HHS Public Access

Author manuscript

Am J Drug Alcohol Abuse. Author manuscript; available in PMC 2017 January 20.

Published in final edited form as:

Am J Drug Alcohol Abuse. 2017 January ; 43(1): 103–110. doi:10.1080/00952990.2016.1191505.

Marijuana Use and Viral Suppression in Persons Receiving Medical Care for HIV-Infection

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Abstract

Background—Marijuana use is common among persons living with HIV (PLWH), but its effect on HIV clinical outcomes has not been thoroughly studied.

Objectives—We determined the association between marijuana use and HIV viral suppression among PLWH.

Methods—Data came from five repeated cross-sections (2009 – 2013) of the Florida Medical Monitoring Project, a population-based sample of PLWH in Florida. Data were obtained via interview and medical record abstraction. Weighted logistic regression models were used to determine the association between marijuana use (past 12-months) and durable viral suppression (HIV-1 RNA value of ≤ 200 copies/milliliter in all measurements within the past 12-months).

Results—Of the 1,902 PLWH receiving antiretroviral therapy and completed an interview and had a linked medical record abstraction, 20% reported marijuana use in the past 12 months (13% less than daily and 7% daily use). Of the total sample, 73% achieved durable viral suppression. In multivariable analysis, marijuana use was not significantly associated with durable viral suppression in daily [Adjusted Odds Ratio (AOR):0.87, 95% confidence interval (CI): 0.58, 1.33] or in less than daily [AOR: 0.83, 95% CI: 0.51, 1.37] users as compared to non-users when

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Conflicts of Interest

No conflicts declared

adjusting for sociodemographic factors, time since HIV diagnosis, depressive symptoms, alcohol, cigarette and other substance use.

Conclusion—In this sample of PLWH receiving medical care in Florida, there was no statistically significant association between marijuana use and viral suppression. As our findings suggest the possibility of a clinical important effect, there is a need for additional evidence from other samples and settings that include more marijuana users.

Keywords

Marijuana; viral suppression; persons living with HIV (PLWH); HIV

Introduction

The widespread use of antiretroviral therapy (ART) has resulted in a significant improvement in morbidity and reduced mortality among persons living with HIV (PLWH) (1), through the increase in CD4+ T-cell count (2,3) and HIV RNA viral suppression(4,5). Furthermore, maintaining suppressed viral loads may help reduce the rate of sexual transmission of HIV(6). Achieving sustained viral suppression is highly dependent on receiving ART and then maintaining near perfect adherence (≥ 80% adherence) to ART(7,8). While the majority of PLWH are able to maintain optimal levels of ART adherence, a substantial portion continue to experience sub-optimal ART adherence. Past studies have identified a number of factors associated with sub-optimal ART adherence including side effects(9), lack of self-efficacy(10), unstable housing or being homeless(11) and depressive symptoms(12). Substance use is one of the most consistently-reported factors that negatively influence ART adherence(13–15). Accordingly, PLWH who use alcohol and other illicit drugs are often less likely to achieve viral suppression(15–17).

Marijuana use is common among PLWH, with 14% to 56% reporting use within the past six months(18–23). Some PLWH report using marijuana to manage HIV-related symptoms as well as side effects of ART including chronic pain, nausea/vomiting, loss of appetite, and mood problems(18,19,22). Data from preclinical studies suggests that marijuana or other synthetic cannabinoids may attenuate HIV viral replication in primary CD4+ T cells(24,25). Further, others using Simian models have reported tetrahydrocannabinol (THC) administration to be associated with attenuation of plasma and cerebrospinal fluid viral load(26). Most of the immunomodulatory effects of marijuana and its constituents are proposed to be mediated via the action of cannabinoids on CB2 receptors which are predominantly located on peripheral immune cells(27). However, marijuana use may negatively influence viral suppression via its effect on the ability to maintain optimal ART adherence. Marijuana comprises a combination of different constituents which may have differential effects. Tetrahydrocannabidiol (THC) – the major psychoactive constituent of marijuana is thought to produce cognitive impairment in a number of relevant domains including memory, planning and organizational skills(28–30) which are critical in the ability to maintain ART adherence. In contrast, cannabidiol (CBD) – another important constituent may have therapeutic effects including: relief of anxiety(31,32) and antipsychotic effects(33). While marijuana may have therapeutic benefits, data on its impact on HIV clinical outcomes in PLWH are limited.

