

Barriers to Antiretroviral Adherence: The Importance of Depression, Abuse, and Other Traumatic Events

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ABSTRACT

Among HIV-infected persons, high-level adherence to antiretroviral medications (> 90%–95%) is associated with improved immunologic, virologic, and clinical outcomes, and is necessary to prevent the emergence of viral resistance. This study examines whether lifetime traumatic events including physical and sexual abuse, are associated with antiretroviral nonadherence. We present a cross-sectional analysis of the Coping with HIV/AIDS in the Southeast (CHASE) Study, analyzing data from the enrollment interview and medical records of study subjects. The CHASE Study is a prospective cohort study of consecutively sampled HIV-infected subjects from infectious diseases clinics in five southern states; Alabama, Georgia, Louisiana, North Carolina, and South Carolina. Four hundred seventy-four (78%) of the 611 CHASE study subjects reported being treated with antiretroviral medications at enrollment and are included in this analysis. Nonadherence was defined as the patient's self-report of missing any doses of their antiretroviral medications over the previous 7 days. Among study subjects, 54% reported a history of physical and/or sexual abuse, 91% reported at least one lifetime traumatic event, and 24% reported nonadherence with their antiretrovirals. In multivariable logistic regression analysis, the number of categories of lifetime traumatic events ($p = 0.03$), the Addiction Severity Index (ASI) alcohol score ($p = 0.02$), and being uninsured ($p = 0.04$) were associated with antiretroviral nonadherence. The finding that lifetime traumatic events are associated with antiretroviral nonadherence, particularly among those who have been traumatized in multiple ways, highlights the complex and often persisting manifestations of such trauma and calls for further investigation.

INTRODUCTION

HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) has proven extremely effective in reducing the morbidity and mortality associated

with HIV infection.¹ Multiple studies have demonstrated that HIV-infected patients with high levels of antiretroviral (ARV) adherence (> 90%–95%) have greater reductions of plasma HIV RNA levels, are more likely to achieve an

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undetectable viral load, and have better immunologic responses to HAART as measured by change in CD4 lymphocyte count.²⁻⁶ Achieving and sustaining a plasma HIV RNA level below the limits of detection for ultrasensitive assays (< 50–80 copies per milliliter depending on the assay used) is an important goal of antiretroviral therapy.⁷ When achieved, this results in a lower likelihood of the emergence of viral resistance in an individual patient, and maximizes the beneficial effects of HAART.^{6,8,9} A recent study demonstrated that among patients initiating HAART at CD4 counts greater than 200 cells per microliter, adherence but not initial CD4 count was predictive of survival.¹⁰

An extensive body of literature describes variables associated with ARV adherence among HIV-infected patients. Previous analyses have focused upon sociodemographic factors (including age, gender, and race/ethnicity), behavioral factors (including alcohol and illicit drug use), psychological factors (including depression, provider trust), and HIV literacy.^{2-4,11-18} Case reports and previous studies have raised concern for an association between traumatic events including sexual and/or physical abuse and ARV nonadherence among HIV-infected patients.¹⁹⁻²³ This study adds to the literature by evaluating the association between lifetime traumatic events and ARV adherence in a cohort of HIV-infected men and women. Evaluating the impact of lifetime traumatic events on ARV adherence and HIV-related outcomes is important given the high prevalence of trauma observed in HIV-infected persons.²⁴⁻²⁷ We report here on predictors of ARV adherence among participants in the Coping with HIV/AIDS in the Southeast (CHASE) study, a large cohort study of HIV-infected persons living in five states in the Southeastern United States. We hypothesize that lifetime traumatic events are associated with antiretroviral nonadherence among HIV-infected patients.

