Prevalence and Factors Associated with Hazardous Alcohol Use Among Persons Living with HIV Across the US in the Current **Era of Antiretroviral Treatment**

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Abstract Hazardous alcohol use is associated with detrimental health outcomes among persons living with HIV (PLWH). We examined the prevalence and factors associated with hazardous alcohol use in the current era using several hazardous drinking definitions and binge drinking defined as ≥ 5 drinks for men versus ≥ 4 for women. We included 8567 PLWH from 7 U.S. sites from 2013 to 2015. Current hazardous alcohol use was reported by 27% and 34% reported binge drinking. In adjusted analyses, current and past cocaine/crack (odd ratio [OR] 4.1:3.3-5.1, p < 0.001 and OR 1.3:1.1–1.5, p < 0.001 respectively), marijuana (OR 2.5:2.2–2.9, p < 0.001 and OR 1.4:1.2–1.6, p < 0.001), and cigarette use (OR 1.4:1.2–1.6, p < 0.001and OR 1.3:1.2-1.5, p < 0.001) were associated with

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increased hazardous alcohol use. The prevalence of hazardous alcohol use remains high in the current era, particularly among younger men. Routine screening and targeted interventions for hazardous alcohol use, potentially bundled with interventions for other drugs, remain a key aspect of HIV care.

Resumen El consumo riesgoso de alcohol se asocia a los resultados adversos de salud entre las personas que viven con VIH (PLWH, por sus siglas en inglés). Estudiamos la preponderancia y los factores asociados al consumo riesgoso en la época actual con el uso de distintas definiciones de beber alcohol en forma riesgosa y consumir alcohol en forma desmedida, que se define como el consumo de > 5tragos para hombres $y \ge 4$ tragos para mujeres. Incluimos a 8567 PLWH de 7 lugares distintos de EE. UU entre 2013 y 2015. El 27% informó de consumo de alcohol en forma

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riesgosa y el 34% informó de consumo de alcohol en forma desmedida en la actualidad. En el análisis ajustado, el consumo actual y pasado de cocaína o crack (índice de probabilidad [OR, por sus siglas en inglés] 4,1:3,3-5,1, p < 0.001 y OR 1.3:1.1-1.5, p < 0.001, respectivamente), marihuana (OR 2,5:2,2-2,9, p < 0,001 y OR 1,4:1,2-1,6, p < 0.001) y consumo de cigarrillo (OR 1.4:1.2-1.6, p < 0,001 y OR 1,3:1,2-1,5, p < 0,001) se asoció al consumo de alcohol cada vez más riesgoso. La prevalencia del consumo de alcohol en forma riesgosa permanece alta en la actualidad, en especial entre los hombres más jóvenes. Los análisis de rutina y las intervenciones dirigidas a públicos específicos para abordar el consumo riesgoso de alcohol, posiblemente en conjunto con intervenciones para abordar el consumo de otras drogas, sigue siendo un aspecto clave del tratamiento contra el VIH.

Keywords HIV \cdot Alcohol use \cdot Hepatitis C \cdot Substance use

Introduction

Hazardous alcohol use is common among persons living with HIV (PLWH) [1] with studies such as the HIV Cost and Service Utilization survey and the HIV Research Network (HIVRN) previously reporting rates of 8 and 11% [1, 2]. Hazardous drinking rates among PLWH have previously been found to be higher than the general population [1]. Predictors of hazardous alcohol use among PLWH include illicit drug use [1, 2] and depression or other mental health disorders [3] while the impact of other factors such as hepatitis C virus (HCV) is less clear.

Hazardous alcohol use is associated with detrimental health outcomes including multiple steps along the HIV treatment cascade such as retention in care [4, 5]; lower CD4 counts among those not on antiretroviral therapy (ART) [6], delayed initiation of and decreased adherence to ART [7, 8], and poorer survival [9]. Hazardous alcohol use potentially increases the risk of HIV transmission by an increased likelihood of risky sexual behavior including unprotected sex with multiple partners [10, 11].

With potent ART, survival has increased dramatically [12, 13]. Consequently, the demographic and clinical characteristics of PLWH in care in the US are changing; for example there is an increasingly disproportionate share of both new HIV diagnoses and individuals living with HIV among Blacks and Latinos and an increasingly larger proportion of those living with HIV among those age 50 or older [14, 15]. However, many earlier studies of alcohol use particularly hazardous alcohol use in PLWH were conducted before the current ART treatment era [1, 2, 8, 16, 17]; had small sample sizes [17, 18]; and unrepresentative patient groups, including few women or

other restrictive patient characteristics [16, 19] yielding results with limited generalizability to PLWH currently in care.

The purpose of this study was to determine the prevalence and factors associated with hazardous alcohol use among PLWH in care across the US in the current era. We hypothesized that in the current ART era substance use and depression would be associated with hazardous alcohol use and HCV co-infection would be associated with no/low alcohol use.

