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Continued Substance Use among People Living with HIV-Hepatitis-C Co-infection and Receiving Antiretroviral Therapy

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Abstract

Background—Co-infection with HIV and Hepatitis-C virus (HCV) poses a significant threat to personal and public health. Substance use among co-infected persons leads to increased morbidity and mortality. The purpose of this study is to examine the continued substance use of people living with HIV-HCV co-infection and receiving antiretroviral therapy (ART).

Methods—Individuals living with HIV infection in Atlanta, GA and currently receiving ART (N = 678) completed audio-computer assisted self-interviews for demographic, health, and behavior characteristics; unannounced pill counts to assess ART adherence over one-month; finger-stick blood specimens collected for HCV antibody testing and urine specimens for drug use screening; and obtained HIV viral load and CD4 cell counts from their medical provider. We performed cross-sectional analyses of behavioral and biological markers of health, health behaviors, and substance use.

Results—Among participants 131 (19%) were HIV-HCV co-infected; 53% of HIV-mono-infected and 60% of HIV-HCV co-infected participants tested positive for use of at least one non-alcohol drug; THC and cocaine were most prevalent. HIV-HCV co-infected individuals were older, with no other significant differences. Within the HIV-HCV co-infected participants, drug users (N = 87) did not differ from non-drug users (N = 53) in terms of ART adherence. However, drug users were significantly more likely to have uncontrolled HIV (17%) compared to those who did not test drug positive (4%).

Conclusions—Substance use is prevalent in persons with HIV-HCV co-infection and may interfere with ART. Research with a larger more representative sample is needed to replicate and confirm these results.

Introduction

As HIV infection has become a manageable chronic illness, morbidity in people living with HIV is now complicated by interactive and co-occurring conditions. Liver disease has emerged as a common cause of death in HIV infected persons, with liver-related mortality closely associated with Hepatitis C virus (HCV) co-infection (Prakash, Mason, Luftig, & Bautista, 2002). An estimated four to five million people in the world are living with HIV-HCV co-infection (Parikh et al., 2012). Furthermore, the hepatotoxicity of antiretroviral

therapy (ART) and substance use places added strain on the liver with the potential to exacerbate organ damage. For example, alcohol use can amplify the hepatotoxicity of antiretroviral therapy and can accelerate liver damage caused by HCV (Braithwaite & Bryant, 2010). Thus, combining antiretroviral medications and substance use contributes to liver disease in people living with HIV, making antiretroviral medications, substance use, and HCV co-infection a particularly hazardous combination (Puoti, Moioli, Travi, & Rossotti, 2012). Limited alcohol use in people living with HIV mono-infection is associated with 8% developing advanced liver fibrosis and cirrhosis, as is the case for 13% of people with HCV mono-infection, compared to 31% in people living with HIV-HCV co-infection (Justice, Sullivan, & Fiellin, 2010). The impact of substance use on ART therefore extends beyond its contributions to treatment non-adherence, with hepatotoxicity interfering with the metabolism of ART and therefore viral suppression (Barve et al., 2010).

HIV-HCV co-infected patients frequently report substance use, with nearly one in ten abusing alcohol (Marcellin et al., 2013). Previous research suggests that despite the increased risks for adverse health effects frequency and quantity of alcohol consumption in HIV-HCV co-infected patients may not differ from HIV mono-infected patients. In addition, co-occurring use of other drugs predicts greater alcohol consumption in HIV-HCV co-infected patients, suggesting multiple substances may be abused in people with HIV-HCV co-infection (Stephens & Havens, 2013). While there is considerable attention to the prevalence of alcohol use in HIV-HCV co-infected individuals taking ART, fewer studies have reported non-alcohol drug use in this population.

Psychoactive substances that are metabolized in the liver pose synergistic risks to individuals with HIV-HCV co-infection. For example, MDMA (ecstasy) and cocaine can cause chronic hepatitis and liver fibrosis (Payance, Scotto, Perarnau, de Muret, & Bacq, 2013). In addition, cocaine use can induce severe hepatotoxicity (Vitcheva, 2012) and cannabis use exacerbates HCV-associated liver disease (Hezode et al., 2005; Ishida et al., 2008). However, few studies to date have reported the use of addictive drugs in people with HIV-HCV co-infection relative to persons with HIV mono-infection. The purpose of this study was to investigate current drug use in a sample of people living with HIV-HCV co-infection and receiving ART, relative to their HIV mono-infected counterparts. Based on the adverse health effects that patients face, we hypothesized that HIV-HCV co-infected individuals would demonstrate significantly less active substance use than their HIV mono-infected counterparts. In addition, we explored sub-analyses of those participants with HIV-HCV co-infection to compare those who were currently using drugs to their non-drug using counterparts.

