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Evaluating Connections Between Polysubstance Use, Social Drivers of Health, and Mental Health Symptoms in People With HIV

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Background. We sought to understand how no, single, and polysubstance use correlate with social drivers of health (SDOH) and mental health symptoms in persons with HIV (PWH).

Methods. Cross-sectional analysis of PWH who use and do not use illicit substances and marijuana. Substance use was defined by self-report and toxicology (urine and hair). Surveys evaluated SDOH and mental health domains. Linear and logistic regression were used to assess the associations of polysubstance and single substance use with SDOH domains at risk and presence of mental health symptom domains compared to controls (no substance use).

Results. A total of 171 participants were enrolled (67 polysubstance, 68 single substance, and 36 controls): 75% were male, 61% were Black, and 13% were of Hispanic ethnicity. Substance using groups were younger, had more transgender women, and higher proportion with income ≤$20 000/year. Ninety-one percent had HIV-1 RNA ≤200 copies/mL. Participants in the polysubstance group reported the most SDOH domains at risk. With adjustment, odds of transportation needs and food insecurity were 2 to 5 times higher for the substance using groups than controls. Odds of mental health symptom domains (depression, mania, anxiety, and posttraumatic stress disorder) were significantly higher in substance using groups than controls.

Conclusions. Substance use is strongly associated with SDOH domains at risk and mental health symptom domains in PWH. Polysubstance use appears to be an important correlate for SDOH domains at risk and this suggests more attention in both future research and clinical care is necessary to determine interventions that will improve SDOH and health-related outcomes.

Keywords. substance use; polysubstance use; social drivers of health; social determinants of health; HIV; mental health.

Substance use among persons with HIV (PWH) is common, including among those who are engaged in HIV care. Though nationally representative samples are limited, more than 50% of PWH report recent marijuana or illicit drug use [1–4]. Similarly, mental health concerns are also more frequent among PWH compared to those without HIV [5–8]. Reported rates vary widely; depression is reported in 22% to 48% of PWH, bipolar disorder in 2.6% to 9.1%, anxiety disorders in 10% to 72%, and posttraumatic stress disorder (PTSD) in 25% to 34% [3–7]. Substance use is frequently associated with worse health outcomes including higher rates of sexually transmitted infections, hepatitis C, lower rates of viral suppression, and more missed visits [2, 9–12]. When substance use and mental health issues are both present, the effects appear to be exacerbated and significant decline in HIV medication adherence are observed [10, 13, 14].

Substance use ranges from intermittent, casual, and recreational use to mild/moderate or severe substance use disorder (defined by associated consequences and complications arising from substance use) [15]. Most substance use research focuses on persons with substance use disorder and is often restricted to a specific drug (ie, opiates, methamphetamines, cocaine, or alcohol). However, among persons who use substances, many use more than 1 substance.

Most of the published literature related to substance use and HIV examines the association of substance use and medication adherence. Little is reported about how different patterns of substance use (ie, polysubstance use, single-substance use, any substance use, or no substance use) are associated with the risk of experiencing health-related social needs or mental health symptoms which often cooccur. The role of socioeconomic status on health is well described [16]. In fact, when examining the effect that modifiable health factors (healthy behaviors, clinical care, physical environment, and socioeconomic conditions) have on

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general health outcomes (longevity and quality of life), socioeconomic factors had the most significant impact on general health outcomes in 33 states [16, 17]. As such, many groups advocate use of the term social drivers of health to describe personal health-related social needs because these are modifiable, whereas social determinants may be more fixed (such as factors at a societal level). Among persons with substance use disorders, mental health symptoms, and health-related social needs (social drivers of health [SDOH]) are common [18, 19]. Similarly, poverty and its association with SDOH is common among PWH [20–24]. In this exploratory study, we sought to understand how substance use including polysubstance use correlates with SDOH domains at risk and presence of mental health symptom domains in PWH engaged in HIV care.