Methods

Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) Cohort

CNICS is a longitudinal observational study of PLWH receiving primary care from 8 clinical sites from 1/1/1995 to the present [20]. CNICS was created to better define the relationship between patient and treatment factors and long-term clinical outcomes among PLWH in the ART era and to investigate questions related to HIV disease management that cannot be readily addressed through traditional randomized controlled trials and other cohort studies [20]. PLWH from 7 CNICS sites with comprehensive collection of the CNICS assessment including hazardous alcohol use during the study time period were included in this study to ensure geographic and racial/ethnic diversity: University of Alabama at Birmingham; University of California, San Francisco; University of Washington; University of California, San Diego; Fenway Community Health Center; University of North Carolina, Chapel Hill; and Johns Hopkins University. Substance use, particularly hazardous alcohol use has been an area of particular interest for CNICS including studies examining how patients and providers prioritize its assessment in clinical care [21] and its impact along with other factors on outcomes such as liver fibrosis, adherence and sexual transmission risk [22–24].

Study Subjects

All PLWH eighteen years of age or older who completed a clinical assessment of patient reported behaviors and outcomes as part of a clinical care visit at least once between 2013-2015 were eligible. We did not include assessments from before 1/2013 to ensure that this was representative of the current treatment era. The clinical assessment is completed approximately every 4–6 months. For those who completed multiple assessments during the study period, the most recent assessment was used. CNICS data

collection was approved by Institutional Review Boards at each site.

Data Sources

The CNICS data repository integrates longitudinal data including comprehensive clinical information from outpatient and inpatient encounters, demographic, clinical, medication, laboratory, and socioeconomic data obtained from each site's electronic health record and other institutional data sources [20].

The CNICS data repository integrates clinical assessment data. Patients used touch-screen tablets to complete the ~ 10 to 12 min clinical assessment including measures of alcohol use (Alcohol Use Disorders Identification Test (AUDIT-C) [25, 26], substance use (modified Alcohol, Smoking, and Substance Involvement Screening Test [ASSIST]) [27, 28], depressive symptoms (Patient Health Questionnaire [PHQ-9]) [29] and other domains.

Instrument Scoring

AUDIT-C scores for current alcohol consumption measured over the prior year were calculated by summing scores for each question [30]. AUDIT-C asks three questions (0-4 points each) about alcohol use during the past year; how often a person has a drink containing alcohol, the usual quantity of drinks consumed, and the frequency of drinking a large number of drinks at one time. We categorized scores as a tertiary variable of No use, Low alcohol use, and Hazardous alcohol use using a cut-off score of ≥ 4 for men and ≥ 3 for women to define Hazardous alcohol use [31]. We repeated analyses using a score of >5 for men and \geq 4 for women to define Hazardous alcohol use [32]. We also created a binary alcohol use variable of no/low use (no use + low alcohol use) and Hazardous alcohol use. Finally, we used binge drinking as an outcome comparing recent binge drinking (less than monthly, monthly, weekly, daily or almost daily) versus no binge drinking. Binge drinking was defined as ≥ 5 drinks for men versus ≥ 4 drinks for women on one occasion.

ASSIST categorizes drug use as current use (past 3 months), prior use, or never used [27, 28]. We examined illicit substance use by (1) specific type of drug used (marijuana, crack/cocaine, methamphetamines/crystal, or illicit opioids/heroin); (2) any drug use; and (3) any drug use excluding marijuana given its evolving legal status. Cigarette use was categorized as current, prior, or never used.

Depressive symptom scores using the PHQ-9 range from 0 to 27 and were categorized as: none (0–4), mild (5–9), moderate (10–19), or severe (\geq 20 points) [29].

Statistical Analyses

We performed bivariate analysis using Chi squared tests. We compared participants who completed the clinical assessment and were therefore included in the study to those who did not complete an assessment during the study period. We compared characteristics among those with no use, low use, and hazardous alcohol use. We examined demographic (age, race/ethnicity, gender, HIV transmission risk factor), and clinical characteristics including $CD4^+$ cell count nadir (≤ 350 , 350-499, and ≥ 500 cells/ mm³), current CD4⁺ cell count (<350, 350–499, and >500 cells/mm³), current HIV-1 RNA viral load level (detectable vs. undetectable), current ART use, HCV infection indicated by either the presence of HCV antibody or HCV RNA, depression category, and substance use (overall and by individual drug class). We examined the percentage of PLWH in different demographic and clinical categories with hazardous alcohol use.

We used multivariate logistic regression to examine factors associated with hazardous versus no/low alcohol use. Inclusion in models was based on hypotheses, known associations, potential confounders, and bivariate results. In addition to including demographic characteristics, we also included HIV treatment related characteristics and substance use. Adjusted models included age, race/ethnicity, gender, HIV transmission risk factor, clinical site, HCV status, CD4 cell count nadir, current viral load level, depression symptoms, substance use, and smoking status. Partial correlations were assessed and too low to create bias due to collinearity. Analyses were repeated excluding those who reported no alcohol use as this is a heterogeneous group including both current non-drinkers who never were hazardous alcohol users and prior hazardous alcohol user who due to illness, consequences of alcohol use, or other reasons became non-drinkers [33, 34]. We repeated analyses using higher cut-offs (AUDIT-C scores of ≥ 5 for men and ≥ 4 for women) to define hazardous alcohol use, and using binge drinking. As odds ratios from logistic regression analyses for common outcomes can be different from underlying prevalence ratios, we conducted secondary analyses using generalized linear models with relative risks rather than odds ratios. We repeated models stratified by individual sites to look for differences across site. Lastly, we conducted sensitivity analyses stratified by gender to examine findings of models specifically for women versus men. Stratified models included similar covariates as the main models except gender and HIV transmission risk factor were excluded from the models. Two-tailed p values <0.05 were considered significant.