Methods

Participants

Men and women living with HIV who were receiving ART (N = 678) were reached through community recruitment strategies. Individuals interested in participating contacted our research program to schedule an intake assessment appointment. The study entry criteria were (a) 18 years of age or older, (b) HIV positive, and (c) prescribed antiretroviral therapy (ART).

Sample Recruitment

The study was conducted in Atlanta, GA, USA and participants were enrolled between October 2012 and March 2014. Men and women living with HIV were recruited through clinical service recruitment and snowball sampling techniques. Study brochures were placed in waiting rooms of HIV service providers and infectious disease clinics throughout metropolitan Atlanta, GA. We also implemented an explicit systematic approach to word-of-mouth chain recruitment. Specifically, participants were given brochures that described the study opportunity with a phone number to the research offices. Participants were encouraged to use the brochures to refer their HIV positive friends to the study.

Procedures

Participants completed an informed consent process where all study procedures were thoroughly explained. Participants provided four sources of data to assess a wide array of demographic, health, and substance use characteristics. First, participants completed audio-computer assisted self-interviews (ACASI) to assess demographic, health and behavioral characteristics at the start of the study (Gribble et al., 2000; Morrison-Beedy, Carey, & Tu, 2006). Second, participants provided finger-stick blood specimens for Hepatitis-C antibody testing. Participants who tested positive for HCV antibodies were informed of their test results and given a written explanation to take to their medical provider. We also asked participants to provide a first catch urine specimen for drug use screening. Drug test results were provided to participants if requested. Third, we collected HIV viral load and CD4 cell counts using a participant assisted medical chart abstraction procedure. Finally, unannounced pill counts were used to assess ART adherence over a one-month prospective period. The specific measures are described below. Participants received US\$145 for completing all aspects of the study. The University of Connecticut Institutional Review Board approved all procedures.

Measures

Computerized interviews

Demographic and health characteristics: Participants were asked their gender, age, years of education, income, ethnicity, and employment status. Participants also reported the year that they first tested HIV positive, completed a measure of 14 HIV-related symptoms of 2-weeks duration (S. Kalichman, Rompa, & Cage, 2000) and reported their experience of common ART side-effects (Carrieri, Villes, & 2007). We also asked participants if they had a history of injection drug use and if they had a history of injection drug using sex partners. Participants reported if they were worried they would run out food or experienced hunger in the previous 4-months.

Hepatitis-C virus antibody test—To screen for HCV co-infection we used the OraQuick rapid HCV antibody test, which has demonstrated high sensitivity and specificity with results comparable to those of laboratory assays (Cha et al., 2013).

Substance use—To assess global alcohol use we administered the Alcohol Use Disorders Identification Test (AUDIT), a 10-item scale designed to measure alcohol consumption and

identify risks for alcohol abuse and dependence (Saunders, Aasland, Babor, DeLaFuente, & Grant, 1993). Scores on the AUDIT range from 0 – 40 and the AUDIT has demonstrated acceptable reliability and validity. Scores of greater than 8 indicate risk for problem drinking, with specificities between .80 and .90 (Maisto, Conigliaro, McNeil, Kraemer, & Kelley, 2000). We included the 4-item CAGE (Cut down, Annoyed, Guilty, Eye opener) questionnaire as a specific measure of alcohol abuse disorders. (Ewing, 1984) In addition, we used Drug Abuse Screening Test (DAST) as an assessment of problem non-alcohol drug use (Maisto, Carey, Carey, Gordon, & Gleason, 2000; Skinner, 1982).

We also screened for drug use with a multi-panel urine dip-test to detect common illicit drugs. This test strip uses a lateral flow chromatographic immunoassay for qualitative detection of 12 drugs and drug metabolites (Redwood Toxicology Labs - Reditest-12). The specific drugs tested are shown in the results. These tests are FDA approved and are reliable and valid for initial drug screening.

