ARTICLE

Longitudinal Antiretroviral Adherence Among Adolescents Infected With Human Immunodeficiency Virus

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Objectives: To longitudinally follow a cohort of adolescents with human immunodeficiency virus (HIV) and to investigate long-term antiretroviral therapy adherence and factors associated with adherence.

Design, Setting, and Patients: Adolescents infected with HIV (N=231; mean age, 18.4 years; 72.7% female; 74.9% African American) from 13 cities throughout the United States were assessed at 3-month intervals.

Main Outcome Measures: Self-reported adherence measures were validated by comparison with HIV-1 RNA viral load, and behavioral factors that may be associated with antiretroviral therapy adherence were assessed.

Results: At the initial visit, approximately 69% of the adolescents reported being adherent to antiretroviral therapy. Adolescents in the later HIV disease stage were less likely to be adherent compared with those in the earlier disease stage. Less alcohol use and being in school were associated with adherence by adolescents on weekends and over the preceding month. Longitudinal adherence was investigated among 65 subjects initially adherent with available information for at least 4 consecutive visits. The median time to nonadherence was 12 months, and failure to maintain adherence was significantly associated with younger age and depression. Among adolescents who attained an undetectable viral load, only about 50% maintained an undetectable viral load for the year.

Conclusions: These findings indicate an urgent need for better interventions to assist adolescents with HIV in adhering to their medication regimens. Adolescents with advanced disease are likely to need more intervention. New treatments recently found effective for adolescent depression may assist in improving adherence for a majority of adolescents with HIV.

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HIGHLY ACTIVE ANTIRETROviral therapy (HAART) can lead to suppression of human immunodeficiency virus type 1 (HIV-1) plasma viremia to undetectable levels for 3 years or more.[1] A robust relationship has been found between adherence to antiretroviral therapy and concurrent HIV-1 viral load. A decrease of 10% in adherence has been associated with a doubling of the HIV RNA level, suggesting that small differences in adherence can result in major differences in virological control.[2]

Adherence is defined as the extent to which a patient's health-related behaviors correspond with medical advice.[3] Adherence to complex HAART medication regimens over an extended period is a key factor in obtaining their health benefit; moreover, nearly perfect adherence is necessary for an optimal benefit from HAART. Successful long-term treatment of HIV/AIDS requires at least 95% adherence to HAART to prevent emergence of drug-resistant HIV that can lead to regimen failure and that may also limit future therapy options.[4] Therefore, patients with HIV are in the extremely difficult position of needing to strive for "perfect" (100%) adherence. Nonadherence to therapy is a significant problem, particularly since the disease process is chronic and therapeutic regimens are employed for prolonged periods.[5] Nonadherence to antiretroviral therapy may be one of the greatest public health challenges associated with the management of HIV/AIDS.[6]

Preliminary longitudinal studies of HAART adherence indicate that long-term adherence to these regimens may be difficult for a majority of patients with HIV. In an observational study of 46 adults with HIV, adherence was assessed at 6 and 12 months.[5] Overall, 63% of patients were ad-

herent to antiretroviral therapy (defined as taking 80% or more of prescribed medication). Among 65 adults with HIV, after a median follow-up of 12 months, only 46% showed adequate adherence.[7] In a comparison of triple-drug therapy (stavudine and lamivudine plus indinavir or nelfinavir), after a median follow-up of 9 months, 32% of the patients in the indinavir group and 50% of the patients in the nelfinavir group showed adequate adherence.[8] It is well documented that medication adherence to antiretroviral therapy is extremely difficult for patients with HIV. Overall, rates of adherence are poor for adolescents, adult women, and adult men.[9-13] Adherence rates in adults with HIV have been found to range from approximately 20% to 70% or 80%,[14-16] with rates likely to be lower with more complex combination therapies. The majority of studies have found adherence rates much lower than the necessary 95%, and a substantial proportion of patients with HIV do not achieve or sustain maximal reductions in viral load.[17]

To our knowledge, there have been no longitudinal studies of HAART adherence among adolescents with HIV. The goal of this study was to investigate longitudinal adherence among adolescents with HIV (mean follow-up, 7.18 months; range, 3-21 months) and factors associated with adherence. Preliminary, cross-sectional work at baseline for the cohort used for this longitudinal study revealed that only 41% of the sample reported full adherence (defined as taking all of their medication most of the time or always).[12] Higher levels of depression were significantly associated with decreased adherence, and a trend was found for an association between the number of prescribed medications and adherence.

