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HIV-infected individuals who use alcohol and other drugs, and virologic suppression

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Abstract

People living with HIV (PLWH) on antiretroviral therapy (ART) who use substances were examined to (a) describe those with virologic control and (b) determine which substance use-factors are associated with lack of virologic control. Participants were adult PLWH taking ART with either past 12-month DSM-IV substance dependence or past 30-day alcohol or illicit drug use. Substance use factors included number of DSM-IV alcohol or drug dependence criteria and

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Disclosure statement

Dr. Saitz is and has been principal investigator of grants awarded to Boston Medical Center and Boston University from the National Institutes of Health (including NIAAA and NIDA, and the Substance Abuse and Mental Health Services Administration) to study the management of unhealthy substance use, including to test the accuracy of screening and the efficacy of screening, brief intervention and referral to treatment and the effectiveness of integrated care. He has been paid to speak or had travel reimbursed to speak or to consult for/at numerous professional and scientific organizations, all non-profit organizations for over a decade, such as the American Society of Addiction Medicine (ASAM), RAND, the Research Society on Alcoholism, The BMJ, the Institute for Research and Training in the Addictions, the International Conference on Treatment of Addictive Behaviors, and the International Network on Brief Intervention for Alcohol and other drugs (INEBRIA), and numerous universities and hospitals. He is an author and editor for Springer, UpToDate, the American Society of Addiction Medicine, the BMJ and the Massachusetts Medical Society (royalties and/or honoraria). Wolters Kluwer has supported conference travel to an editors meeting. Systembolaget, a Swedish government agency that aims to minimize alcohol related problems, supported transportation and lodging for a presentation on brief intervention at an INEBRIA thematic meeting in 2016. Alkermes provided medication for an NIH-funded trial of alcohol disorder treatment effectiveness. He has been paid to serve as an expert witness in malpractice cases related to the management of alcohol and other drug disorders. In 2009 he consulted for Inflexxion and Medical Directions, in 2008 and 2004 for Saatchi and Saatchi healthcare, in 2006 for Fusion Medical Education, in 2004 for the Lewin Group, in 2002 for Axis-Shield ASA and Forest Pharmaceuticals. He has also consulted regarding research for Yale University, Brandeis University, Group Health Inc, Beth Israel-Deaconess Hospital, and other universities. He spoke at a National Press Foundation event on the terminology of addiction and received no compensation but the meeting was funded by ASAM, Open Society Foundations, Pew Charitable Trusts, Shatterproof, Hazelden Betty Ford Foundation and the Addiction Technology Transfer Center Network. All other authors have no conflicts to declare.

past 30-day specific substance use. Associations with HIV viral load (HVL) (<200 vs. 200 copies/mL) were tested using logistic regression models. Multivariable analyses adjusted for age, sex, homelessness and anxiety or depression. Participants ($n = 202$) were median age 50 years, 66% male, 51% African American and 75% self-reported 90% past 30-day ART adherence. Though HVL suppression (HVL <200 copies/mL) was achieved in 78% (158/202), past 30-day substance use was common among this group: 77% cigarette use; 51% heavy alcohol use; 50% marijuana; 27% cocaine; 16% heroin; and 15% illicit prescription opioid use. After adjusting for covariates, specific substance use was not associated with a detectable HVL, however number of past 12-month DSM-IV drug dependence criteria was (adjusted odds ratio = 1.23 for each additional criterion, 95% CI: 1.04–1.46). Three-quarters of a substance-using cohort of PLWH receiving ART had virologic control and 90% ART adherence. Substance dependence criteria (particularly drug dependence), not specifically substance use, were associated with lack of virologic control. Optimal HIV outcomes can be achieved by individuals who use alcohol or drugs and addressing symptoms of substance dependence may improve HIV-related outcomes.

Keywords

HIV; antiretroviral; medication adherence; injection drug use; substance use

1. Introduction

Approximately one-third of the 1.2 million people living with HIV (PLWH) in the United States drink alcohol in unhealthy amounts or use illicit drugs (Substance Abuse and Mental Health Services Administration, 2010), which are associated with negative consequences (Carrico, 2011; Carrieri et al., 1999; Celentano et al., 1998; Friedman, Pross, & Klein, 2006; Hinkin et al., 2007; Kipp et al., 2011; Kipp, Desruisseau, & Qian, 2011; Lucas, Cheever, Chaisson, & Moore, 2001; Moore et al., 2012; Palepu et al., 2003; Purcell, Parsons, Halkitis, Mizuno, & Woods, 2001; Strathdee et al., 1998). Despite this, some PLWH who use substances adhere to ART and achieve sustained virologic control. Studies among PLWH who use substances typically concentrate on injection drug use (Mathers et al., 2008; Palepu et al., 2006; Poundstone, Chaisson, & Moore, 2001), although alcohol and marijuana use are more common (Substance Abuse and Mental Health Services Administration, 2014). Few studies have focused on the full spectrum of substance use, specific substances, patterns of use or disorder criteria and their association with HIV viral load (HVL).