Chart abstracted viral load and CD4 cell counts—We used a participant assisted method for collecting chart abstracted viral load and CD4 cell counts from participants' medical records. Participants were given a form that requested their doctor's office to provide results and dates of their most recent, and not older than 3-months, viral load and CD4 cell counts. These data were therefore obtained directly by the participant from their HIV care provider. The form included a place for the provider's office stamp or signature to assure data authenticity. HIV RNA below detection was defined as less than 400 copies/mL for uniformity across providers.

HIV treatment adherence—Participants consented to three unannounced telephone-based pill counts that occurred over a six-week period. Unannounced pill counts are reliable and valid in assessing medication adherence when conducted in homes (D. R. Bangsberg, Hecht, Charlebois, Chesney, & Moss, 2001) and on cell-phones (S. C. Kalichman et al., 2008; S. C. Kalichman et al., 2007). In this study we conducted unannounced cell-phone based pill counts using study-provided free cell phones. Following an office-based interview that included a full accounting of all prescription medications and training in the pill counting procedure, participants were called at three unscheduled times over 12 to 16 day intervals. The first of the three pill counts is used to establish the initial number of pills in possession with the subsequent two pill counts allowing for calculation of adherence, defined as the ratio of pills counted relative to pills prescribed, taking into account the number of pills dispensed. We used pill count adherence to define adherent participants as having taken greater than 85% of their medications, a level of adherence commonly associated with HIV treatment failure (D. Bangsberg & Deeks, 2002).

Data analyses—We conducted two stages of data analyses. First, logistic regressions were performed to compare characteristics of participants who tested HIV mono-infected (N = 547) and HIV-HCV co-infected (N = 131). Second, we performed sub-analyses on those participants who were HIV-HCV co-infected. For these exploratory analyses we compared HIV-HCV co-infected participants who tested positive for any of the 12 drugs on the urine screens (n = 78) to those who did not test positive for any drugs (N = 53). We also conducted sensitivity analyses where all HIV-HCV co-infected participants with any

indicators of current alcohol or drug use ($n = 92$) were compared to those with no substance use ($n = 39$) to remove any confounding effects of alcohol use. Multi-variable models were performed for variables found significant in bivariate models. For all analyses we report odds ratios with 95% confidence intervals, defining statistical significance as $p < .05$.

Results

Among the 678 participants, 547 (81%) tested HCV negative, 117 (17%) tested HCV-positive and previously diagnosed, and 14 (2%) tested HCV-positive for the first time at this screening. Table 1 shows the demographic and health characteristics of HIV mono-infected and HIV-HCV co-infected participants. Logistic regressions indicated that HIV-HCV co-infected persons were significantly older than HIV mono-infected participants. As expected, HIV-HCV co-infection was associated with a history of injection drug use and having had an injection drug using sex partner. No other demographic characteristics were significantly associated with HCV co-infection.

Health status and treatment adherence

Results indicated that 84% of HIV mono-infected and 88% of HIV-HCV co-infected participants were HIV viral suppressed and 82% and 88% had CD4 counts greater than 200 cells/cc, respectively. (see Table 2) In addition, 32% of HIV mono-infected and 29% of HIV-HCV co-infected participants were less than 85% adherent to their ART regimen over the one-month observation period. There were no significant differences between HIV mono-infected and HIV-HCV co-infected persons on any health status measure.

Substance use

Results showed that 55% of HIV mono-infected and 41% of HIV-HCV co-infected participants reported recent alcohol use, a non-significant difference. (see Table 3) In addition, 13% of participants indicated hazardous drinking on the AUDIT and 7% responded positively to more than two indicators of alcohol abuse on the CAGE. Fifty-three percent of HIV mono-infected and 60% of persons with HIV-HCV co-infection screened positive for at least one non-alcohol drug, with THC and cocaine use being most prevalent. Prescription drugs did not account for opiate use; twice as many participants screened positive for opiates as those prescribed opiates. Again, there were no differences between HIV mono-infected and HIV-HCV co-infected participants.

