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Marijuana Use and Achievement of Abstinence from Alcohol and Other Drugs among People with Substance Dependence: A Prospective Cohort Study

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Abstract

Background—Many with alcohol and other drug dependence have concurrent marijuana use, yet it is not clear how to address it during addiction treatment. This is partially due to the lack of clarity about whether marijuana use impacts one's ability to achieve abstinence from the target of addiction treatment. We examined the association between marijuana use and abstinence from other substances among individuals with substance dependence.

Methods—A secondary analysis of the Addiction Health Evaluation And Disease management study, a randomized trial testing the effectiveness of chronic disease management. Individuals met criteria for drug or alcohol dependence and reported recent drug (i.e. opioid or stimulant) or heavy alcohol use. Recruitment occurred at an inpatient detoxification unit, and all participants were referred to primary medical care. The association between marijuana use and later abstinence from drug and heavy alcohol use was assessed using longitudinal multivariable models.

Results—Of 563 study participants, 98% completed at least one follow-up assessment and 535 (95%) had at least one pair of consecutive assessments and were included. In adjusted analyses, marijuana use was associated with a 27% reduction in the odds of abstinence from drug and heavy alcohol use (adjusted odds ratio 0.73 [95% CI, 0.56–0.97], P=0.03).

Conclusions—Marijuana use among individuals with alcohol or other drug dependence is associated with a lower odds of achieving abstinence from drug and heavy alcohol use. These findings add evidence that suggests concomitant marijuana use among patients with addiction to other drugs merits attention from clinicians.

Keywords

Marijuana use; Abstinence; Relapse; Substance dependence; Alcohol dependence; Drug dependence

1. INTRODUCTION

Although marijuana is thought to be less harmful than other drugs (Nutt et al., 2007), its use has well-documented health consequences including detrimental effects on the cardiopulmonary, endocrine and central nervous systems (Khalsa and ElSohly, 2007; Tetrault et al., 2007). Despite these health effects, some have perceived that marijuana use among substance dependent persons is inconsequential or even beneficial and it may not be a clinical focus during addiction treatment (DuPont and Saylor, 1989; Morgan et al., 2010, 2013), Published principles of addiction treatment do not mention how marijuana use or addressing it might affect the outcome of treatment for other substances (National Institute on Drug Abuse, 2012). A guideline for opioid treatment programs recommends addressing marijuana use in subjects with opioid addiction to reduce activities that might increase the risk of opioid relapse (Center for Substance Abuse Treatment, 2005).

The use of marijuana is increasing: in the United States, 17.4 million people age 12 and older used marijuana in the past month (Substance Abuse and Mental Health Services

Administration (SAMHSA), 2011). This high prevalence in part explains its accounting for 17% of admissions nationwide, ranking third after alcohol and opioid admissions and above cocaine, and amphetamines (SAMHSA, 2011). Marijuana use occurs commonly among people with substance dependence, even during the course of addiction treatment in specialty treatment programs (DuPont and Saylor, 1989; Scavone et al., 2013). Thus, it is important to understand its effect on those dependent on other drugs.

Use of multiple drugs portends worse addiction treatment outcomes compared to the use of a single drug (McLellan et al., 1994). But findings about marijuana's effects on use of other substances and the need to address it during addiction treatment for other substances are not uniform (Hill et al., 2013; Wasserman et al., 1998; Church et al., 2001; Epstein and Preston, 2003; Nirenberg et al., 1996; Saxon et al., 1993; Aharonovich et al., 2005; Alessi et al., 2011; Budney et al., 1996; Kadden et al., 2009). Many find no association between marijuana use and outcome of addiction treatment for other substances (Budney et al., 1996; Church et al., 2001; Epstein and Preston, 2003; Hill et al., 2013; Nirenberg et al., 1996; Saxon et al., 1993) and one small study suggested that marijuana use helped crack cocaine addiction (Labigalini et al., 1999). Another small study, however, suggests that addressing marijuana use may lead to more use of alcohol (Peters and Hughes, 2010) and at least two prospective studies suggest that marijuana use is associated with worse addiction treatment outcomes (Aharonovich et al., 2005; Wasserman et al., 1998).

