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Depressive Symptoms and Substance Use: Changes Overtime among a Cohort of HIV-positive and HIV-negative MSM

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Abstract

Background—The objective of this study was to examine depressive symptoms overtime and quantify the variance in symptoms attributable to substance use among a cohort of HIV-positive and HIV-negative men.

Methods—Participants were enrolled in an NIH/NIDA funded cohort, with 534 men resulting in 1,888 visits between August 2014 and June 2018. Participants were between 18 and 45 years, and half were HIV-positive. At baseline and semi-annual visits, information was collected on depressive symptoms, sexual behaviors, and substance use. Changes overtime in symptom scores were evaluated using individual growth curve modeling.

Results—The average CES-D_{20} score was 19.5 (SD=12.7). Depressive symptoms were highest among daily/weekly methamphetamine users (56% vs. 39% occasional users and 27% non-users; p value<.01). Factors independently associated with depressive symptoms included methamphetamine use (adjusted OR=1.5; 95% CI 1.1–2.3) and transactional sex (adjusted OR=1.8; 95% CI 1.4–2.5). Based on growth curve modeling, methamphetamine was the most influential predictor of depressive symptoms, accounting for 10% of individual variance (p value<.01). Declines in depressive symptoms were noted for heavy users of a number of drugs, except for methamphetamine. For instance, those reporting daily/weekly heroin had a 3.38 point decline in

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Contributors

MJ formulated the research question and MJ, SS, and PG designed the study. MJ conducted statistical analyses and drafted the initial manuscript. MJ, RB, SS, and PG contributed to the conception of the analyses. All authors contributed to the interpretation of the results, manuscript writing, and approved the final manuscript.

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Conflict of Interest

No conflict declared

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$CESD_{20}$ scores overtime (p value=0.01). However, heavy methamphetamine users had much higher $CESD_{20}$ scores and their scores remained high overtime (p value for change=0.91).

Conclusions—The prevalence of depressive symptoms among this cohort of HIV-negative and HIV-positive MSM was high, especially among frequent methamphetamine users. These findings suggest that reducing methamphetamine use may have the potential to reduce depressive symptoms.

Keywords

Depressive symptoms; Substance use; Methamphetamine; HIV; MSM

1. Introduction

Health disparities and inequalities across a wide range of health outcomes, including mental health have been noted among sexual minorities (Buchmueller and Carpenter, 2010; Dilley et al., 2010; Lee et al., 2009; Medley et al., October 2016; NSDUH Data Review. Retrieved from http://www.samhsa.gov/data; Roberts et al., 2010; Struble et al., 2010). A recent population-based study found that compared to heterosexuals, sexual minorities were twice as likely to have a diagnosis of a mood disorder (including depression) even after adjusting for other factors such as age and education (Stinchcombe et al., 2018). Disparities in mental health and depression are often linked to experiences with stigma, discrimination, and substance use and further exaggerated among those who are younger, identify as bisexual, or are HIV-positive (Bing et al., 2001; Bjorkenstam et al., 2017; Dyer et al., 2012; la Roi et al., 2016; Medley et al., October 2016; NSDUH Data Review. Retrieved from http://www.samhsa.gov/data). Depression and substance use are often comorbid conditions with evidence indicating common genetic factors for both conditions (Kendler et al., 2003). However, disentangling the causal relationship between these conditions is challenging, especially given the bidirectional nature of substance use and depression. Data from the few studies that have explored this are mixed, with some studies finding that drug use precedes depression, while others note that drug use serves as a potential form of self-medication and follows the onset of depression (Grant et al., 2009; Grant et al., 2016).

Findings in the literature on the association between depressive symptoms and sexual behavior have been somewhat mixed among men who have sex with men (MSM). While some studies have found decreased interest in sex and sexual activity during times of increased depressive symptoms, others have found no association (Bradley et al., 2008; Crepaz and Marks, 2001; Dilley et al., 1998; Shiu et al., 2014). In studies where an association was noted, those with depressive symptoms had increases in the number of sexual partners, condomless sex, sexual encounters under the influence of drugs and alcohol, rates of exchange sex, and risk of sexually transmitted infections including HIV (Koblin et al., 2006; Meade and Sikkema, 2005; Reisner et al., 2009). Additionally, the co-occurrence of other issues such as substance use disorders along with depression increased the risk of HIV acquisition given the increased engagement in sexual transmission behaviors (Meade and Sikkema, 2005).

