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# Overload: The Impact of Incident Stressful Events on Antiretroviral Medication Adherence and Virologic Failure in a Longitudinal, Multi-site HIV Cohort Study

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## Abstract

**Background—**HIV-infected individuals frequently experience traumatic and stressful events such as sexual and physical assault; housing instability; and major financial, employment, and legal difficulties. Past trauma history predicts poorer medication adherence and health outcomes, yet little research has examined the influence of incident stressful experiences on antiretroviral medication adherence and treatment outcomes.

**Methods—**We prospectively measured incident stressful and traumatic events, medication adherence, and viral load over 27 months in an 8-site, 5-state study. Using multivariable logistic and generalized estimating equation modeling, we assessed the impact of incident stressful events on 27-month changes in self-reported medication adherence and virologic failure (viral load ≥400 c/mL).

**Results—**Of 474 participants on antiretroviral therapy at baseline, 289 were interviewed and still on treatment at 27 months. Participants experiencing the median number of incident stressful events (n=9) had over twice the predicted odds (OR=2.32) of antiretroviral medication non-adherence at follow-up compared to those with no events. Stressful events also predicted increased odds of virologic failure during follow-up (OR=1.09 per event).

**Conclusions—**Incident stressful events are exceedingly common in the lives of HIV-infected individuals and negatively impact antiretroviral medication adherence and treatment outcomes. Interventions to address stress and trauma are needed to improve HIV outcomes.

### Keywords

HIV; AIDS; Stress; Adherence; Virologic failure; Disparities

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## Introduction

Combination antiretroviral (ARV) therapy has dramatically reduced morbidity and mortality for people living with HIV/AIDS (PLWHA). In developed nations, life expectancy of PLWHA is approaching that of the general population and has consistently improved since the introduction of highly active antiretroviral therapy in 1996 (1). Achieving and sustaining suppression of plasma HIV RNA (viral load [VL]) is a principal tenet of HIV treatment that guidelines endorse as a goal for both ARV-naïve and ARV-experienced patients (2, 3). To achieve this goal, sustained high levels of ARV adherence are required. It is generally accepted that >95% adherence was required to reliably maintain virologic suppression with first-generation unboosted protease inhibitor combination ARV regimens (4), although evidence is accumulating that 80% adherence may be a more appropriate threshold for the newer boosted PI and non-nucleoside reverse transcriptase regimens (5, 6).

A broad literature describes factors associated with ARV adherence and consistently recognizes the importance of mental health disorders, substance abuse, and alcohol abuse in contributing to non-adherence (7–11). Recent studies have highlighted other psychosocial factors, including stressful and traumatic events, as contributors to ARV non-adherence among individuals with HIV infection (11–15). Traumatic experiences, especially histories of childhood sexual and physical abuse, are much more prevalent among PLWHA than in the general population (16). Further, given the concentration of HIV in disadvantaged populations, the lives of PLWHA tend to be heavily characterized by a range of moderately and severely stressful events such as major financial, employment, and legal difficulties; housing instability; injuries, accidents, or assault; and death or illness of close family members. While many of these events may not satisfy the diagnostic definition of a traumatic experience, this tapestry of “life chaos” is increasingly recognized as having important implications for patients’ engagement and success in care (17).

To date, many studies of ARV adherence have been cross-sectional and therefore unable to assess the impact of changes in psychosocial factors, including incidence of stressful and traumatic events, on changes in ARV adherence. Although stressful events have been linked with ARV non-adherence in cross-sectional analyses (12), the impact of incident stressful and traumatic events on longitudinal changes in ARV adherence among patients engaged in clinical care has not been well studied. Therefore we conducted the current study to address the influence of incident stressful and traumatic events on changes in self-reported ARV adherence and on virologic failure in the CHASE cohort over 27 months of follow-up. We hypothesized that incident stressful and traumatic events would be associated with decreases in ARV adherence and failure to sustain an undetectable VL during longitudinal follow-up.