Results

Between 2013 and 2015 the clinical assessment was completed by 8567 PLWH. Demographic and clinical characteristics are presented in Table 1 categorized by current alcohol use. Mean age of participants was 46 years with 3441 (41%) aged 50 or older, 1305 (15%) women, and 1298 with HCV (15%). Demographic and clinical characteristics of participants were similar to those of CNICS patients who did not complete an assessment during the study period and to 345 individuals who started the assessment but did not complete it (data not shown).

Hazardous Alcohol Use

No current alcohol use was reported by 33%, 41% reported low alcohol use and 27% reported hazardous alcohol use (AUDIT-C scores of \geq 4 for men and \geq 3 for women). Binge drinking was reported by 34%. Rates of hazardous alcohol use were higher among men, those with a detectable viral load, and those not receiving ART (Table 1). Hazardous alcohol use was less common with older ages. Hazardous alcohol use was less frequently reported by PLWH with HCV (21%) compared to no HCV (27%).

Hazardous alcohol use was more prevalent among PLWH who reported current illicit drug use (38%) compared with past (22%) or no substance use (15%) (Table 2). This pattern was consistent across all drugs except methamphetamine use where hazardous alcohol use was most prevalent among those with past not current use (Table 2), with particularly prevalent hazardous alcohol use with cocaine/crack use.

Factors Associated with Hazardous Alcohol Use

In bivariate analyses (Table 3, column 1), factors associated with hazardous alcohol use included male gender, younger age, white race, not having HCV, and having a detectable VL. Past methamphetamine/crystal use, past and current cocaine/crack and marijuana use, and current opioid/heroin use were associated with hazardous alcohol use.

In adjusted logistic regression analyses of hazardous alcohol use (AUDIT-C scores of ≥ 4 for men and ≥ 3 for women), compared to those reporting no/low alcohol use, current illicit drug use *including marijuana* were associated with hazardous alcohol use (OR 3.21: 2.75–3.73, p < 0.001) and past (OR 1.60: 1.37–1.87, p < 0.001). In adjusted models, current substance use *excluding marijuana* were also associated with hazardous alcohol use (OR 1.74: 1.48–2.06, p < 0.001) and past (OR 1.24: 1.09–1.42, p < 0.001).

We repeated analyses using individual illicit drugs. Factors associated with no/low alcohol use included older age, black race, and HCV co-infection while past and present cocaine/crack use and marijuana use were associated with hazardous alcohol use as was past and current cigarette use (Table 3, column 2).

We conducted sensitivity analyses comparing those with hazardous alcohol use to those with low use excluding those reporting that they did not drink at all (Table 3, column 3). This was to exclude those with prior hazardous alcohol use who had become non-drinkers [33–35]. Findings were similar to results including nondrinkers except HCV was no longer associated with low alcohol use. We also repeated analyses using a higher cutoff to define hazardous alcohol use (Table 3, column 4) with a similar pattern of results.

In adjusted analyses using binge drinking to characterize drinking patterns (Table 3, column 5), female gender was associated with a lower odds of binge drinking than male gender as was older age. Past and current cocaine/crack and marijuana use, and past and current cigarette smoking were all associated with increased odds of binge drinking. In contrast to several other alcohol measures, HCV was not associated with significantly less binge drinking. In addition, we examined those with hazardous alcohol use versus no/low alcohol use using relative risk rather than odds ratios and found similar findings (Table 3, column 6).

Because there are differences in CNICS sites in terms of participants (e.g. California sites have a higher proportion of Latino PLWH than the site in Birmingham, Alabama), we repeated models looking at individual sites. The pattern of findings in the adjusted models were similar by site although not all findings that were statistically significant in the overall model were significant in the individual site models with smaller sample sizes.

Lastly we conducted analyses stratified by gender (Table 4). Results were similar to overall findings, however a few differences were notable. The stratified analyses highlighted that associations between black race and no/ low alcohol use were driven by men and associations between CD4 nadir >350 cells/ml³ and hazardous alcohol use were driven by women. In contrast, past and current cocaine/crack and marijuana use were associated with hazardous alcohol use among both men and women.