This study aimed to bridge these knowledge gaps and provide insights to achieving virologic control through two objectives: (i) to identify participants with virologic control (HVL <200 copies/mL) within a cohort of adult PLWH on ART who used substances, and describe their substance use; (ii) to determine which substance use-related factors were associated with a lack of HIV virologic control and, secondarily, ART adherence.

2. Methods

2.1. Study design

This cross-sectional study derived data from the Boston ARCH Cohort (<http://www.bumc.bu.edu/care/research-studies/boston-arch/>).

2.2. Participants

Between December 2012 and November 2014 participants were recruited from an urban academic hospital-based HIV primary care clinic and an affiliated community health center-based homeless HIV primary care clinic.

Inclusion criteria for Boston ARCH were: age ≥ 18 years, HIV infection, prior 12-month DSM-IV substance dependence or ever injection drug use, English-speaking and willingness to provide contact information for at least one person for follow-up. Additional inclusion criteria for this analysis were: (1) receiving ART (i.e., “yes” response to “Are you currently taking anti-retroviral therapy?”) and; (2) current substance use or disorder, defined as having at least one of the following: (i) past 12-month DSM-IV alcohol or drug dependence or (ii) any past 30-day alcohol or illicit drug use. Exclusion criteria included pregnancy, plans to leave the Boston area in the next year or cognitive impairment hindering informed consent. Participants provided written informed consent and were compensated (US \$50 dollars). The Boston University Medical Campus Institutional Review Board approved the study.

2.3. Data collection and variable definitions

2.3.1. Dependent variables—The primary dependent variable was HIV virologic control defined as HVL of <200 vs. ≥ 200 copies/mL (Department of Health and Human Services, 2016; Ribaudo, 2009). We also conducted a confirmatory analysis using HVL <50 vs. ≥ 50 copies/mL as a threshold.

At enrollment, each participant’s medical record was reviewed. The most recent CD4 cell count (cells/mm³) and HVL (copies/mL) within 3 months was recorded. If documentation was lacking, one or both biomarkers were assessed. Our secondary dependent variable was self reported past 30-day ART adherence (<90% vs. ≥ 90%) measured using a validated Visual Analogue Scale (VAS).¹

2.3.2. Main independent variables: Substance use-related factors—Substance use factors (specific substances used and severity of use disorder) were our independent variables of interest. We selected these variables a priori according to what we suspected clinically would affect HVL and included: past 30-day specific substance use including alcohol, marijuana or cocaine (due to low prevalence of opioid use in our cohort we did not include opioids as a main independent variable); past 30-day number of heavy drinking days (≥ 4 drinks/day for women or ≥ 5 drinks/day for men); and severity of alcohol dependence, drug dependence or both, defined by the number of DSM-IV criteria met in the preceding 12

¹The VAS instrument used in this study included designated lines at 10% intervals between 0 and 100% (i.e., a line at 90% and not 95%), though participants were encouraged to mark anywhere on the line that best represented their adherence, we chose to use a past 30-day ART adherence cutoff value of <90% vs. ≥ 90%.

months using the Mini International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998). Frequency and quantity of alcohol use was assessed using the validated 30-Day Timeline Follow Back (Sobell, Maisto, Sobell, & Cooper, 1979) and past 30-day drug use was assessed using questions from the Addiction Severity Index (Leonhard, Mulvey, Gastfriend, & Shwartz, 2000; McLellan, Luborsky, Woody, & O'Brien, 1980; Zanis, McLellan, Cnaan, & Randall, 1994).

2.3.3. Secondary independent variables—Secondary independent variables included each of the following: past 30-day use of tobacco, alcohol in heavy amounts (defined as 4 drinks/day or >7 drinks/week for women, 5 drinks/day or >14 drinks/week for men), heroin, illicit prescription opioids or sedatives and in the past 30 days the number of days using drugs or alcohol, the number of days using >1 substance, or any injection drug use (yes vs. no). Past 12-month DSM-IV alcohol and drug dependence were also examined. All substance use data were obtained through self-report.

