attendance and the observed increases in client adherence, these encouraging findings deserve mention and will be the topic of future research endeavors.

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