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Patient-Related Risks for Nonadherence to Antiretroviral Therapy among HIV-Infected Youth in the United States: A Study of Prevalence and Interactions

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Abstract

Adherence continues to be a major barrier to successful treatment with highly active antiretroviral therapy (HAART) for HIV-infected individuals. HIV-infected adolescents and young adults face a lifetime of treatment with HAART. Often, individuals who struggle with adherence to HAART face multiple barriers that would therefore impact on the success of any single modality intervention. Thus, we conducted a cross-sectional, observational study to determine the prevalence of personal barriers to adherence and to identify associations between these barriers in HIV-infected subjects, 12 to 24. We studied the following personal barriers to adherence: mental health barriers, high/low self-efficacy and outcome expectancy, and the presence of specific structural barriers. There were 396 subjects infected after age 9 recruited from sites from the Adolescent Trials Network for HIV/AIDS Interventions or the Pediatric AIDS Clinical Trials Group. Of the 396 subjects, 148 (37.4%) self-identified as nonadherent. No significant differences were found between adherent and nonadherent subjects for the presence of mental health disorders. Adherence was significantly associated with all but one structural barrier. Both self-efficacy and outcome expectancy were higher among adherent versus nonadherent subjects ($p < 0.0001$). Grouping subjects according to low self-efficacy and outcome expectancy for adherence, adherence differed according to the presence or absence of mental health disorders and structural barriers ($p < 0.0001$). Our data suggest that adolescents have significant rates of non-adherence and face multiple personal barriers. Adherence interventions must address multiple barriers to have the maximum chance for positive effects.

Introduction

HIV-infected individuals who require therapy must adhere to prescribed antiretroviral therapies to prevent progression to AIDS, opportunistic infections, and the development of resistant virus. Adherence remains a significant problem for those who have been prescribed highly active antiretroviral therapy (HAART).[1–6] Factors influencing adherence can be divided into three major categories: patient factors, medication factors, and factors related to the system of care.[7] In each of these areas, there may be numerous barriers depending on the specific population and on the unique life situations of the individual. In this study, we have chosen to focus on patient factors in an adolescent population prescribed HAART in the United States.

The most commonly cited categories of patient factors linked to non-adherence are (1) cognitive/behavioral factors related to antiretroviral therapy (ART) such as self-efficacy to adhere to antiretroviral treatment, and outcome expectancies regarding effectiveness of antiretroviral treatment; (2) mental health and substance abuse disorders; and (3) structural barriers such as homelessness and lack of insurance.[3,8–14] Most studies related to adherence have been completed in adults with few focusing specifically on adolescents. The influence of these factors on antiretroviral adherence has been documented in the literature, at least among adult samples. For cognitive behavioral factors, Murphy et al.[9] found that self-efficacy regarding staying with treatment through environmental changes, and in the face of negative influences, was a significant predictor of medication adherence among

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HIV-positive women, and that positive outcome expectations about following the antiretroviral regimen also predicted better adherence. Regarding mental health issues, Tucker et al.[15] found that patients with depression, generalized anxiety disorder, or panic disorder were more likely to be nonadherent than those without a psychiatric disorder. Furthermore, nonadherence was associated with use of cocaine, marijuana, amphetamines, or sedatives. In a longitudinal investigation of adherence among HIV-positive adolescents prescribed antiretrovirals, Murphy et al.[8] found failure to maintain adherence was significantly associated with depression. Finally, numerous studies have found a variety of structural barriers that impact adherence to antiretrovirals. These have included barriers related to the overall health-care system, socioeconomic status, cost of treatment, lack of transportation, and place of treatment.[16,17]

Young people who struggle with maintaining good adherence to HAART may face more than a single barrier. Few studies have described how these various patient-related categories are distributed among behaviorally HIV-infected adolescents, i.e., how these barriers coexist within individuals. The lack of such information limits the design of the next generation of research that seeks to be comprehensive in scope and focused on improving adherence. The purpose of this study was to address these gaps in knowledge by determining how the various patient barriers coexist within behaviorally HIV infected adolescents and the prevalence of multiple barriers within this population, focusing on the three major categories of factors associated with nonadherence that were noted above (i.e., self-efficacy and outcome expectancies related to antiretroviral treatment, mental health and substance abuse disorders, and structural barriers). As this was a cross-sectional study, it was not designed to develop a strategy for predicting adherence or to understand changes in adherence barriers over time, but rather to assess the most prevalent patient factors associated with HIV medication nonadherence and how these barriers are associated in adolescents.