2.3.4. Covariates—We identified covariates for this analysis that were likely to be associated with virologic control and could potentially confound the relationship with substance use factors. These covariates included: age (Mann et al., 2012; Palepu et al., 2004), sex (Mann et al., 2012; Palepu et al., 2004), homelessness (having spent 1 night in a shelter or on the street, without shelter, in the previous 6 months) (Knowlton et al., 2006), anxiety (Overall Anxiety Severity and Impairment Scale [OASIS] score 8) and depression (Patient Health Questionnaire version 2 [PHQ-2] score 3) (Bouhnik et al., 2005).

2.4. Statistical analysis

Colinearity was determined for independent variables and covariates using Spearman correlation matrix. None of the covariates had a correlation coefficient of 0.40 or greater. Associations with HIV virologic control and past 30-day ART adherence were tested using separate univariate and multivariable logistic regression models for each main independent variable of interest and each dependent variable (multivariable models were not conducted for secondary independent variables as no statistically significant differences were detected at baseline for our primary dependent variable). Independent variables found to be associated with both ART adherence and HIV virologic control were further analyzed using the previously described Baron and Kenny (1986) approach to investigate whether ART adherence was a mediating factor in the association with HIV virologic control. A two-sided *p* value <0.05 was considered statistically significant. All analyses were performed using SAS software version 9.3 (SAS institute Inc., Cary, NC, USA).

3. Results

3.1. Sample characteristics

Of 673 patients screened, 374 were eligible and 250 (67%) enrolled in the Boston ARCH Cohort; 202 were included in our analysis; 18 were excluded for not reporting substance use and 30 for not receiving ART (see Table 1).

3.2. Description of substance use factors and HIV virologic control

Most participants (86%) had past 12-month DSM-IV substance dependence (54% both alcohol and drug dependence, 22% drug dependence only and 10% alcohol dependence only) and 14% had past 30-day substance use without substance dependence (see Table 2).

3.3. Associations of substance use factors with virologic control and ART adherence

After adjusting for potential confounders, only number of drug dependence criteria remained significant (OR = 1.23, 95% CI: 1.04–1.46). Our confirmatory analysis using an HVL threshold of <50 vs. ≥50 copies/mL revealed similar results. Number of drug dependence criteria was also associated with <90% ART adherence. Past 30-day cocaine use and number of heavy drinking days were both independently and significantly associated with <90% ART adherence (but not with HVL). A covariate, homelessness was consistently associated with both a detectable HVL and <90% ART adherence (see Tables 3 and 4).

Mediation: ART non-adherence was strongly associated with detectable HVL (OR = 3.54, 95% CI: 1.64–7.64) but the association between the number of drug dependence criteria and detectable HVL was slightly attenuated (OR = 1.18, 95% CI: 0.99–1.41), consistent with partial mediation by ART adherence.

4. Discussion

Approximately three-quarters of a substance using HIV cohort receiving ART achieved virologic control and self-reported ART adherence ≥90%. Criteria for drug dependence, but not specific substance use, were associated with a detectable HVL after accounting for mediation by ART adherence, suggesting that poor HIV virologic control is driven by the effect of substance use on one's life rather than use itself. Although heavy drinking and cocaine use were associated with ART non-adherence, no association was found with HVL.

This study's findings confirm and advance existing literature by demonstrating that virologic control can be achieved by substance using PLWH (Malta, Magnanini, Strathdee, & Bastos, 2010; Ustinov et al., 2016). Several studies have shown an association between specific substance use and a detectable HVL (Baum et al., 2009, 2010; Bonn-Miller, Oser, Bucossi, & Trafton, 2014). These studies, either used abstainers as a comparator (Arnsten et al., 2002; Azar, Springer, Meyer, & Altice, 2010; Egger et al., 2002; Lucas, Chaisson, & Moore, 1999; Palepu et al., 2003; Tran, Nguyen, Do, Nguyen, & Maher, 2014; Weber et al., 2009), focused on PWID (Larsen et al., 2010) or did not quantify substance use as thoroughly (i.e., differentiate use from dependence) (Arnsten et al., 2002; Baum et al., 2009). Our study sample included a range of people who used substances and received ART.

Our study is also unique in its determination of the severity of substance use disorder using DSM-IV criteria and its association with HVL. This was not fully explained by ART adherence and may signify the functional consequences of increasing severity of substance use disorder (e.g., reduced health care compliance, poor nutrition, poor self-care etc.) or a direct effect of increased substance use itself (i.e., increased severity of substance use disorder may be a marker of increased substance use).