MATERIALS AND METHODS

Sample and procedure

The CHASE study consecutively sampled HIV-infected men and women who received care at one of eight infectious diseases clinics

in five southern states: Alabama, Georgia, Louisiana, North Carolina, and South Carolina. From 2000–2002 incident AIDS cases increased 29% in these states while increasing 9% across other southern states and less than 1% throughout the rest of the country.²⁸ This study was approved by the Institutional Review Boards at Duke University and all study sites. Our primary goal was to examine the sociodemographic characteristics, coping strategies, life histories, and care utilization patterns of persons receiving HIV-related care outside the three major cities (Atlanta, Charlotte, and New Orleans) in the South. Each of the clinics had at least 50% of their patients living in rural areas. HIV-infected English-speaking patients at the eight clinics were eligible to participate if they passed the Short-Portable Mental Status Questionnaire,²⁹ which tests for major cognitive impairment. From December 2001 through April 2002, a total of 789 patients were approached about participating; 16 were excluded because they did not meet study inclusion criteria; of the 773 remaining eligible subjects, 611 (79%) participated in the CHASE study. In this paper a cross-sectional analysis of the 474 patients who reported being treated with antiretroviral medications at the time of their enrollment interview is presented.

Information from patients used for this analysis was obtained through extensive interviews that took place in the clinics, nearby locations, or patient's homes. Interviews lasted an average of approximately 2 hours. Because of the sensitive nature of some of the questions asked in the survey, interviewers engaged in a week-long training on instrument administration followed by certification in the field. In addition to the interviews, clinical information from patients' medical records were prepared by trained health care providers on standardized chart abstraction forms.

Measures

Prior to being asked about antiretroviral adherence study subjects were asked questions about the antiretroviral medications they were taking and were shown antiretroviral medication picture cards to assist with recall. Antiretroviral medication adherence was measured

by the patient's self-reported response to the question, "When was the last time you skipped any of your HIV medicines?" This global question was asked in conjunction with other questions regarding adherence over each of the previous three days including the number of missed doses and the number of doses taken off schedule. The Patient Care Committee and the Adherence Working Group of the Outcomes Committee of the Adult AIDS Clinical Trial Group (AACTG) used this global question to measure adherence when evaluating adherence instruments.¹⁸ For the purposes of this analysis, patients were considered nonadherent if they reported missing any doses of their HIV medication during the past 7 days. This was chosen given the proven benefit of more than 95% adherence in decreasing the rates of antiretroviral drug resistance, and achieving successful virologic and immunologic outcomes.^{2-6,8-10} Patient self-report and 1-week adherence are validated measures in assessing antiretroviral adherence that have been shown to predict immunologic and virologic responses.^{2,4,5,30} In our study, an undetectable viral load (HIV RNA < 400 copies per milliliter) was observed in 60% of subjects in the adherent group and 43% of subjects in the nonadherent group ($p < 0.01$).

The number of categories of lifetime traumas was constructed by assigning 1 point for each of 15 trauma categories with details about each trauma component described below. The categorical evaluation of the number of types of traumatic events experienced has been widely used³¹⁻³⁶; patients experiencing more categories of traumatic events have been shown to have higher rates medical conditions including diabetes,³⁴ ischemic heart disease,^{34,35} and substance abuse.^{32,33}

The measure of lifetime sexual and physical abuse history was based on our previous studies,^{37,38} which were originally adapted from other research.³⁹⁻⁴¹ This instrument has been shown to correlate with several indicators of poor health.^{37,38,42} Subjects were asked structured questions regarding all sexual experiences: (1) before the age of 13 with anyone 5 or more years older than the subject and (2) at age 13 or older involving force or the threat of harm. Additionally, subjects were asked an

open-ended question about any other forced or unwanted sexual experiences. Subjects were directly asked about the perpetrator of any unwanted or forced sexual experiences including family members. To meet criteria for adult sexual abuse there must be clear force or threat of harm. However, in children (< 13 years) the threat of force or harm is implied by a 5-year age differential between victim and perpetrator. We define sexual abuse to include the following experiences where force or threat of force is used: (1) touching of the subject's breasts, pubic area, vagina or anus with hands, mouth, or objects, (2) making the subject touch the perpetrator's pubic area or anus with hands, mouth, or objects, and (3) making the subject have vaginal or anal intercourse. We define physical abuse as incidents separate from sexual abuse that include: (1) life threat (being physically attacked with or without a weapon with the intent to kill or seriously injure) and (2) other physical abuse (being beaten, hit, kicked, bit, or burned by another person, incidents outside the range of normal spanking or children fighting).