Methods

This was a cross-sectional, observational study designed to assess the most prevalent patient factors associated with HIV medication non-adherence and how these barriers are associated in adolescents. The target population consisted of HIV-infected youth ages 12 through 24 years, who were infected through risk behaviors after age 9, who were eligible and offered and/or prescribed HAART by their healthcare provider based on the US Public Health Services (DHHS) guidelines, including: individuals who were currently being prescribed HAART; those who were prescribed HAART in the past; and subjects who had never been on HAART because they refused to initiate treatment. The study was approved by the Institutional Review Boards at each site recruiting subjects.

Procedures

Participants were recruited from clinical sites that are funded through either the Adolescent Trials Network for HIV/AIDS Interventions (ATN) or the Pediatric AIDS Clinical Trials Group (PACTG) to conduct HIV-related research. These sites offer comprehensive HIV services to adolescents and young adults. A total of 19 sites recruited subjects to this study ($n = 396$) for this specific study. Subjects who were prescribed HAART for prevention of mother to child transmission were excluded. Consent was obtained from either the subject or parent, depending on the requirements of the Institutional Review Board at the site and the age of the subject. At each site, study questions were asked via face-to-face interviews with the subject by a study coordinator trained in clinical research. Specific variables were considered present only if they were reported as present at the time of either the interview or chart review. The chart abstraction and subject interview were performed within 14 days of subject enrollment into this study. The interview was performed prior to chart abstraction.

Think aloud/intensive interview to pilot face-to-face measures

Given that many of the measures were to be utilized with adolescents for the first time, a pilot study of the measures was conducted prior to the main trial. A "think aloud"/intensive interview procedure was conducted with a pilot sample of adolescents ($n = 25$) for the adherence self-efficacy, adherence outcome expectancy, and environment questions (scales are described below in the Interview Measures section). Such intensive individual interviews are often utilized to learn what respondents are thinking when they are trying to answer questions, and to improve comprehension prior to a full-scale implementation of the instrument.[18] Each of the questions was read to the participant and they were allowed to answer. A series of questions was then asked of the respondents to ascertain: their understanding of certain terms within each item; how confident they were that they gave an accurate answer; whether they would ask the question in a different way, and if so, how. Their responses were reviewed and suggested clarifications to items made by the pilot sample of adolescents were incorporated into the measures when there was consistency of recommendations and a significant number of the pilot sample subjects indicated that a term or phrase in an item was confusing. Only a few items were changed as a result of the think aloud procedure, and involved minor wording changes to make an item more easily understood by using a more common term. These pilot data are not shown.

Interview/study procedures

A study coordinator at each site, trained in clinical research, conducted the face-to-face interview in a private setting with the adolescent and recorded subject responses on hard copy interview forms. Interviews were conducted prior to chart abstraction of medical record data. As this was a cross-sectional, single time point study, questions regarding adherence and other measures were assessed at the time the study was conducted. Study coordinators reviewed patient charts and abstracted the following information: diagnoses of substance abuse and mental health disorders; most recent $CD4^+$ T cell counts and HIV RNA levels; occurrence of category C AIDS-defining conditions; and current antiretroviral regimen. As youth were engaged in comprehensive HIV treatment programs, barriers related to mental health diagnoses and substance abuse were collected by chart abstraction. Also, any youth with mental health diagnoses (including substance abuse) were collected by chart abstraction, with the presence of these disorders based on clear documentation of a disorder in the medical record. Mental health disorders were classified into the following categories: mood disorders,

schizophrenia, anxiety, attention deficit hyperactivity disorder (ADHD), developmental delay, and "other" mental health disorders. Data on substance use and abuse were poorly and inconsistently documented in the medical record. Thus, data on substance abuse are not considered further.