This study has limitations. Its cross-sectional design does not allow causal inferences. Additionally, our sample was recruited from health care settings and includes a large proportion of individuals with substance dependence (one of the study's inclusion criteria) and may not be representative of all PLWH receiving ART who use substances. Power was limited to detect some associations. The odds ratios for the effects of the number of drinking days and the number of dependence criteria on lack of viral control and poor ART adherence appear to be small, but these variables are ordinal count variables and the ratios describe the increase in risk for each additional heavy drinking day or criterion. Our substance use data rely on self-report and could be biased, though the expected direction of effect would be towards the null, and such was minimized by using validated tools in confidential circumstances (Babor, Stephens, & Marlatt, 1987). As our primary dependent variable (i.e., HVL) was objective, the potential for these biases to affect our results is further reduced.

Despite substance use, approximately three-quarters of HIV-infected participants receiving ART achieved virologic control, reinforcing that optimal HIV outcomes, including a reduction in the risk for HIV transmission, key to a Treatment as Prevention strategy, can be achieved by this population. Furthermore, monitoring of substance use and determining its overall impact, as represented by a substance use disorder diagnosis, should be incorporated into HIV care. One way to do that may be to assess and address disorder symptoms, not just use.

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Table 1

Characteristics of HIV-infected adults on antiretroviral therapy (ART) reporting past 30-day substance use or with past 12-month substance dependence stratified by HIV viral load (HVL) ($n = 202$).

Characteristic	Overall (%) ($n = 202$)	Undetectable HVL (<200 copies/mL) (%) ($n = 158$)	Detectable HVL (≥ 200 copies/mL) (%) ($n = 44$)	<i>p</i> value
Sociodemographic factors				
Age (median ± IQR)	50 (43–56)	50 (44–56)	50 (41–55)	0.675
Male ^a	133 (65.8)	104 (65.8)	29 (65.9)	0.992
Race				
Hispanic	50 (24.8)	37 (23.4)	13 (29.5)	0.236
Non-Hispanic Black	102 (50.5)	77 (48.7)	25 (56.8)	
Non-Hispanic White	40 (19.8)	36 (22.8)	4 (9.1)	
Non-Hispanic Other ^b	10 (5.0)	8 (5.1)	2 (4.5)	
High school education	132 (65.3)	104 (65.8)	28 (63.6)	0.788
Married or living with partner	46 (22.8)	36 (22.8)	10 (22.7)	0.994
Unemployed last 6 months	173 (85.6)	131 (82.9)	42 (95.5)	0.036
Homeless last 6 months ^a	50 (24.8)	29 (18.4)	21 (47.7)	<0.001
Anxiety ^{a,c} or Depression ^{a,d}	105 (52.2)	75 (47.8)	30 (68.2)	0.017
Current OAT ^e prescription	37 (20.2)	28 (19.9)	9 (21.4)	0.824
CD4 cell count, Median (IQR)	559 (348–779)	620 (406–839)	332 (217–587)	<0.001
>90% ART adherence ^f	149 (74.5)	128 (82.1)	21 (47.7)	<0.001

Note: IQR – Interquartile range.

^aWe identified covariates for this analysis that were likely to be associated with HVL and could potentially confound the relationship with substance use factors. These covariates included: age (Mann et al., 2012; Palepu et al., 2004), sex (Mann et al., 2012; Palepu et al., 2004), homelessness (having spent >1 night in a shelter or on the street, without shelter, in the previous 6 months) (Knowlton et al., 2006), anxiety (Overall Anxiety Severity and Impairment Scale [OASIS] score >8) and depression (Patient Health Questionnaire version 2 [PHQ-2] score >3) (Bouhnik et al., 2005).

^bAmerican Indian or Alaskan Native, Multi-Racial or Other,

^cOASIS score > 8,

^dPHQ 2 score > 3,

^eOAT – opioid agonist therapy (methadone or buprenorphine),

^f $n = 2$ missing values

Table 2

Associations between substance-related factors and HVL and ART adherence for HIV-infected adults on ART reporting past 30-day substance use or with past 12-month substance dependence ($n = 202$).

