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Antiretroviral Therapy Use, Medication Adherence, and Viral Suppression among PLWHA with Panic Symptoms

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Abstract

Panic symptoms are prevalent among PLWHAs, yet few studies have examined their relationship with HIV outcomes. Using data from an observational cohort study in Baltimore, MD, we examined the association between panic symptoms and ART use, medication adherence, and viral suppression. Data were analyzed using GEE and adjusted for age, sex, race/ethnicity, cocaine and/or heroin use, clinic enrollment time, alcohol use, and depressive symptoms. Between June 2010 and September 2012, 1195 individuals participated in 2080 audio computer assisted interviews; 9.9% (n=118) of individuals endorsed current panic symptoms. In multivariate analysis, panic symptoms were associated with decreased ART use (IRR 0.94; p = 0.05). Panic symptoms were neither associated with medication adherence nor viral suppression. These findings were independent of depressive symptoms and substance use. Panic symptoms are under-recognized in primary care settings and present an important barrier to ART use. Further studies investigating the reasons for this association are needed.

INTRODUCTION

Mental disorders are twice as common in PLWHAs as the general population (63% vs. 30.5%) (1, 2). The most common mental disorder in PLWHA is major depression (3-5). Two systematic reviews of the literature on mental disorders in HIV concluded that depression was significantly associated with antiretroviral nonadherence (6, 7). The association between antiretroviral adherence and other mental health disorders however is less well established and further investigation has been recommended (7).

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In the general population, the National Institute of Mental Health estimated an average expenditure per person of $1591 using healthcare data from 2006 and ranked panic disorder among the top 10 neuropsychiatric disorders contributing to the total burden of disability in the United States and Canada (8, 9). Panic disorder has a prevalence of eleven percent in PLWHA, 3 to 5 times higher than the general population (10). Despite this prevalence, few studies have explicitly examined panic symptoms or panic disorder and HIV treatment outcomes in PLWHAs. Panic symptoms can occur at any time and are characterized by a fear of disaster or of losing control. Panic disorder is characterized by sudden and repeated episodes of panic symptoms. In a study by Tucker et al, panic disorder was associated with twice the odds of antiretroviral nonadherence (11). This association was independent of substance misuse. Similar findings were noted by Mellins et al (12). By contrast, Palmer et al showed no significant association between panic disorder and nonadherence (13). Neither study examined the relationship between panic disorder or symptoms and antiretroviral therapy use or viral suppression.

Given the significant prevalence of panic disorder among PLWHA and the few studies of panic disorder or symptoms and HIV treatment outcomes, we investigated the association between panic symptoms and antiretroviral therapy use, medication adherence, and viral suppression in an urban HIV outpatient setting. We hypothesized that current panic symptoms would be associated with lower antiretroviral therapy use, medication nonadherence, and a non-suppressed viral load.

METHODS

Study Design

This is a prospective cohort study of individuals enrolled in the Johns Hopkins HIV Clinical Cohort (JHHCC) who participated in an Audio Computer Assisted Interview (ACASI) between June 2010 and September 2012. The JHHCC is a longitudinal cohort of HIV-infected adults receiving care in the Johns Hopkins HIV Clinic. All patients receiving care are eligible to participate. Data collected on enrollees include demographic, clinical, diagnostic, laboratory, and pharmacy data. Laboratory data are obtained electronically. A description of the data collection methods for the JHHCC has been published previously (14). Written informed consent is obtained to enroll participants.

Participants were eligible for this study if they were either on antiretroviral therapy (ART) or had a CD4 count <500 cells/mm. The CD4 cell count cut-off of 500 was based on antiretroviral therapy prescribing guidelines during the study period (15). For analyses examining ART adherence and viral suppression, only individuals receiving ART were included.

Survey

In July 2000, an ACASI collecting patient reported outcomes was added to the data collection procedures of JHHCC (16). The survey takes approximately 15 minutes to complete and collects alcohol use, illicit drug use, adherence to antiretroviral therapy, and depressive symptoms over the prior six months. In June 2010, 5 panic items (described

below) from the Patient Health Questionnaire (PHQ) were added to the ACASI. The Johns Hopkins University School of Medicine Institutional Review Board approved this study.