The Childhood Trauma Questionnaire⁴³ was used to assess physical and emotional neglect during childhood. Cronbach's reliability has been reported at 0.89 for emotional neglect and 0.66 for physical neglect. Both have substantial test-retest reliability (0.81 and 0.79, respectively). These two scales are each composed of five items and can range from 5 to 25. We used the cutoff suggested by Bernstein and Fink for moderate physical neglect (9 or higher) and moderate emotional neglect (12 or higher) for adding 1 point each to the total number of lifetime trauma categories.

The interview also included questions concerning a variety of other traumas before the age of 18 and lifetime. This list of traumas was adapted from other research,^{34,41} in which the more categories of traumatic events experienced have been associated with later poor health outcomes.³¹⁻³⁶ Presence of other trauma before the age of 18 included: (1) parental alcohol/drug use, (2) parental depression or parental suicide or attempted suicide, (3) imprisonment of a parent, (4) domestic violence in the home (e.g., beating of mother at least sometimes, mother being threatened with a

weapon at least once), (5) subject sent to reform school, prison, foster care, or adopted, (6) death of an immediate family member, and (7) subject having a life-threatening illness or injury not HIV related. Lifetime traumas include: (1) murder of a close family member, (2) death of a child, (3) death of a spouse/partner, and (4) other similar trauma written in by the subject.

The Brief COPE,⁴⁴ a six-scale version of the COPE, was used to measure patient coping. These included: active, denial, substance use, emotional support, self-blame, and positive reframing coping. Patients were asked what they have been doing to deal with the stress of HIV infection. Responses to items were recorded using a Likert scale ranging from 1 ("not doing this at all") to 4 ("doing this a lot"). Each scale contains two items with Cronbach's α reliability reported from 0.54 to 0.9. Coping techniques were divided into two categories. Positive coping techniques included active, emotional support, and positive reframing coping. Negative coping techniques included denial and self-blame coping. Substance use coping was not included in the negative coping techniques category as alcohol and illicit drug use were measured directly using the Addiction Severity Index (ASI). The positive and negative coping scales demonstrated Cronbach α scores of 0.61, and 0.58, respectively.

Depression was measured using the Brief Symptom Inventory (BSI).⁴⁵ The BSI is a shortened version of the well-validated Symptoms Checklist-90. For this analysis we focused on the depression subscale of the BSI. The depression subscale has previously been shown to have adequate internal consistency (Cronbach $\alpha = 0.85$) and test-retest reliability.⁴⁵ The six-item depression scale can range between 0 and 4 with a higher score indicating more depressive symptoms.

The ASI is a semistructured interview that assesses seven domains including alcohol use and drug use.⁴⁶ The ASI alcohol and the ASI drug composite scores were used to measure substance use among study subjects. These composite scores measure the severity of alcohol use and drug use over the past 30 days. Given the broad range of ASI scores observed, odds ratios were calculated and are reported

for a 10-point increase in ASI score. Living in poverty was calculated by taking subject reported total income from all sources and comparing it to the Federal Poverty Level (FPL). The FPL takes into consideration the number of dependents living in the house; therefore, the number of dependents in the household was used in our calculation as well. Race and ethnicity were obtained by patient self-report and are included in this analysis because some prior studies have shown associations between these variables and ARV nonadherence.^{12,15} Because the vast majority of Caucasian/non-Latino respondents were African American (89%), we created one variable labeled minority. Baseline CD4 counts and HIV RNA levels were obtained from the medical charts. The most recent CD4 count and HIV RNA within 6 months prior to the baseline interview was used for this analysis.

Statistical analysis

Univariable analyses were performed on all study variables to ensure that distributional assumptions were met. Comparison of means and proportions between the adherent and nonadherent groups was performed using the Student's *t* test. A multivariable logistic regression model was estimated including predictor variables specified *a priori*. Predictor variables include the number of categories of lifetime traumatic events, positive coping, negative coping, ASI alcohol score, ASI drug score, depression, age, gender, race/ethnicity, and insurance status. The depression and coping variables were highly correlated. Consequently, given the clinical importance of depression and the consistent association of depression with nonadherence in previous studies,^{3,11,17} the coping variables were dropped from the final model. A moderate correlation was observed between the trauma variable and both depression and coping. As such, additional multivariable logistic regression models were estimated to evaluate the individual effects of depression and coping on antiretroviral nonadherence with trauma excluded from the models. All statistical analyses were performed using STATA Version 8.1 (STATA Corporation, College Station, TX).