Findings from the few studies on the effect of marijuana use on viral suppression in PLWH have been mixed. One study found marijuana use to have no significant effect on plasma HIV viral loads (34), and two others reported lower plasma HIV viral loads in marijuana users(35,36). In another study, sex while under the influence of marijuana was significantly associated with increased odds of elevated seminal plasma viral load(37). Many of these previous studies have been limited by, lack of a control group of non-marijuana users(35), or lack of adjusting for relevant confounding factors in the relationship between marijuana and viral suppression(35,37). Florida is very relevant to this question, because it has the 3rd highest number of PLWH and the highest number of newly diagnosed HIV infections in the United States(38). As of early 2016, there are no laws allowing marijuana to be legally used (either recreationally or medically) for PLWH in Florida(39). However, voters will be considering a constitutional amendment to legalize medical marijuana in late 2016. Therefore, it is important to fully understand the potential impact of marijuana use in this population. Given recent findings suggesting a reduced HIV viremia(35,36), we hypothesized that marijuana use would be associated with greater odds of viral suppression in a dose-dependent manner. To this end, the objective of this analysis was to determine the relationship between marijuana use and durable viral suppression among a sample of PLWH.

Methods

Study sample

Data for this analysis come from the Florida Medical Monitoring Project (MMP), a multi-site national HIV surveillance system funded by the U.S Centers for Disease Control and Prevention to monitor clinical and behavioral characteristics in HIV-infected adults receiving medical care in the United States(40). Detailed methods of the MMP have been described previously(41). Briefly, the MMP uses a three-stage probability-based sampling method to obtain nationally representative, annual, cross-sectional adult samples of PLWH receiving medical care for HIV in the United States. In the first stage, U.S states and territories were sampled to participate. In the second stage, eligible facilities providing HIV care were selected to participate and in the final stage, PLWH within the participating facilities were sampled. Participant eligibility criteria for the MMP include a confirmed HIV diagnosis, age 18 or older, ability to complete a survey in English or Spanish, ability to complete an informed consent, and a HIV primary care visit at one of the sampled facilities. For the present analysis, we used data collected from 5 cross-sections of data collection cycles (2009 to 2013) from Florida. Data were collected via face-to-face interviews with sampled participants and a linked medical record abstraction. Given the 5 years of data, there were few persons in the analysis who completed the MMP survey more than once (n=73). However, MMP statistical guidelines indicate that these persons' data should be retained because excluding them tends to distort the variance calculations and thus produce spurious inferences. To determine the association between marijuana use and viral suppression, we restricted the analysis to only those participants on ART at the time of completing the survey (N=1,902).

Ethics Statement

The National Center for HIV, Viral Hepatitis, STD and TB Prevention's Office of the Associate Director for Science at the Centers for Disease Control and Prevention (CDC) has determined the MMP to be a nonresearch, public health surveillance activity used for disease control program and policy(42). As such, MMP is not subject to human subjects regulations, however participating states or territories and facilities obtained local institutional review board approval to conduct MMP if required locally. The present analysis was approved by the Institutional Review Board at the University of Florida.

Measures

Outcome variable

Durable Viral Suppression: Participants HIV-1 RNA value in the past 12 months was obtained via medical record abstraction. To account for the possibility that participants may have used marijuana at any time during the past 12 months prior to the interview, we defined durable viral suppression, as an HIV-1 RNA level that was undetectable or ≤ 200 copies per milliliter at every measurement in the past 12 months.