METHODS

Study Design and Population

This is a cross-sectional analysis of baseline data from the Case Western Reserve University Center for Excellence on the Impact of Substance Use on HIV (Center). The Clinical Core for the Center has created a prospective cohort of persons who use substances or do not use substances, with and at risk for HIV. This cohort was designed to establish a comprehensive database of sociodemographic, clinical, social, and behavioral health data, as well as a biorepository of biological samples to be utilized in future multidisciplinary research spanning the spectrum from bench to bedside investigating factors associated with HIV infection and substance use. Enrollment is ongoing and potential participants are identified by study coordinators using substance use screening results performed annually in the MetroHealth System Infectious Disease clinic. Eligibility criteria for the cohort include: adults ≥18 years with and at risk for HIV, with and without substance use, and able to read and understand the informed consent. Substances considered for inclusion are marijuana, cocaine, methamphetamine, opioids, sedatives, and hallucinogens. Tobacco and alcohol use are not included as eligibility criteria for the cohort although detailed assessment of use is collected. Prescribed medications including opioids for pain or treatment for opioid use disorder and stimulants are not considered "substance use" in this study. Participants with any substance use complete entry (baseline), 6- and 12-month visits, and annual visits for the subsequent years. Participants with no substance use (controls), complete only the entry visit, regardless of HIV status. All study activities and the protocol were approved by the MetroHealth System institutional review board. All participants provide written informed consent before study participation. Study data were collected and managed using the secure REDCap electronic data capture tools hosted at MetroHealth [25, 26].

For this cross-sectional analysis of evaluations performed at the entry visit, all PWH enrolled through October 2024 were included. People without HIV were excluded because there were too few enrolled to provide appropriate power for between group comparisons. For this analysis, participants were categorized as controls if they reported no substance use in the past year and tested negative for all illicit substances and marijuana in urine and hair toxicology screens. Participants with substance use were classified by the number of substances they used identified by self-report or by toxicology. Single-substance use was defined by reported use of or tested positive for 1 of the following substances: marijuana, cocaine, methamphetamine, opioid, sedative, or hallucinogen. Polysubstance use was defined as having 2 or more positive substances as described previously on urine and/or hair toxicology testing.

Study Evaluations

The entry visit includes completion of the NIDA-Modified Alcohol, Smoking, and Substance Involvement Screening Test (nmASSIST), an SDOH questionnaire, the Friendship Scale, the Adverse Childhood Experiences (ACEs) questionnaire, the PTSD Checklist Civilian, and the DSM-5 Cross-Cutting Symptom Measure (CCSM1) by participant self-report to study staff. Study visits take place in a private environment with the participant and 1 study staff member present during completion of surveys. Participants are encouraged to be truthful in their responses and that their responses will not adversely affect their clinical care. The nmASSIST details lifetime and current use (within the past 3 months) [27]. The tool provides substance specific risk score (low, moderate, high). For the cohort, the tool has been supplemented with questions to calculate lifetime use and age at first use. Self-reported substance use in the past 3 months on nmASSIST is used along with toxicology data to categorize participants. Urine toxicology screening is performed on all participants at MetroHealth in the clinical laboratory using an automated chemistry analyzer and enzyme immunoassay. Positives are confirmed using gas chromatography/mass spectrometry when discrepant from self-reported data. Hair toxicology is performed on all participants by Quest Diagnostics (Lenexa, KS). Collection occurs as per Quest's Hair Testing for Drugs of Abuse Specimen Collection Procedures and Information guide. Hair is screened by laser diode thermal desorption-tandem mass spectrometry and immunoassay at the initial screen cutoff levels. Positives are confirmed by mass spectrometry at confirmatory cutoff level.

The SDOH questionnaire is a compilation of validated screening questions embedded in our electronic health record that is used by our institution to ascertain SDOH domains at risk by self-report. Responses to the questionnaire are entered in the electronic health record as well as the research database to ensure that referral pathways are triggered when indicated. The specific SDOH domains assessed are financial resource strain [28, 29], housing [30], transportation [31], food insecurity [32], intimate partner violence [33], utilities, and internet

access. Each domain is scored as "at risk" or "not at risk." For housing instability, transportation needs, intimate partner violence, utility, and internet access needs, any "yes" answer is categorized as "at risk." For financial resource strain, a response of at least "somewhat hard" and for food insecurity, a response of at least "sometimes true" are categorized as "at risk." The total number of SDOH domains at risk was defined as the sum of SDOH domains that met at "at risk" designation. The Friendship Scale is a 6-item survey of social isolation that has been validated and used in studies with PWH [34, 35]. The ACEs questionnaire is a 10-question survey about common traumatic experiences that occur in early life which provides a quantitative assessment of self-reported prior trauma [36]. The survey covers abuse, household challenges and neglect before the age of 18 years. Each question is answered yes or no, with 1 point assigned to each yes answer. A higher score indicates higher risk for social-, emotional-, and health-related problems as an adult. The PTSD Checklist Civilian is a validated and reliable, self-report instrument designed to assess for symptoms of PTSD that map to DSM-IV diagnostic criteria [37, 38]. The CCSM1 is an established measure that has good to excellent test–retest reliability and has been subjected to psychometric validation. Participants who respond with ≥2 on CCSM1 (symptoms for several days in past 2 weeks) were assigned a value of 1 for that mental health domain. Total number of DSM-5 domains was defined as the sum of CCSM1 positive screening (as discussed previously) for depression, anger, mania, anxiety, somatic symptoms, psychosis, sleep problems, memory, repetitive thoughts and behavior, dissociation, and personality functioning [39–41].