Subjects were classified into the following adherence categories according to self-report: offered/prescribed HAART but refused (36 [9.1%]), started HAART but now stopped (83 [21%]), prescribed HAART but currently taking less than HAART (4 [1.0%]), started HAART but currently nonadherent (25 [6.3%]), and started HAART and adherent (248 [62.6%]). Subjects on HAART were considered adherent if they were taking all prescribed medications all the time or most of the time (missed no more than two doses per week if on a twice a day regimen and no more than one dose per week if they were on a once-a-day regimen). As an adolescent's adherence can vary depending on the week, this was a global assessment of self-reported adherence, meaning that subjects were asked by the study coordinator to respond for an average week in order to distinguish those subjects who were either primarily adherent or primarily non-adherent. Thus, the responses to the adherence questions were dichotomized as "started HAART and currently adherent" versus "other," with the other including all nonadherent subjects.

Interview Measures

Self-efficacy for adherence

Self-efficacy for antiretroviral adherence is one's sense of being able to adhere to the medications prescribed. Ten items adapted from the Adult AIDS Clinical Trials Group (AACTG) adherence instrument[3] were administered. All items were prefaced with "How confident are you that you can . . . ", and were scored on a scale ranging from 0 (Not at all confident) to 10 (Completely confident). Items addressed issues related to the treatment schedule (e.g., How confident are you that you can: make taking your medication part of your daily routine?; stick to taking your medications even if you aren't feeling well?"). Selected items from this scale have been utilized in research studies with adults and found to have very good internal consistency.[19]

Outcome expectancy for adherence

Outcome expectancy for antiretroviral adherence was assessed through 7 items on the subject's impression of the impact of taking antiretroviral therapy. Murphy et al.[20] adapted questions from a medication adherence study with adults,[21] and those items with high internal consistency were selected for use in this study. A 5-point Likert scale, from strongly disagree to strongly agree, was used. Both positive expectancies (e.g., taking medications as prescribed will help to stay well), and negative expectancies (e.g., taking medication as prescribed will result in troublesome side effects) were assessed.

Both the Self-Efficacy (SE) for adherence and Outcome Expectancy (OE) regarding antiretroviral treatment were derived as the sum of responses to each series of questions.

Although data were collected on substance abuse through chart review, this variable was not included in this analysis due to its low documented prevalence. As will be discussed, the low prevalence was most likely due to the manner of collection as opposed to true prevalence.

Environment

Seven questions were asked to investigate the environment of the adolescent that may impact medication adherence. Subjects were asked if any of the following made it difficult for them to take their HIV medications: a place to sleep, medical insurance, transportation to get medications, transportation to the clinic, getting the medications filled, problems related to job or school, and problems related to family or child care, either their own children or someone else's children. Items were selected from both literature review and clinical experience of the investigators.

Statistical analysis

Simple univariate statistics (mean, standard deviation [SD], median, percentages) were used describe the characteristics of the study populations. Student's t test and Wilcoxon rank sums test were used to assess associations with adherence for continuous characteristics and Fisher's Exact test for categorical measures. HIV-1 RNA was $\log_{10}$-transformed for analysis. For scaled measures such as adherence self-efficacy and outcome expectancy regarding antiretroviral treatment, Cronbach α was used to assess how well a set of variables measured a single unidimensional latent construct. Logistic regression was used to investigate the association of SE and OE to adherence to medication regimen. A composite variable was created to capture the eight possible combinations of the three specific binary barriers to medication adherence investigated in this study. These barriers include mental health disorders (present versus absent), structural barriers (present versus absent) and cognitive-behavioral barriers (present [low SE/low OE] versus. absent [high SE/high OE]). The derivation of the composite measure was restricted to those subjects with both high SE and OE or low SE and OE given inherent ambiguity in interpreting the relationship of SE and OE to adherence that would otherwise arise if discordant categories (high SE/low OE or low SE/high OE) were included. A generalized Fisher's exact test was used to examine the relationship of adherence to this eight-level measure, with logistic regression modeling being used to further investigate this relationship.