METHODS

PARTICIPANTS

Study subjects were enrolled in the Reaching Excellence in Adolescent Care and Health (REACH) Project of the Adolescent Medicine HIV/AIDS Research Network. A detailed description of the national REACH study objectives and procedures can be found elsewhere.[18] Briefly, REACH was an observational study of HIV disease progression in adolescents with HIV enrolled at 12 to 18 years of age who were infected as teens primarily through sexual behaviors. All of the subjects were engaged in medical care and were enrolled between 1996 and 1999 in 13 cities throughout the United States. For this analysis, only subjects who were receiving HAART consistent with Public Health Service guidelines for the use of antiretroviral agents in adults and adolescents with HIV were included. At that time, the treatment guidelines recommended that the regimen should include a combination of 2 nucleoside reverse-transcriptase inhibitors and either a protease inhibitor or a nonnucleoside reverse-transcriptase inhibitor. Subjects contributed information to the analysis during visits occurring every 3 months.

INFORMED CONSENT

The study protocol was reviewed and approved by the institutional review board at each of the participating sites. All of the subjects were informed of study requirements and gave written consent. Parental permission was obtained where required by local site review boards.

ASSESSMENT MEASURES

Data used in this analysis were obtained from 4 sources: direct face-to-face interview, audio computer-assisted self-administered interview, laboratory analysis, and medical record abstraction.

Medication Adherence

The medication adherence assessment was obtained through the face-to-face interview and from medical record abstraction. The adherence assessment was conducted only regarding the current antiretroviral drugs prescribed to the subjects. Current prescriptions were identified through abstraction of the subjects' medical records shortly before the interviews. The prescribed drugs were copied into the questionnaire and the subjects were asked about the medications they were supposed to be taking. Those subjects who could identify all of the drugs prescribed were asked about the frequency with which each drug was taken in the preceding month ("last month adherence"), on the preceding Saturday ("last Saturday adherence"), or on the preceding nonweekend day ("yesterday adherence"). The variable of adherence in the preceding month (the response to the question "How often did you take your medication last month?") was originally structured as a 5-point Likert scale (1 indicated "none"; 2, "once in a while"; 3, "half the time"; 4, "most of the time"; and 5, "all the time"). For this analysis, the variable of adherence in the preceding month was dichotomized into adherence (responses 4 and 5) vs nonadherence (responses 1-3).

For the 2 other adherence variables (adherence either the preceding Saturday or the preceding nonweekend day), subjects were considered adherent if they correctly identified the number and timing of the prescribed medications. Among this sample, the mean±SD number of doses per day was 6.6±4.3 doses (range, 1-24 doses).

Mental Health and Coping

The Center for Epidemiologic Studies Depression Scale[19] is a 20-item self-report symptom rating scale developed to measure depressive symptoms among adults in community surveys. Different cut points are recommended for adolescents than those used for adults, and sex differences in cut points have also been recommended. For the current study, cut points at age 21 years or older for females and 16 years or older for males for depression[20,21] were adapted from Garrison et al.[20] To assess anxiety, 2 scales were administered. The first was a brief 4-item scale assessing health-related anxiety.[22] The scale (score range, 0-16) taps 4 domains that can be significantly affected by anxiety: sleep, appetite, social contact, and concentration. Cronbach α for this sample was .85. In addition, 2 subscales from the Reynold and Richmond manifest anxiety scale,[23] one of the most widely used and researched self-report anxiety instruments for youth, were also administered.[24,25] The overall Reynold and Richmond manifest anxiety scale score was used as a continuous variable (score range, 0-21) based on 10 physiological anxiety and 11 worry/oversensitivity questions.

The adaptive coping measure[26] is constructed from 5 subscales: positive action, self-destructive escape, passive problem solving, spiritual hope, and seeking social support. The coping scale has undergone confirmatory factor analysis among 2 cohorts with HIV, with 7 factors identified. All factor subscales show adequate α values (range, .76-.89) and adequate eigenvalues (range, 2.12-7.94). Spearman correlations between behaviors and coping were conducted to validate the scale, and subscales were associated with behaviors anticipated to be related to coping styles in expected directions.