Statistical Analysis

Descriptive statistics were calculated for all variables. Continuous variables were summarized using means and standard deviations, whereas categorical variables were summarized using frequencies and percentages. Differences in clinical and demographic characteristics between substance use groups were assessed using chi-squared tests for categorical variables and 1-way analysis of variance for continuous variables.

Linear regression models were fit using maximum likelihood estimation to examine the association between the independent variable of interest, substance use status categorized as polysubstance, single substance, or no substance use/controls, and continuous outcomes including: total number of SDOH domains at risk, total number of positive DSM-5 domains, and ACES score. Cofounding variables included in each model included: sex at birth, age, race, and income level categorized as >$20 000 and ≤$20 000.

Logistic regression models were employed to assess the odds of experiencing SDOH domains at risk (financial resource strain, housing stability, transportation needs, food insecurity, intimate partner violence, utilities, and internet access), screening positive for DSM-5 domains (depression, anger, mania, anxiety, somatic symptoms, psychosis, sleep problems, impaired memory, repetitive thoughts/behaviors, dissociation, and personality functioning), having moderate to high PTSD symptoms, and experiencing social isolation (each outcome dichotomized as yes vs no) for PWH with polysubstance use and single substance use compared to PWH with no substance use. Again, all models were adjusted for sex, age, race, and income.

Given the exploratory nature of this study, we did not perform adjustments for multiple comparisons. The primary goal of this analysis was to generate hypotheses and identify potential associations for future research. An alpha level of 0.05 was used in the analysis to determine statistical significance for all models and tests. Statistical analysis was conducted using SAS 9.4 for Windows.

RESULTS

Demographics, HIV and Substance Use-related Characteristics

From May 2022 through October 2024, 171 PWH were enrolled. Of these, 135 (79%) were PWH with any substance use and 36 (21%) were controls. Polysubstance use was present in half of the participants with any substance use (67 of 135 or 50%). See Table 1 for demographic, HIV, and substance use-related characteristics for the 3 groups (polysubstance use, single substance use, and control groups). Participants in the substance use groups were younger than controls with mean ± standard deviation age of 52 ± 12 versus 49 ± 14 versus 57 ± 13 years for polysubstance versus single substance versus controls, respectively ($P = .02$, overall). The majority of participants (75%) were male at birth and there were more transgender women in the substance use groups (4% vs 12% vs 0%; $P = .05$ for polysubstance use vs single substance use vs controls, respectively). Most participants (61%) were Black and 13% were of Hispanic ethnicity. Sexuality was similar across groups with 41% identifying as gay or lesbian, 12% as bisexual, and 36% as straight. HIV characteristics were similar between groups. All participants had prescriptions for antiretroviral therapy and the majority (91%) had HIV-1 RNA levels ≤200 copies/mL. Mean ± standard deviation current CD4+ cell count was 651 ± 369 cells/mm^3.

All but 2 participants had medical insurance (both without insurance were in the polysubstance use group). Income level did differ between the groups with higher proportions of participants with income below poverty level (≤$20 000 annually) in both substance use groups compared to controls (70% vs 61% vs 42%; $P = .02$ for polysubstance use vs single-substance use vs control, respectively). There were also differences in proportion of participants with children between groups; PWH with polysubstance use were more likely to have children than controls (61% vs 36%; $P = .02$). See Table 2 for distribution of substances used in the substance use groups. Substance use groups were more likely to report daily nicotine use (55% vs