Analyses were carried out using SAS, version 8 (SAS Institute, Cary, NC), with p values of 0.05 or less to define statistical significance.[22] Multiple comparison corrections were not used, and missing values (varying in number among the outcomes) were not imputed.

Results

A total of 396 HIV-infected adolescents and young adults infected after age 9 years were enrolled into the study. The modes of infection were as follows: 270 (68.2%) were infected through a sexual partner, 2 (0.5%) were infected through sharing hypodermic needles, 62 (15.7%) were unsure as to the source of their infection, 37 (9.3%) were infected through blood products, 20 (5.1%) were infected through sexual abuse, and 5 (1.3%) reported their source of infection as "other." The demographic characteristics of the population are described in Table 1. Among the 396 study participants, 248 (62.6%) were adherent and 148 (37.4%) were non-adherent to HAART. Adherence was not significantly associated with gender, age, or AIDS-defining condition. Adherence was

Table 1. Demographic Characteristics of Study Population According to HAART Medication Adherence

Demographic characteristics	*Adherence*		
	Adherent (n = *248*)	*Nonadherent* (n = *148*)	p *value*[a]
Gender: *n* (%)			
Female	131 (65.5)	69 (34.5)	
Male	117 (59.7)	79 (40.3)	0.25
Age:			
Mean (SD)	21.6 (2.3)	21.5 (2.2)	0.59
Median	22.1	21.8	0.48
Race: *n* (%)			
Asian/Pacific Islander	2 (50.0)	2 (50.0)	
Black/African American	157 (59.0)	109 (41.0)	
Native American/Alaskan Native	0	2 (100.0)	
White	33 (78.6)	9 (21.4)	
Other/mixed race	56 (68.3)	26 (31.7)	0.018
Hispanic or Latino origin: *n* (%)			
Yes	67 (72.0)	26 (28.0)	
No	181 (59.7)	122 (40.3)	0.037
AIDS defining condition: *n* (%)			
Yes	127 (62.3)	77 (37.7)	
No	118 (64.1)	66 (35.9)	
Unknown	3 (37.5)	5 (62.5)	0.32
CD4 count (cells/mm^3):			
Mean (SD)	472.6 (343.0)	293.2 (208.5)	< 0.0001
Median	414.5	266.5	< 0.0001
Unknown	2	0	
HIV-1 RNA (copies/mL):			
Mean (SD)	117377 (651100)	102232 (153918)	0.79
Median	1734	36130	< 0.0001
Unknown	110	12	
Geometric mean[b]	2994	31261	< 0.0001

[a]Fisher's exact test was used to assess associations of adherence with categorical measured variables. For continuous variables (age, CD4 count, and HIV-1 RNA) Student's *t* test was used for assessing differences in means and non-parametric testing for medians.
[b]The geometric mean is the antilog of the mean of $\log_{10}$-transformed HIV-1 RNA values and is interpreted similarly to the simple mean.
HAART, highly active antiretroviral therapy; SD, standard deviation.

associated with race, with larger proportions of subjects self-identifying as white or as Hispanic/Latino reporting being adherent compared to subjects not self-reporting these ethnicities. Self-reported adherent subjects had significantly higher mean $CD4^+$ T cell counts (473 cells/mm^3 versus 293 cells/mm^3, $p < 0.0001$) and lower geometric mean plasma HIV-1 RNA levels (2994 copies per milliliter versus 31,261 copies per milliliter, $p < 0.0001$); due to the skewed nature of the distribution of HIV-1 RNA measures, statistical testing was conducted on the log transformed data.

The relationship of mental health disorders to adherence is shown in Table 2. Mental health disorders were classified into six categories: attention deficit/hyperactivity disorder, anxiety disorder, mood disorders, developmental delay, schizophrenia, and other. There were 148 subjects (38.3%) with a formal mental health diagnosis; mood disorders were the most common, reported in 124 (32.1%) subjects. Having a formal diagnosis of a major mental health disorder was not associated with adherence in this population, nor was any individual category of mental health disorders ($p > 0.1$).