Outcome description

Our outcomes were 1) antiretroviral therapy (ART) use 2) ART adherence and 3) HIV-1 RNA suppression on ART. Antiretroviral therapy use was abstracted from the medical record by trained coders and was defined as documentation of a regimen containing a combination of protease inhibitors, non-nucleoside transcriptase inhibitors, integrase strand transfer inhibitors, CCR5 inhibitors, or nucleoside transcriptase inhibitors at the time of the ACASI interview. ART adherence was determined using a self-report visual analog scale asking participants to mark the point on the line (between 0 and 100%) that reflected how much of their HIV medication they had taken in the last month (17). Self-reported adherence of <90% on the ACASI was classified as non-adherence. HIV-1 RNA was obtained from laboratory records and was defined as an HIV-1 RNA of <50 copies/mL. HIV-1 RNAs were included if drawn either on the date of the interview, or within 6 months of the interview.

Independent variables

Our primary independent variable was the presence or absence of panic symptoms. This was ascertained using the following questions from the panic module of the PHQ: 1) In the past four weeks have you had an anxiety attack? 2) If you had an anxiety attack, has this ever happened before? 3) Do some of the attacks come out of the blue, that is in situations where you do not expect to be nervous or uncomfortable? 4) Do these anxiety attacks bother you a lot or are you bothered about having another attack? 5) During your last anxiety attack did you have any symptoms like shortness of breath, sweating, heart pounding, dizziness, faintness, tingling, numbness, nausea, or upset stomach? (18) Individuals were classified as having panic symptoms if they answered yes to the first and fifth questions, and had an affirmative response to at least one of the remaining three questions. This algorithm was based on two studies determining the sensitivity and specificity of the number of positive responses to the individual items on the five item scale (19, 20). As an affirmative response to all 5 questions has increased specificity for panic symptoms, we also performed sensitivity analyses for the three outcomes using this stricter definition of panic symptoms.

Additional independent variables were chosen a priori. These included sex, race/ethnicity, age, illicit drug use, alcohol use, depressive symptoms, and clinic enrollment time (defined as the time between first clinic visit and the ACASI interview). Sex, age, and race/ethnicity were obtained from clinical records. Illicit drug use was obtained via self-report on the ACASI. Individuals were categorized as neither heroin nor cocaine use, heroin use only, cocaine use only, or both heroin and cocaine use. We examined opioid and stimulant use specifically given their prevalence in this cohort and previous literature suggesting a negative association between stimulant use and our outcomes of interest (21, 22). Methamphetamine was not examined as there was little self-reported use on the ACASI. Alcohol use was measured using the three-item version of the alcohol use disorders identification test (AUDIT-C) (23, 24) and categorized as: hazardous/binge, moderate, and none per the National Institute on Alcohol Abuse and Alcoholism's definitions (NIAAA) (25). Hazardous drinking was defined as >14 drinks per week or >4 drinks per occasion for

men and >7 drinks per week or >3 drinks per occasion for women. Moderate drinkers consumed alcohol below hazardous levels. Depressive symptoms were measured using a two item screen. The first question asked how frequently in the past two weeks an individual experienced either 1) little interest or pleasure in doing things or 2) felt depressed, down, or hopeless. An answer of mostly or always on either question was defined as the presence of depressive symptoms (26). The CD4 cell count closest in time following the interview was obtained from the laboratory records.

Statistical Methods

Descriptive statistics were calculated for the outcome variables and independent variables for the entire cohort and separately by the presence or absence of panic symptoms. To account for multiple measurements on participants, we used generalized estimating equations (GEE). The multiple measurements on individuals create a correlation structure within the data that must be accounted for in analyses. GEE accounts for this correlation within participants, giving proper estimation of regression coefficients and standard errors (27). These methods were applied to each of the dichotomous outcomes (ART utilization, adherence, and viral suppression) in separate models using log link, a Poisson model and an independent correlation matrix (28). To adjust for age, race/ethnicity, sex, illegal drug use, hazardous drinking, depressive symptoms, and enrollment time, these variables were included in the models. Interaction terms were created between the following variables and panic symptoms-sex, race/ethnicity, cocaine use, heroin use, hazardous drinking, and depressive symptoms. Sex and race/ethnicity were fixed variables. All other predictors including panic symptoms, depressive symptoms, and substance use varied over time. The data were analyzed using STATA, version 12.0 (StataCorp, College Station, TX).