Table 1. Demographic, HIV, and Substance Use–related Characteristics by Group

	Polysubstance (Group 1) n = 67	Single Substance (Group 2) n = 68	Control (Group 3) n = 36	*P* 1 versus 3	*P* 2 versus 3	*P* 1 + 2 versus 3	*P* 1 versus 2
Age, y	52 ± 12	49 ± 14	57 ± 13	.07	<.01	.01	…
Sex							
Male	52 (78%)	52 (76%)	25 (69%)	…	…	…	…
Female	15 (22%)	16 (24%)	11 (31%)	…	…	…	…
Gender				…	.04	.09	…
Cisgender	64 (96%)	60 (88%)	34 (100%)	…	…	…	…
Transgender	3 (4%)	8 (12%)	0 (0%)	…	…	…	…
Race				.07	…	.06	…
Black	44 (66%)	43 (63%)	17 (47%)	…	…	…	…
Other	23 (34%)	25 (37%)	19 (53%)	…	…	…	…
Ethnicity							
Hispanic/Latino	9 (14%)	8 (12%)	5 (14%)	…	…	…	…
Sexuality							
Gay or lesbian	29 (43%)	25 (37%)	16 (44%)	…	…	…	…
Bisexual	9 (13%)	9 (13%)	2 (6%)	…	…	…	…
Straight	21 (31%)	27 (40%)	13 (36%)	…	…	…	…
Declined/blank	8 (12%)	7 (10%)	5 (14%)	…	…	…	…
HIV-related							
HIV-1 RNA ≤ 200 cps/mL	58 (87%)	63 (93%)	34 (94%)	…	…	…	…
CD4, cells/mm^3	646 ± 407	636 ± 366	688 ± 302	…	…	…	…
Financial							
No insurance	2 (3%)	0 (0%)	0 (0%)	…	…	…	…
Income <$20 000	40 (70%)	35 (61%)	15 (42%)	<.01	.06	.01	…
Has children	35 (61%)	29 (48%)	13 (36%)	.02	…	.05	…
Substances Used							
Cannabis	57 (53%)	50 (47%)	-	-	-	-	.09
Cocaine	50 (81%)	12 (19%)	-	-	-	-	<.001
Methamphetamine	19 (95%)	1 (5%)	-	-	-	-	<.001
Opioids	16 (89%)	2 (11%)	-	-	-	-	<.001
Sedatives	6 (100%)	0 (0%)	-	-	-	-	.01
Hallucinogens	6 (100%)	0 (0%)	-	-	-	-	.01
Daily nicotine	35 (52%)	28 (41%)	6 (17%)	<.01	.01	<.01	…
Moderate/high Risk alcohol use[a]	35 (56%)	38 (56%)	7 (19%)	<.01	<.01	<.001	…

Values shown are frequency (column percent) for categorical variables and mean ± standard deviation for continuous variables. *P* values shown were those ≤.1 for between-group comparisons.

[a]Moderate- to high-risk Substance Involvement Score for alcohol use by NIDA-modified Alcohol, Smoking, and Substance Involvement Screening Test.

41% vs 17%; $P < .01$ for polysubstance use vs single substance use vs control, respectively) and moderate- to high-risk alcohol consumption (56% vs 56% vs 19%; $P \leq .01$).

Social Drivers of Health

Of the 7 SDOH domains assessed (see Table 3), proportions of participants at risk financially (12%), for intimate partner violence (15%), and for lack of internet access (31%) were similar among the groups ($P > .3$ for all, for overall among 3 groups). However, for housing instability ($P = .05$ for any substance use vs controls), transportation needs ($P < .01$), food insecurity ($P < .01$), and utilities ($P < .01$), PWH who use any substances were more likely to be at risk than controls. Further, the polysubstance group had the highest proportion of participants with SDOH domains at risk. In unadjusted analysis, nearly half of PWH in the polysubstance use group were at risk for housing insecurity and this was significantly higher than for controls (48% vs 25%; $P = .02$). However, this association did attenuate with adjustment with adjusted odds of housing instability of 2.22 (95% confidence interval, 0.84-5.84) and 1.48 (0.56-3.93) for polysubstance use and single-substance use compared to controls, respectively. Similar trends were apparent for transportation (31% vs 29% vs 8%), food insecurity (64% vs 60% vs 35%), and utilities (43% vs 38% vs 14%) with lesser differences between the substance use groups. Each of these differences remained significant with adjustment (see Figure 1) with 2 to 5 times odds of SDOH domains at risk for PWH with polysubstance use or single substance use compared with controls, except for utilities, which was no longer significant in the adjusted model. Last, the total number of SDOH domains at risk was highest in

Table 2. Combinations of Substances Used by Toxicology Screens of Participants Who Use Substances