RESULTS

Demographic characteristics of the 474 CHASE subjects included in this analysis are displayed in Table 1. Overall the mean age of subjects was 40.6 ± 8.7 years; 29.1% were female; 67.5% were minorities; 15.6% were college graduates; 71.3% had incomes below the FPL, and 22.2% were uninsured. The mode of HIV transmission was reported as men who have sex with men (MSM) in 35.4%, heterosexual transmission in 41.6%, and injection drug use (IDU) in 5.9%. There were no statistically significant differences in these sociodemographic characteristics among the adherent and nonadherent groups. In this sample, 54% of study subjects reported a history of physical and/or sexual abuse, and 91% of subjects reported at least one lifetime traumatic event. Most study subjects (90%) had experienced all their traumatic events more than 2 years before the study. Among the CHASE cohort nonadherence in the last week was reported in 23.6% of subjects.

Bivariable analyses

Being uninsured ($p = 0.03$), the number of categories of lifetime traumatic events ($p < 0.01$), the use of negative coping techniques (denial and self-blame coping) ($p < 0.01$), the ASI alcohol score ($p < 0.01$), the ASI drug score ($p < 0.01$), and depression ($p < 0.01$) were associated with nonadherence (Table 2). The use of positive coping techniques (active, emotional support, and positive reframing coping) was associated with complete adherence ($p = 0.01$). Age, gender, race/ethnicity, education, and living in poverty were not associated with nonadherence in the last week. A significant increase in the rate of nonadherence was observed in subjects that experienced more categories of lifetime traumatic events (Fig. 1). Antiretroviral nonadherence was reported in 9.5% of subjects with no trauma history, 22.4% of subjects reporting 3 categories of trauma, and 34% of subjects with 5 or more categories of trauma (Fig. 1, $p < 0.01$).

Multivariable analyses

The following variables were associated with nonadherence in multiple logistic regression

analysis: the number of categories of lifetime traumatic events (odds ratio [OR] = 1.11, $p = 0.03$, 95% confidence interval [CI] = 1.01, 1.22), the ASI alcohol score (OR = 1.57, $p = 0.02$, 95% CI = 1.06, 2.32), and being uninsured (OR = 1.71, $p = 0.04$, 95% CI = 1.03, 2.83) (Table 3). Age, gender, race/ethnicity, depression, and the ASI drug score were not associated with antiretroviral nonadherence in multivariable logistic regression analysis. Given that a moderate correlation was observed between the trauma and both the depression and coping variables, additional multivariable logistic regression models were estimated to evaluate the effects of depression and coping on nonadherence with trauma removed from each model. Depression was significantly associated with nonadherence in the multivariable model when the trauma variable was removed (OR = 1.29, $p = 0.05$, 95% CI = 1.00, 1.66). In a model evaluating the effects

TABLE 1. PATIENT CHARACTERISTICS OF FOUR HUNDRED SEVENTY-FOUR HIV-INFECTED SUBJECTS REPORTING ANTIRETROVIRAL USE AT ENROLLMENT INTERVIEW IN THE CHASE STUDY

Characteristics	Mean \pm SD or frequency (%)
Age (years)	40.6 \pm 8.7
Gender	
Female	138 (29.1%)
Male	336 (70.9%)
Race/ethnicity	
Minority	320 (67.5%)
Caucasian/Non-Latino	154 (32.5%)
Education	
Less than high school graduate	87 (18.4%)
High school graduate	157 (33.2%)
Some college	155 (32.8%)
College graduate	74 (15.6%)
Reported mode of HIV transmission	
Men who have sex with men	168 (35.4%)
Heterosexual contact	197 (41.6%)
Intravenous drug use	28 (5.9%)
Other	81 (17.1%)
Insurance ^a	
Private insurance	125 (26.4%)
Medicare	141 (29.7%)
Medicaid	206 (43.6%)
Uninsured	105 (22.2%)
Income	
Below Federal Poverty Line	338 (71.3%)
Above Federal Poverty Line	136 (28.7%)
CD4 Lymphocyte count (cells/ μ L)	441 \pm 413
Log HIV RNA (copies/mL)	2.85 \pm 1.26

^aSubjects may have more than one category of insurance provider.