Structural barriers to adherence are presented in Table 3. We analyzed the association of each barrier to adherence and all, except for having a place to sleep at night, were significantly associated with adherence ($p < 0.02$). The number of structural barriers experienced was also associated with adherence, with increasing numbers associated with worse adherence ($p < 0.0001$). Of those with no barriers, 72.7% were adherent compared to 62.1% experiencing one barrier and 40.2% of subjects experiencing two or more barriers.

The mean and median SE and OE scores differed significantly according to adherence; adherent subjects had higher adherence self-efficacy and outcome expectancy regarding antiretroviral treatment than those nonadherent to medication (Table 4). Cronbach α for self-efficacy was 0.91 and for outcome expectancy was 0.62. Although this value for outcome expectancy is somewhat lower than generally acceptable for this type of scale, outcome expectancy regarding antiretroviral treatment was included in the remaining analyses as it was significantly associated with adherence (p value <0.0001).

To better understand the relationship between SE, OE and adherence, subjects were grouped into quartiles from low to high for SE and OE and were categorized by adherence (Table 5). The highest rates of adherence were observed among those subjects with high SE (Q3 and Q4) and high OE (Q4). As can be seen in the table, when examined jointly (shaded area of table), high SE was typically associated with high rates of adherence, whereas adherence was high in subjects with high

Table 2. Examination of Mental Health History According to HAART Medication Adherence

Subject carries a formal diagnosis of:	*Adherence*		
	Adherent	*Nonadherent*	p *value*[a]
A major mental health disorder:			
Yes	90 (60.8)	58 (39.2)	
No	154 (64.7)	84 (35.3)	0.45
Unknown	4	6	
Attention deficit hyperactivity disorder (ADHD):			
Yes	0	1 (100.0)	
No	244 (63.4)	141 (36.6)	0.37
Unknown	4	6	
Anxiety:			
Yes	1 (50.0)	1 (50.0)	
No	243 (63.3)	141 (36.7)	1.00
Unknown	4	6	
Developmental delay:			
Yes	0	0	
No	244 (63.2)	142 (36.8)	NA
Unknown	4	6	
Mood disorder:			
Yes	72 (58.1)	52 (41.9)	
No	172 (65.6)	90 (34.4)	0.18
Unknown	4	6	
Schizophrenia:			
Yes	5 (83.3)	1 (16.7)	
No	239 (62.9)	141 (37.1)	0.42
Unknown	4	6	
Other mental health disorders:			
Yes	12 (80.0)	3 (20.0)	
No	232 (62.5)	139 (37.5)	0.27
Unknown	4	6	

[a]*P* value obtained using Fisher's exact test for association of mental health disorders with adherence. The relatively small number of subjects with "unknown" status for formal diagnosis of mental health disorders were excluded from this testing.
HAART, highly active antiretroviral therapy.

OE only when SE was high. Logistic regression analyses were carried out to further explore the association of SE and OE to adherence. SE and OE were significantly and independently associated with adherence ($p < 0.0001$ and 0.0318, respectively). The estimated odds ratios (OR; 95% confidence interval [CI]) for predicting adherence (adherent versus nonadherent) associated with SE for comparisons of the first (lowest), second and third quartile to the fourth (highest) quartile were 0.04 (0.02–0.11), 0.10 (0.04–0.22) and 0.29 (0.12–0.69), respectively. For OE the comparable OR (95% CI) estimates were 0.33 (0.15–0.69), 0.58 (0.29–1.16) and 0.69 (0.34–1.38), respectively. However, there was no evidence of a significant interaction with respect to SE modifying the relationship of OE to adherence or, equivalently, of OE modifying the relationship of SE to adherence ($p = 0.15$).