Exploratory analyses among HIV-HCV co-infected drug users

In sub-analyses focused on HIV-HCV co-infected individuals, those who tested positive for drug use were significantly more likely to report not having reliable transportation to their health care provider and reported drinking alcohol more frequently. (see Table 4) In addition, HIV-HCV co-infected participants were significantly less likely to have undetectable (< 400 c/ml) HIV RNA. Participants who tested positive for drugs did not differ from non-drug users on any other demographic or health characteristic. In the exploratory multivariable model we entered variables that were significant in the bivariate analyses, specifically transportation, alcohol frequency, and HIV viral load. Results indicated that only viral load was marginally associated with continued substance use, $OR =$

4.8, $p = .054$, 95%CI = 0.97-23.8. Finally, we conducted sensitivity analyses comparing participants who both did not test positive for drugs and did not report alcohol use, to those who indicated any substance, including alcohol use. Results did not differ from the original analyses.

Discussion

The current study found that nearly one in five participants living with HIV and receiving ART were also HCV seropositive. Although ninety percent of those who tested HCV positive had been previously diagnosed with chronic HCV infection, we found high-rates of current alcohol and drug use among people with HIV-HCV co-infection. Specifically, 41% of HIV-HCV co-infected individuals reported current alcohol use and 60% tested positive on the drug use-screening test, with 24% testing positive for more than one drug. There were no differences between HIV-HCV co-infected and HIV mono-infected persons on any indicators of substance use. Indeed, there were few characteristics that distinguished co-infected individuals from those with HIV mono-infection. The overall health status of the HIV-HCV co-infected participants is concerning, with more than half of HIV-HCV co-infected participants lacking adequate access to food and one in four failing to achieve 85% ART adherence.

Among HIV-HCV co-infected individuals in exploratory sub-analysis there were no significant associations between drug use and demographic characteristics and ART adherence. While HIV suppression was related to current substance use in the unadjusted model, this association was no longer significant in the multivariable analysis. These results are based on a small sub-sample with sparse cells, including the number with detectable viral loads, and should be interpreted with caution. Further research is needed with a larger sample size given that the same pattern of results has been reported in previous research, where poorer HIV suppression was observed in HIV-HCV co-infected persons (Cescon et al., 2013). Future studies with larger samples should investigate whether poorer viral suppression in HIV-HCV co-infected patients is accounted for by ART pharmacokinetics and metabolism, possibly involving liver dysfunction including fibrosis and cirrhosis, in substance users.

The current research results should be interpreted in light of the study limitations. First, we relied on a convenience sample that cannot be considered representative of people living with HIV infection. The sample also came from a wide-range of providers that likely varied in health services. In addition, we performed exploratory analyses on variables that included sparse cells, such as the number of participants within groups who had detectable viral loads. Thus, interpretation of all of the study findings should be tentative and call for replication with a larger sample. The study also relied on self-report instruments to assess social and behavioral characteristics, including alcohol use. Although we used reliable and valid measures, these data may still be subject to social response biases. We used urine screening to detect drug consumption within 48 to 96 hours of use. Substance use in this sample was therefore likely higher than observed. With these limitations in mind, we believe that our findings have implications for future research.

Substance use is prevalent in this sample of people living with HIV infection and the rates of alcohol and drug use were just as high among those with HIV-HCV co-infection. Given the well-established hazards posed by active substance use among persons with HCV infection, and even more dire consequences of substance use by HIV-HCV co-infected patients receiving ART, it is likely that our participants have been informed to avoid alcohol and other drugs. Thus, our findings suggest that there are substantial challenges facing a significant number of HIV-HCV co-infected individuals in terms of ceasing substance use. Drug addiction itself is a severe chronic disease and these patients should be considered triply diagnosed. Within this context, our participants had high-rates of food insecurity, poor transportation, poor medication adherence, and incomplete viral suppression. When their older age and added health threats posed by HCV infection and drug addiction are considered, the need for focused substance use treatment in HIV-HCV co-infected persons receiving ART is apparent. The role of drinking and drug use in the lives of people living with HIV should also be addressed, especially in HIV-HCV co-infected patients. For example, adults who are HIV-HCV co-infected may drink or use other drugs to alleviate the pain that commonly occurs in co-infected patients (Tsui, Cheng, Libman, Bridden, & Samet, 2012). Research is needed to determine optimal means for treating continued substance use in people living with HIV, with even greater urgency for persons with HIV-HCV co-infection.

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Biography

Seth C. Kalichman is a Professor of Psychology at the University of Connecticut. His research focuses on social and behavioral aspects of AIDS, particularly sexual risk behavior intervention and medication adherence research in the southeastern US and South Africa.