Table 1. Characteristics of the Sample of 231 Adolescents at First Available Visit*

Characteristic	Percentage
Male sex	27.3
Race	
African American	74.9
Hispanic	11.3
White/others	13.8
Viral load, µL	
≤10	68.6
CD4 cell count, µL	
<200	11.9
200-499	44.9
≥500	43.2
Adherence preceding month	
All the time/most of the time	69.8
Not all the time	30.2
Adherence preceding nonweekend day	
Yes	69.3
Adherence preceding Saturday	
Yes	62.8

*Mean age ± SD, 18.4 ± 1.5 years (range, 15-22 years).

Substance Use

The substance use variables included the 4-question CAGE instrument[27] variable. Subjects were categorized as a problem drinker if they indicated yes for at least 2 of the following 4 questions: (1) ever felt that you should *c*ut down on your drinking; (2) people ever *a*nnoyed you by criticizing you about your drinking; (3) ever felt bad or *g*uilty about your drinking; and (4) ever had a drink first thing in the morning to steady nerves or get rid of a hangover ("*e*ye-opener"). Other substance use variables measuring intensity of alcohol or marijuana use were structured as 5-point Likert variables ("no use in the past 3 months/never used"; "once per month or less"; "more than once per month, but less than once per week"; "1 or more times per week, but not every day"; and "used every day").

Quality of Life

Four subscales of the RAND 36-Item Health Survey,[28] including social functioning, physical pain, physical functioning, and general health, were administered to REACH adolescents. We used the T-scores of the quality of life variables to equate central tendency.[28]

Laboratory Measures

Two laboratory evaluations were used in this study. Quantitative immunophenotyping of CD4 T-lymphocyte counts was performed at the individual clinical sites in certified laboratories using AIDS Clinical Trials Group standardized flow cytometry protocols. Quantitative HIV-1 RNA viral load in plasma was measured on frozen specimens in a centralized laboratory using either nucleic acid sequence–based amplification or NucliSens assays (Organon Teknika, Durham, NC). The laboratory was certified by the Virology Quality Assessment laboratory proficiency testing program (National Institutes of Health, Bethesda, Md). The lower limits of detection for the nucleic acid sequence–based amplification and NucliSens assays were 400/µL and 80/µL, respectively. The Centers for Disease Control adult/adolescent disease progression stage variable was obtained by combining the CD4 cell count and the HIV clinical infection category.[29] This was categorized at 3 levels: early (A1, A2, B1), intermediate (A3, B2, C1), and late (B3, C2, C3) stages of disease progression.

STATISTICAL ANALYSIS

The third author (S.J.D.) had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All of the statistical tests were performed using SAS 8.1 software (SAS Institute Inc, Cary, NC). We generated means, as well as simple proportions as appropriate, to describe the study population. Adjusted and unadjusted generalized estimating equations[30] models were used to study the association between each of the 3 adherence variables (adherence the preceding nonweekend day, preceding Saturday, and preceding month) and the independent variables.

A covariate was included in the adjusted repeated-measures model if it attained a 2-tailed *P* value of .20 or less in the unadjusted model. Backward elimination models were later computed with a *P* value of less than .05 being required for covariates to be kept in the final models. Odds ratios were used to measure the strength of association between covariates and outcomes. For continuous explanatory variables, the odds ratio corresponds to a unit increase in the explanatory variable.[31]

To deal with its skewed distribution, CD4 T-cell count was log transformed (to the base of 10).

Survival analysis (Kaplan-Meier) was used to estimate the time to becoming nonadherent to HAART for 38 subjects initially adherent to the drug regimen. Cox proportional hazard analysis[32] was used to assess demographic characteristics associated with maintenance of adherence.

Repeated-measure analysis was performed using the generalized estimating equations approach[30] for the analyses involving virological rebound and its association with self-reported adherence.

RESULTS

CHARACTERISTICS OF THE STUDY SAMPLE

At the time of this analysis, 353 adolescents with HIV were participating in the REACH study. We excluded 122 subjects with HIV not receiving HAART. Our final study sample included 231 adolescents with HIV. The new adherence questions used in this article were added to the REACH face-to-face interview in July 1998, approximately 2 years after the beginning of the study. The "first available visit" is defined as the first visit the participants attended after the introduction of the new adherence questions.