## Methods

### Sample and Procedure

The Coping with HIV/AIDS in the SouthEast (CHASE) study has been described in detail previously (11, 18). Briefly, the study recruited 611 consecutively sampled HIV-infected patients receiving care at one of eight infectious diseases clinics in 5 Southeastern U.S. states (AL, GA, LA, NC, SC) in 2001–2002. Patients completed detailed interviews with trained, field-certified interviewers at baseline and after 9, 18, and 27 months. Additionally, clinical information from patients’ medical records was recorded by trained health care providers on standardized chart abstraction forms. The current study includes the 474 CHASE participants (78%) who reported receiving antiretroviral medications at their baseline interview. All study procedures were approved by the Institutional Review Boards at Duke University and all study sites.

## Measures

**Antiretroviral Medication Adherence—**Derived from the Patient Care Committee and the Adherence Working Group of the Outcomes Committee of the Adult AIDS Clinical Trial Group (19), our self-report measure of ARV medication adherence has been described in detail previously (11). Briefly, study participants were asked questions about the ARV medications they were taking and were shown ARV medication picture cards to assist with recall prior to being asked a series of questions related to adherence. ARV 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?" with possible response options In the past week; 1–2 weeks ago; 3–4 weeks ago; 1–2 months ago; 3 or more months ago; and Never. Patients were considered to have non-adherence if they reported missing any ARV doses during the past 7 days; results were consistent in sensitivity analyses when the outcome was modeled as an ordinal response variable with ordinal logistic regression. Patient self-report and one-week adherence are validated measures for assessing ARV adherence that predict immunologic and virologic responses (20–22); in the present sample, self-reported adherence was strongly correlated with an undetectable viral load at baseline (OR=2.09, p = 0.002). The adherence questionnaire was administered at the baseline and 27-month follow-up interviews.

**HIV Virologic Failure—**We considered as a second endpoint virologic failure, defined as VL≥400 c/mL. From the medical record abstraction, we selected the earliest VL (as quantified by each recruitment clinic's standard laboratory practices) within 3 months after each interview (baseline and 9, 18, and 27 months). We used a cutoff of 400 to indicate viral suppression because of the varying minimum detection thresholds in use at the time at the different labs. Results were consistent in sensitivity analyses when viral load (on the log scale) was modeled as a continuous outcome.

**Incident stressful events, severe stressful events, and traumatic events—**We used a modified version of the Life Events Survey (12, 23) to measure the occurrence of stressful events in the 9 months preceding the baseline interview and in the intervals between consecutive interviews. We included only events considered to be moderately to severely stressful based on previous studies with interviewer-based objectively rated stresses; these measures have consistently predicted HIV disease progression (24). Moderate stressors included experiences such as relationship difficulties; death or serious illness of a close friend or family member; employment difficulties (e.g. loss of job); and non-HIV-related serious illnesses, injuries, and accidents (see Table 4). Severe stressors included divorce/separation, death or illness of an immediate family member, major financial problems (e.g., foreclosure), more than a week in prison, and sexual and physical assault. We further considered as traumatic events those severe stressors that would satisfy criterion A(1) of the definition of post-traumatic stress disorder (25): sexual and physical assault and death of a spouse/partner or child. We considered three continuous global measures of stressors: the number of all stressors (moderate and severe), the number of severe stressors, and the number of traumatic events. We calculated these measures for the 9 months before baseline and for the 27 months between baseline and last follow-up. Additionally, we created a count variable reflecting the number of types of lifetime traumatic experiences based on a detailed trauma assessment completed by each participant at baseline, as described previously (11, 18, 26).

**Other psychosocial covariates—**Depressive symptoms at baseline and 9, 18, and 27 months were measured using the Brief Symptom Inventory (BSI) (27), a shortened version of the well-validated Symptoms Checklist-90. Here we focused on the 6-item BSI depression subscale, which has adequate internal consistency (Cronbach's alpha=0.85) and

test-retest reliability. We standardized the scale to range from 0–100 with 10 units representing one standard deviation in the general population.

The Addiction Severity Index (ASI) is a semi-structured interview that assesses seven domains including alcohol use and drug use (28). The ASI alcohol composite score, ranging from 0–100, measures the severity of alcohol use over the past 30 days and was assessed in study subjects at baseline and 27 months.

Coping styles were evaluated with 16 items from the Brief Cope at baseline and 27 months (29). Consistent with previous definitions (11, 29, 30) and an exploratory factor analysis, we formed two scales of adaptive (positive reframing, using emotional support, acceptance, religion, active) and maladaptive (denial, self blame, and behavioral disengagement) coping styles, each ranging from 1–4, which were uncorrelated ($\rho = -0.07$) and had satisfactory internal reliability (Cronbach's alpha = 0.74 and 0.72, respectively).