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Depression is not only a risk factor for HIV acquisition, but evidence also indicates that among those who are HIV-positive, the prevalence of depression is high with up to half of HIV-positive patients living with depression (Choi et al., 2016; Ciesla and Roberts, 2001; Meade and Sikkema, 2005; Nacher et al., 2010). The co-occurrence of depression and HIV has been associated with negative outcomes including reduced quality of life and functionality, increases in medical comorbidities, as well as reduced rates of antiretroviral therapy (ART) prescriptions, decreases in ART adherence, and higher viral loads (independent of adherence behavior) (Ammassari et al., 2004; Mayston et al., 2012; Mitchell et al., 2012; Nanni et al., 2015). However, most studies on depression have used a cross sectional study design and less is known about changes in depressive symptomatology over time and patterns of persistence over time, particularly in populations with competing risks for depression including sexual minority status, HIV-positivity, and substance use. Given the potential fluctuating nature of depressive symptoms and its association with HIV transmission and acquisition, our study aimed to examine the prevalence, correlates, and changes in depressive symptoms over time, among a cohort of HIV-positive and high risk HIV-negative young men who have sex with men (MSM). Correlates of interest included sociodemographic characteristics, sexual risk behaviors, and substance use. Beyond the shape and direction of change in depressive symptoms (i.e., does it remain flat, increase, or decrease), we also aimed to quantify the extent to which substance use including the various patterns of drugs used contribute to the differences in depressive symptomatology. We recognize the complex and ongoing interaction between these two disorders and hypothesize that substance use impacts the trajectory of depressive symptoms and can vary by type of substance used. Understanding changes in depressive symptoms overtime and the extent to which various substance use patterns serve as a facilitator for these changes will contribute to our understanding of the intersection of substance use and mental health. Furthermore, unique to our study is our specific focus on a highly vulnerable population and our ability to explore differences by HIV-status.

2. Methods

2.1 Study population and design

Data for this study were based on those collected from participants in the mSTUDY – an NIH/NIDA funded cohort of racial/ethnically diverse, HIV-positive and high-risk HIV-negative MSM. The mSTUDY has been described elsewhere (Fulcher et al., 2018; Javanbakht et al., 2018; Okafor et al., 2017), but briefly, study enrollment started in August 2014 and participants were recruited from two different study sites in Los Angeles, CA including a community-based organization providing services for the lesbian, gay, bisexual, and transgender community and a community-based university research clinic. Participants enrolled in the mSTUDY between August 2014 and June 2018 were included in this analysis and were if they were: (1) between 18 and 45 years of age, (2) identified as male at birth, (3) if HIV-negative, reported condomless anal intercourse with a male partner in the past 6-months, (4) capable of providing informed consent, and (5) willing and able to return to the study every six months to complete study related activities. By design, half of the participants were HIV-positive and half were HIV-negative.

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2.2 Study procedures and data collection

All participants provided written informed consent prior to study participation. At each study visit participants completed a self-administered, computer-based questionnaire. The questionnaire collected information on current depressive symptoms as well as demographics, substance use, and sexual risk behaviors. Current symptoms of depression were measured using the 20-item Center for Epidemiological Studies Depression Scale ($CES\text{-}D_{20}$), first at baseline and again during follow-up visits. The scale was originally developed to measure depressive symptomatology in the general population and has since been used in other populations including those with HIV (Choi et al., 2015; Eaton et al., 2004; Meader et al., 2011; Natamba et al., 2014; Radloff, 1977). The $CES\text{-}D_{20}$ measures depressive symptoms experienced in the past seven days as defined by the American Psychiatric Association Diagnostic and Statistical Manual (DSM-V) for a major depressive episode.

As part of the self-administered study questionnaire, participants were asked to report on the frequency of substance use in the past six months including the use of the following drugs: (1) cocaine powder; (2) crack cocaine; (3) ecstasy; (4) heroin; (5) marijuana; (6) methamphetamine; (7) 'party drugs' including GHB and ketamine; (8) poppers, and (9) illicit use of prescription medications. Frequent users for each drug was defined as those who reported weekly use or more often, occasional users were those who reported monthly use or less often, and non-users were those who reported no use. Questions on sexual behaviors relevant to this analysis focused on recent behaviors (past six months) and included information on number and gender of sex partners, reports of new sex partners, concurrent partnerships (i.e., sexual partnerships that overlap in time), and transactional sex defined as an exchange of money, drugs, shelter, or other goods for sex.

At each study visit samples were collected for STI/HIV testing. Urine samples as well as rectal and pharyngeal swabs were collected for chlamydia and gonorrhea testing using nucleic acid amplification testing (NAAT) technology (Aptima Combo 2®, GenProbe, San Diego, CA). Blood samples were collected for HIV testing among those who were HIV-negative and HIV-1 RNA levels for those who were HIV-positive. Blood samples were also collected for syphilis testing using the rapid plasma regain test (RPR), with confirmatory testing using the *Treponema pallidum* particle agglutination test (TPPA). All participants were scheduled to return every six months and the study procedures were repeated at each visit. The study was approved by the Institutional Review Board at the University of California Los Angeles.

2. 3 Analytic Strategy

The primary outcome of this analysis was depressive symptomatology. In order to create a dichotomous variable indicative of depressive symptoms we used a cut-point of 23 on the $CES\text{-}D_{20}$ score. The cut-point was found to be more optimal for use among HIV-positive individuals (sensitivity: 1.0; specificity: 0.87) as compared to the cut-point of 16, which is more widely used in the general population (Choi et al., 2015). Univariate analyses provided descriptive statistics for the sample overall and by depressive symptomatology status (i.e., $CES\text{-}D_{20} \geq 23$ vs. $CES\text{-}D_{20} < 23$). Comparisons of demographics, substance use, sexual risk

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behaviors, as well as clinical and laboratory characteristics between those who reported depressive symptoms compared to those who did not report depressive symptoms were based on chi-square methods adjusting for the effect of the subject (i.e., repeated measures). Factors associated with depressive symptomatology were assessed using regression analysis with generalized estimating equations (GEE) in order to account for the within subject correlations (Liang and Zeger, 1986; Zeger et al., 1988). We fit models with random intercepts and time effects to accommodate the repeated measures gathered from each participant and to allow participant-specific changes in the responses over time. Univariate analyses along with *a priori* knowledge informed variables for inclusion in the multivariable models.