Discussion

This study describes alcohol use among a population of >8000 PLWH in care across the U.S. in the current treatment era. It demonstrates the high prevalence of hazardous alcohol use (27%) which has important implications on outcomes among PLWH such as adherence to ART and

	N = 850	57							
	Total		No alcoh	ol use	Low alco	hol use	Hazardous	alcohol use	p value
	N = 850	57	N = 280	4	N = 3493	3	N = 2270		
	N	100%	N	33%	N	41%	N	27%	
Gender									
Male	7262	85%	2211	30%	3068	42%	1983	27%	
Female	1305	15%	593	45%	425	33%	287	22%	< 0.001
Age (years)									
<30	793	9%	145	18%	313	39%	335	42%	
30–39	1768	21%	427	24%	763	43%	578	33%	
40-49	2565	30%	854	33%	1096	43%	615	24%	
50-59	2615	31%	995	38%	1018	39%	602	23%	
≥60	826	10%	383	46%	303	37%	140	17%	< 0.001
Race/ethnicity									
White	4164	49%	1257	30%	1736	42%	1171	28%	
Black	2677	31%	970	36%	1102	41%	605	23%	
Hispanic	1268	15%	436	34%	466	37%	366	29%	
Other	458	5%	141	31%	189	41%	128	28%	< 0.001
HIV transmission		570	141	5170	10)	4170	120	2070	<0.001
MSM	5392	63%	1433	27%	2392	44%	1567	29%	
IDU*	1082	13%	500	46%	374	35%	208	19%	
Heterosexual	1854	22%	500 788	43%	639	33 <i>%</i> 34%	208 427	23%	
		3%							< 0.001
Other	239		83	35%	88	37%	68	28%	<0.001
CD4 + cell count			1746	2501	2072	4107	1014	240	
≤350 251,500	5033	59%	1746	35%	2073	41%	1214	24%	
351-500	1285	15%	400	31%	511	40%	374	29%	0.001
≥500	2238	26%	654	29%	904	40%	680	30%	< 0.001
CD4 + cell count	. , .	,							
≤350	1638	19%	602	37%	641	39%	395	24%	
351-500	1382	16%	435	31%	579	42%	368	27%	
≥500	5536	65%	1763	32%	2268	41%	1505	27%	0.003
Currently receivin	ng ART (N =	,							
No	742	9%	229	31%	286	39%	227	31%	
Yes	7723	91%	2534	33%	3169	41%	2020	26%	0.03
Current viral load	(N = 8539))							
Detectable	1113	13%	326	29%	455	41%	332	30%	
Undetectable	7426	87%	2471	33%	3024	41%	1931	26%	0.007
Hepatitis C virus									
No	7269	85%	2228	31%	3049	42%	1992	27%	
Yes	1298	15%	576	44%	444	34%	278	21%	< 0.001
Depression sympt	oms (N $= 8$	3548)							
None	4718	55%	1521	32%	1973	42%	1224	26%	
Mild	1969	23%	624	32%	810	41%	535	27%	
Moderate	1517	18%	525	35%	578	38%	414	27%	
Severe	344	4%	125	36%	125	36%	94	27%	0.09

Table 1 Clinical and demographic characteristics by alcohol use among persons living with HIV in clinical care at 7 CNICS sites across theU.S. in 2013–2015

IDU injection drug use, MSM men who have sex with men, ART antiretroviral therapy

* IDU includes patients who report being both MSM and IDU

	N = 8567						p value
	No alcoho	l use	Lower risk a	lcohol use	Hazardous a	lcohol use	
	N = 2804		N = 3493		N = 2270		
	N%		N%		N%		
Illicit drug us	e (including mar	rijuana)					
None	996	43%	987	42%	349	15%	
Past	1131	38%	1154	39%	658	22%	
Current	677	21%	1352	41%	1263	38%	< 0.001
Illicit drug us	e (excluding ma	rijuana)					
None	1378	34%	1778	44%	848	21%	
Past	1096	34%	1200	37%	907	28%	
Current	330	24%	515	38%	515	38%	< 0.001
Methampheta	mine/crystal use						
None	1803	33%	2293	42%	1347	25%	
Past	746	33%	827	37%	682	30%	
Current	255	29%	373	43%	241	28%	< 0.001
Cocaine/crack	use						
None	1614	34%	2049	44%	1017	22%	
Past	1107	33%	1268	38%	941	28%	
Current	83	15%	176	31%	312	55%	< 0.001
Opiate/heroin	use						
None	2233	32%	2957	42%	1809	26%	
Past	513	38%	455	34%	383	28%	
Current	58	27%	81	37%	78	36%	< 0.001
Marijuana use	2						
None	1224	43%	1163	41%	477	17%	
Past	1086	36%	1199	40%	713	24%	
Current	494	18%	1131	42%	1080	40%	< 0.001
Cigarette use							
Never	1148	35%	1469	45%	662	20%	
Past	740	31%	961	40%	707	29%	
Current	916	32%	1063	37%	901	31%	< 0.001

Table 2 Substance use by alcohol use among persons living with HIV in clinical care at 7 CNICS sites across the U.S. in 2013–2015

survival. There was a lower prevalence of hazardous alcohol use among older individuals and those with HCV co-infection, though alcohol use was still substantial among these groups. Past and present cocaine/crack use and marijuana use were associated with increased odds of hazardous alcohol use. The results of this study have important implications for the care of PLWH including highlighting the crucial need for on-going screening and improved treatment delivery for alcohol use in clinical care systems.