**Socio-demographic and Clinical covariates—**Patient age, sex, race/ethnicity, education, and insurance status were recorded at the baseline interview. Because nearly all participants were either Caucasian/Non-Latino (31%) or African American/Non-Latino (63%), we classified participants as either Caucasian/Non-Latino or of minority race/ethnicity. Baseline CD4 T lymphocyte count was defined as the measurement closest to the baseline interview date within a window of 3 months on either side.

## Statistical analyses

We examined the distribution of study variables among all participants on ARVs at baseline and among those who completed the 27-month interview and were still on ARVs at that time to assess the potential for selection bias in the adherence analysis; we compared these distributions using chi-square and Wilcoxon rank sum test statistics. To evaluate predictors of changes in ARV adherence from baseline to the 27-month interview, we used logistic regression to model non-adherence at 27 months while controlling for baseline non-adherence. We considered predictors that were of interest *a priori*, with a particular focus on the association between incident stressful events and changes in adherence. Given the collinearity between incident stressful events, incident severely stressful events, and incident traumatic events, we fit three separate multivariable models, each containing one of these three variables. We hypothesized that all three variables would be predictive of deteriorations in adherence but that the effect size per traumatic event would be greater than the effect size per severely stressful event, which in turn would be greater than the effect size per any stressful event. In sensitivity analyses, we considered those participants who went off ARVs between baseline and 27-month follow-up (and were therefore excluded from the primary analysis of change in adherence) to have failed treatment, and we fit models comparing those who either reported non-adherence or had gone off ARVs to those who reported complete adherence. We recoded the continuous variables representing age, CD4 count, BSI, and ASI so that odds ratios corresponded to the change per 10 years of age, per 100 CD4 cells/$mm^3$, per 10 BSI units (one normed standard deviation), and per 10 ASI units.

To model the probability of virologic failure (≥400 c/mL) at each of the four survey time points, we used generalized estimating equations with a logit link and binomial error distribution to account for the dependency in repeated observations within individuals. These models included only baseline characteristics and covariates that were measured every 9 months (depression and incident events). These models did not include an adherence measure since adherence data were only collected at baseline and 27 months. Primary analyses included patients with available VL measurements at each interview (344 participants – 73% – contributed 725 separate VL measures in the appropriate time

windows). In sensitivity analyses, we reclassified patients with missing VL measures as having virologic failure at each time point for which a value was not available ("missing=failure").

## Results

Among 474 study participants, the median age was 40 years, 29% were female, and roughly two-thirds of patients belonged to minority racial/ethnic groups (Table 1). At baseline, patients had experienced a median of 3 types of lifetime traumatic events. The longitudinal ARV adherence analysis included those who completed the 27-month interview and were still on ARVs. Compared to the overall sample, this group (n=289, 61%) tended to be older, more educated, and less likely to belong to a racial/ethnic minority group (Table 1). During the 27-month period following baseline, patients reported a median of 9 incident stressful events, including 3 incident severely stressful events, and 21% reported ARV non-adherence.

In bivariable analyses, baseline non-adherence was associated with ARV non-adherence at the 27-month follow-up interview (Table 2). Depressive symptoms, alcohol use, and maladaptive coping measured at the 27-month interview also predicted ARV non-adherence at 27 months, as did the three measures of incident stressful events between baseline and 27 months. We observed an exposure-response relationship between incident stressful events and ARV non-adherence (Figures 1a, 1b). After adjustment for covariates, measures of association remained unchanged for all incident stressful events (OR=1.10 per event, 95% CI=1.04–1.16) and incident severely stressful events (1.13 per event, 0.99–1.29) while the OR for incident traumatic events was somewhat attenuated (OR=1.43, 0.97–2.09). These ORs represent the change in the odds of non-adherence associated with a single additional event. Based on predictions from these models, an individual with the median number of stressful experiences during follow-up (9) had over twice the predicted odds of non-adherence compared to an individual with none (OR=2.32), and an individual with the median number of severely stressful experiences (3) had 1.44 times the predicted odds of non-adherence compared to an individual with none. Similar estimates were obtained in sensitivity analyses from models combining those who went off ARVs with those reporting non-adherence.