At the first available visit (**Table 1**), the mean±SD age was 18.4±1.5 years (range, 15-22 years). The majority of the subjects were female (72.7%) and African American (74.9%). Relatively few participants (11.9%) had a CD4 T-cell count of less than 200/µL, and 68.6% of the sample had an HIV-1 RNA viral load of 10/µL or less. During the first available visit, 69.8% of the participants reported being adherent in the preceding month, 62.8% reported adherence on the preceding Saturday, and 69.3% reported adherence on the preceding nonweekend day.

Table 2. Validation of Self-reported Adherence by Viral Load Measures

Characteristic	Patients With Respective Viral Load, No. (%)		OR* (95% CI)	*P* Value
	Viral Load <10/μL (Low)	Viral Load >10/μL (High)		
Adherence preceding nonweekend day				
No	91 (58.71)	64 (41.29)	1	NA
Yes	278 (74.73)	94 (25.27)	2.30 (1.47-3.59)	<.001†
Adherence preceding Saturday				
No	143 (58.37)	102 (41.63)	1	NA
Yes	371 (75.25)	122 (24.75)	2.16 (1.47-3.17)	<.001†
Adherence preceding month				
No	131 (53.25)	115 (46.75)	1	NA
Yes	421 (72.81)	158 (27.19)	2.29 (1.56-3.35)	<.001†

Abbreviations: CI, confidence interval; NA, not applicable; OR, odds ratio.
*Odds ratio from repeated-measure analyses using the generalized estimating equations models.
†$P<.05$ derived from generalized estimating equations models comparing lower viral load (<10/μL) vs higher viral load (≥10/μL).

AGREEMENT BETWEEN ADHERENCE MEASURES

Moderate agreements were found between adherence on the preceding nonweekend day and the preceding Saturday ($\kappa=0.63$; $P<.001$) and between adherence on the preceding nonweekend day and in the preceding month ($\kappa=0.55$; $P<.001$). Poor agreement was observed between preceeding Saturday and preceeding month adherence ($\kappa=0.38$; $P<.001$; data not shown).

VALIDATION OF ADHERENCE MEASURES

The adherence measures were validated by comparison with HIV-1 RNA viral load (**Table 2**). We found significantly lower viral load measures among those who were adherent in the preceding month ($P<.001$), on the preceding nonweekend day ($P<.001$), and on the preceding Saturday ($P<.001$) than among those who were nonadherent (<10/μL vs ≥10/μL, respectively).

ADHERENCE ON THE PRECEDING NONWEEKEND DAY

The only variable significantly associated with adherence on the preceding nonweekend day in the univariate analyses was the Centers for Disease Control HIV disease assessment (**Table 3**). Subjects in the late HIV disease stage were less likely to be adherent compared with those in the early stage of the disease ($P=.005$). In the multivariate analyses, only this Centers for Disease Control HIV disease assessment variable remained in the final model and was the only independent predictor of adherence on the preceding nonweekend day ($P=.005$).

ADHERENCE ON THE PRECEDING SATURDAY

In the univariate analyses, we found significant associations between being adherent to HAART during the preceding Saturday and the following variables: higher CD4 cell count ($P=.003$); lower intensity of alcohol use ($P<.001$); not dropping out of high school ($P=.01$); and early stage of the HIV infection vs late stage ($P=.02$) (Table 3). In the multivariate analyses, independent positive predictors of adherence during the preceding Saturday were high CD4 cell count ($P=.01$), low intensity of alcohol use ($P<.001$), and not dropping out of high school ($P=.03$). The Centers for Disease Control disease progression variable was not included in the multivariate model owing to its known correlation with the CD4 cell count variable already in the model.

ADHERENCE IN THE PRECEDING MONTH

In the univariate analyses, being adherent in the preceding month was significantly associated with lower intensity of alcohol use ($P<.03$) and not dropping out of high school ($P=.002$) (Table 3). In the multivariate models, both lower intensity of alcohol use ($P=.03$) and not dropping out of high school ($P=.003$) remained significantly related to being adherent in the preceding month.

MAINTENANCE OF ADHERENCE TO HAART

Sixty-five subjects initially adherent to HAART with available information for at least 4 consecutive visits (at 3-month intervals) were selected and considered for this analysis. The adherence variable was dichotomized into adherence ("most of the time" or "all the time") vs nonadherence ("none," "once in a while," or "half the time").