Prevalence of Hazardous Alcohol Use

The prevalence of hazardous alcohol use was higher in this study compared to the HIV Cost and Services Utilization

survey or the HIV Research Network (HIVRN) where 8% or 11% reported heavy/hazardous alcohol use [1, 2]. These differences may be explained in part by definitions. For example, HIVRN defined hazardous drinking as >14 drinks/week or \geq 5 drinks/occasion for men and >7 drinks/ week or ≥ 4 drinks/occasion for women. Of note, even when using the more stringent AUDIT-C definition of >5for men and >4 for women, 18% in the current study reported hazardous alcohol use. Differences in how alcohol use was collected may also contribute to the higher prevalence in CNICS. CNICS uses touch-screen tablets to collect assessments, lessening some of the social desirability bias and underreporting associated with interviewerbased collection. Several studies have indicated patient preference self-administered for electronic over

	Bivariate	Multivariate				
	Hazardous vs. no/low* alcohol use	Hazardous vs. no/low* alcohol use	Hazardous vs. low risk** alcohol use	Hazardous vs. no/low*** alcohol use using higher	Binge drinking vs. not binge drinking	Hazardous vs. no/low* alcohol use with relative
	OR: 95% CI, p value	OR: 95% CI, p value	OR: 95% CI, p value	cut-on OR: 95% CI, p value	OR: 95% CI, p value	RR: 95% CI, p value
Sex						
Male	Ref	Ref	Ref	Ref	Ref	Ref
Female	0.75: 0.65 - 0.86, < 0.001	1.03: 0.85-1.25, 0.8	1.16: 0.93-1.45, 0.2	0.94: 0.75-1.19, 0.6	0.77: 0.64-0.93, 0.007	0.96: 0.83-1.11, 0.6
Age						
<30	Ref	Ref	Ref	Ref	Ref	Ref
30–39	0.66: 0.56-0.79, < 0.001	0.70: 0.58 - 0.84, < 0.001	0.66: 0.54 - 0.81, < 0.001	0.78: 0.63-0.96, 0.02	0.75: 0.62-0.90, 0.002	$0.86:\ 0.78-0.94,\ 0.002$
40-49	0.43: 0.36-0.51, < 0.001	0.47: 0.39-0.57, < 0.001	0.48: 0.39-0.59: <0.001	0.54: 0.44-0.66, < 0.001	0.44: 0.37-0.53, <0.001	0.69: 0.62 - 0.77, < 0.001
50-59	0.41: 0.35 - 0.48, < 0.001	0.44: 0.37 - 0.53, < 0.001	0.51: 0.42 - 0.63, < 0.001	0.50: 0.41-0.62, < 0.001	0.34; 0.28-0.41, < 0.001	0.65: 0.58 - 0.72, < 0.001
≥60	0.28: 0.22 - 0.35, < 0.001	0.33: 0.26 - 0.42, < 0.001	0.42: 0.32 - 0.55, < 0.001	0.34; 0.25-0.46, < 0.001	0.21: 0.16-0.26, < 0.001	0.52: 0.44–0.62, <0.001
Race/ethnicity						
White	Ref	Ref	Ref	Ref	Ref	Ref
Black	0.75: 0.67 - 0.84, < 0.001	0.74: 0.64 - 0.85, < 0.001	0.77: 0.66-0.90, 0.001	0.86: 0.73-1.01, 0.07	0.81: 0.71 - 0.92, 0.002	$0.85:\ 0.77-0.93,\ 0.001$
Hispanic	1.04: 0.90-1.19, 0.6	1.05: 0.89-1.22, 0.6	1.13: 0.95-1.34, 0.2	1.03: 0.86-1.23, 0.7	1.24: 1.07 - 1.43, 0.005	1.03:0.94-1.14,0.5
Other	0.99: 0.80-1.23, 0.9	0.88: 0.70-1.12, 0.3	0.89: 0.69-1.15, 0.4	0.88: 0.67–1.15, 0.4	0.96: 0.77–1.20, 0.7	0.96: 0.84–1.10, 0.6
HIV transmission risk factor	on risk factor					
MSM	Ref	Ref	Ref	Ref	Ref	Ref
IDU*	0.58: 0.49 - 0.68, < 0.001	0.56: 0.46-0.68, < 0.001	0.69: 0.56 - 0.86, 0.001	0.65: 0.52 - 0.81, < 0.001	0.58: 0.49-0.70, < 0.001	0.68: 0.59–0.77, <0.001
Heterosexual	0.73: 0.65 - 0.83, < 0.001	1.08: 0.90-1.29, 0.4	1.34:1.10-1.63,0.004	1.14: 0.93-1.39, 0.2	0.96: 0.81–1.13, 0.6	1.06: 0.93–1.20, 0.4
Other	0.97: 0.73-1.29, 0.8	1.06: 0.77-1.45, 0.7	1.15: 0.81-1.63, 0.4	0.81: 0.55-1.19, 0.3	1.16: 0.87–1.56, 0.3	1.05: 0.86-1.28, 0.6
CD4 + cell count nadir	int nadir					
≤350	Ref	Ref	Ref	Ref	Ref	Ref
351-499	1.29: 1.13 - 1.48, < 0.001	1.14 0.98-1.32, 0.09	$1.18\ 1.01 - 1.39,\ 0.04$	1.13: 0.95–1.34, 0.2	1.11: 0.97-1.28, 0.1	1.08 0.99-1.19, 0.09
≥500	1.37: 1.23 - 1.53, < 0.001	1.16: 0.99–1.34, 0.06	1.17: 0.99–1.38, 0.06	1.22: 1.03–1.45, 0.02	1.09: 0.95–1.26, 0.2	1.10: 1.00-1.21, 0.04
Current viral load	ad					
Detectable	Ref	Ref	Ref	Ref	Ref	Ref
Undetectable	0.83: 0.72 - 0.95, 0.007	0.95: 0.81-1.10, 0.5	0.98: 0.83-1.15, 0.8	0.92: 0.77-1.09, 0.3	0.90: 0.78-1.04, 0.2	0.97: 0.88-1.07, 0.6
Hepatitis C virus	IS					
No	Ref	Ref	Ref	Ref	Ref	Ref
Yes	0.72: 0.63-0.83, <0.001	0.83: 0.70 - 0.98, 0.03	0.97: 0.80-1.17, 0.7	0.75: 0.62-0.92, 0.004	0.88: 0.75-1.03, 0.1	0.84: 0.75 - 0.95, 0.004
Depression symptoms	lptoms					
None	Ref	Ref	Ref	Ref	Ref	Ref
Mild	1 06: 0 95-1 20 0 3	0.91 · 0.80 - 1.04 0.2	0.95; 0.82-1.09, 0.4	0.97:0.84-1.12.0.7	0.98: 0.87–1.22. 0.8	0.93: 0.86-1.01, 0.1