	Marijuana	Cocaine	Meth	Opioid	Sedative	Hallucin	N = 132[a]
1 drug 65 (49.2%)	XXX						50 (37.9)
	…	XXX	…	…	…	…	12 (9.1)
	…	…	…	XXX	…	…	2 (1.5)
	…	…	XXX	…	…	…	1 (0.8)
2 drugs 50 (37.9%)	XXX	XXX					31 (23.5)
	XXX	…	XXX	…	…	…	6 (4.5)
	XXX	…	…	XXX	…	…	5 (3.8)
	XXX	…	…	…	XXX	…	2 (1.5)
	…	XXX	XXX	…	…	…	2 (1.5)
	…	XXX	…	…	XXX	…	1 (0.8)
…	…	…	…	XXX	XXX		1 (0.8)
	…	XXX	…	XXX	…	…	1 (0.8)
	…	…	XXX	…	XXX	…	1 (0.8)
3 drugs 14 (10.6%)	XXX	XXX		XXX			7 (5.3)
	…	XXX	XXX	…	…	XXX	3 (2.3)
	XXX	XXX	XXX	…	…	…	2 (1.5)
	XXX	…	XXX	XXX	…	…	1 (0.8)
	XXX	…	XXX	…	…	XXX	1 (0.8)
4 drugs 3 (2.3%)	XXX	XXX	XXX			XXX	2 (1.5)
	…	XXX	XXX	XXX	XXX	…	1 (0.8)

The column furthest to the right shows the frequency (column percent) of participants that tested positive by toxicology screen for the substance or combination of substances indicated in the corresponding row by XXX.

Abbreviations: Meth, methamphetamine; hallucin, hallucinogen.

[a]Three participants who reported substance use had no positive toxicology results.

Table 3. Social Driver of Health Domains at Risk by Group

	Polysubstance (Group 1) n = 67	Single Substance (Group 2) n = 68	Control (Group 3) n = 36	*P* 1 versus 3	*P* 2 versus 3	*P* 1 + 2 versus 3	*P* 1 versus 2
SDOH domains at Risk[a]							
Financial	8 (12%)	8 (12%)	4 (11%)				
Housing	32 (48%)	26 (38%)	9 (25%)	.02		.05	
Transportation	21 (31%)	20 (29%)	3 (8%)	<.01	.01	>.01	
Food	43 (64%)	41 (60%)	13 (36%)	<.01	.02	>.01	
Safety	11 (16%)	12 (18%)	3 (8%)				
Utilities	29 (43%)	26 (38%)	5 (14%)	<.01	.01	>.01	
Internet access	25 (37%)	17 (25%)	11 (31%)				
Number of SDOH Domains at risk	3.3 ± 2	2.9 ± 2.2	2.0 ± 1.7	<.01	.04	>.01	
Social isolation[b]	34 (51%)	34 (50%)	13 (36%)				

Values shown are frequency (column percent) for categorical variables and mean ± standard deviation for continuous variables. *P* values shown were those ≤.1 for between-group comparisons.

Abbreviation: SDOH, social drivers of health.

[a]At risk by domain from the Social Drivers of Health Survey.

[b]Some isolation to very isolated by the Friendship Scale.

PWH with polysubstance use, followed by single substance use, and then controls (3.3 ± 2 vs 2.9 ± 2.2 vs 2 ± 1.7, respectively; $P < .01$ overall). With adjustment, total number of SDOH domains at risk remained significantly different between groups overall ($P < .05$), which was driven by the difference between the polysubstance use and control groups where PWH with polysubstance use had 1.08 higher number of SDOH domains at risk than controls ($P = .02$).

Social isolation was measured separately in the cohort and proportion of participants reporting at least some isolation to being very isolated (48%) was similar among the groups ($P = .29$).

Mental Health Diagnoses

For all the DSM-5 domains assessed, there was at least some evidence that PWH in the substance use groups had higher proportions of participants that screened positive than the control