Bivariable predictors of virologic failure (≥400 c/mL) over 27 months of follow-up included membership in a minority racial/ethnic group, lower baseline CD4, more lifetime traumatic experiences, more incident stressful events, and more incident severely stressful events (Table 3). With the exception of lifetime traumatic experiences, these associations all persisted in multivariable models (minority race/ethnicity: OR=1.67, 95%CI=1.06–2.62; incident stressful events: OR=1.09, 95%CI=1.02–1.17; incident severe stressful events: OR=1.19, 95%CI=1.02–1.39). Results remained substantively unchanged in sensitivity analyses using a missing=failure approach for patients with missing VL measures at a given 9-month interval.

To further understand the relationship between incident stressful events, adherence, and virologic failure, we separately considered sexual assault, physical assault, and 9 other groupings of incident events (e.g., health-related, financial; Table 4). Experiences of sexual and physical assault during follow-up were the least common, with incidence of 1.1 and 9.3 per 100 person-years, respectively, whereas financial stressors were the most common (78.6 events per 100 person-years). Incident events reported at one third or more of interviews included major illness, injury or accident (non-HIV related); major illness of a family member or close friend; death of a family member or close friend; financial stresses; and relationship stresses. We fit a series of multivariable models for ARV non-adherence and

virologic failure, each including one type of stressful event and all other covariates from either Table 2 or 3. In these models, relationship, safety-related, and life transition stresses were associated with decreased adherence while relationship stresses and injuries, accidents, and non-HIV related illnesses predicted virologic failure (Table 4).

## Discussion

In this multi-site study of patients with established HIV infection, occurrence of incident stressful and traumatic events between interviews predicted deteriorations in ARV adherence during 27 months of prospective follow-up, even after adjustment for baseline characteristics, depression, alcohol use, and coping styles. We observed a strong exposure-response relationship between incident stressful and traumatic events and ARV non-adherence (Figure 1). Participants experiencing the median number of incident stressful events (n=9) had over twice the predicted odds of ARV non-adherence at follow-up compared to those with no events after controlling for baseline adherence. Incident stressful (but not traumatic) events were also associated with an increased risk of virologic failure over the follow-up period.

The clinical relevance of the relationship between incident stressful events and adherence is underscored by the high frequency of such events during longitudinal follow-up. Participants experienced a median of 9 stressful events and 3 severely stressful events over 27 months. In any 9-month period, over half of participants experienced a major financial stressor; approximately one-third experienced a major injury or illness not related to HIV, the death of a family member or close friend, a serious illness of a family member or friend, and a major relationship stressor; and approximately one in five experienced employment-related stressors and safety-related stressors.

Our study advances previous research on the impact of stressful and traumatic events on HIV adherence and virologic outcomes, as most prior studies have employed a cross-sectional design (11, 12, 14, 15) and therefore have been unable to model changes in adherence, a behavior that is known to vary over time.(31) Our findings support other research which has documented both high lifetime prevalence and high ongoing incidence of stressful and traumatic experiences which characterize the lives of many people living with HIV/AIDS (16, 32–36). A relationship between stressful events and ARV adherence may explain the increased risk of virologic failure observed in the present study and the higher rates of clinical disease progression and mortality that have been reported previously in patients experiencing more stressful and traumatic events (15, 26, 37, 38), although some evidence also suggests that stress may have a direct adverse effect on the immune system which may hasten disease progression (39).

These findings inform clinical practice and intervention development. While prior traumatic experiences such as childhood sexual abuse certainly influence health behaviors and outcomes in HIV-infected individuals (15, 24, 26, 38, 40–42), the less severe but more frequent stressful experiences also have important implications for treatment outcomes. The development of evidence-based interventions to reduce the impact of stressful events on PLWHA, for example by teaching coping skills, as well as interventions to prevent the occurrence of stressful events when possible, may prove vital to maintaining adherence and improving health outcomes in HIV-infected individuals. While some of the stressful events considered in this study may not be preventable through intervention (e.g., death or illness of a family member), the occurrence of other types of events such as financial, employment, and relationship-related stressors could plausibly be reduced through the effective marshalling of targeted support resources.