Finally, we examined the unique trajectories and changes over time in depressive symptom scores using individual growth curve modeling (Goldstein et al., 1994; Willett JB, 1994). The individual growth model estimates both average and individual trajectories overtime thus allowing for an examination of inter- and intra-individual changes. Specifically, we used the *unconditional* growth model to express a mixed effects model in which the outcome (CES-D_{20} score) was modeled as a function of time allowing for a random intercept and slope. The *conditional* growth models were developed to consider substance use and HIV status as an explanatory variable. Separate *conditional* models were developed to consider substance use including a dichotomous substance use variable (i.e., yes, no), a three level substance use variable comparing methamphetamine, other drugs not including methamphetamine, and no drugs, as well as frequency of use. For the purposes of this analysis, the use of individual growth models allowed us to describe the overall trend in symptom scores over time – i.e., whether symptoms scores increased, decreased, or remained the same overtime both at the individual level and across individuals.

Additionally, we used the conditional linear growth models to determine whether, and to what extent HIV status and specific substance use patterns were associated with differences in changes in depressive symptom scores. All analyses were conducted using SAS version 9.4 (SAS Inc., Cary, NC).

3. Results

3.1 Characteristics of study population

Between August 2014 and June 2018, a total of 534 participants were enrolled in the mSTUDY with as much as 3.7 years of follow-up data. These participants accumulated a total of 1,888 visits, with 86% of participants having two or more visits, and 66% having 3 or more visits (median visits=3; range (1–7 visits). At baseline the average age of participants was 31.4 years (SD 7.0) with 43% identifying as African American, followed by 37% Hispanic/Latino and 14% white (Table 1). Nearly half reported being unemployed and 35% reported experiencing unstable housing in the 6 months prior to study enrollment. By design, half of the study participants (n=267) were HIV-positive. At baseline, HIV-positive patients were slightly older, were more likely to report being unemployed, and more likely to have a history of incarceration (Table 1).

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3.2 Prevalence of depressive symptomatology

The median CES-D_{20} score was 19 (interquartile range: 9–26) and prevalence of depressive symptoms (i.e., CES-$D_{20} \geq 23$) as reported across all study visits was 35% (n=656)(Table 2). Nearly half of those with a current prescription for antidepressants had depressive symptoms as compared to 29% of those without a prescription. The prevalence of depressive symptoms was higher in visits where participants reported unemployment (49% vs. 24%; p value<.01) as well as unstable housing (48% vs. 30%; p value <.01) and slightly higher among those who were HIV-positive (38% vs. 31%; p value=0.02). Additionally, differences in the prevalence were noted by both substance use and sexual behaviors. Among visits where participants reported methamphetamine use, nearly half reported depressive symptoms, as compared to 31% in visits where other drugs were reported (but not methamphetamine) and lowest in visits with no substance use (23%; p value<.01). Further exploration of substance use reveals a dose response relationship between amount of substance use and prevalence of depressive symptoms, with those in the highest use category (i.e., weekly or more often) having the highest prevalence of depressive symptoms as compared to those in the monthly or less often, and no drug use categories (Figure 1).

Analyses stratified by HIV-status showed differences in sexual risk behaviors associated with depressive symptoms by HIV-status. HIV-positive participants who reported having new sex partners in the past 6 months had a higher prevalence of depressive symptoms as compared to those without a new sex partner (42% vs. 31%; p value <.01). Among HIV-negative participants a higher prevalence of depressive symptoms was noted during visits in which both male and female sex partners were reported as compared to male only partners, as well as visits in which transgender sex partners were reported (45% vs. 30%; p value=0.04; 46% vs. 30%; p value <.01 respectively).

Based on multivariable analyses, adjusting for unemployment, antidepressant medication use, depressive symptoms at prior visit, and HIV-status, methamphetamine use was independently associated with CES-D_{20} scores ≥ 23. Specifically, we found that methamphetamine users were 1.5 times as likely to have high depressive symptoms scores as compared to non-substance users (adjusted odds ratio (AOR)=1.5; 95% confidence interval (CI) 1.1–2.3), which was also higher than those who reported substance use not including methamphetamine (AOR=1.4; 95% CI 1.0–2.1). Additionally, transactional sex was independently associated with high depressive symptom scores (past 3 months) (AOR=1.8; 95% 1.4–2.5).