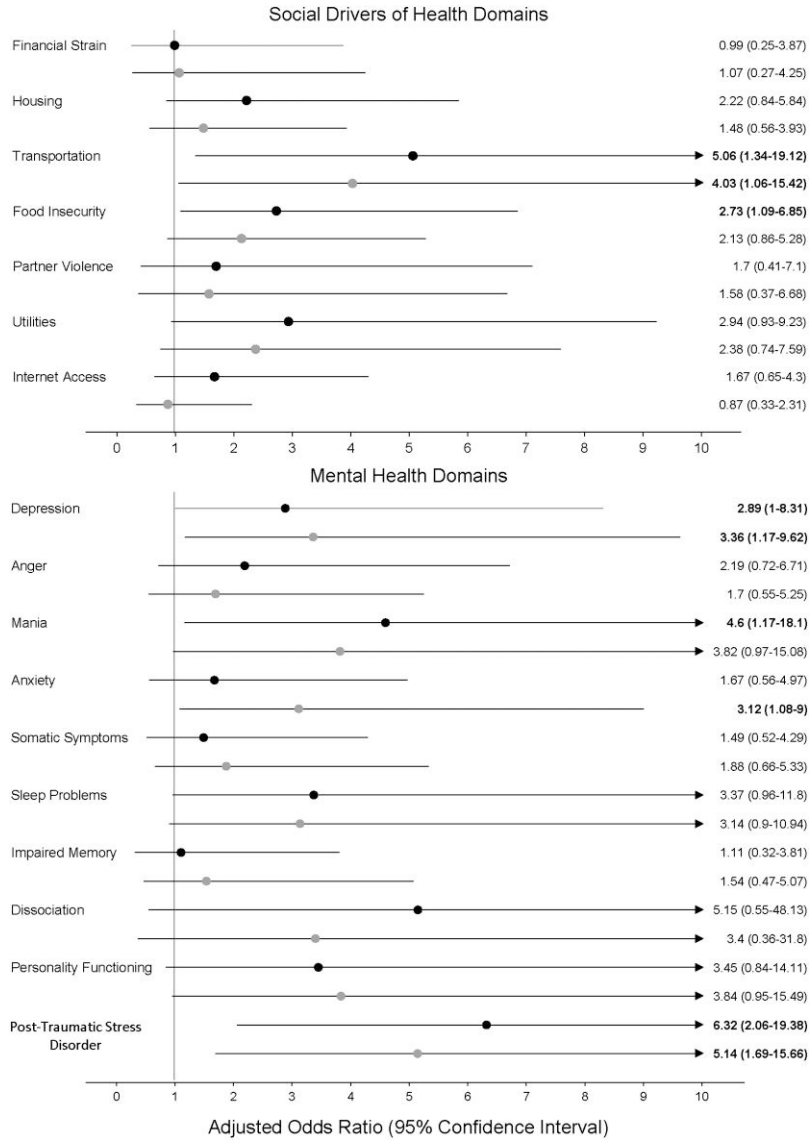

Figure 1. Odds of social driver of health domains at risk and presence of mental health symptoms for people with HIV with polysubstance use and single-substance use compared to no substance use. Dots represent adjusted odds ratio for each social driver of health and mental health domain and lines represent 95% confidence intervals around each odds ratio. Black dots represent the adjusted odds ratios for participants with polysubstance use compared with controls; gray dots are for participants with single-substance use compared with controls. Values on the right are the adjusted odds ratios described. Bolded adjusted odds ratios have *P* value <.05. Odds ratios for psychosis and repetitive thoughts and behaviors not reported (zero participants in control group reported these symptoms).

group. Five of the DSM-5 domains were significantly different among the 3 groups in unadjusted analyses; these included depression, mania, anxiety, repetitive thoughts and behaviors, and personality functioning (all $P \leq .02$) (see Table 4). Although some associations attenuated slightly in adjusted analyses, the adjusted odds of depression symptoms were 2.89 (95% confidence interval, 1-8.31) and 3.36 (1.17-9.62), of mania were 4.6 (1.17-18.1) and 3.82 (0.97-15.08), and of anxiety were 1.67 (0.56-4.97) and 3.12 (1.08-9) for PWH with polysubstance use and single-substance use compared to controls, respectively. There was also some evidence that sleep problems with adjusted odds of 3.37 (0.96-11.8) and 3.14 (0.9-10.94), and personality functioning with adjusted odds of 3.45 (0.84-14.11) and 3.84 (0.95-15.49) were more likely for PWH with polysubstance use and single substance use compared to controls, respectively, as well. Additionally, PWH in the substance use groups had higher total number of DSM-5 domains screen positive compared to controls (adjusted differences in means 1.24 [$P < .05$] and 1.46 [$P = .02$] for polysubstance use and single substance use versus control, respectively).