Christopher Washington, Christopher Kegler, and Tamar Grebler are Research Associates with the University of Connecticut working exclusively on studies of HIV prevention, treatment, and care in the southern US and South Africa.

Moirá O. Kalichman and Chauncey Cherry, are Program Managers at the University of Connecticut. They have dedicated their careers to conducting social and behavioral research with underserved populations affected by HIV/AIDS.

Lisa Eaton is an Assistant Professor of Human Development and Family Studies at the University of Connecticut. Her research is focused on improving the health of underserved and understudied populations. Her current research is developing behavioral interventions to reduce HIV transmission risks and increase HIV testing access among men who have sex with men.

Glossary

Adherence	the ratio of pills counted relative to pills prescribed, taking into account the number of pills dispensed
ART	antiretroviral therapies, medications used for treating HIV infection
Co-infection	in this study, dually diagnosed with HIV infection and Hepatitis-C virus infection
HIV RNA	the genetic material of human immunodeficiency virus
Viral load	refers to a measure of active virus in a given unit of a body fluid; e.g., the amount of HIV RNA in a standard unit of blood plasma

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Table 1

Demographic characteristics of people living with HIV mono-infection and HIV-HCV co-infection.

Characteristic	HIV mono-Infection (N = 547)		HIV-HCV Co-Infection (N = 131)		OR	95%CI
	M	SD	M	SD		
Age	45.6	9.0	53.0	6.4	1.12**	1.09-1.16
Years education	12.6	1.8	12.4	1.8	0.94	0.85-1.04
	N	%	N	%		
Male	384	70	94	72		
Female	163	30	37	28	0.92	0.61-1.41
Caucasian	41	8	22	16		
African-American	507	92	109	83	0.40	0.22-0.70
Unemployed	156	29	24	18		
Employed/Student	86	16	20	8		
Disability	306	55	97	74	1.41	1.14-1.74
Income < \$10,000	186	34	43	33	1.05	0.70-1.56
IDU history	22	4	62	47	21.4**	12.4-37.06
IDU partner history	86	16	71	54	6.35**	4.20-9.61
Lacks transportation	183	33	40	30	0.88	0.58-1.32
Home Insecure	222	41	82	37	0.88	0.59-1.29
Worried that food would run out without money for more	309	56	67	51	0.81	0.55-1.18
Experienced hunger	161	29	36	27	0.91	0.59-1.39

Note :

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p < .01

Table 2

Health characteristics of people living with HIV mono-infection and HIV-HCV co-infection.

Characteristic	HIV mono-Infection (N = 547)		HIV-HCV Co-Infection (N = 131)		OR	95%CI
	M	SD	M	SD		
Years since HIV diagnosis	13.3	7.8	18.9	7.6	1.09	1.06-1.12
HIV symptoms	3.7	3.6	3.5	3.3	0.98	0.92-1.03
ART side effects	5.4	5.6	5.1	5.2	1.00	0.96-1.03
ART adherence	87.2	16.5	86.9	18.0	0.91	0.28-2.93
CD4 cell count	501.4	337.3	554.1	484.6	1.00	1.00-1.01
	N	%	N	%		
ART Adherence < 85%	170	32	35	29	1.17	0.76-1.81
HIV RNA < 400c/ml	449	84	112	88	0.71	0.39-1.27
CD4 < 200	435	82	112	88	1.65	0.92-2.95

Note: ART = antiretroviral therapy; HIV RNA < 400 c/ml defined undetectable viral load; CD4 cell count < 200 defines AIDS diagnosis.

Table 3

Substance use among people living with HIV mono-infection and HIV-HCV co-infection.