The CHASE cohort is largely representative of HIV-infected individuals engaged in care in the Southeast U.S., but may not be generalizable to patients in other regions of the country, large cities, or internationally. Selection bias may influence our results as the number of patients completing the 27-month interview and still on ARVs at that time (n=289) differed from the eligible sample for study participation who were receiving ARVs at the baseline interview (n=474) across a number of variables. The ARV adherence sample tended to be older and more educated and was less likely to be of minority race/ethnicity and to have experienced stressful events in the 9 months before baseline. These differences partially reflect differences in who was retained at 27 months and partially reflect differences in who remained on ARVs through 27 months. The observation that those with more stressful experiences were more likely to be lost and more likely to go off ARVs may suggest that our study actually underestimated the impact of stressful events on non-adherence. We obtained nearly identical results in a sensitivity analysis that combined those who went off ARVs with those who reported non-adherence. The lack of association between incident traumatic events and virologic failure in this analysis may reflect the rarity of traumatic experiences relative to moderate and severe stressful events during prospective follow-up.

A number of methods may be used to assess medication adherence, and patient self-report may overestimate adherence (43). However, there is no accepted gold standard to measure adherence; patient self-report is widely used and has been shown to correlate with clinical outcomes (11, 21, 44). In this study, incident stressful events predicted not only self-reported non-adherence but also virologic failure, a widely accepted biomarker of non-adherence.

As nearly any HIV clinician could attest, incident stressful events are exceedingly common in the lives of HIV-infected individuals engaged in outpatient care; this study concludes that such events negatively impact ARV adherence and virologic outcomes over time. Efforts to improve health outcomes for HIV-infected individuals should address history of severe traumatic experiences (41, 42), but must also pay particular attention to less severe but more frequent stressful events that may occur while the patient is engaged in clinical care, such as financial, relationship, safety-related and life-transition stresses. Interventions to prevent such stressful events where possible and to improve the ability of patients to cope with events that do occur may play an important role in optimizing health outcomes for HIV patients.

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## Abbreviations

| | |
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| **ARV** | Antiretroviral therapy |
| **ASI** | Addiction Severity Index |
| **BSI** | Brief Symptoms Inventory |
| **CHASE** | Coping with HIV/AIDS in the Southeast |

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| **CI** | Confidence interval |
| **OR** | Odds ratio |
| **PLWHA** | People living with HIV/AIDS |
| **VL** | Viral load |

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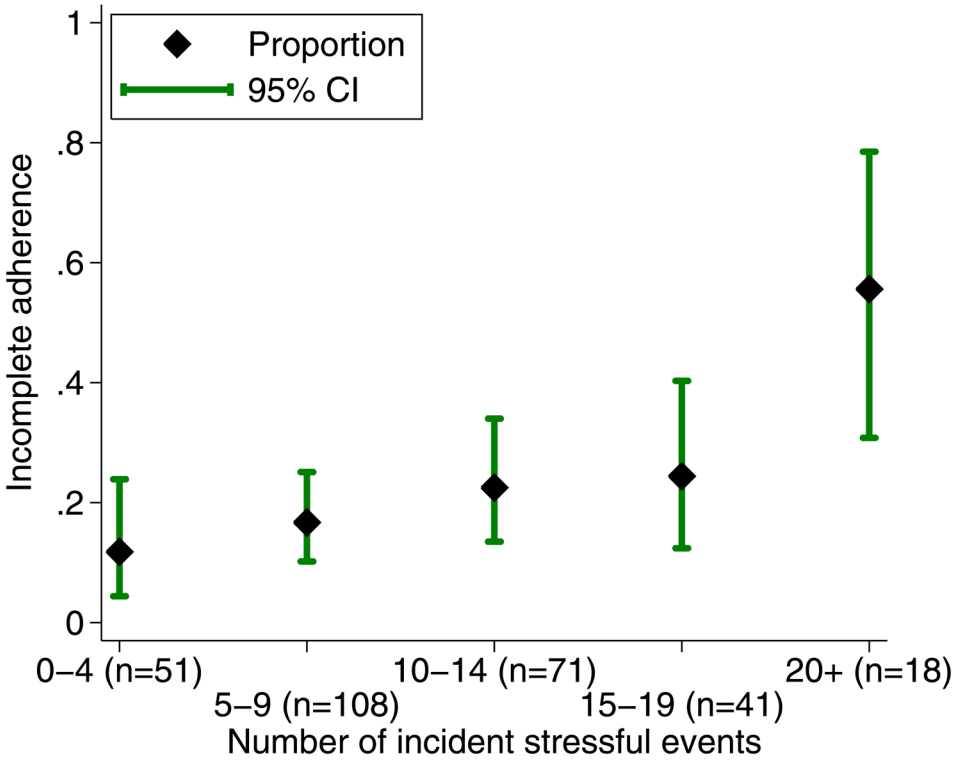