TABLE 2. BIVARIABLE ANALYSIS: VARIABLES ASSOCIATED WITH NONADHERENCE^a AMONG CHASE STUDY SUBJECTS

Variable	Adherent (n = 362)	Nonadherent (n = 112)	Range	Odds ratio	95% CI	p value
Age (years)	40.7 ± 8.9	40.3 ± 7.7	20–71	0.99	0.97, 1.02	0.68
Gender						
Female	105 (76%)	33 (24%)		1.00		
Male	257 (76%)	79 (24%)		0.98	0.61, 1.56	0.93
Race/ethnicity						
Minority	252 (79%)	68 (21%)		1.00		
Caucasian/Non-Latino	110 (71%)	44 (29%)		1.48	0.96, 2.3	0.08
Education						
Less than high school graduate	66 (76%)	21 (24%)		1.00		
High school graduate	119 (76%)	38 (24%)		1.02	0.55, 1.88	0.95
Some college	115 (74%)	40 (26%)		1.11	0.60, 2.04	0.74
College graduate	61 (82%)	13 (18%)		0.68	0.31, 1.47	0.33
Insurance ^b						
Private insurance	101 (81%)	24 (19%)		0.70	0.42, 1.17	0.18
Medicare	108 (77%)	33 (23%)		0.97	0.61, 1.55	0.90
Medicaid	161 (78%)	45 (22%)		0.83	0.54, 1.28	0.41
Uninsured	72 (69%)	33 (31%)		1.68	1.04, 2.72	0.03
Income						
Above Federal Poverty Line	98 (72%)	38(28%)		1.00		
Below Federal Poverty Line	264 (78%)	74 (22%)		0.72	0.46, 1.14	0.16
Lifetime trauma categories	2.9 ± 2.3	3.6 ± 2.3	0–11	1.14	1.05, 1.25	< 0.01
Depression	0.63 ± 0.78	0.88 ± 0.92	0–3.83	1.4	1.10, 1.77	< 0.01
Positive coping ^c	3.11 ± 0.6	2.95 ± 0.6	1–4	0.63	0.44, 0.91	0.01
Negative coping ^d	1.56 ± 0.5	1.75 ± 0.6	1–4	1.69	1.19, 2.40	< 0.01
ASI ^e Alcohol	1.6 ± 4.3	3.6 ± 8.7	0–58.9	1.71	1.18, 2.45	< 0.01
ASI ^e Drug	1.0 ± 3.1	2.4 ± 6.5	0–45.6	1.97	1.21, 3.19	< 0.01

^aNonadherence is defined as patients' self-report of missing any doses of prescribed antiretroviral medications in the past week.

^bSubjects may have more than one category of insurance provider.

^cPositive coping is defined as active, emotional support, and positive reframing.

^dNegative coping is defined as denial, and self-blame coping.

^eASI, Addiction Severity Index; odds ratio per 10-point increase in ASI score.

Continuous variables recorded as mean ± SD, Categorical variables recorded as frequency (row%).

of coping, negative coping was significantly associated with nonadherence (OR = 1.51, $p = 0.03$, 95% CI = 1.05, 2.18) and positive coping maintained borderline significance (OR = 0.71, $p = 0.08$, 95% C = I 0.49, 1.04) when trauma and depression were excluded from the model.

DISCUSSION

Our study demonstrates an association between lifetime traumatic events and antiretroviral nonadherence among a large cohort of consecutively sampled HIV-infected patients from five southern states. Among the CHASE cohort 54% of subjects reported a history of physical and/or sexual abuse (females, 59%; males, 51%), and 91% of subjects reported at least one lifetime traumatic event (females,

94%; males, 90%). Considering the high prevalence of trauma among HIV-infected persons,^{24–27} our finding that rates of antiretroviral nonadherence increase for each additional category of trauma experienced (adjusted OR = 1.11) is sobering. An exposure/response relationship was observed such that subjects experiencing more lifetime traumatic events were incrementally more likely to be non-adherent with their antiretroviral medications (Fig. 1). Among study participants, nonadherence was reported in 9.5% of subjects with no history of trauma, 22.4% of subjects who had experienced three categories of trauma, and 34% of subjects experiencing five or more categories of trauma ($p < 0.01$). Given the critical importance of antiretroviral adherence on clinical outcomes in HIV infection this is an important finding that deserves further evaluation.