	Bivariate	Multivariate				
	Hazardous vs. no/low* alcohol use	Hazardous vs. no/low* alcohol use	Hazardous vs. low risk** alcohol use	Hazardous vs. no/low*** alcohol use using higher cut-off	Binge drinking vs. not binge drinking	Hazardous vs. no/low* alcohol use with relative risks rather than odds ratios
	OR: 95% CI, p value	OR: 95% CI, p value	OR: 95% CI, p value	OR: 95% CI, p value	OR: 95% CI, p value	RR: 95% CI, p value
Moderate	1.07: 0.94–1.22, 0.3	0.90: 0.78-1.03, 0.1	0.97: 0.83-1.14, 0.7	1.03: 0.88-1.21, 0.7	0.99: 0.87–1.13, 0.9	0.89: 0.81-0.97, 0.01
Severe	1.07: 0.84-1.37, 0.6	0.88: 0.68-1.15, 0.4	0.98: 0.73-1.31, 0.9	1.06: 0.79–1.41, 0.7	0.86: 0.66–1.10, 0.2	0.85: 0.71-1.03, 0.09
Methamphetar	Methamphetamine/crystal use					
None	Ref	Ref	Ref	Ref	Ref	Ref
Past	1.32: 1.18 - 1.47, < 0.001	0.88: 0.75-1.02, 0.09	0.95: 0.80-1.11, 0.5	0.90; 0.76-1.07, 0.2	0.94: 0.81–1.09, 0.4	0.93: 0.85-1.02, 0.1
Current	1.17: 0.99–1.37, 0.06	0.58: 0.47 - 0.71, < 0.001	0.60: 0.48-0.75, < 0.001	0.62: 0.50-0.78, < 0.001	0.70: 0.58-0.85, < 0.001	0.70: 0.61-0.80, <0.001
Cocaine/crack use	use					
None	Ref	Ref	Ref	Ref	Ref	Ref
Past	1.43: 1.29 - 1.58, < 0.001	1.31: 1.14–1.51, <0.001	1.33: 1.14–1.55, <0.001	1.28: 1.08-1.50, 0.003	1.28: 1.12 - 1.46, < 0.001	1.16: 1.05-1.28, 0.003
Current	4.34: 3.63-5.19, <0.001	4.08: 3.29–5.05, <0.001	3.34: 2.65-4.21, <0.001	4.05: 3.25-5.06, <0.001	4.09: 3.29-5.08, <0.001	1.92: 1.72-2.14, < 0.001
Opiate/heroin use	use					
None	Ref	Ref	Ref	Ref	Ref	Ref
Past	1.14; 1.00–1.29, 0.06	0.95; 0.81-1.11, 0.5	1.10; 0.92–1.31, 0.3	1.12: 0.94–1.33, 0.2	0.92: 0.801.07, 0.3	1.00; 0.91–1.09, 1.0
Current	1.73; 1.21–2.14, 0.001	1.05: 0.76-1.45, 0.8	1.09: 0.76–1.56, 0.6	1.14: 0.81-1.63, 0.4	0.97: 0.71-1.34, 0.9	1.12: 0.94–1.33, 0.2
Marijuana use						
None	Ref	Ref	Ref	Ref	Ref	Ref
Past	1.56: 1.37–1.78, <0.001	1.37: 1.17 - 1.59, < 0.001	1.21: 1.03-1.42, 0.02	1.23: 1.03–1.48, 0.02	1.22: 1.06 - 1.40, 0.005	1.28: 1.12 - 1.45, < 0.001
Current	3.33: 2.94–3.77, <0.001	2.50: 2.15–2.91, <0.001	1.69: 1.44–1.99, <0.001	2.17: 1.82–2.58, <0.001	2.20: 1.91–2.53, <0.001	1.84: 1.63–2.09, <0.001
Cigarette use						
Never	Ref	Ref	Ref	Ref	Ref	Ref
Past	1.64: 1.45 - 1.86, < 0.001	1.33: 1.16–1.52, <0.001	1.37: 1.18-1.59, <0.001	1.39: 1.19-1.64, < 0.001	1.40: 1.23 - 1.59, < 0.001	1.18: 1.07-1.29, 0.001
Current	1.80: 1.60-2.02, <0.001	1.38: 1.20–1.58, <0.001	1.55: 1.34 - 1.80, < 0.001	1.60: 1.37-1.87, <0.001	1.39: 1.23 - 1.58, < 0.001	1.18: 1.07-1.29, 0.001
Results with p	Results with p values <0.05 are given in bold	bloc				