RESULTS

Baseline characteristics by the absence or presence of panic symptoms

1195 eligible individuals participated in 2080 ACASI interviews. Of these, 1119 individuals (1922 interviews) were on ART and are included in analyses of medication adherence. Of the 1119 individuals on ART, 1106 (1904 interviews) had an HIV-1 RNA available for analysis. In our sample, 9.9% of participants (n=118) endorsed panic symptoms (Table 1). There was a higher proportion of women among patients with panic symptoms (48.3%) compared to patients without panic symptoms (33%). Also patients reporting panic symptoms were significantly younger (48.6 years) than those not reporting panic symptoms (49.9 years). Twice the percentage of Caucasian participants screened positive for panic symptoms. Additionally, over twice the percentage of participants with depressive symptoms also screened positive for panic symptoms. Finally, twice the percentage of individuals screening positive for panic symptoms used both heroin and cocaine. For both groups, the median clinic enrollment time was approximately 8 years with median CD4 counts over 400. The majority of our participants had undetectable viral loads and were prescribed antiretroviral therapy with greater than 90% adherence; participants who screened positive for current panic symptoms were less likely to be on antiretroviral therapy than those without panic symptoms. The median follow-up time from the first ACASI

interview where panic symptoms were included to the study end was 1.5 years (IQR 1.1-1.8).

Antiretroviral Therapy Use

Table 2 displays the relationship between panic symptoms and antiretroviral therapy use, medication adherence, and HIV-1 RNA viral suppression.

In bivariate analyses, panic symptoms (IRR 0.93; 95% CI 0.88-0.99; p=0.024) and both heroin and cocaine use (IRR 0.83; 95% CI 0.70-0.99; p=0.035) were associated with decreased rate of antiretroviral therapy use. In multivariate analysis, the association between panic symptoms and lower rate of antiretroviral therapy use persisted (IRR 0.94; 95% CI 0.89-1.00; p=0.05) as did the association between both heroin and cocaine use and lower rate of ART use (IRR 0.85; 95% CI 0.72-1.00; p=0.051). Interactions between panic symptoms and sex, race/ethnicity, hazardous drinking, heroin use, cocaine use, and depressive symptoms were not statistically significant.

Antiretroviral Adherence

In bivariate analysis, panic symptoms (IRR 0.88; 95% CI 0.80-0.98; p=0.02), depressive symptoms (IRR 0.88; 95% CI 0.79-0.97; p=0.009), and either heroin (IRR 0.81; 95% CI 0.71-0.93; p=0.004) or cocaine (IRR 0.73; 95% CI 0.56-0.95; p=0.021) use were associated with a decreased rate of medication adherence. In multivariate analysis, the association between depressive symptoms and decreased rate of medication adherence remained statistically significant (IRR 0.90; 95% CI 0.81-0.99; p=0.031) as did the association between decreased medication adherence, heroin use only (IRR 0.82; 95% CI 0.71-0.94; p=0.005), and cocaine use only (IRR 0.73; 95% CI 0.56-0.94; p=0.016). Panic symptoms were not associated with medication adherence (IRR 0.92; 95% CI 0.82-1.02; p=0.102). Interactions between panic symptoms and sex, race/ethnicity, hazardous drinking, heroin use, cocaine use, and depressive symptoms were not statistically significant.

HIV-1 RNA Suppression

Panic symptoms were not associated with the rate of HIV-1 RNA viral suppression in bivariate or multivariate analyses. Interactions between panic symptoms and sex, race/ethnicity, hazardous drinking, heroin use, cocaine use, and depressive symptoms were not statistically significant.

Sensitivity analyses

Individuals with positive responses to all 5 items on the PHQ panic module were classified as having panic symptoms. Using this stricter definition, the prevalence of panic symptoms in our sample was 5.8%. Similar associations were found between panic symptoms and the outcomes of interest in adjusted analyses: ART use (IRR 0.91; 95% CI 0.84-0.99; p=0.03), medication adherence (IRR 0.91; 95% CI 0.78-1.04; p=0.17), and HIV-1 RNA viral suppression (IRR 1.05; 95% CI 0.92-1.19; p=0.47).

DISCUSSION

In this study of HIV-infected individuals, the prevalence of panic symptoms was 9.9% which is slightly lower than that noted in the literature. Panic symptoms were significantly associated with decreased rate of antiretroviral therapy use but were not significantly associated with medication adherence or HIV-1 RNA viral suppression. These results suggest that symptoms of panic may be an under-recognized barrier to antiretroviral therapy use.