Independent variable—The primary independent variable was marijuana use in the past 12 months assessed via self-report. Participants reported how often they used marijuana in the past 12 months with the following response options: daily, weekly, monthly, less than monthly or none. In the present analysis, marijuana use was categorized into a three-level variable: daily; less than daily, or none.

Covariates

Sociodemographic characteristics: Sociodemographic variables assessed via self-report included: age (in years), gender, race/ethnicity status (categorized as white, non-Hispanic; black, non-Hispanic; Hispanic/Latino and Asian) and homelessness (defined as living on the street, in a shelter, a single-room occupancy hotel or in a car) in the past 12 months.

Clinical and Psychosocial Factors: Time since HIV diagnosis was assessed via self-report as the time (in years) since first positive test for HIV. A modified 8-item version of the Patient Health Questionnaire depression scale (PHQ-9) was used to assess the level of current (past two weeks) depressive symptomatology in the sample(43). Items from the PHQ-8 were summed with a resulting range of 0 to 24. We categorized scores <5 as none/minimal depression, 5–14 as mild/moderate depression and scores ≥ 15 as severe depression(44).

Alcohol, cigarette and other substance use: Participants self-reported their alcohol and cigarette use in the past 12 months. Alcohol use in the past 12 months was operationalized as hazardous drinking (defined as ≥ 7 drinks per week for women or ≥ 14 drinks per week for men(45), low or moderate use (any drinking not meeting criteria for hazardous use) or no alcohol use. Recent cigarette use was categorized as daily smoking, less than daily smoking or no smoking. For other substance use, we created a dichotomous summary variable that

indicated any use of illicit substances including: cocaine, heroin, methamphetamines, hallucinogens and other non-prescribed sedatives in the past 12 months versus no use.

Data Analysis

We computed weighted univariate frequencies of sociodemographic characteristics, clinical and psychosocial factors of the sample and compared their distributions by marijuana use using modified Rao-Scott chi-square tests. Next, bivariate and multivariable logistic regression analysis was conducted to assess the relationship between covariates of interests and durable viral suppression. Our strategy for constructing the multivariable models was to include the primary independent variable (frequency of marijuana use), covariates established a priori related to viral suppression from previous literature, covariates that were significant at the Bivariate analysis ($p \leq .10$) and the survey year that data was collected. In addition, we did not adjust for covariates that could potentially be in the causal pathway in the relationship between marijuana use and viral suppression (such as ART adherence). Two sensitivity analyses were conducted to understand: (1) the effect of varying the cut-off of viral suppression (i.e. defining viral suppression as a HIV-1 RNA level <75 copies/mL or <400 copies/mL) and (2) treating HIV-1 RNA levels on a $\log_{10}$ transformed scale in the analysis and back transformed to geometric means. For the second sensitivity analysis, we selected participant's most recent HIV-1 RNA measurement in the past 12 month as the outcome and to allow for statistical analysis, undetectable viral load values or values below the detection limit (<75 copies/mL or 50 copies/mL) were counted as 20 copies/mL prior to log transformation. Alpha was set at .05 in the multivariable analysis, crude and adjusted odds ratios are reported. All analysis accounted for the complex sampling design and unequal selection probabilities by using the PROC SURVEYLOGISTIC procedures in SAS version 9.4 (SAS Institute., Cary, NC, USA).

Missing data—Overall, missing data on the primary independent variable and covariates of interests were minimal (most ≤ 2%), however, approximately 8% (n=155) of participants had missing HIV-1 RNA measurement in their medical record. Among all covariates assessed, gender, race/ethnicity status and alcohol use were significantly associated ($p<.05$) with missing HIV viral load measurements (data not shown). We excluded participants with missing HIV viral load, however, in order to address the potential for biased estimates as a result of missing outcome data, we retained all predictors associated with missingness of HIV RNA measurement in the multivariable model(46).