Characteristic	HIV viral load		ART Adherence ^d	
	<200 copies/mL n (%) $n = 158$	200 copies/mL n (%) $n = 44$	90% n (%) $n = 149$	<90% n (%) $n = 51$
Main independent variables				
No. heavy drinking days (median, IQR) ^{b,c}	1 (0–4)	2 (0–13)	0 (0–4)	2 (0–16)
Marijuana used	79 (50.0)	18 (40.9)	67 (45.0)	28 (54.9)
Cocaine used	43 (27.2)	15 (34.1)	35 (23.5)	21 (42.2)
No. DSM IV substance dependence criteria met, past 12 months ^e				
Alcohol (median, IQR)	4 (0–7)	6 (2–7)	4 (0–7)	6 (2–7)
Drug (median, IQR)	5 (2–7)	7 (6–7)	5 (1–7)	6 (4–7)
Secondary independent variables				
Tobacco use	121 (76.6)	38 (86.4)	114 (76.5)	44 (86.3)
Heavy alcohol use ^{c,f}	81 (51.3)	26 (59.1)	72 (48.3)	34 (66.7)
Heroin use	25 (15.8)	7 (15.9)	18 (12.1)	14 (27.5)
Rx opioid use ^g	24 (15.2)	6 (13.6)	21 (14.1)	9 (17.6)
Tranquilizer or sedative use ^g	15 (9.5)	3 (6.8)	12 (8.1)	6 (11.8)
No. drinking days (median, IQR)	3 (0–10)	5 (0–17)	2 (0–9)	8 (1–19)
No. drug use days (median, IQR)	5 (0–25)	6 (0–20)	4 (0–21)	17 (2–28)
> 1 substance use (in a day)	44 (27.8)	12 (27.3)	35 (23.5)	19 (37.3)
Injection drug use	17 (10.8)	7 (15.9)	12 (8.1)	12 (23.5)
Alcohol and drug dependence ^h	80 (50.6)	29 (65.9)	73 (49.0)	34 (66.7)

Note: ART – antiretroviral, IQR – interquartile range, Rx – prescription.

^a $n = 2$ missing.

^b 4 drinks in a day for women or 5 drinks in a day for men.

^c 30-day Timeline follow back.

^d Addiction severity index, past 30-day use.

^e MINI (past 12-month, number of DSM-IV criteria).

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f 4 drinks in a day or > 7 in a week for women or 5/14 for men,
 g illicit use.

Table 3

Bivariable and multivariable analyses of substance-related factors and HIV viral load ≥ 200 copies/mL among HIV-infected adults on antiretroviral therapy (ART) who report past 30-day substance use or past 12-month substance dependence ($N = 202$).

Characteristic	Unadjusted OR (95% CI)	Adjusted OR (95% CI) ^a
Main independent variables		
No. heavy drinking days ^{b,c}	1.03 (0.99–1.07)	1.03 (0.99–1.07)
Marijuana use ^d	0.69 (0.35–1.36)	0.68 (0.33–1.41)
Cocaine use ^d	1.38 (0.68–2.83)	1.21 (0.56–2.60)
No. DSM IV substance dependence criteria met, past 12 months ^e		
Alcohol	1.15 (1.01–1.30)	1.09 (0.95–1.26)
Drug	1.29 (1.09–1.52)	1.23 (1.04–1.46)

Note: OR – odds ratio, CI- confidence interval.

^a Each row represents a separate multivariable model, all models adjusted for: age, sex, homelessness, anxiety or depression.

^b 4 drinks for women or 5 drinks for men in a day,

^c 30 day timeline follow back,

^d Addiction severity index, past 30 d use,

^e MINI (past 12-month number of DSM-IV criteria met).

Table 4

Bivariable and multivariable analyses of substance-related factors and <90% antiretroviral (ART) adherence^a among HIV-infected adults on ART who report past 30-day substance use or past 12-month substance dependence ($N = 200$).

Characteristic	Unadjusted OR (95% CI)	Adjusted OR (95% CI) ^b
Main Independent variables		
No. heavy drinking days ^{c,d}	1.06 (1.02–1.10)	1.06 (1.02–1.10)
Marijuana use ^e	1.49 (0.79–2.82)	1.74 (0.88–3.45)
Cocaine use ^e	2.28 (1.16–4.47)	2.08 (1.03–4.20)
No. DSM IV substance dependence criteria met, past 12 months ^f		
Alcohol	1.10 (0.98–1.24)	1.06 (0.93–1.20)
Drug	1.23 (1.07–1.43)	1.20 (1.04–1.40)

Note: OR – odds ratio, CI- confidence interval.

^aPast 30 days,

^b each row represents a separate multivariable model, all models adjusted for: age, sex, homelessness, anxiety or depression,

^c 4 drinks for women or 5 drinks for men in a day,

^d 30 day timeline follow back,

^e Addiction severity index, past 30 day use,

^f MINI (past 12-month number of DSM-IV criteria met).