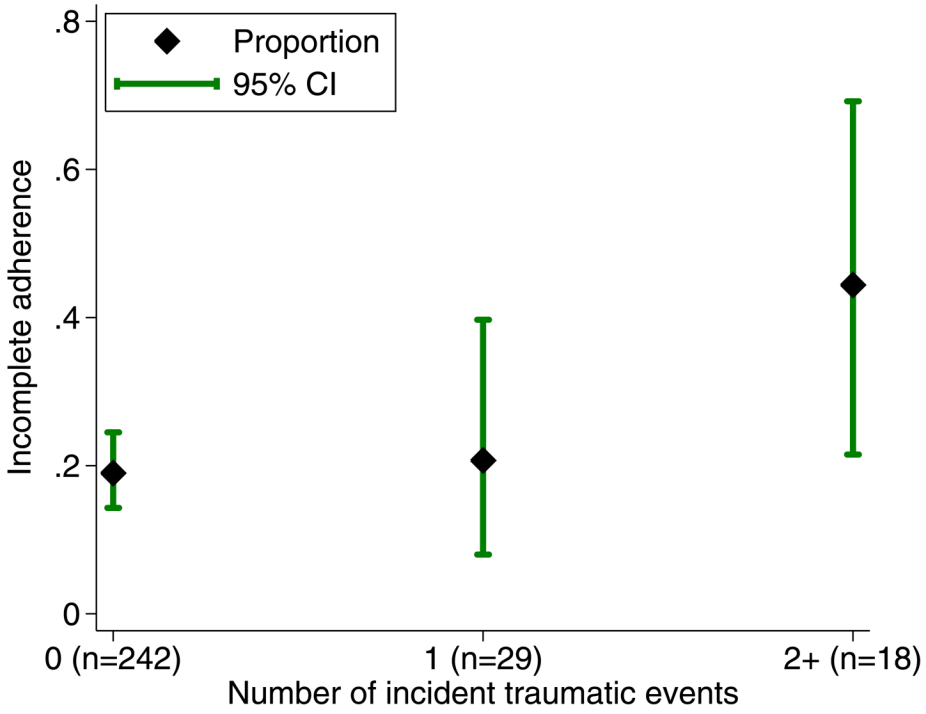


**Figue 1.**

Figure 1a. The relationship between incident stressful events and antiretroviral non-adherence during 27-month follow-up in Coping with HIV/AIDS in the SouthEast (CHASE) study participants.

Figure 1b. The relationship between incident traumatic events and antiretroviral non-adherence during 27-month follow-up in Coping with HIV/AIDS in the SouthEast (CHASE) study participants.

**Table 1**

Baseline and follow-up characteristics of Coping with HIV/AIDS in the SouthEast (CHASE) study participants included in analyses of sustained virologic suppression and longitudinal antiretroviral medication adherence.