Results

Sample Characteristics

The majority of the sample were 40 years of age or older (35% were 40 – 49 years and 47% were 50 years of age or older), of male gender (69%), of racial/ethnic minority status (43% black, non-Hispanic, 18% Hispanic/Latino and 3% Asian) and had 10 or more years since HIV diagnosis (60%; Table 1). Sixty-percent of the sample reported alcohol use (46% low to moderate and 14% hazardous use) and 36% reported cigarette use (7% less than daily and 29% daily use) and 11% reported other substance use. Twenty-percent of the sample reported marijuana use in the past 12 months (13% less than daily and 7% daily use; Table

1). Seventy-three percent of the sample (n=1,259) were durably virally suppressed, the mean number of viral load measurements for the whole sample was 3.8 with standard deviation (SD) =1.87. Number of viral load measurements was similar by viral suppression status: suppressed (mean=3.8, SD=1.83) and not suppressed (mean=3.9, SD=1.98).

Factors associated with marijuana use

Covariates that were associated with marijuana use are also shown in Table 1. As expected, alcohol, cigarette and other substance use were significantly associated with marijuana use (all ps <.0001). Marijuana use was also associated with younger age, male gender, white, non-Hispanic race/ethnicity status, homelessness and depressive symptoms.

Durable Viral Suppression

In bivariate analyses, marijuana users were significantly less likely to have suppressed viral load (68% vs. 74%; p=.0362) as compared to non-users (Table 1). In bivariate analysis of frequency of use, daily marijuana use was significantly associated with a decreased odds of viral suppression (OR= 0.68; 95% CI: 0.46, 0.99) as compared to non-users (Table 2). However, less than daily use of marijuana was not significantly associated with viral suppression compared to non-use (OR=0.76; 95% CI: 0.53, 1.10). In multivariable analysis that adjusted for age, gender, race/ethnicity status, homelessness, time since HIV diagnosis, depressive symptoms, alcohol, cigarette and other substance use, there was no statistically significant association between either daily (AOR=0.87; 95% CI: 0.58, 1.33) or less than daily marijuana use (AOR=0.83; 95% CI: 0.51, 1.37) and durable viral suppression. In sensitivity analysis that varied the cut-off threshold of viral suppression to <75 copies/mL and <400 copies/mL the results for the association between marijuana use and viral suppression remained relatively identical (data not shown). Similarly, when we conducted our analysis treating HIV-1 RNA level on a logarithm transformed scale; the results were in agreement with the analysis using the dichotomous cut-off threshold of viral suppression with no significant difference between adjusted geometric mean viral loads between both less than daily use (104.7; 95% CI=30.2, 362.1 copies/mL; p=0.0684) and daily use (125; 95% CI=35.4, 446.8 copies/mL; p=0.1610) as compared to nonuse (81.2; 95% CI: 37.2, 242.8 copies/mL).

Discussion

In this sample of PLWH who are engaged in medical care in Florida, we did not find a statistically significant association between daily or less than daily marijuana use in the past 12 months and durable viral suppression when adjusting for possible confounders.

A detailed online literature search identified four studies that have examined the relationship between marijuana use and HIV viral suppression and they each had different findings. *Abrams et al.* found no significant short term differences in plasma viral load among 67 HIV-infected individuals who were randomly assigned either to a 3.95% THC marijuana cigarette, a 2.5mg dronabinol (delta-9-teterahydrocannibol) capsule or a placebo capsule three times daily in a small, short duration (21 days) intervention clinical trial (34). In a more recent study by Ghosn et al.(2014), sex while under the influence of cannabis was

significantly associated with increased odds of a detectable HIV-1 RNA in the semen(37), among a sample of 157 HIV-infected men who have sex with men (MSM). Two studies have found lower viral load among marijuana users(35,36). Thames et al (2015), in a sample of 55 PLWH recruited from HIV clinics in the Los Angeles area, found lower viral load among light and moderate-to-heavy marijuana users as compared to non-users(36). A fourth study found daily cannabis use to be significantly associated with lower plasma viral load as compared to less than daily use among in a sample of 88 newly infected PLWH in Vancouver, Canada participating in an injection drug use study (35).