OR odds ratio, 95% CI 95% confidence interval, RR relative risk

All models also adjusted for site

* No/low alcohol use includes no alcohol use and lower risk alcohol use defined as AUDIT-C scores of less than 4 for men and less than 3 for women

** Low risk alcohol use defined as AUDIT-C scores of less than 4 for men and less than 3 for women, excluding those with no alcohol use

*** No/low alcohol use using the higher cut-off includes no alcohol use and lower risk alcohol use defined as AUDIT-C scores of less than 5 for men and less than 4 for women

Table 3 continued

Table 4 Factors associated with hazardous alcohol use compared with no/low alcohol use among persons living with HIV in clinical care at 7 CNICS sites across the U.S. in 2013–2015 in multivariate analyses stratified by sex

	Multivariate OR	Multivariate OR
	Females	Males
Age		
<30	1 Ref	1 Ref
30–39	0.74: 0.40-1.38, 0.3	0.68: 0.56-0.82, <0.001
40-49	0.66: 0.36-1.23, 0.2	0.44: 0.36-0.53, <0.001
50-59	0.65: 0.34-1.21, 0.2	0.41: 0.34–0.50, <0.001
≥ 60	0.34: 0.16-0.74, 0.006	0.31; 0.24–0.41, <0.001
Race/ethnicity		
White	1 Ref	1 Ref
Black	0.94: 0.65-1.35, 0.7	0.71: 0.61–0.83, <0.001
Hispanic	1.11: 0.64–1.94, 0.7	1.05: 0.89-1.24, 0.5
Other	0.40: 0.17-0.97, 0.04	0.96: 0.75-1.23, 0.8
CD4 + cell collision	ount (nadir)	
≤350	1 Ref	1 Ref
351-500	1.50: 0.99-2.25, 0.05	1.09: 0.93-1.27, 0.3
>500	1.23: 0.82–1.87, 0.3	1.14: 0.96–1.34, 0.1
Current viral le	oad	
Detectable	1 Ref	1 Ref
Undetectable	0.84: 0.57-1.24, 0.4	0.97: 0.82–1.14, 0.7
Hepatitis C via	rus	
No	1 Ref	1 Ref
Yes	0.81: 0.53-1.25, 0.3	0.69: 0.58–0.82, <0.001
Depression syn	nptoms	
None	1 Ref	1 Ref
Mild	0.96: 0.67–1.37, 0.8	0.90: 0.79–1.03, 0.1
Moderate	1.35: 0.94–1.94, 0.1	0.83: 0.71-0.97, 0.02
Severe	1.71: 0.93–3.13, 0.09	0.76: 0.57–1.03, 0.08
Methamphetan	nine/crystal use	
None	1 Ref	
Past	0.58: 0.35-0.97, 0.04	0.88; 0.75–1.04, 0.1
Current	1.09: 0.51-2.33, 0.8	0.53: 0.42–0.65, <0.001
Cocaine/crack	use	
None	1 Ref	1 Ref
Past	1.55: 1.03–2.34, 0.04	1.26: 1.08-1.47, 0.003
Current	3.66: 2.10–6.37, <0.001	4.11: 3.25–5.19, <0.001
Opiate/heroin	use	
None	1 Ref	1 Ref
Past	0.88; 0.55–1.41, 0.6	0.87: 0.74–1.02, 0.1
Current	0.65: 0.27-1.53, 0.3	0.99: 0.70–1.41, 1.0
Marijuana use		
None	1 Ref	1 Ref
Past	1.60: 1.07-2.40, 0.02	1.30: 1.10–1.53, 0.002
Current	2.79: 1.85–4.21, <0.001	2.47: 2.11–2.91, <0.001
Cigarette use		
Never	1 Ref	1 Ref

Table 4 continued

	Multivariate OR Females	Multivariate OR Males
Current	1.10: 0.74–1.63, 0.7	1.38: 1.19–1.59, <0.001

Results with p values <0.05 are given in bold

interviewer-based data collection, and electronic administration has yielded more disclosure of sensitive behaviors [36–39]. It may be that study differences can also be explained in part by changes in demographic and clinical characteristics of PLWH in the US in recent years. Only 33% in CNICS reported no alcohol use which is notable given increasing evidence that perhaps no level of alcohol consumption is 'safe' among PLWH [40]. The high prevalence of hazardous alcohol use found in this study has clinical implications in terms of ensuring clinical care settings have enough resources to ensure adequate identification and treatment of this complex and yet crucial issue among PLWH.