To our knowledge, no studies have explicitly examined panic symptoms and antiretroviral therapy use. Among other studies that have investigated the association between all psychiatric disorders and antiretroviral therapy use, most have been associated with decreased self-reported utilization of antiretroviral therapy; results similar to our study (3, 29). Prior studies reported lower baseline ART use of 63-69% among participants with any psychiatric diagnosis; the relationship between individual psychiatric diagnoses and ART use was not reported in these studies to allow for direct comparison (11-13). Given the promotion of universal HIV treatment, further understanding of the barriers involved in the receipt of antiretroviral therapy among individuals with panic symptoms is of utmost importance. We hypothesize that in patient-provider discussions panic symptoms, co-occurring substance use, and/or multiple complaints in the setting of panic symptoms, may take priority over ART initiation resulting in decreased prescription of ART (30-32). Additionally, patient anxiety may interfere with the uptake of ART. These hypotheses could be examined in future studies and serve as potential targets for future interventions.

There was no significant association between panic symptoms and medication non-adherence. This is in contrast to previously published work by Tucker and Mellins (11, 13) where a significant association was found. The findings from younger, largely Caucasian samples may not generalize to our older, largely African-American sample. Additionally, there may have been restrictions in range in the independent variable of panic. In both Mellins et al and Tucker et al in, participants were defined by the presence of panic or other psychiatric disorders whereas our sample was defined by the presence of panic symptoms. Thus the level of psychiatric impairment may have been more severe than in our population. Notably, our sample appears to have been more stable as evidenced by their higher CD4 counts and ART use, better adherence, and greater viral suppression compared with their samples. As a corollary to this, the strength of the association between panic symptoms and medication adherence may have been attenuated by the greater likelihood of panic symptoms than a full criterion disorder as panic symptoms may fluctuate.

We also found no association between panic symptoms and HIV-1 RNA viral suppression. In the presence of panic symptoms, patients may have short periods of medication nonadherence that are insufficient to affect the measured viral load or they may continue to take their antiretroviral medications despite the presence of panic symptoms.

Notably, our prevalence of panic symptoms was lower than reported in the literature. There are four possible explanations for this. First, panic symptoms and disorder have a higher prevalence among Caucasians; our population was composed of over 80% African-

Americans. Second, we were unable to account for the impact of psychotropic medications on current symptoms which may have resulted in an underestimate of the true prevalence in our population. Few studies to date have explored the effect of treatment of panic symptoms and panic disorder in PLWHAs. In the non-HIV population however, appropriate treatment with SSRIs was associated with a reduction in the mean number of emergency room and laboratory visits (33-34). Third, panic items were queried over the four weeks prior to the time of the ACASI and may have missed individuals with panic symptoms more than four weeks before completion of the ACASI. Fourth, the English version of the panic module of the PHQ has not been rigorously studied among individuals living with HIV. In the non-HIV population, panic disorder has a relatively low prevalence and the sensitivity of the panic module has varied widely, especially in samples with high psychiatric comorbidity. Wittkampf et al studied the test characteristics of the panic module in a selected primary care population of people without HIV (patients with unexplained somatic complaints, the highest 10% consultation rates, and individuals presenting to their primary provider with a new mental health problem three months before selection date) and found that the panic module performed moderately well in screening for panic disorder but the sensitivity and specificity of the module was affected by the presence of other psychiatric comorbidities (20). In PLWHAs where there is high psychiatric comorbidity, the panic items used may not have allowed us to fully capture the prevalence of symptoms.

Consistent with prior research, our study did show significant associations between depressive symptoms and substance use and lower ART adherence. However, there was no significant association between these variables and viral suppression. The lack of stronger associations could be sample specific or related to statistical power. Compared to other studies, this study population had a lower prevalence of depressive symptoms and substance use (11, 35). In addition, lack of associations between depressive symptoms and substance use and viral suppression could be secondary to more durable ART regimens resulting in less viral rebound with brief episodes of non-adherence.

There are limitations to this study. Panic disorder is commonly comorbid with other mental conditions; we did not assess other mental disorders outside of panic and depressive symptoms. Previous literature however suggests higher viral loads among individuals with SMI (35). Panic symptoms were based on self-report symptoms experienced the month prior to completion of the ACASI, which is completed every 6 months. This raises the potential for recall and social desirability biases. We did not evaluate the use of psychotropic medications and mental health service utilization in this study. We hypothesize that both would result in a decrease in panic symptoms and a resultant increase in ART utilization among individuals with HIV and co-occurring panic symptoms. If mental health service utilization and psychotropic medicine use mediate the relationship between panic symptoms and ART use, this will elucidate targets for intervention. Finally, we used a clinic based sample therefore our results may not be generalizable to the broader population of PLWHAs.