A potential reason for the disparate results may be related to differences in the study samples, as participants in our study were comprised of PLWH who are in care and were recruited from a variety of clinic settings in Florida. Prior studies that found marijuana use to be associated with reduced viral load(35,36), included samples that were recruited from regions that have legalized medical marijuana. It is possible that there are differences in the marijuana consumed (including the THC/CBD contents) in these samples than in our sample where medical marijuana is prohibited. Another significant difference in our study is that we analyzed marijuana use by frequency of use (i.e. daily, less daily and none), whereas the studies by Ghosn et al. (2014) averaged marijuana use into a yes vs. no category. Milloy et al. (2015) analyzed frequency of use but did not include a group of non-users. Some previous studies have revealed differential effects of marijuana use by frequency of use. For instance, a recent study from the Women's Interagency HIV Study (WIHS), found lower adherence to ART among all current marijuana users compared to non-users, but found that ART adherence was not reduced in daily marijuana users compared to non-users(18). Another plausible reason for the different results is in our adjustment for potential confounders in the association between marijuana use and viral suppression.

Data from preclinical studies suggest that marijuana or other synthetic cannabinoids may have a beneficial effect on reducing HIV viral loads and replication. In vitro studies have shown that THC may reduce HIV viral replication in primary CD4+ T cells(24,25). Investigators using non-human primates reported that chronic THC administration initiated prior to and throughout the asymptomatic phase of simian immunodeficiency virus (SIV) was associated with reduction of plasma and cerebrospinal fluid viral load(26). Our results reported here are in somewhat contrast with findings from these studies; however caution is advised when extrapolating findings from non-human primates to humans. One potential explanation for our contrasting findings is that marijuana consumption in humans is often highly correlated with the use of other substances and past studies have found alcohol(15), cigarette (47) and cocaine (48) to impact negatively on viral suppression.

The present study found a statistically significant association between daily marijuana use and reduced odds of viral suppression in bivariate analysis which was no longer significant in a multivariable analysis, suggesting that marijuana use is associated with some other factors that are in need of further investigation in the relationship between marijuana use and viral suppression. The confidence intervals around the adjusted odds ratios for the association between daily and less than daily marijuana use were relatively wide – spanning both the negative, null and positive range – but particularly toward the negative range. Furthermore, the lower limits of the confidence intervals of the odds ratios include sets of

odds ratios that may be considered clinically significant (i.e. 42% decreased odds and 49% decreased odds of viral suppression for daily and less than daily marijuana use respectively). It is possible that confidence intervals may have been narrower if more marijuana users were available for analysis; therefore such considerations are important in planning future work where a more targeted recruitment of marijuana users would allow for more precise inference of effects within this group. Additionally, future studies should consider collecting more precise measures of marijuana use (e.g. quantity, dose, and specific THC/CBD ratio of the marijuana consumed) in order to clarify this relationship. The strengths of our study include the use of probabilistic sampling of a large racial/ethnically diverse sample of PLWH receiving care. However, we offer some caution in the interpretation of our study findings. As our study utilized a cross-sectional design we are not able to infer whether the findings reported here are causal. In addition, marijuana use was assessed via self-report over a period of 12 months, and data may be subject to recall or social desirability bias. Finally, this analysis was conducted among PLWH receiving medical care in Florida between 2009 and 2013, thus our findings may not be generalizable to other settings among PLWH that are not receiving routine HIV care.

Conclusion

Currently there are shifting trends to legalize marijuana for medical and recreational purposes, with 23 states passing laws that allow medical use of marijuana for patients with qualifying conditions. Persons living with HIV may have increased access to marijuana, despite limited scientific data on the therapeutic and or harmful effects of marijuana use in this population. In this study there was no statistically significant association between daily and less than daily marijuana use and viral suppression. Our results should not be interpreted as definitive evidence that marijuana use is harmless for viral suppression. In order to inform the field and clarify the clinical importance of the effect of marijuana use on viral suppression and other HIV-related outcomes, there is a need for additional evidence in other samples and settings, with larger samples and finer measures of marijuana use.