To understand the typology of adherence, the association of the eight-level composite variable created to capture the combinations of the three personal barriers to medication adherence was examined (Table 6). As can be seen in the table, the composite measure was significantly associated with adherence ($p < 0.0001$) and clustering of barriers does occur in subjects with poor adherence. For example, of the 32 subjects with low SE/low OE, a mental health disorder, and at least one structural barrier, 22 (68.8%) were non-adherent. In contrast, among the 25 subjects with low SE and low OE but without either a mental health disorder or structural barrier, only 9 (36.0%) were nonadherent. If, on the other hand, both SE and OE are high, the majority of subjects were adherent regardless of the presence of either a mental health disorder or structural barrier.

Logistic regression modeling, used to explore interactions among the three personal barriers to adherence, failed run when the three-way interaction of the personal barriers was included. However, a model with all possible two-way interactions included indicated that all three were significant ($p < 0.02$). This indicates that the effect of low SE/low OE on adherence varies according to whether or not a mental health disorder was present (or equivalently that the effect of the presence of a mental health disorder on adherence varies according to SE and OE). Similarly, this model indicated that the effect of low SE/low OE or the presence of a mental health disorder on adherence varies according to whether or not a structural barrier was present.

Discussion

HAART therapy has greatly reduced both morbidity and mortality in individuals infected with HIV.[23–25] However, a major impediment to the success of therapy is the poor adherence encountered in subjects prescribed HAART.[1,3,4,26,27]

Table 3. Examination of Structural Barriers (Currently and/or in the Past Six Months) According to HAART Medication Adherence

Do you face any of the following problems that make it difficult for you to take your HIV medications?	*Adherence*		
	Adherent	*Nonadherent*	p *value*[a]
Do you always have some place to sleep at night?			
Yes	17 (50.0)	17 (50.0)	
No	231 (63.8)	131 (36.2)	0.14
Problems with medical insurance?			
Yes	32 (43.8)	41 (56.2)	
No	216 (66.9)	107 (33.1)	0.0004
Problems with transportation to pick up your medicines?			
Yes	16 (36.4)	28 (63.6)	
No	232 (65.9)	120 (34.1)	0.0002
Problems with transportation to get to the clinic for your visit with your provider?			
Yes	35 (47.9)	38 (52.1)	
No	213 (65.9)	110 (34.1)	0.0049
Problems getting your medication prescriptions filled?			
Yes	24 (47.1)	27 (52.9)	
No	224 (64.9)	121 (35.1)	0.019
Problems related to your job or school?			
Yes	20 (42.6)	27 (57.4)	
No	228 (65.3)	121 (34.7)	0.0035
Problems dealing with your family or taking care of your children, either your own or someone else's children?			
Yes	16 (35.6)	29 (64.4)	
No	232 (66.1)	119 (33.9)	0.0001
Number of structural barriers:			
None	152 (72.7)	57 (27.3)	
One barrier	59 (62.1)	36 (37.9)	
Two or more barriers	37 (40.2)	55 (59.8)	< 0.0001

[a]*P* values were obtained from Fisher's exact test examining the association of structural barriers with adherence.
HAART, highly active antiretroviral therapy.

We specifically looked at personal barriers to adherence that included the following three areas: mental health/substance abuse, adherence self-efficacy and outcome expectancy regarding antiretroviral treatment, and structural barriers. It was hypothesized that these barriers may coexist in certain nonadherent subjects, defining a typology of nonadherence that might direct the development of interventions that impact on multiple barriers that coexist.

In creating the typology, we focused on nonadherent subjects. Of those subjects with low SE/low OE, a mental health disorder and at least one structural barrier, 68.8% were nonadherent. These findings, along with results identifying significant interactions among barriers, support the notion that a large percentage of youth with adherence issues face more than a single barrier and that these barriers occur together in nonadherent patients. This approach of assessing multiple

Table 4. Examination of Adherence Self-Efficacy and Outcome Expectancy Regarding Antiretroviral Treatment According to HAART Medication Adherence

Self-efficacy and outcome expectancy	*Adherence*		
	Adherent	*Nonadherent*	p *value*
Self-efficacy (SE):			
Mean (SD)	85.1 (14.3)	61.4 (23.1)	< 0.0001
Median	89.0	67.5	< 0.0001
Outcome expectancy (OE):			
Mean (SD)	29.5 (4.3)	26.4 (5.0)	< 0.0001
Median	31.0	27.0	< 0.0001

Cronbach α: Self-efficacy (SE): Cronbach α is equal to 0.91; the value of Cronbach α obtained with the deletion of a single variable from the scale ranged from 0.90 to 0.92.