During the follow-up period, 33 incident cases were reported and 7 participants were censored because they dropped out of the study or were lost to follow-up. The average time subjects contributed to the analysis was 10.61 months (range, 3-21 months). The median time to becoming nonadherent to the HAART regimen for this study group was 12 months (95% confidence interval [CI], 9-15 months). Univariate Cox proportional hazard analyses (**Table 4**) showed that failure to maintain adherence was not associated with participants' sex or race. On the other hand, we found that younger age (hazard ratio=0.11; 95% CI, 0.4-0.30) and being depressed (hazard ratio=2.21; 95% CI, 1.10-4.42) were significantly associated with failure to maintain adherence.

Table 3. Predictors of Adherence During Preceding Nonweekend Day, Preceding Saturday, and Preceding Month*

	Adherence Variables					
	Adherence Preceding Nonweekend Day		Adherence Preceding Saturday		Adherence Preceding Month	
Predictors	UOR (95% CI)	AOR (95% CI)	UOR (95% CI)	AOR (95% CI)	UOR (95% CI)	AOR (95% CI)
Age	1.05 (0.91-1.21)	NA	0.99 (0.89-1.10)	NA	1.01 (0.87-1.16)	NA
Sex (female vs male)	0.83 (0.50-1.40)	NA	1.14 (0.78-1.66)	NA	1.14 (0.69-1.87)	NA
CD4 cell count (log)	1.39 (0.88-2.21)	NA	2.06 (1.28-3.33)†	1.89 (1.13-3.15)†	1.28 (0.73-2.22)	NA
High school dropout (nondropouts vs dropouts)	0.76 (0.49-1.20)	NA	0.63 (0.44-0.91)†	0.61 (0.39-0.94)†	0.52 (0.34-0.78)†	0.54 (0.36-080)†
Race						
African American	1	NA	1	NA	1	NA
Hispanic	1.43 (0.45-2.71)	NA	1.24 (0.73-2.11)	NA	1.00 (0.48-2.10)	NA
White	0.86 (0.76-1.62)	NA	1.00 (0.60-1.66)	NA	0.69 (0.37-1.26)	NA
Intensity of alcohol use	0.91 (0.71-1.16)	NA	0.68 (0.55-0.83)†	0.67 (0.55-0.82)†	0.79 (0.65-0.97)†	0.80 (0.66-0.98)†
CDC disease progression stage						
Early stage	1	1	1	NA	1	NA
Intermediate stage	0.68 (0.41-1.15)	0.68 (0.41-1.15)	0.78 (0.52-1.17)	NA	0.95 (0.57-1.56)	NA
Late stage	0.47 (0.28-0.80)†	0.47 (0.28-0.80)†	0.56 (0.35-0.92)†	NA	0.75 (0.42-1.37)	NA

Abbreviations: AOR, adjusted odds ratio; CDC, Centers for Disease Control and Prevention; CI, confidence interval; NA, not applicable; UOR, unadjusted odds ratio.
*The analyses also included the variables of health anxiety, adaptive coping, depression, anxiety, physical pain, general health, physical functioning, social functioning, alcohol drinking problems (ever: yes, no), intensity of marijuana/illicit drug use, number of prescribed drugs, number of prescribed doses, and number of times consumed 5 alcoholic drinks or more. Those variables, not shown in the table, did not present a significant association with the adherence variables (adherence during preceding nonweekend day, preceding Saturday, and preceding month). The demographic variables (age, sex, and race) were included in the table regardless of the significance of association with the adherence variables.
†$P<.05$.

Table 4. Incidence of Nonadherence by Selected Characteristics*

Predictors	Hazard Ratio (95% CI)	*P* Value
Age	0.11 (0.04-0.30)	<.001†
Sex (male vs female)	1.38 (0.62-3.06)	.43
African American	1	NA
Hispanic	1.35 (0.40-4.49)	.63
White	0.81 (0.28-2.33)	.70
Depression	2.21 (1.10-4.42)	.02†

Abbreviation: CI, confidence interval; NA, not applicable.
*n = 38.
†$P<.05$.