Acknowledgments

The authors will like to thank Karalee Poschman, MPH and all MMP staff for their interviewing and medical record abstraction efforts. The authors will also like to thank MMP patients for their cooperation and participation in the project.

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Am J Drug Alcohol Abuse. Author manuscript; available in PMC 2017 January 20.

Table 1

Characteristics of the MMP sample by marijuana use

Characteristics	Total[P] (N=1,902) [95% CI]		Marijuana use (n=372) [95% CI]		No marijuana use (n=1,530) [95% CI]		*p*-value
	N	(%)	n	(%)	n	(%)	
Age (years)							**.0093**
18–29	103	(5) [4, 7]	28	(7) [4, 11]]	74	(5) [3, 6]]	
30–39	248	(13) [12, 15]	58	(15) [12, 19]	189	(13) [11, 14]	
40–49	662	(35) [32, 37]	143	(39) [32, 47]	517	(33) [31, 36]	
≥ 50	889	(47) [44, 50]	143	(39) [32, 43]	742	(49) [46, 52]	
Gender							
Male	1294	(69) [64, 75]	293	(80) [74, 85]	995	(67) [61, 72]	**<.0001**
Female	608	(31) [25, 36]	79	(20) [15, 26]	527	(33) [28, 39]	
Race							**.0004**
White, non-Hispanic	659	(36) [30, 43]	171	(47) [39, 54]	485	(34) [27, 40]	
Black, non-Hispanic	854	(43) [37, 49]	137	(35) [29, 42]	714	(44) [38, 51]	
Hispanic/Latino	337	(18) [15, 21]	53	(15) [10, 20]	282	(19) [15, 22]	
Asian	52	(3) [2, 4]	11	(3) [1, 5]	41	(3) [2, 4]	
Homeless[†]							
No	1770	(93) [92, 94]	338	(90) [87, 93]	1424	(94) [92, 95]	**.0113**
Yes	132	(7) [6, 8]	34	(10) [7, 13]	98	(6) [5, 8]	
Years since HIV diagnosis							
≤ 5	342	(18) [16, 20]	65	(18) [14, 23]	276	(18) [16, 20]	.2301
6 – 10	437	(22) [20, 25]	73	(19) [16, 23]	362	(23) [21, 26]	
10+	1120	(60) [57, 63]	233	(62) [27, 68]	882	(59) [56, 62]	
Depression – Past 2 weeks							**<.0001**
None-minimal	1499	(79) [77, 82]	278	(75) [70, 80]	1221	(81) [78, 83]	
Moderate/severe	214	(12) [10, 14]	39	(10) [7, 13]	175	(12) [10, 14]	
Severe	167	(9) [7, 11]	53	(15) [11, 18]	114	(7) [6, 9]	
Alcohol use[†]							**<.0001**
None	754	(39) [35, 43]	67	(18) [14, 22]	687	(44) [40, 49]	

Characteristics	Total[ρ] (N=1,902) [95% CI]		Marijuana use (n=372) [95% CI]		No marijuana use (n=1,530) [95% CI]		*p*-value
	N	(%)	n	(%)	n	(%)	
Low to moderate	853	(46) [43, 50]	207	(56) [50, 61]	645	(44) [40, 48]	
Hazardous	274	(14) [13, 16]	96	(27) [21, 32]	178	(11) [10, 13]	
Cigarette use[†]							**<.0001**
None	1214	(64) [61, 67]	157	(42) [36, 48]	1055	(70) [67, 72]	
Less than daily	126	(7) [5, 88]	35	(9) [6, 13]	91	(6) [5, 7]	
Daily	553	(29) [26, 32]	180	(49) [43, 54]	373	(24) [22, 27]	
Other substance use[†¶]							
No	1691	(89) [87, 91]	241	(63) [57, 70]	1450	(95) [94, 96]	
Yes	202	(11) [9, 13]	130	(37) [30, 43]	72	(5) [4, 6]	
Durable viral suppression[‡]							**.0362**
≤ 200 copies/ml	1259	(73) [70, 75]	236	(68) [63, 73]	1019	(74) [71, 77]	
> 200 copies/ml	488	(27) [25, 30]	114	(32) [27, 37]	371	(26) [23, 29]	
Marijuana use[†]							
None	1530	(80) [78, 83]	–		–		
Less than daily	238	(13) [11, 14]	–		–		
Daily	134	(7) [6, 8]					