PWH who use any substances had higher ACEs scores indicating a greater history of childhood trauma compared to controls ($P = .01$ for any substance use vs control) (see Table 4). The difference in mean ACEs score remained significant for

Table 4. Positive Mental Health Domain Screens by Group

	Polysubstance (Group 1) n = 67	Single Substance (Group 2) n = 68	Control (Group 3) n = 36	*P* 1 versus 3	*P* 2 versus 3	*P* 1 + 2 versus 3	*P* 1 versus 2
Positive DSM-5 domains[a]							
Depression	26 (39%)	30 (44%)	6 (17%)	.02	<.01	>.01	
Anger	21 (31%)	22 (32%)	6 (17%)		.09	.07	
Mania	20 (30%)	23 (34%)	3 (8%)	.01	<.01	>.01	
Anxiety	20 (30%)	30 (44)	6 (17%)		<.01	.02	.09
Somatic Symptoms	24 (36%)	26 (38%)	7 (19%)	.08	.05	.05	
Psychosis	8 (12%)	8 (12%)	0 (0%)	.03	.03	.03	
Sleep problems	20 (30%)	18 (26%)	4 (11%)	.03	.07	.04	
Impaired memory	11 (16%)	14 (21%)	5 (14%)				
Repetitive	10 (15%)	13 (19)	0 (0)	.02	<.01	>.01	
Thoughts/behaviors	8 (12%)	8 (12%)	1 (3%)				
Dissociation	16 (24%)	20 (29%)	3 (8)	.05	.01	.02	
Personality Functioning							
Number of DSM-5 Domains	2.7 ± 3	3.1 ± 3.2	1.1 ± 1.6	<.01	<.001	>.001	
ACEs score	3.9 ± 2.9	3.4 ± 2.7	2.3 ± 2.8	<.01	.06	.01	
Moderate/high PTSD symptoms[b]	33 (49%)	34 (50%)	5 (14%)	<.001	<.001	>.001	

Values shown are frequency (column percent) for categorical variables and mean ± standard deviation for continuous variables. *P* values shown were those ≤.1 for between group comparisons.

Abbreviations: ACEs, Adverse Childhood Experiences; PTSD, posttraumatic stress disorder.

[a]Symptoms for several days in the past 2 weeks by DSM-5 Self-Rated Level 1 Cross-Cutting Symptom Measure.

[b]Moderate to high symptoms on Post-Traumatic Stress Disorder Checklist-Civilian instrument.

polysubstance use versus control in adjusted analysis (adjusted difference in mean ACEs score 1.34; $P = .03$, and .87; $P = .16$ for polysubstance use and single substance use compared to control, respectively). Further, proportion of participants having moderate to high PTSD symptoms were significantly higher in PWH who use substances (see Table 4) with adjusted odds of at least moderate PTSD symptoms of 6.32 (2.06-19.38) and 5.14 (1.69-15.66) for polysubstance use and single substance use, respectively, compared to control.

DISCUSSION

In this study, among PWH who use substances and are engaged in HIV care, polysubstance use was common. It is especially notable that polysubstance use, but not single-substance use, was independently associated with reporting more SDOH domains at risk, and more adverse childhood trauma than PWH with no substance use. Also, PWH who use any substances reported more mental health symptom domains than controls and whether polysubstance use or single-substance use was less important than for SDOH where only polysubstance use was associated with number of SDOH domains at risk in adjusted analysis.

Although prior studies have demonstrated the association of mental health, prior trauma, and SDOH with substance use [23, 42], we found that polysubstance use specifically was associated with higher proportions of participants with SDOH domains at risk than the other groups and even with adjustment for demographics and income level, PWH with polysubstance use had on average 1 more SDOH domain at risk than controls. Although single-substance use was associated with several SDOH domains at risk, after adjustment, only transportation need was significant compared to controls.

Interestingly, even though the frequency of SDOH domains at risk was consistently greater in the polysubstance group in the adjusted models, mental health symptom domains were more frequent among both substance using groups compared with controls. Future research should more thoroughly explore how the frequency, duration, and severity of substance use patterns interact with and affect SDOH and mental health domains.

Because this is cross-sectional analysis, it is unclear whether substance use preceded and led to lower income and higher social needs or if the higher social needs increased the likelihood of substance use. Experiencing childhood trauma has been associated with increased substance use; the association of PTSD symptoms with polysubstance use supports the possibility of substance use being a coping mechanism related to trauma. Screening for prior trauma when patients first engage in care and especially in those with polysubstance use may be helpful to identify individuals who will need more support, resources, and time from the care team.