VIROLOGICAL REBOUND AFTER SUPPRESSION

Thirty-five subjects with undetectable levels of viral load during the first available visit and with available viral load information for at least 4 consecutive visits (at 3-month intervals) were selected and considered for analysis. This cohort was 71% female, 88% African American, 6% Hispanic, and 6% white/other. The mean±SD age of the sample was 17.71±1.56 years. Subjects were followed up from their first HIV-1 RNA viral load less than 0.4/µL to the first viral load measure higher than 0.4/µL or virological rebound. During the first 12-month follow-up period, 17 participants (48.57%) experienced virological rebound. The incidence of rebound decreased over time from 9 cases after the first 3-month follow-up to 6 cases after the 6-month follow-up, and to only 1 case at the 9-month follow-up and 1 case at the 12-month follow-up. During the 12-month follow-up, univariate generalized estimating equations analysis showed a positive association between a lack of virological rebound and self-report of adherence to the HAART regimen ($P=.02$; data not shown).

COMMENT

The average adherence rate (ie, adhering most of the time or all of the time) reported by this adolescent sample (approximately 69%) is consistent with rates found in other adherence research studies.[14-16] The fact that adolescents in the later HIV disease stage were less likely to be adherent compared with those who are in the earlier disease stage may be owing to those former adolescents being more affected physically and therefore being less able to tolerate adverse effects of medication, or it may be owing to their depression over disease progression and lowered outcome expectancies that the medications can help them.

In terms of longitudinal adherence, the median time to becoming nonadherent was 12 months. Failure to maintain long-term adherence was significantly associated with younger age and depression. As the REACH investigators have noted previously,[12] depressive symptoms and disorders in adolescents are often underidentified and, therefore, undertreated.[33] In the past, adolescents have had a relatively poor response to antidepressants that are typically efficacious with adults.[33,34] However, the Treatment Adolescent Depression Study[35] has recently compared fluoxetine, cognitive behavioral therapy, a combination of both, and a placebo medication—the first

comparison study in adolescents—and found support for antidepressant therapy with adolescents, especially when combined with cognitive behavioral therapy. Thus, there are now better avenues of treatment for adolescent depression. Adolescents being considered for receiving a prescription of HAART should be screened for depression. Those who are depressed may need both treatment for depression as well as interventions to assist them in adhering to their new treatment regimen for successful long-term adherence.

Of those adolescents who could attain an undetectable viral load in this study (n=35), only about half (51.4%) maintained an undetectable viral load for a year. From these findings, it appears that only a small percentage of teens starting therapy will have long-term suppression. The low rates of both achievable and readily sustainable undetectable viral suppression found in this study of adolescents have implications for initial HAART regimen planning in this population. Clearly, more insight and work are needed to determine how to best prepare adolescents for the difficulties of sustaining adherence to the medication regimen prior to initiating HAART. These findings also suggest that ease of selection of viral resistance needs to be a more prominent factor for the selection of initial HAART regimens in adolescents. Multiple once-daily regimens that have generally higher barriers to viral resistance than those used in the timeframe of this study are now being evaluated and will warrant further effectiveness testing in adolescents.

Overall, the findings from this study indicate an urgent need for better interventions to assist adolescents infected with HIV with their medication regimen. Based on the findings from this study, intervention should include assisting adolescents in problem-solving issues concerning substance use and lowered adherence. This may include teaching them to plan their medication-taking schedule for times when they will not be drinking and/or using drugs, or referral to substance use treatment for those adolescents with problematic levels of use. In addition, intervention should include teaching adolescents to maintain a consistent schedule during the week to assist in facilitating adherence. Moreover, adolescent patients with advanced HIV disease are likely to need more intervention support than do patients in an earlier disease stage. Finally, many adolescent patients may need intervention that focuses on dealing with depression over time. Patient-level intervention, health care provider–level interventions, and health care system modification may all be necessary if the challenge of antiretroviral medication adherence by adolescents with HIV is to be successfully surmounted.

A potential limitation of this study is that adherence was assessed only through adolescents' self-reports. However, self-reporting of medication adherence by adolescents has been found to be reasonably accurate,[36,37] and rates of adolescent nonadherence reported in studies using laboratory assays are consistent with rates reported in studies using self-report.[38,39] In the REACH Project, we have investigated the accuracy of self-reports of marijuana use in a comparison of self-report data with urinalysis[40] and found that the level of self-report among the adolescents with HIV was exceptionally high. Finally, the longitudinal group of 65 subjects who had at least 4 consecutive visits was, in some sense, a subgroup of more adherence. That is, they were adherent to study visits more than subjects who did not obtain as many visits.

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