Aging

Effective ART has resulted in many PLWH living into middle and old age. Of note, among older PLWH, hazardous alcohol use was less likely for those \geq 60, who were less than half as likely to report hazardous alcohol use compared with those <30. This is consistent with general population studies which have found an association between older age and less alcohol use [41, 42]. Despite this, 17% of PLWH \geq 60 reported hazardous alcohol use suggesting that there is still need for additional interventions targeting all ages of PLWH, and for additional research to better understand the effectiveness of interventions across the age spectrum for PLWH, particularly given the associations between alcohol and poor outcomes among the elderly such as falls, fatal injuries and adverse drug reactions [43, 44].

Substance Use

We found hazardous alcohol use was more common among current substance users and that this association varied by individual drug. Both current and past cocaine/crack and marijuana use were associated with a higher odds of hazardous alcohol use. These findings highlight the importance of research that evaluates associations between individual substances and alcohol use as it can vary across drugs and may differentially affect outcomes. Further research is needed to identify whether certain patterns of substance use, for instance alcohol and cocaine/crack, are particularly detrimental to HIV outcomes and warrant specific interventions and to better identify the role of joint interventions that simultaneously target both alcohol and drug use.

HCV

HCV co-infection is common among PLWH and liver disease is a leading cause of non-AIDs mortality [45, 46]. Hazardous alcohol use exacerbates HCV-related liver disease through increased HCV viral replication, toxic effects on the liver, and indirectly via effects on ART adherence and decreased HCV treatment eligibility [47–51]. In addition, alcohol use among PLWH co-infected with HCV is associated with faster liver fibrosis progression, while sustained virological response to HCV therapy is associated with slower liver fibrosis progression [52]. HCV treatment is rapidly evolving with higher treatment success rates and easier treatment regimens, however alcohol use remains a potential contraindication to HCV treatment among PLWH [53]. This is an important target population for interventions to reduce preventable morbidity and mortality.

We found 56% of PLWH co-infected with HCV reported alcohol use with 21% reporting hazardous alcohol use. This rate is high given the negative consequences. HCV was associated with a lower odds of hazardous alcohol use. One possible explanation for this could be selection effects with the combination of HCV and hazardous alcohol use making it less likely for a PLWH to survive and thereby be part of the cohort. However, in a sensitivity analysis that excluded non-drinkers, there was not a decreased odds of hazardous alcohol use among those co-infected with HCV. These findings raises the possibility that those with HCV are to some extent making different decisions about drinking than those without HCV, possibly heeding advise to reduce their risk for liver toxicity from alcohol.

Strengths

A study strength is the large, diverse cohort of PLWH. This cohort represents the changing epidemiology of HIV across the US with substantial numbers of women, racial and ethnic diversity, and a population increasing in mean age. A second strength is the focus on 2013 and after. Finally, the comprehensive measurement of not just alcohol but other drug use allows assessment of the role of individual drugs among PLWH who may have high rates of co-occurring substance use.

Limitations

Several limitations are worth noting. We evaluated associations with alcohol use, but associations do not necessarily indicate causation. Alcohol and drug use were collected in the clinical assessment which could lead to underestimates. However, use of electronic collection allows patient burden to be reduced permitting integration into care and decreasing underreporting of risk behaviors due to social desirability bias [54]. While the clinical assessment has expanded to include additional languages such as Amharic, this study included only English and Spanish-speaking PLWH which may reduce generalizability to PLWH who do not speak English or Spanish and/ or are not in care. Studies are needed that focus more broadly, including additional socioeconomic and contextual factors to inform public policies and interventions, with effective interventions that can be routinely incorporated into clinical settings being of particular value.

Conclusions

We describe prevalence and factors associated with hazardous alcohol use among PLWH in care across the U.S in the current era. The purpose is to better understand alcohol use not to stigmatize PLWH but instead to ensure that risk behaviors are identified and addressed to prevent negative consequences. Rates of alcohol use remain high. Factors associated with hazardous alcohol use included younger age and past and present cocaine use and marijuana use. Strengths include inclusion of women, the large sample size and examining individual substances and patterns of substance use while accounting for overlapping use. While rates of hazardous alcohol use were lower among PLWH with HCV, the rates remained substantial given the negative consequences. Routine screening and targeted interventions for hazardous alcohol and other substance use remain a key aspect of HIV care.

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Compliance with ethical standards

Conflicts of interest The authors declare they have no conflicts of interest.

Informed consent All sites have approval from Human Subjects committees at their local institution and participants signed informed consent to participate in CNICS. All data submitted to the CNICS Data Repository are deidentified. For this retrospective data analysis of existing deidentified data in the CNICS Data Repository, no additional formal consent is required.

Ethical approval This article does not contain any studies with animals performed by any of the authors.

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