3.3 Trajectory of depressive symptomatology

Results of the growth model analyses are presented in Table 3. Based on the unadjusted linear growth model, we find that the estimated variance of the intercept and slope (80.72 and 1.99, respectively) are statistically meaningful (p<.01), suggesting that individuals varied in depressive symptoms scores and that the rate and direction of change overtime also varied by individual. Looking across all participants, the average CES-D_{20} score of 19.08 decreased slightly over time (i.e., across visits), though this change was neither clinically or statistically meaningful (0.33 points; p value=0.06). In our multivariable analyses (as presented above), we found that substance use was an important factor associated with

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depressive symptoms with the individual growth model analyses further demonstrating that substance use – methamphetamine in particular – was an influential predictor of the rate of change in depressive symptoms. When examining substance use overall (i.e., as a dichotomous variable) we found that the variance of the intercept changed from 80.72 to 78.47, meaning substance use over time accounted for 2.8% change in the individual difference in CES-D_{20} scores (Table 3). However, when we further delineated the impact of methamphetamine use, including the frequency of use, we found that methamphetamine use accounted for 10.2% of the individual differences in depressive symptoms (80.72–72.51)/ 80.72], more than any of the other substance we examined including cocaine, ecstasy, heroin, marijuana, party drugs, poppers, and prescription drugs which only accounted for anywhere between <1 to 1.5% of the individual variance in depressive symptoms (Table 4). Additionally, we found that frequent methamphetamine users had a 5.37 point increase in depressive symptom scores compared to non-users (p value<.01), reduced to a 2.51 point increase among occasional methamphetamine user (compared to non-users; p value<.01) and this remained even after controlling for HIV-status (Table 3). With inclusion of HIV status in the model, we find that variance in mean depressive symptoms remained the same (72.51 vs. 72.56) – in other words, the temporal impact of HIV on depressive symptoms scores was negligible. Likewise the unexplained individual variance over time did not change; HIV positive participants had CES-D_{20} scores that were 0.90 points higher and a 0.43 point faster increase in scores per visit when compared to those without HIV, though this difference was not statistically significant (p value=0.38 and 0.18, respectively).

Across study visits we see clinically and statistically meaningful differences between depressive symptom scores when comparing methamphetamine users to other substance users and non-substance users (Figure 2). However, given that the interaction between methamphetamine use and time was not statistically significant, the modest changes in depression scores overtime are not different for methamphetamine users compared to non-users (Table 3). In fact, we find significant declines in depressive symptoms for heavy users of a number of drugs, though this is not the case for methamphetamine (Table 4). For instance, participants who reported using heroin weekly or more often had a 3.38 point decline in $CESD_{20}$ scores overtime (p value=0.01), with similar patterns noted for heavy users of cocaine, ecstasy, and party drugs). However, methamphetamine users, especially heavy methamphetamine users on average had much higher $CESD_{20}$ scores (Figure 2, Table 3) and their scores remained high overtime (non-significant change of 0.13; p value=0.91) (Table 3).

4. Discussion

Findings from this study indicate that more than a third of this cohort of younger MSM reported symptoms consistent with depression. The longitudinal nature of our study and our extensive data on the various types and frequency of substances used allowed us to quantify the contribution of each substance to differences in depressive symptoms overall and with time. We found that while substance use was associated with symptoms of depression, methamphetamine use more than any other drug accounted for increases in depressive symptoms and was a more influential determinant of depressive symptom scores than HIV-status. Furthermore, we found that frequent methamphetamine use was associated with

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persistence of depressive symptoms even though frequent users of other drugs showed declines in depressive symptoms overtime. Finally, the equal distribution of HIV-positive and negative participants allowed us to identify sexual risk behaviors associated with depressive symptoms while considering the specific risk profiles for both HIV transmission and acquisition.

Our finding that non-substance users had the lowest depression scores was not unexpected, though our result showing that those who used substances less frequently had lower depression scores suggests that reductions in the amount of substance use even in the absence of abstinence may be associated with improvements in symptoms of depression. Additionally, relative to other substances, reduced use of methamphetamine had the greatest impact on depressive symptoms. While the cessation of drug use is the principal objective of any drug abuse treatment program, substance use disorders are often described as chronic relapsing conditions with relapse rates as high as 60% (Connors et al., 1996; McLellan et al., 2000). Consequently, consideration to 'harm reduction strategies' that lead to a decrease in methamphetamine use (not just abstinence) may still be helpful in this context. In fact, a randomized study of a 16-week substance use treatment program among methamphetamine dependent men found that reductions in negative outcomes (including depression) were linearly correlated with methamphetamine use (Jaffe et al., 2007). While the greatest benefit was seen for those who achieved methamphetamine abstinence, there were still benefits gained from reduced methamphetamine use. Likewise, another study specifically among methamphetamine using MSM found that those who reported a decrease in stimulant use showed reductions in sexual risk behaviors and improvements in indicators of HIV care (Carrico et al., 2014).

Management of depression has its own treatment cascade and despite the fact that depression is highly prevalent among sexual minorities, including those who are HIV-positive, it is widely underdiagnosed, untreated, and undertreated (Pence et al., 2012; Weaver et al., 2008). In fact, a recent analysis of the depression treatment cascade in the context of HIV care found that less than half of patients with a major depressive disorder were diagnosed clinically, 18% were receiving any treatment with only 7% receiving adequate treatment (Pence et al., 2012). Findings from our study support this in that nearly one-third of our participants who reported symptoms consistent with depression were not receiving pharmacological treatment. Additionally, our finding that half of those who reported depressive symptoms were in fact receiving medication for depression lends support to results that suggest that substance use may in fact affect medications used in the treatment of depression resulting in less benefit from these treatments (Grelotti et al., 2017). Although it has been suggested that strategies are needed to treat depression in parallel with substance use (Delaney et al., 2018), our data suggest that interventions that initially target reductions in substance use (methamphetamine in particular) may be useful in evaluating the extent to which co-morbid conditions such as depression decline before starting treatment regimen that target depression.