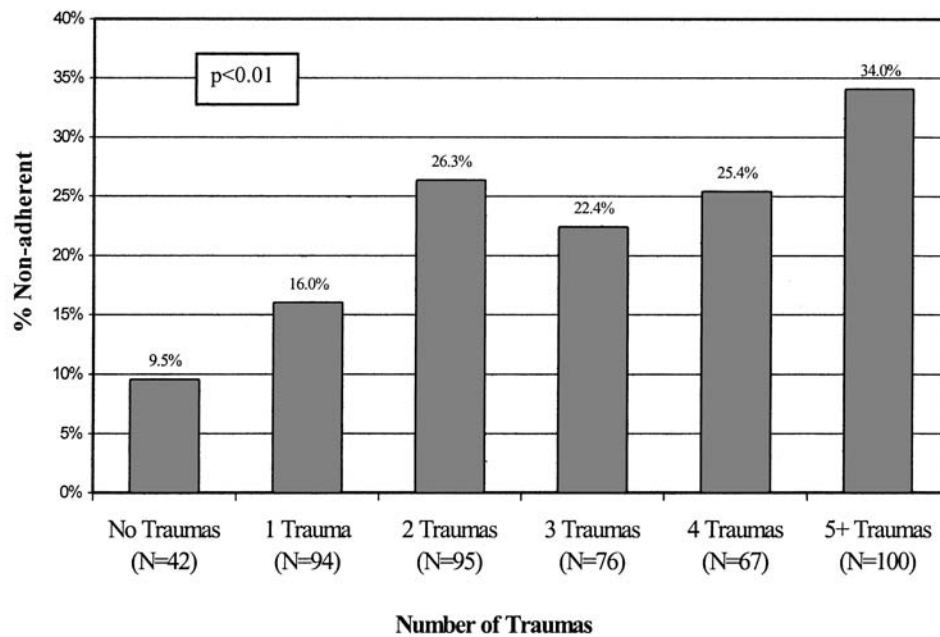


FIG. 1. The association of the number of categories of lifetime traumatic events on the prevalence of antiretroviral nonadherence among CHASE study subjects. $p < 0.01$ pertains to trend test. Nonadherence is defined as patients' self-report of missing any doses of prescribed antiretroviral medications in the past week.

Several studies have reported the association of physical/sexual abuse, and the number of categories of lifetime traumatic events with high-risk sexual behavior, alcohol use, and illicit drug use in other patient populations.^{33,34,47-50} Among HIV-infected patients, trauma has been associated with HIV disease progression.^{51,52} Now in the HAART era, ARV nonadherence may partially mediate the relationship of trauma and HIV disease progression. Previous studies have shown worse im-

munologic responses as measured by CD4 count, and worse virologic responses as measured by plasma HIV RNA among HIV-infected subjects with less than 90%–95% adherence to their prescribed ARV regimen.²⁻⁶ Among CHASE subjects the rate of ARV nonadherence increased considerably for each additional category of trauma experienced (Fig. 1).

Cohen et al.⁵³ recently reported that HIV-infected women with a history of physical abuse

TABLE 3. MULTIVARIABLE LOGISTIC REGRESSION ANALYSIS: VARIABLES ASSOCIATED WITH NONADHERENCE^a AMONG CHASE STUDY SUBJECTS

Variable (range)	Adjusted OR	95% CI	p value
Age (20–71)	1.00	0.98, 1.03	0.82
Male	0.94	0.57, 1.55	0.80
Caucasian	1.38	0.86, 2.21	0.18
Lifetime trauma categories 0–11)	1.11	1.01, 1.22	0.03
Depression (0–3.83)	1.22	0.94, 1.58	0.14
ASI ^b Alcohol (0–58.9)	1.57	1.06, 2.32	0.02
ASI ^b Drug (0–45.6)	1.42	0.85, 2.37	0.19
Uninsured	1.71	1.03, 2.83	0.04

^aNonadherence is defined as patients' self-report of missing any doses of prescribed antiretroviral medications in the past week.