The lack of focus on a seemingly less problematic but addictive substance in addiction treatment is not new. Cigarette smoking was not addressed and was even accommodated within addiction treatment programs until recently, based on the belief that addressing tobacco simultaneously would interfere with treatment for the primary drug. But studies now suggest that addressing smoking during addiction treatment doesn't worsen but improves outcomes (Olsen et al., 2005; Prochaska et al., 2004; Satre et al., 2007; Tsoh et al., 2001), and smoking cessation has become more a part of addiction treatment (Baca and Yahne, 2009; Schroeder and Morris, 2010). In sum, study results are conflicting regarding whether marijuana use affects use of other substances, and some perceive marijuana use to be inconsequential during addiction treatment. A larger, prospective and longitudinal study could contribute to the existing literature. Therefore, our aim was to explore whether marijuana use adversely impacts achievement of abstinence from other substances. We assessed the association between marijuana use and abstinence from drug (i.e., opioid and stimulant) and heavy alcohol use in people with alcohol or other drug dependence. The study hypothesis was that marijuana use would decrease the odds of subsequent abstinence.

2. METHODS

2.1 Study Design

This is an analysis of data collected prospectively from participants in a randomized clinical trial testing the effectiveness of chronic disease management (the Addiction Health Evaluation And Disease management (AHEAD) study, NCT00278447; Saitz et al, 2013). Those who had at least one pair of consecutive assessments (i.e., study entry and 3-month or 3-month and 6-month or 6-month and 12-month) were included in this study so that

exposure could be assessed during at least one assessment and outcome assessed during the second assessment in the pair.

2.2 Participants

AHEAD study participants were recruited primarily at a residential detoxification unit by approaching patients, as well as by referral from ambulatory clinics, an emergency department, urgent care center, and inpatient settings at one hospital, and through local advertisements. Inclusion criteria were the following: (1) age 18 years or greater; (2) current Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV) diagnosis of alcohol dependence (determined by the Composite International Diagnostic Interview Short-Form (CIDI-SF) (Kessler et al., 1998) and *very* heavy alcohol use in the past 30 days (defined as ≥4 standard drinks for women and ≥5 standard drinks for men at least *twice*, or ≥15 drinks per week for women or ≥22 drinks per week for men -- weekly average based on typical daily drinking in the past month) or current DSM-IV diagnosis of drug dependence (determined by the CIDI-SF) (Kessler et al., 1998) and any drug use in the past 30 days, defined as cocaine (or any other psychostimulant) or heroin (or any other opioids or prescription painkiller without a prescription, in larger amounts than prescribed, or for a longer period of time than prescribed); and (3) willingness to continue or establish primary care at one hospital-based clinic and attend an outpatient (study) disease management visit within that primary care clinic.

The exclusion criteria were the following: (1) unable to be interviewed due to acute illness; (2) breath alcohol ≥100 mg/dL; (3) unable to provide the names, phone numbers, and addresses of 2 contact persons; (4) not fluent in English or Spanish; (5) cognitive impairment (score of less than 21 of 30 on the Mini-Mental State Examination; Smith et al., 2006) (6) pregnancy; and (7) inability to provide informed consent. All enrollees provided written informed consent. The Institutional Review Board (IRB) at Boston University Medical Campus approved this study. Additional privacy protection was secured by the issuance of a Certificate of Confidentiality by the Department of Health and Human Services (DHHS), to protect participants from release of their research data even under a court order or subpoena.

2.3 Assessments

Participants were evaluated at study entry, 3, 6 and 12 months after enrollment. All underwent the same structured interview in English or Spanish (based on participant preference) conducted by a trained research associate. Assessments addressed demographics, past 30-day cigarette use, past 30-day alcohol use by validated calendar method (Timeline Follow-back [TLFB]; Sobell and Sobell, 1995), other drug use by the Addiction Severity Index (ASI; McLellan et al., 1992) alcohol and drug consequences using the Short Inventory of Problems (SIP for alcohol, SIP-DU for drugs; Allensworth-Davies et al., 2012; Smith et al., 2009), depressive symptoms using the 9-item Patient Health Questionnaire (PHQ-9; Kroenke et al., 2001), anxiety symptoms categorized as minimal, mild, moderate or severe using the Beck Anxiety Inventory (BAI; Beck and Steer, 1993), medical comorbidity using a validated comorbidity questionnaire (Charlson et al., 1987; Katz et al., 2003), recent incarceration based on if the participants had spent time in a jail,

prison, correctional institution or had been arrested in the past 3 months (McLellan et al., 1992), and homelessness based on if the participants spent any nights on the street or in a shelter in the past 3 months (Kertesz et al., 2005). Interviews usually occurred at the General Clinical Research Unit in the medical school but were also conducted at jails/prisons (with DHHS, IRB and jail/prison approval), inpatient settings, in other outpatient locations or by phone as a last alternative. In order to obtain accurate information and encourage truth-telling by participants, Research Assistants administered breath alcohol testing at every assessment. They also reminded participants that interviews were confidential, would not be shared with their clinicians, or affect their health care in any way. The study also obtained a certificate of confidentiality which further protects participant data.