Our study has significant implications for the clinical care of patients with anxiety disorders. Although panic symptoms were associated with a decreased rate of ART use, our findings suggest that once participants with panic symptoms are prescribed ART, optimal

antiretroviral adherence, and viral suppression are attainable. Studies of depression and anxiety disorders in PLWHAs reported improved antiretroviral adherence with treatment of the mental health condition (11, 12). Similar improvement in HIV treatment outcomes may result with treatment of panic disorder. Unfortunately, there remains significant under-recognition and under-treatment of panic disorder in primary care settings (36, 37). This appears to stem from limited provider knowledge about anxiety disorders and lower treatment seeking behaviors by the patients (30, 38). The importance of addressing panic disorder however is underscored by evidence showing that appropriate treatment of panic disorder is associated with a reduction in the mean number of emergency room visits and improved clinical outcomes (33, 34, 39). Early clinical detection and treatment of panic symptoms and disorder is of paramount importance to successful management of HIV given the potential disruption in ART contributing to drug resistance, disease progression, and increased healthcare costs. Educational interventions targeting both providers and individuals with panic disorder may improve the likelihood of recognition and treatment. Additionally, integration of medical and behavioral health within an HIV primary care setting will allow for improved evaluation and management of this population.

In summary, we found that panic symptoms were associated with decreased likelihood of antiretroviral therapy use. Future studies investigating reasons for decreased ART use in patients with panic symptoms and engagement in care among individuals with panic symptoms and the impact on ART use are needed. Identification of these facilitators of ART use among individuals with panic symptoms will elucidate targets for intervention.

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Table 1

Baseline Characteristics by the Absence or Presence of Panic Symptoms (n=1195)

Characteristics	No Panic Symptoms (n=1077)	Panic Symptoms (n=118)	Probability
Sex, n (%) **Male** **Female**	722 (67) 355 (33)	61 (51.7) 57 (48.3)	0.001
Median Age, y (IQR)	49.9 (44.2-55.5)	48.6 (40.8-54.4)	0.005
Age, n (%) **< 50yo** **≥ 50yo**	546 (50.7) 531 (49.3)	67 (56.8) 51 (43.2)	0.209
Race/Ethnicity, n (%) **African-American** **Caucasian/Other**[a]	917 (85.1) 160 (14.9)	81 (68.6) 37 (31.4)	0.000
Heroin/Cocaine Use, n (%) **Neither Heroin nor Cocaine** **Heroin Only** **Cocaine Only** **Both Heroin and Cocaine**	989 (91.8) 49 (4.6) 24 (2.2) 15 (1.4)	100 (84.8) 12 (10.2) 2 (1.7) 4 (3.4)	0.019
Depressive Symptoms, n (%) **No** **Yes**	963 (89.4) 114 (10.6)	89 (75.4) 29 (24.6)	0.000
Hazardous Drinking, n (%) **None** **Moderate** **Hazardous**	636 (59.1) 381 (35.4) 60 (5.6)	64 (54.2) 46 (39.0) 8 (6.8)	0.582
Median Clinic Enrollment Time, y (IQR)	8.3 (3.2-13.0)	7.9 (2.9-11.4)	0.107
Median ACASI Follow-up Time, y (IQR)	1.6 (1.1-1.9)	1.5 (1.1-1.8)	0.283
Median CD4 count, n (IQR)	444 (270-642)	464.5 (322-664)	0.151
On Antiretroviral Therapy, n (%)	984 (91.4)	99 (83.9)	0.008
Medication Adherence[b]**, n (%)**	790 (77.8)	77 (74.8)	0.488
Undetectable Viral Load[c]**, n (%)**	666 (66.3)	77 (75.5)	0.06

Abbreviations: IQR=interquartile range, y=year, ACASI-Audio computer assisted interview

[a] Less than 2% of the Moore Clinic patient population self-identifies as Hispanic, Asian, Native-American, or Other therefore these racial/ethnic groups were included among the population self-identifying as Caucasian for the purposes of this analysis.