| | N (%) or median (IQR) | | |
|---|---|---|---|
| **Characteristic** | **Overall sample (n=474)** | **ARV Adherence Sample (n=289)[1]** | **P Value** |
| Age, years (range 20–71) | 40 (35–46) | 41 (36–47) | 0.01 |
| Female gender | 138 (29.1%) | 89 (30.8%) | 0.31 |
| Minority race/ethnicity | 320 (67.5%) | 172 (59.5%) | <0.01 |
| Education, years (range: 3–18) | 12 (12–13) | 13 (12–14) | <0.01 |
| No health insurance | 101 (21.3%) | 56 (19.4%) | 0.2 |
| Baseline: | | | |
| CD4 count, cells/mm$^3$ (range: 0–1,580) | 364 (230–577) | 399 (250–617) | <0.01 |
| Lifetime traumatic experiences (range: 0–12)[2] | 3 (1–4) | 2 (1–4) | 0.57 |
| Incident stressful events, all types (range: 0–14)[2] | 3 (2–5) | 3 (1–5) | 0.02 |
| Incident severely stressful events (range: 0–6)[2] | 1 (0–2) | 1 (0–1) | <0.01 |
| Incident traumatic events (range: 0–2)[2] | 0 (0-0) | 0 (0-0) | 0.08 |
| Not adherent to ARVs[3] | 112 (23.6%) | 61 (21.1%) | 0.11 |
| 27-month follow-up: | | | |
| Incident stressful events, all types (range: 0–35)[4] | N/A | 9 (5–14) | N/A |
| Incident severely stressful events (range: 0–17)[4] | N/A | 3 (1–5) | N/A |
| Incident traumatic events (range: 0–6)[4] | N/A | 0 (0-0) | N/A |
| Not adherent to ARVs[3] | N/A | 60 (20.8%) | N/A |
| BSI depression score (range: 0–100) | N/A | 55 (44–65) | N/A |
| ASI alcohol score (range: 0–100) | N/A | 0 (0–12) | N/A |
| Adaptive coping score (range: 1–4) | N/A | 3.1 (2.7–3.5) | N/A |
| Maladaptive coping score (range: 1–4) | N/A | 1.3 (1–1.7) | N/A |

BSI: Brief Symptoms Inventory. ASI: Alcohol severity index.

[1] Includes patients on ARVs at baseline (n=474) who completed a 27-month interview and were receiving ARVs at the time of the 27-month interview (n=289)

[2] In 9 months preceding baseline interview

[3] Missed at least one dose in past week

[4] Between baseline and 27-month follow-up interviews (assessed every 9 months)

## Table 2

Factors associated with change in antiretroviral non-adherence from baseline to 27-month follow-up in Coping with HIV/AIDS in the SouthEast (CHASE) study participants.

| Characteristic (n=289) | Bivariable OR (95% CI) | Multivariable OR (95% CI)[1] |
|---|---|---|
| Baseline characteristics | | |
| Age, per 10 years | 0.77 (0.56, 1.06) | 0.74 (0.49, 1.11) |
| Female gender | 0.91 (0.51, 1.61) | 0.70 (0.31, 1.54) |
| Minority race/ethnicity | 0.80 (0.47, 1.37) | 1.01 (0.51, 2.00) |
| Education, per year | 0.97 (0.85, 1.11) | 0.98 (0.81, 1.18) |
| No health insurance | 1.64 (0.89, 3.02) | 1.61 (0.76, 3.40) |
| Not adherent to ARVs[2] | 3.46 (1.85, 6.46) | 3.27 (1.64, 6.53) |
| Lifetime traumatic experiences, per type | 1.09 (0.97, 1.21) | 0.94 (0.81, 1.09) |
| 27-month follow-up: | | |
| BSI depression score, per 10 units | 1.32 (1.06, 1.64) | 0.96 (0.70, 1.33) |
| ASI alcohol score, per 10 units | 1.42 (1.04, 1.93) | 1.18 (0.76, 1.83) |
| Adaptive coping score, per SD | 0.89 (0.68, 1.17) | 0.84 (0.59, 1.19) |
| Maladaptive coping score, per SD | 1.43 (1.11, 1.83) | 1.19 (0.84, 1.69) |
| Incident stressful events, per event[3] | 1.09 (1.04, 1.13) | 1.10 (1.04, 1.16) |
| Incident severely stressful events, per event[3] | 1.14 (1.03, 1.26) | 1.13 (0.99, 1.29) |
| Incident traumatic events, per event[3] | 1.73 (1.24, 2.39) | 1.43 (0.97, 2.09) |

[1] Three separate multivariable models were evaluated, each including one of the following: incident stressful events, incident severely stressful events, and incident traumatic events, along with all other listed covariates. Parameter estimates for covariates were consistent across the 3 multivariable models and are presented for the model that included incident stressful events.