Note: ρ Data does not always sum to total sample size due to missing data for specific variables

[†]Past 12 months,

[¶]Includes cocaine, heroin, methamphetamines, hallucinogens, and other non-prescribed sedatives;

[‡]Obtained via medical record abstraction and is based on those individuals on ART with an HIV RNA measurement available.

Table 2

Bivariate and multivariable associations between marijuana use and durable viral suppression

	Durable Viral Suppression (≤ 200 copies/ml)			
Characteristics	**OR 95% CI**	***p-value***	**AOR 95% CI**	***p-value***
Age (vs. 18–29)		**.0036**		.2145
30–39	1.51 (0.95, 2.39)		1.16 (0.67, 2.01)	
40–49	1.68 (1.13, 2.51)		1.31 (0.80, 2.14)	
≥ 50	2.28 (1.45, 3.58)		1.58 (0.97, 2.57)	
Gender (vs. Female)		**.0133**		.5738
Male	1.34 (1.06, 1.70)		1.09 (0.81, 1.45)	
Race/ethnicity (vs. White, Non-Hispanic)		**<.0001**		**<.0001**
Black, non-Hispanic	0.45 (0.35, 0.57)		0.51 (0.38, 0.69)	
Hispanic/Latino	0.67 (0.48, 0.95)		0.72 (0.50, 1.04)	
Asian	0.46 (0.24, 0.89)		0.51 (0.24, 1.05)	
Homeless (vs. No)		**<.0001**		**<.0001**
Yes	0.24 (0.18, 0.34)		0.31 (0.21, 0.46)	
Time since HIV diagnosis (vs. <5 yrs.)		**.0067**		**.0481**
5 – 9	1.91 (1.26, 2.88)		1.85 (1.13, 3.03)	
≥ 10	1.59 (1.14, 2.23)		1.39 (1.00, 1.95)	
Depression (vs. None-minimal)		**.0178**		.2322
Moderate/severe	0.88 (0.60, 1.28)		1.04 (0.71, 1.52)	
Severe	0.64 (0.47, 0.87)		0.75 (0.54, 1.05)	
Alcohol use (vs. None)		.3443		.8783
Low to moderate drinking	1.07 (0.81, 1.43)		1.02 (0.74, 1.40)	
Hazardous	0.82 (0.58, 1.17)		0.92 (0.59, 1.41)	
Cigarette use (vs. None)		**.0007**		**.0443**
Less than daily	0.88 (0.55, 1.39)		1.03 (0.64, 1.65)	
Daily	0.59 (0.45, 0.77)		0.67 (0.49, 0.92)	
Other substance use (vs. None)[¶]				
Yes	0.67 (0.49, 0.90)	**.0102**	0.92 (0.57, 1.49)	.7492
Marijuana use (vs. None)		.0580		.7205
Less than daily	0.76 (0.53, 1.10)		0.83 (0.51, 1.37)	
Daily	0.68 (0.46, 0.99)		0.87 (0.58, 1.33)	

Note – Model adjusted for survey year; OR=Odds Ratio; AOR=Adjusted Odds Ratio;

[¶]Includes cocaine, heroin, methamphetamines, hallucinogens, and other non-prescribed sedatives;