We were curious about the correlation between polysubstance use and having greater number of children despite relatively equal proportions of males and females in the 3 groups. Research suggests that individuals with moderate to severe polysubstance abuse patterns generally have higher levels of

impulsivity, often associated with novelty and sensation seeking [43]. Poor impulse control and decision-making abilities may contribute to limited preplanning and higher levels of condomless sex with consequent pregnancies. However, it is also possible that the stress of parenting led to an increase in substance use. Although our data do allow us to examine general substance abuse patterns, we are unable to sequence substance use history and patterns with childbirth dates to inform this intriguing finding more fully.

We were pleased to see there was no difference in HIV viral suppression rates or mean CD4+ cell counts between groups; however, it is concerning that substance use correlated with regular tobacco use and moderate to high-risk alcohol use. The negative health effects of both are well studied; however, future studies should seek to understand their role in health outcomes among persons who use other substances.

It is essential that we consider the intersecting epidemics of poverty, substance use, and mental health and its associated impact on health. Thus, when screening for substance use, it is important to also screen for SDOH domains at risk as well as mental health symptoms. Developing patient-centered, integrated care models are necessary to improve overall health outcomes, especially among persons who use substances. Rather than siloing care for substance use and mental health, strategies to integrate services are needed. It may be appropriate and necessary to focus on addressing health-related social needs before either mental health needs or substance use needs can be addressed such as seen in the MAX clinic in Seattle or Housing First initiatives [44, 45]. Addressing these immediate health and concrete social needs enhances patient engagement, which then optimizes the referral and retention of patients in a second tier of much-needed mental health and substance abuse treatment services. Our results support integration of social services including assistance with housing, transportation, and food into care as well; however, in our study population of PWH who use substances engaged in HIV care where links to these resources are readily available, it is clear that additional novel approaches to improve SDOH domains at risk are needed.

Although these study results are not generalizable to all PWH, the participants in this study represent a broad range of substances used and the spectrum from occasional to daily use reflecting real-world substance use among PWH engaged in HIV care. It should be noted that in our study population the prevalence of cocaine use was higher and prevalence of methamphetamine and opioid use was less than has been described in other studies of PWH. Peak opioid, methamphetamine, and cocaine use commonly occurs in adults ages 18 to 34 years, and use generally declines with advancing age. We suspect that the difference in prevalence is because our study population was older with mean age older than 50 years. This too reflects our clinic population. As the population of PWH ages, it has become increasing important to study older populations to understand the cumulative effects and patterns of substance use in PWH. Our finding regarding the prevalence of cocaine use is an example of this. We suspect PWH who developed cocaine addictions earlier in life may persist in their use patterns as they age. Furthermore, based on the low reported subject income levels and the higher price of powdered cocaine, crack versus powdered cocaine may be more prominently used, although we cannot verify this from our data.

Some additional limitations warrant discussion. In this cross-sectional study, we are unable to infer causality as temporality of the exposure versus outcome could not be established. Although our total sample size was not small, we did have limited power to include all potential confounders and interaction terms in the multivariable modeling, and in this observational study, unmeasured confounding is possible. Defining our exposure of interest in terms of number of substances used does not allow distinguishing the effect of individual substances on the outcomes. However, we chose this exposure to understand correlates of polysubstance use given the challenge in research of accounting for multiple substances used to add to the literature on this trend. The SDOH survey identifies risk status related to 7 important domains. Although the risk status assessment and related frequency count totals supply important information, they do not provide a method to rank the impact of each driver on the quality of life or health. Likewise, the CCSM1 provides a screening triggering the need for a more detailed assessment of select mental health disorders. Further in-depth analyses of mental health disorder severity, interactions and contributions to SDOH, and other outcomes were beyond the scope of this study. With regard to generalizability, as mentioned previously our study population encapsulates PWH engaged in HIV care. Further, this study was performed at a single hospital system based in an academic institution and may not generalize to other locations given difference in substance use, social context, and resources. Last, it is important to acknowledge that this study did not adjust for multiple comparisons, which increases the risk of Type I errors. Given the exploratory nature of this research, our primary goal was to generate hypotheses and identify potential associations for future confirmatory studies. Although some of our findings may be due to chance, the reporting of effect sizes and confidence intervals provides a more comprehensive understanding of the magnitude and precision of our results. Future research should replicate these findings with larger sample sizes and more stringent control for multiple comparisons.

In conclusion, the results of this study exemplify the importance of understanding HIV and substance use disorder health challenges through the lens of the complex social contexts that impact patient care. The intersections of health, behavioral, and social factors highlight the importance of utilizing holistic, integrated, person-centered care models to more effectively address the individual and environmental complexities present within this population.

Notes

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