^bASI, Addiction Severity Index; adjusted odds ratio per 10-point increase in ASI score.

and/or sexual abuse were less likely to receive antiretroviral therapy when such treatment was indicated. They hypothesized that an inability to trust health providers and barriers to self-care associated with abuse and the psychological sequelae of abuse may lead women to decline antiretroviral therapy.^{19,20,53–55} These factors may also explain the association of lifetime traumatic events and ARV non-adherence observed in our study.

In our multivariable logistic regression analysis depression was not associated with antiretroviral nonadherence, although this variable was highly statistically significant in bivariable analyses. This finding is likely the result of the moderate correlation observed between the trauma and depression variables. When trauma was dropped from the multivariable logistic regression model, depression was significantly associated with antiretroviral nonadherence. The association between depression and nonadherence has been observed in previous studies.^{3,11,17} Similarly, negative coping was associated with nonadherence in a multivariable model when the collinear trauma and depression variables were excluded. Consistent with previous studies we found an association between alcohol use and antiretroviral nonadherence.^{2,12–14,18} We hypothesize that traumatic events are the earliest in a series of circumstances associated with poor adherence. The interplay between trauma and subsequent depression, negative coping, alcohol abuse, and medication adherence in HIV-infected patients is complex and requires further investigation. Our findings suggest that each of these factors is important with regards to antiretroviral adherence, and that screening for trauma, depression, and alcohol abuse is warranted in the routine care of HIV-infected patients. Specific interventions targeting each of these factors are needed in an effort to improve adherence. Among traumatized patients, cognitive-behavioral approaches to improving antiretroviral adherence are being investigated and merit further study.⁵⁶

Our study demonstrates that HIV-infected patients who are uninsured are more likely to be nonadherent with their antiretroviral medications even after adjustment for other covariates. We hypothesize that patients who are

uninsured have more difficulty in consistently obtaining their medications and this may contribute to the higher rate of nonadherence observed.

We note several important strengths of this study. The CHASE cohort is one of the largest and most representative samples of HIV-infected subjects in the southeast United States. By including subjects from five southern states, and focusing on clinics providing services to a high proportion of patients from rural locales, this cohort allows for investigation of the impact of HIV-infection on a population that has not been well studied. Given that the South is the region with the highest rates of HIV and AIDS in the United States,²⁸ the evaluation of such a cohort is of critical importance. The CHASE cohort is larger than most other ARV adherence studies, which have typically included subjects from a single clinic or medical center. Another methodological strength of our study is the consecutive sampling approach. Much of the literature investigating ARV adherence describes convenience samples derived from patient and provider referral or from clinical trials. This inherently introduces volunteer bias that we were able to reduce with our consecutive sampling approach.

Our study has several limitations. There are multiple ways to assess medication adherence including patient self-report, pill counts, and monitored electronic monitoring devices (MEMS). Each measure has advantages and disadvantages and patient self-report may overestimate adherence.^{18,57} However, self-reported adherence has been shown to correlate with clinical outcomes,^{2,4,5,30} and is the most widely used measure to evaluate ARV adherence in HIV-infected patients. Additionally, responses to the global question used in our study correlated well with virologic outcomes. Because this study is cross-sectional we cannot be certain whether trauma affects nonadherence, or whether those patients who are nonadherent are recalling more traumas. We identify an association between trauma and antiretroviral nonadherence but are not able to establish causality. Subjects' reports of lifetime traumatic events raise concern for recall bias, especially because most events occur many years prior to the study interview. In practice,

health care providers can elicit and address only those lifetime traumas remembered and reported by patients under their care. Because HIV-infected subjects in our study who recall and report having experienced more traumatic events are less likely to be adherent with their antiretroviral medications, we believe the issue of recall bias is of minimal significance in clinical practice.

CONCLUSIONS

ARV adherence is one of the key principles of successful management in the care of HIV-infected persons. The association between high-level ARV adherence and clinical, immunologic, and virologic outcomes are strong. Given the high prevalence of physical abuse, sexual abuse, and other lifetime traumatic events among HIV-infected persons and the association between these variables and poor ARV adherence, trauma deserves more attention in clinical practice. The majority of HIV-infected patients do not receive in-depth psychological evaluation and counseling in their routine HIV care. Providers caring for HIV-infected persons need to be aware of the association between lifetime traumatic events and ARV nonadherence in order to provide appropriate care and referrals for their patients.

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