The relationship between substance use, depression, and risky sexual behaviors is likely complex and may be difficult to disentangle the effect of one factor on the other. For instance, our finding that those who reported transactional sex had a two fold increase in the

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odds of depressive symptoms may not only suggest a direct path from sex work to depression but may likely be indicative of an indirect path where sex work becomes an economic necessity for people who use drugs regularly. Other studies along with our previous work demonstrate that not only is transactional sex associated with substance use, but that a majority of the transactions may be occurring for the purpose of obtaining drugs (Bauermeister et al., 2017; Javanbakht et al., 2018; Weber et al., 2001). The intertwined nature of substance use, depression, and sexual risk behaviors suggests that this "syndemic" of conditions should be addressed concurrently particularly relevant to those who are dually effected.

There are several limitations to this study. First, the majority of our data elements including sexual risk behaviors and substance use were based on self-report which can result in an underestimation of these behaviors. Our use of computer assisted self-interviews may help to minimize reluctance in reporting behaviors that are socially stigmatized or illegal and may help to minimize the potential response bias (Catania et al., 1990; Fendrich et al., 1999). While the CES-D_{20} is a widely used validated tool for measuring depressive symptoms, it is not intended as a diagnostic tool for major depressive disorders. However, we hope that the use of a more conservative cut-point, validated among HIV-positive populations will help to increase the construct validity of the scale and allow for measurement of symptoms that are more closely aligned with a clinical diagnosis of depression (Choi et al., 2015). Disentangling the temporal ordering of substance use and depressive symptoms is challenging given our data and it's difficult to say whether substance use led to depressive symptoms or whether the symptoms led to substance use. Our data measure depressive symptoms in the past seven days and substance use in the past six months so in that sense our measure of substance use precedes symptoms. Additionally, when we lagged the substance use by one visit (i.e., substance use reported 12 months prior to visit when depressive symptoms were reported) the results remained the same (data not shown). However, the potential chronicity and persistence of the behaviors and our outcome of interest makes it difficult to determine which is the cause and which is the effect. Finally, this study was based on participants recruited from a community based sexual health clinic and a university based research clinic and may not be generalizable to other populations.

The prevalence of depressive symptoms among this cohort of high risk HIV-negative and HIV-positive MSM was relatively high, especially among substance users. Additionally, frequent methamphetamine use was associated with persistence of depressive symptoms even though frequent users of other drugs showed declines in depressive symptoms overtime. Our findings reinforce the importance of providing effective substance use treatment and suggest that interventions targeted at reducing substance use and methamphetamine in particular may reduce depressive symptoms and impact other co-occurring issues such as sexual risk behaviors.

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Highlights

- Frequent heroin and methamphetamine users had the highest prevalence of depressive symptoms
- Compared to other substances, methamphetamine was the most influential predictor of depressive symptoms accounting for 10% of individual variance in symptoms
- Declines in depressive symptoms overtime noted for most drugs, except for methamphetamine users who showed no change overtime

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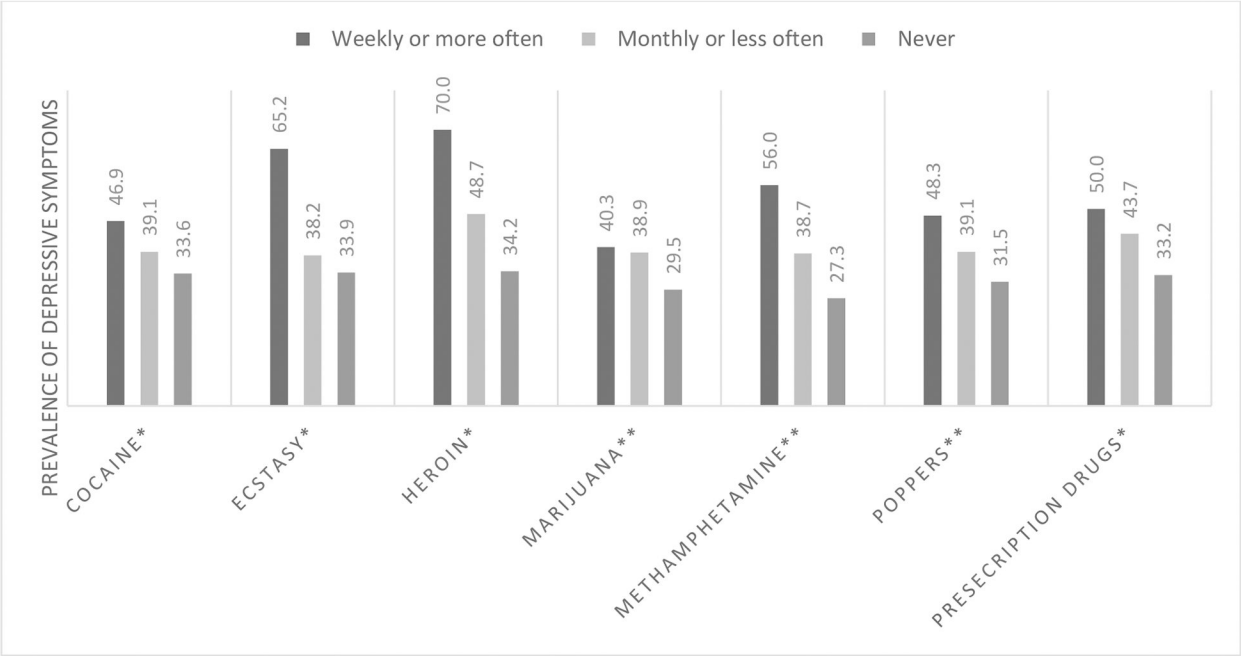

Figure 1.