Outcome expectancy (OE): Cronbach α is equal to 0.62; the value of Cronbach α obtained with the deletion of a single variable from the scale ranged from 0.52 to 0.66.

HAART, highly active antiretroviral therapy; SD, standard deviation.

Table 5. Number and Percentage Adherent to HAART Medication According to Quartiles of the Self-Efficacy and Outcome Expectancy Distribution

	OE quartile				
SE quartiles	*Low (Q1)* n *(%)*	*Q2* n *(%)*	*Q3* n *(%)*	*High (Q4)* n *(%)*	*Total* n *(%)*
Low (Q1)	10 (22.2)	6 (23.1)	6 (40.0)	5 (45.5)	27 (27.8)
Q2	8 (47.1)	14 (53.8)	18 (50.0)	11 (52.4)	51 (51.0)
Q3	3 (30.0)	**24 (85.7)**	**16 (72.7)**	**27 (87.1)**	**70 (76.9)**
High (Q4)	**7 (87.5)**	**15 (78.9)**	**30 (96.8)**	**48 (96.0)**	**100 (92.6)**
Total	28 (35.0)	59 (59.6)	70 (67.3)	**91 (80.5)**	248 (62.6)

SE, self-efficacy; OE, outcome expectancy; HAART, highly active antiretroviral therapy.

barriers within a population may prove to be very useful for the development of future adherence interventions, as an individual who faces multiple barriers can be offered more than a single, unimodal intervention to intervene with non-adherence. As noted, our study was not designed to determine the predictors of adherence but rather to identify combinations of barriers present in nonadherent adolescents.

Adherence self-efficacy has been shown to positively correlate with adherence in patients prescribed HAART.[3,4,28] In a recent review, adherence self-efficacy was consistently associated with HAART adherence.[29] Outcome expectancy regarding antiretroviral treatment has also been shown to enhance adherence.[12,30–32] In our study, adherence self-efficacy and outcome expectancy regarding antiretroviral treatment were independently associated with adherence, although adherence self efficacy had greater sensitivity as a predictor than outcome expectancy. Thus, use of these scales would allow identification of subjects with low SE/OE for antiretroviral treatment among subjects who are truly nonadherent. Our data support the inclusion of these variables in measures of personal barriers to adherence and support the use of interventions to enhance self-efficacy and outcome expectancy as it relates to adherence to HAART in this population. Cronbach α for outcome expectancy for antiretroviral treatment was lower than what is generally accepted for this type of measure. As outcome expectancy was independently associated with adherence, this scale was included in subsequent analyses. Clearly, refinement of this scale is warranted for use in this population.

Depression has been shown to negatively correlate with adherence in adolescents and adults.[1,2,33] In our study, mood disorders were the most prevalent mental health diagnosis. However, the overall prevalence of mental health disorders was 38% and no category of disorder was associated with adherence. There are a number of possible reasons for this. First, we relied on a documented mental health diagnosis obtained through chart abstraction. The actual prevalence of mental health issues may actually be higher than what was found through chart review. Many studies that report mental health impacting adherence use direct measures of depressive symptoms. Thus, many youth who have mental health issues, such as depressive symptoms, may have been missed in gathering the data through these methods and a more immediate measure, that assesses anxiety and depression at nonclinical levels, may be more prudent in future studies. In addition, those youth who have a documented mental health disorder may be far more likely to be receiving care for this disorder, which may explain why there was no association between adherence and mental health disorders.