Characteristic	HIV mono-Infection (N = 547)		HIV/HCV Co-Infection (N = 131)		OR	95% CI
	M	SD	M	SD		
AUDIT	3.0	4.6	3.0	5.4	1.00	0.96-1.04
DAST	1.1	1.6	1.4	1.8	1.07	0.99-1.21
	N	%	N	%		
Does not drink alcohol	243	45	77	59	Ref	
Drinks monthly	108	20	17	13	2.64	0.77-8.98
Drinks weekly	111	20	22	17	0.68	0.35-4.82
Drinks 2-3 times/week	58	11	12	9	1.65	0.45-5.95
Drinks 4+ times / week	25	5	3	2	1.72	0.44-6.64
AUDIT < 7	477	87	113	86		
AUDIT 8	71	13	18	14	1.07	0.61-1.86
CAGE < 2	509	93	120	92		
CAGE 3	39	7	11	8	1.19	0.59-2.40
Prescription opiates	12	2	4	3	1.40	0.44-4.43
Urine Screening Tests						
Opiates (morphine)	21	4	11	8	NP	
Oxycodone	14	3	8	6	NP	
Propoxyphene(PPx)	1	<1	1	1	NP	
Phencyclidine(PCP)	3	1	1	1	NP	
Barbiturates	1	1	0		NP	
Benzodiazepines	51	9	11	8	NP	
Cocaine	141	26	36	26	1.08	0.70-1.66
Amphetamine	8	2	4	3	NP	
Methamphetamine	15	3	4	3	NP	
Marijuana (THC)	143	26	39	30	1.19	0.78-1.81
Methadone (MTD)	4	1	1	1	NP	
Methylenedioxymethamphetamine (MDMA)	1	1	0		NP	
No Drug Use	256	47	53	40	Ref	
One drug	195	35	48	36	0.50	0.19-1.27
Two Drugs	76	14	23	18	0.59	0.23-1.52
Poly-substance use	17	4	7	6	0.74	0.27-1.99

Note : AUDIT=Alcohol Use Disorders Identification Test; DAST=Drug Abuse Screening Test; CAGE= CAGE (Cut down, Annoyed, Guilty, Eye opener) questionnaire; NP = not performed due to sparse or empty cells.

Table 4

Demographic characteristics of HIV-HCV co-infected non-drug users and drug users.

Characteristic	Non-Drug Users (N = 53)		Drug Users (N = 78)		OR	95%CI
	M	SD	M	SD		
Age	53.2	6.5	52.8	6.4	0.99	0.93-1.04
Years education	12.5	1.6	12.3	1.8	0.95	0.78-1.16
Years since HIV diagnosis	19.7	6.2	18.3	8.3	0.97	0.93-1.02
HIV Symptoms	3.6	3.7	3.4	3.1	0.98	0.89-1.09
ART side effects	4.6	5.2	5.8	5.2	1.04	0.97-1.12
ART Adherence	88.0	14.2	86.2	20.3	0.65	0.07-4.47
CD4 count	530.2	319.2	570.1	571.0	1.00	0.99-1.01
AUDIT score	3.16	6.9	2.9	4.2	0.99	0.93-1.05
	N	%	N	%		
Male	40	76	54	69		
Female	13	24	24	31	1.36	0.62-3.01
Caucasian	7	13	15	19		
African-American	46	87	63	81	0.63	0.24-1.69
Unemployed	11	21	13	17		
Employed/Student	5	9	5	6		
Disability	36	68	57	73	1.21	0.81-1.80
Income < \$10,000	19	36	24	31	1.25	0.60-2.63
IDU history	27	51	35	45	0.78	0.38-1.57
IDU partner history	28	53	43	55	1.09	0.54-2.20
Lacks transportation	11	21	29	37	2.26*	1.01-5.06
Housing Insecure	20	37	29	37	0.97	0.47-2.00
Worried that food would run out without money for more	24	45	43	55	1.48	0.73-2.99
Experienced hunger	12	22	24	31	1.51	0.68-3.39
ART Adherence <85%	13	26	22	31	0.82	0.36-1.84
HIV RNA 400c/ml	49	96	63	83	5.05*	1.08-23.46
CD4 200	44	86	68	89	1.35	0.45-3.99
Drinking Frequency						
Never	39	73	38	48		
Monthly	4	8	13	17		
Weekly	4	8	18	23		
2-3 × week	5	9	7	9		
4+ × week	1	2	2	3	1.41*	1.01-1.97
AUDIT 8	8	15	10	12	0.82	0.30-2.25
CAGE 3	5	10	6	8	0.80	0.23-2.79

Note :

* $p < .05$; ART = antiretroviral therapy; HIV RNA < 400 c/ml defined undetectable viral load; CD4 cell count < 200 defines AIDS diagnosis; AUDIT=Alcohol Use Disorders Identification Test; CAGE= CAGE (Cut down, Annoyed, Guilty, Eye opener) questionnaire

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