Prevalence of depressive symptoms by type and amount of substance use (past 6 months) among mSTUDY participants (8/2014–6/2018)

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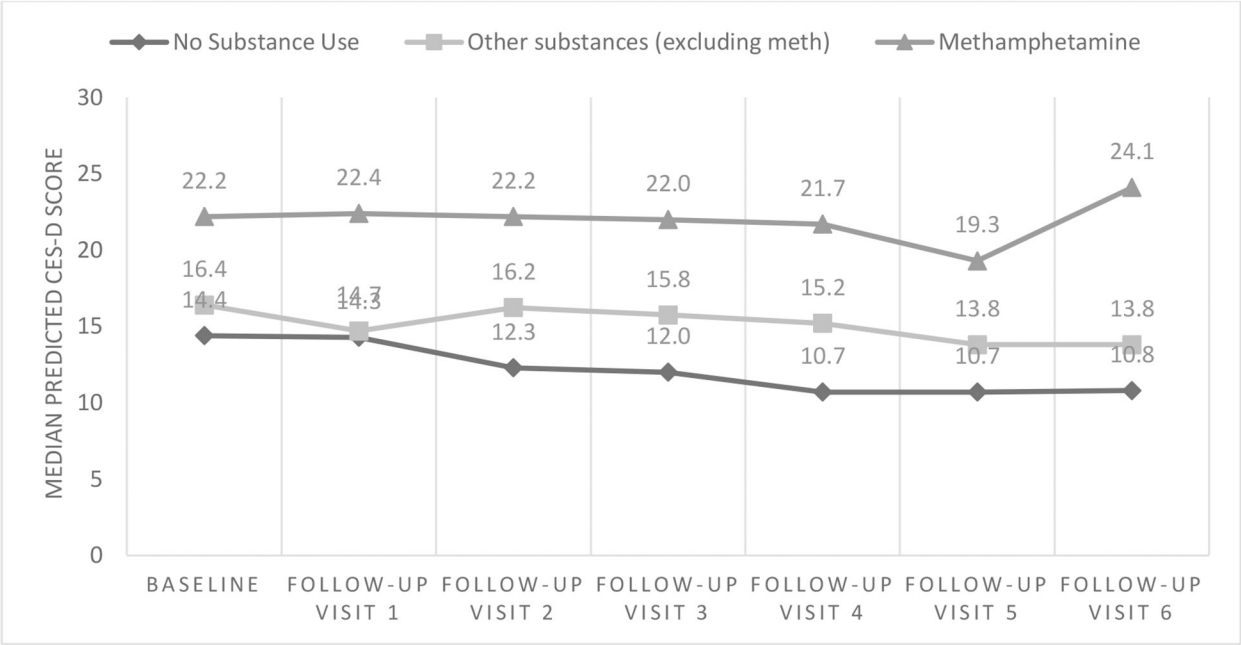

Figure 2.

Predicted CESD scores across study visit, by substance use status among mSTUDY participants (8/2014–6/2018)

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Table 1.

Baseline characteristics among mSTUDY participants, by HIV status (8/2014 – 6/2018)

	Total (n=534)^		HIV-positive (n=267)^		HIV-negative (n=267)^		P value
	n	%	n	%	n	%	
Socio-demographic characteristics							
Age, mean(SD)	31.4 (7.0)		33.8 (6.6)		29.1 (6.6)		<.01
Race/ethnicity							0.13
African American	228	42.7	110	41.3	118	44.1	
Hispanic/Latino	196	36.7	97	36.3	99	37.1	
Other	37	6.9	15	40.5	22	8.2	
White	73	13.7	45	16.9	28	10.5	
Education							0.06
< High School	66	12.5	41	15.7	25	9.4	
High School Graduate	193	36.5	97	37.2	96	36.0	
> High School Graduate	269	51.0	123	47.1	146	54.6	
Unemployed	237	45.8	145	56.4	92	35.4	<.01
Unstable Housing, past 6 months *	189	35.4	94	35.2	95	35.6	0.93
Ever Incarcerated	208	39.1	117	44.1	91	34.1	0.02

Abbreviations. SD=Standard deviations

^ Sum may not equal total due to missing information

* Defined as not having a regular place to stay in the past 6 months

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Table 2.