[b] Medication adherence is assessed only in those on antiretroviral therapy (n=1119) and is defined as >90%.

[c] Undetectable viral load is based on those individuals on ART who had an HIV-1 RNA available for analysis (n=1106) and is defined as <50 copies/mL.

Table 2

Bivariate and Multivariate Analyses (IRR) of the Effect of Panic Symptoms on the Rate of Prescribed Antiretroviral Therapy Use, Medication Adherence, and HIV Viral Suppression[a]

Variable	Outcomes											
	ART Use (n=1195)				Adherence (n=1119)				Viral Suppression (n=1106)			
	Bivariate	p-value	Multivariate	p-value	Bivariate	p-value	Multivariate	p-value	Bivariate	p-value	Multivariate	p-value
Panic Symptoms	0.93 (0.88-0.99)	0.024	0.94 (0.89-1.00)	0.050	0.88 (0.80-0.98)	0.020	0.92 (0.82-1.02)	0.102	1.05 (0.95-1.17)	0.318	1.06 (0.95-1.17)	0.295
Age **< 50** **≥ 50**	1.0 (Ref) 1.05 (1.02-1.08)	0.003	1.03 (1.00-1.06)	0.025	1.01 (0.96-1.06)	0.677	1.00 (0.95-1.05)	0.894	1.12 (1.03-1.19)	0.007	1.11 (1.03-1.20)	0.006
Sex	1.02 (0.98-1.05)	0.341	1.01 (0.98-1.04)	0.609	1.00 (0.95-1.05)	0.967	1.00 (0.95-1.06)	0.940	1.00 (0.93-1.08)	0.999	0.99 (0.92-1.07)	0.847
Race/Ethnicity **Caucasian/Other** **African-American**	1.0 (Ref) 0.98 (0.95-1.02)	0.342	0.97 (0.94-1.01)	0.148	1.10 (1.01-1.19)	0.031	1.09 (1.00-1.19)	0.042	0.93 (0.84-1.02)	0.121	0.94 (0.85-1.03)	0.182
Heroin/Cocaine **Neither** **Heroin Only** **Cocaine Only** **Both**	1.0 (Ref) 0.94 (0.87-1.02) 0.96 (0.85-1.08) 0.83 (0.70-0.99)	0.147 0.467 0.035	0.95 (0.88-1.03) 0.96 (0.85-1.08) 0.85 (0.72-1.00)	0.231 0.489 0.051	0.81 (0.71-0.93) 0.73 (0.56-0.95) 0.90 (0.71-1.15)	0.004 0.021 0.408	0.82 (0.71-0.94) 0.73 (0.56-0.94) 0.90 (0.71-1.14)	0.005 0.016 0.370	0.86 (0.70-1.05) 0.88 (0.68-1.14) 1.07 (0.85-1.35)	0.133 0.327 0.568	0.85 (0.69-1.04) 0.88 (0.68-1.14) 1.07 (0.84-1.35)	0.108 0.339 0.589
Hazardous Drinking **None** **Moderate** **Hazardous**	1.0 (Ref) 0.99 (0.96-1.02) 0.93 (0.86-1.01)	0.371 0.095	0.99 (0.96-1.02) 0.95 (0.87-1.02)	0.596 0.166	1.01 (0.95-1.06) 0.97 (0.85-1.10)	0.826 0.627	1.03 (0.97-1.09) 1.01 (0.89-1.15)	0.307 0.878	0.97 (0.90-1.05) 0.99 (0.85-1.16)	0.479 0.915	0.99 (0.91-1.06) 1.02 (0.87-1.18)	0.690 0.831
Depressive Symptoms	0.99 (0.94-1.03)	0.524	0.99 (0.95-1.04)	0.800	0.88 (0.79-0.97)	0.009	0.90 (0.81-0.99)	0.031	1.07 (0.97-1.17)	0.182	1.07 (0.97-1.18)	0.156
Enrollment Time	1.00 (1.00-1.00)	0.006	1.00 (1.00-1.00)	0.056	1.00 (1.00-1.00)	0.372	1.00 (1.00-1.00)	0.429	1.00 (1.00-1.00)	0.538	1.00 (1.00-1.00)	0.973

[a] adjusted for age at the time of ACASI interview, sex, race/ethnicity, heroin and/or cocaine use, hazardous drinking, depressive symptoms, and clinic enrollment time.