[2] Missed at least one dose in the past week

[3] Between baseline and 27-month follow-up interviews (assessed every 9 months)

## Table 3

Factors associated with virologic failure (>400 c/mL) during longitudinal follow-up in Coping with HIV/AIDS in the SouthEast (CHASE) study participants.

| Characteristic (n=344) | Bivariable OR (95% CI) | Multivariable OR (95% CI)[1] |
|---|---|---|
| Baseline characteristics | | |
| Age, per 10 years | 0.87 (0.70, 1.07) | 0.90 (0.71, 1.13) |
| Female gender | 1.35 (0.90, 2.03) | 1.15 (0.73, 1.81) |
| Minority race/ethnicity | 2.33 (1.55, 3.50) | 1.67 (1.06, 2.62) |
| Education, per year | 0.85 (0.77, 0.94) | 0.90 (0.80, 1.00) |
| No health insurance | 0.74 (0.45, 1.20) | 0.76 (0.45, 1.30) |
| CD4, per 100 cells/$mm^3$ | 0.79 (0.73, 0.86) | 0.79 (0.73, 0.86) |
| Lifetime traumatic experiences | 1.08 (1.00, 1.17) | 1.05 (0.96, 1.15) |
| Time-varying characteristics | | |
| BSI depression score, per 10 units | 1.07 (0.93, 1.25) | 1.05 (0.89, 1.25) |
| Incident stressful events, all types | 1.08 (1.01, 1.15) | 1.09 (1.02, 1.17) |
| Incident severely stressful events | 1.16 (1.01, 1.33) | 1.19 (1.02, 1.39) |
| Incident traumatic events | 0.89 (0.59, 1.35) | 0.88 (0.55, 1.39) |

[1] Multivariable generalized estimating equation (GEE) logistic regression models account for dependent observations in individual patients. Three separate multivariable models were evaluated, each including one of the following: incident stressful events, incident severely stressful events, and incident traumatic events, along with all other listed covariates. Parameter estimates for covariates were consistent across the 3 multivariable models and are presented for the model that included incident stressful events.

## Table 4

Incidence rates of stressful events and association with antiretroviral non-adherence and virologic failure (>400 c/mL) during longitudinal follow-up in Coping with HIV/AIDS in the SouthEast (CHASE) study participants.

| Type of stressful event[1] | Incidence (no. events per 100 person-years) | Non-adherence OR (95% CI) | Virologic failure OR (95% CI |
|---|---|---|---|
| Sexual assault | 1.1 | 4.97 (0.74, 33.41) | 1.64 (0.42, 6.50) |
| Physical assault | 9.3 | 1.35 (0.81, 2.22) | 0.74 (0.40, 1.36) |
| Health: Major illness, injury, accident | 69.5 | 1.19 (0.98, 1.44) | 1.32 (1.09, 1.60) |
| Death of family member or close friend | 57.5 | 1.13 (0.90, 1.42) | 1.11 (0.88, 1.40) |
| Major illness of family member/close friend | 55.0 | 1.07 (0.87, 1.31) | 1.14 (0.89, 1.45) |
| Financial stresses | 78.6 | 1.05 (0.78, 1.41) | 0.92 (0.66, 1.29) |
| Relationship stresses | 56.6 | 1.28 (1.03, 1.61) | 1.28 (1.02, 1.61) |
| Employment stresses | 46.0 | 1.12 (0.93, 1.33) | 0.94 (0.76, 1.17) |
| Legal stresses | 16.1 | 1.12 (0.71, 1.78) | 1.01 (0.67, 1.50) |
| Safety-related stresses | 28.3 | 1.36 (1.04, 1.77) | 1.05 (0.77, 1.45) |
| Life transition stresses | 23.5 | 1.50 (1.09, 2.06) | 1.35 (0.91, 2.00) |

[1] Financial stresses: Foreclosure; repossession of car; no money for basic needs; had to sell possessions; being called by bill collectors; months behind in bills; other major problems with money. Relationship stresses: divorce; estrangement from spouse; increase in arguments; marriage or engagement. Employment stresses: lost job; unemployed and not able to find work; long hours; difficulties with boss or other major employment difficulties. Legal stresses: arrested for serious crime; >1 week in jail or prison; spouse or relative arrested for serious crime. Safety-related stresses: burglarized; felt unsafe in neighborhood. Life transition stresses: respondent or partner became pregnant or had or adopted a baby; ended formal schooling; left home for the first time; had a child leave home; moved multiple times.