Prevalence of depressive symptoms across study visits among mSTUDY participants, by HIV-status (8/2014 – 6/2018)

	Total (n=1,888 visits)			HIV-positive (n=964 visits)			HIV-negative (n=924 visits)		
	CES-D Score ≥ 23		P value~	CES-D Score ≥ 23		P value~	CES-D Score ≥ 23		P value~
	n	%		n	%		n	%	
Total	656	34.8	--	366	37.8	--	290	31.4	--
Socio-demographic characteristics									
Age at study visit, mean (SD)			0.76			0.45			0.46
CES-D Score ≥ 23	32.4 (6.8)			34.6(6.3)			29.9(6.6)		
CES-D Score < 23	32.5 (7.1)			35.0(6.7)			30.5(6.6)		
Race/ethnicity			0.95			0.95			0.87
African American	279	35.1		143	38.0		136	32.5	
Hispanic/Latino	218	32.7		133	35.6		85	28.9	
Other	61	37.9		26	42.6		35	35.0	
White	98	37.0		64	41.6		34	30.6	
Unemployed			<.01			<.01			<.01
Yes	385	49.2		242	50.2		143	47.5	
No	248	23.9		106	24.0		142	23.8	
Unstable Housing, past 6 months *			<.01			0.08			<.01
Yes	252	48.2		125	50.8		127	45.9	
No	404	29.6		241	33.6		163	25.2	
Substance use behaviors									
Smoker, current (cigarettes)			<.01			0.03			<.01
Yes	266	49.3		152	46.9		114	52.8	
No	325	29.1		172	33.5		153	25.3	

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	Total (n=1,888 visits)			HIV-positive (n=964 visits)			HIV-negative (n=924 visits)		
	CES-D Score ≥ 23		P value~	CES-D Score ≥ 23		P value~	CES-D Score ≥ 23		P value~
	n	%		n	%		n	%	
Binge drinking, past 6 months			0.73			0.28			0.82
Yes	329	35.5		155	39.1		174	32.7	
No	326	34.2		211	37.4		115	29.7	
Substance use (mutually exclusive categories), past 6 months			<.01			<.01			<.01
Methamphetamine use	338	47.1		230	47.4		108	46.6	
Other substance use (excluding methamphetamine)	204	30.6		78	34.4		126	28.6	
No substance use	113	22.8		58	23.3		55	22.3	
Specific drugs used, past 6 months									
Cocaine			0.03			0.32			0.02
Yes	143	40.2		64	41.8		79	38.9	
No	512	33.6		302	37.8		210	29.3	
Ecstasy			0.05			0.09			0.20
Yes	104	40.6		57	45.6		47	35.9	
No	551	33.9		309	37.0		242	30.7	
Heroin			0.02			0.33			0.02
Yes	32	56.1		12	57.1		20	55.6	
No	623	34.2		354	37.7		269	30.5	
Marijuana			<.01			<.01			0.01
Yes	388	39.8		203	45.1		185	35.2	
No	267	29.5		163	31.9		104	26.5	
Methamphetamine			<.01			<.01			<.01
Yes	338	47.1		230	47.4		108	46.6	

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	Total (n=1,888 visits)			HIV-positive (n=964 visits)			HIV-negative (n=924 visits)		
	CES-D Score ≥ 23		P value[~]	CES-D Score ≥ 23		P value[~]	CES-D Score ≥ 23		P value[~]
	n	%		n	%		n	%	
No	317	27.3		136	28.6		181	26.4	
Poppers			<.01			<.01			0.71
Yes	253	41.8		167	49.4		86	32.2	
No	402	31.5		199	31.9		203	31.1	
Prescription drugs			0.01			0.02			0.18
Yes	115	45.6		62	54.9		53	38.1	
No	540	33.2		304	35.6		236	30.3	
Sexual behaviors									
Gender of Sex Partners, past 6 months			0.07			0.50			0.04
Male only	598	34.0		354	37.8		244	29.7	
Male and Female	58	45.0		12	44.4		46	45.1	
New Sex Partner, past 6 months			0.01			0.03			0.08
Yes	461	37.4		246	42.3		215	33.0	
No	195	29.8		120	31.4		75	27.6	
Transgender Anal Sex Partner, past 6 months			0.01			0.22			<.01
Yes	66	49.3		22	56.4		44	46.3	
No	590	33.7		344	37.2		246	29.7	
Intimate Partner Violence, past 12 months[**]			<.01			<.01			<.01
Yes	158	54.5		91	55.8		67	52.8	
No	478	30.9		266	34.2		212	27.5	
Concurrent Sexual Partnership, past 6 months			0.98			0.66			0.84

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	Total (n=1,888 visits)			HIV-positive (n=964 visits)			HIV-negative (n=924 visits)		
	CES-D Score ≥ 23		P value~	CES-D Score ≥ 23		P value~	CES-D Score ≥ 23		P value~
	n	%		n	%		n	%	
Yes	248	34.4		132	40.9		116	29.2	
No	323	32.8		186	34.3		137	30.9	
Received $/drugs/shelter for sex, past 3 months			<.01			<.01			<.01
Yes	172	57.5		99	62.7		73	51.8	
No	449	29.7		252	32.6		197	26.6	
Clinical and Laboratory Factors									
HIV-serostatus			0.02						
HIV-positive	366	37.8		--	--		--	--	
HIV-negative	290	31.4		--	--		--	--	
HIV-1 RNA ≤ 20 copies/mL^						0.09			
Yes	--	--		188	34.8		--	--	
No	--	--		174	41.6		--	--	
Any STI (Chlamydia, Gonorrhea, or Infectious Syphilis)			0.39			0.35			0.96
Yes	131	38.5		81	39.5		50	37.0	
No	521	33.9		284	37.5		237	30.5	
Prescription for Antidepressant#			<.01			<.01			<.01
Yes	270	49.4		168	48.3		102	51.3	
No	386	28.8		198	32.1		188	26.0	