Substance use has also been associated with poorer adherence in subjects prescribed HAART.[8,34,35] One limitation of this study was that we were unable to utilize the substance abuse data. The numbers of subjects who were found on chart review to have a formal substance abuse diagnosis was lower

Table 6. Distribution of Adherence for Subjects According to Personal Barriers to Adherence

Personal barriers to adherence			*Adherence*		
SE/OE combination	*Mental health disorders*	*Structural barriers*	*Adherent* n	*Nonadherent* n *(%)*	*Total*
Present (low/low)	Present	Present	10	22 (68.8)	32
Present	Present	Absent	4	14 (77.8)	18
Present	Absent	Present	7	28 (80.0)	35
Present	Absent	Absent	16	9 (36.0)	25
Absent (high/high)	Present	Present	14	0 (0.0)	14
Absent	Present	Absent	28	3 (9.7)	31
Absent	Absent	Present	29	2 (6.5)	31
Absent	Absent	Absent	49	8 (14.0)	57

Adherence differs significantly according to different combinations of the personal barriers to adherence (Fisher's exact test p value < 0.0001).

SE, self-efficacy; OE, outcome expectancy.

than expected based on prior literature. We therefore excluded this variable from the analysis, as the data were poorly recorded in the medical records reviewed. Documentation of subjects meeting criteria for a substance abuse disorder, as well as subjects with a high level of use but not meeting criteria for a disorder, would have been important to capture. As this study was not intended to predict adherence in subjects initiating HAART, but rather to describe youth already prescribed HAART and reporting nonadherence, at the study development phase it was decided that subject burden required for administration of additional measures to assess current substance abuse was not warranted. At that time we thought the chart data would be accessible and well-documented. However, such instruments would be needed when planning for the implementation of specific adherence interventions.

As low SE/OE for antiretroviral treatment was found in many nonadherent subjects and many of these subjects also had an additional structural barrier, interventions designed to enhance these personal characteristics would need to either exclude subjects with other barriers or address the other barriers as well in order to adequately assess the impact of the intervention. For example, if one were designing an intervention to address low OE and low SE in non-adherent adolescents, assessment for depression and structural barriers and inclusion of interventions to address these issues may potentially enhance the impact on adherence and may also enhance the durability of the effect. As noted, this should be addressed in future adherence research in adolescent populations. In addition, interventions that address a number of barriers simultaneously could be developed. For example, motivational interviewing has been found to not only have an impact on adherence, but to decrease other risk behaviors such a substance abuse.[36] Such approaches may be preferable in an adolescent population since some youth may have limited capacity to deal with multiple interventions.

The issue of structural barriers to adherence is particularly significant in an adolescent population. In HIV-infected adolescents 12 to 18 years of age, data from the REACH Project revealed a number of important issues that could lead to structural barriers to adherence. At their baseline evaluation (females vs. males), 26% and 25% had no health insurance, 29% and 31% had dropped out of school, 27% and 27% reported being homeless at some time, and 24% and 27% had been in a detention facility.[37] In a study of barriers to adherence in the same population, Murphy and colleagues found two factors most strongly associated with adherence versus nonadherence: medication-related adverse effects and complications in day to day routines.[38] It is thus not surprising that we found that structural barriers have an impact on adherence. Given that this study was conducted at sites with comprehensive, multidisciplinary services, these day to day barriers continue to impact adherence in adolescents and young adults.

It is clear that there may be associations among personal barriers to adherence. In a recent study by Remien and colleagues,[39] depressive symptomatology was assessed in HIV-positive women utilizing a stress and coping model. These investigators found that stress was a mediating factor for depressive symptoms and that adherence self-efficacy mediated the relation of psychosocial support to depression. Although beyond the scope of our study, it is clear that the relationships among these barriers leading to poor adherence are quite complex and deserve further study in the adolescent population.

There are a number of limitations to our study. First, our study was not designed to predict adherence, but rather to better describe the prevalence of certain personal barriers to adherence and how these personal barriers to adherence cluster in patients with self-reported poor adherence. Second, chart review for identifying subjects with mental health and substance abuse barriers appears to have under-reported these barriers in the population. Finally, we only evaluated personal barriers to adherence and did not address medication-related barriers or barriers related to the clinical system of care. With that said, our study did show that many youth face a number of barriers and was successful in suggesting an approach to designing adherence interventions in populations where many barriers may exist.

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