Abbreviations. SD=Standard Deviation; PrEP=Pre-exposure Prophylaxis

~p value adjusts for the effect of the subject (i.e. multiple observations for the same participant)

*Defined as not having a regular place to stay in the past 6 months

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** Defined as being hit, kicked, or slapped by a lover, boyfriend/girlfriend when that person meant to hurt you physically

^ Among HIV-positive participants

Includes prescription for antidepressants including SSRIs, SNRIs, and TCAs

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Table 3.

Individual growth models for longitudinal changes in depressive symptoms among mSTUDY participants (8/2014–6/2018)

	Unconditional growth model			Conditional growth model: Substance Use (yes vs. no)			Conditional growth model: Substance Use (meth vs. other drugs vs. no drugs)			Conditional growth model: Meth Use Frequency			Conditional growth model: Meth Use Frequency and HIV status		
	Estimate	(SE)	P value	Estimate	(SE)	P value	Estimate	(SE)	P value	Estimate	(SE)	P value	Estimate	(SE)	P value
Random Variance															
Intercept	80.72	6.61	<.01	78.47	6.51	<.01	73.67	6.25	<.01	72.51	6.16	<.01	72.56	6.14	<.01
Linear slope	1.99	0.55	<.01	1.93	0.55	<.01	1.88	0.54	<.01	1.85	0.52	<.01	1.82	0.52	<.01
Residual	61.22	2.60	<.01	61.48	2.63	<.01	61.79	2.63	<.01	61.26	2.60	<.01	61.22	2.60	<.01
Fixed Effects															
Intercept	19.08	0.48	<.01	17.29	0.82	<.01	17.14	0.81	<.01	17.36	0.56	<.01	16.93	0.68	<.01
Visit	−0.33	0.16	0.06	−0.26	0.29	0.36	−0.26	0.29	0.36	−0.18	0.19	0.36	−0.28	0.23	0.11
Meth use															
Weekly or more often										5.37	0.95	<.01	5.33	0.97	<.01
Monthly or less often										2.51	0.89	<.01	2.47	0.91	<.01
Never										0.00			0.00		
Meth Use*Time															
Weekly or more often										0.13	0.39	0.73	0.04	0.39	0.76
Monthly or less often										−0.04	0.36	0.91	−0.11	0.37	0.91
Never										0.00			0.00		
HIV-positive													0.90	0.92	0.36
HIV-positive*Time													0.43	0.32	0.18

Abbreviations. SE=standard error; meth=methamphetamine

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Note. Unconditional growth model only includes the temporal predictor of time without other explanatory variables; the conditional growth models include random effects (i.e., slope and intercept) and is conditioned on the specific predictor variable noted in the column

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Table 4.

Individual growth models examining association with type and amount of substance use and variation and change in depressive symptoms scores overtime among mSTUDY participants (8/2014 – 6/2018)

	% Difference in individual variation explained in CES-D_{20} scores*	Change in CES-D_{20} Score overtime (95% CI)	P value
Cocaine	0.7%		
Weekly or more often		−2.42 (−3.24 to −1.60)	<.01
Monthly or less often		−0.21 (−0.60 to 0.18)	0.59
Never		0	
Ecstasy	0.3%		
Weekly or more often		−3.23 (−4.54 to −1.92)	0.01
Monthly or less often		0.23 (−0.21 to 0.67)	0.61
Never		0	
Heroin	0.9%		
Weekly or more often		−3.38 (−4.69 to −2.07)	0.01
Monthly or less often		−2.70 (−4.04 to −1.36)	0.03
Never		0	
Marijuana	1.2%		
Weekly or more often		−0.29 (−0.60 to 0.02)	0.32
Monthly or less often		−0.33 (−0.73 to 0.07)	0.40
Never		0	
Methamphetamine	10.2%		
Weekly or more often		0.13 (−0.23 to 0.49)	0.91
Monthly or less often		−0.04 (−0.42 to 0.34)	0.73
Never		0	
Party drugs	1.5%		
Weekly or more often		−1.86 (−2.75 to −0.97)	0.04
Monthly or less often		−0.09 (−0.53 to 0.35)	0.84

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	% Difference in individual variation explained in CES-D_{20} scores*	Change in CES-D_{20} Score overtime (95% CI)	P value
Never		0	
Poppers	0.7%		
Weekly or more often		−0.83 (−1.34 to −0.32)	0.10
Monthly or less often		0.16 (−0.18 to 0.50)	0.63
Never		0	
Prescription drugs	1.4%		
Weekly or more often		−0.86 (−1.51 to −0.21)	0.19
Monthly or less often		0.69 (0.16 to 1.22)	0.19
Never		0	

*differences are measured as a change in the variance of the intercept of linear mixed model accounting for substance use and time