2.4 Independent Variable

The main independent variable was any (versus no) days of marijuana use in the past 30 days at study entry, 3- and 6-month follow-up assessments as determined by the Addiction Severity Index (ASI).

2.5 Dependent Variable

The outcome was abstinence from drug (i.e., opioid and stimulant) and heavy alcohol use as determined at 3-, 6- and 12-month follow-up assessments. Stimulant and opioid use were evaluated using the ASI, with abstinence defined as zero days reported use of cocaine, amphetamines, heroin, methadone, or other opioids. In all cases, use of prescription medications (i.e., opioids including methadone) was counted only if the substance was used without a doctor's prescription, in amounts greater than prescribed, or for a longer period than prescribed. Heavy alcohol use was defined as ≥4 standard drinks for women and ≥5 standard drinks for men at least once in the past 30 days and was assessed using the Timeline Follow-back calendar method, administered by a trained research associate in an interview format. In order to confirm the findings based on self-reported abstinence, we performed a similar analysis to the main study question, looking at the association between marijuana use at 3 months and the outcome abstinence at 6 months by biochemical testing (abnormal carbohydrate deficient transferrin (CDT), any drug by saliva or hair testing).

2.6 Covariates

Covariates were added to multivariable models to control for factors that could potentially confound the association between marijuana use and abstinence from drug (i.e. opioid and stimulant) and heavy alcohol use. In general, potential confounders were chosen based on the literature, clinical knowledge, and the assessment of potential differences in a variety of subject characteristics by marijuana use, rather than statistical testing alone as our study may have been underpowered to identify some associations. In one study, factors predictive of failure to achieve abstinence were homelessness, duration of alcohol consumption, cigarette smoking, and multiple addictions (Gelsi et al., 2007). In another, factors independently associated with failure to remain abstinent included male gender, homelessness, HIV infection, multiple addictions, and sexual abstinence (Shah et al., 2006).

The following covariates were used in this study: age, gender, race/ethnicity, recent incarceration, recent homelessness, anxiety, recent cigarette smoking, alcohol and drug

consequences (baseline SIP and SIP-DU, respectively), use of more than one substance other than marijuana, and any medical comorbidity. Use of more than one substance other than marijuana was defined as heavy alcohol use (based on TFLB) or any of the following drugs listed in the ASI: heroin, methadone, other opiates/analgesics, barbiturates, sedatives, hypnotics, tranquilizers, cocaine, amphetamines, hallucinogens, inhalants). We also included randomization group (assignment to attend the AHEAD clinic verses no assignment to attend the AHEAD clinic [all participants were given a referral to primary medical care]) as a covariate. ASI-alcohol and ASI-drugs were not used as covariates as they each were highly correlated with SIP and SIP-DU, respectively. Anxiety and depression were also highly correlated; we chose anxiety as a covariate since it has been linked to marijuana use (Cheung et al., 2010).

2.7 Statistical Analysis

Descriptive statistics were used to characterize the study sample at study entry overall and stratified by any (versus no) marijuana use. Continuous variables were compared using t-tests or the Wilcoxon rank sum test and chi-square and Fisher's exact tests were used as appropriate to compare categorical variables. We examined the relationship between marijuana use and the outcome (abstinence from drug (i.e., opioid and stimulant)and heavy alcohol use) by fitting generalized estimating equations (GEE) logistic regression models, to account for correlation in the data due to incorporating repeated measures from the same participant. The GEE models were fit using a logit link and an independence working correlation matrix. Results are reported using the empirical variance estimator. To ensure the independent variable (marijuana use) preceded the dependent variable (abstinence from drug (i.e., opioid and stimulant) and heavy alcohol use), the independent variable was "lagged" to predict the dependent variable at the subsequent assessment. This approach required subjects to have at least one pair of consecutive interviews to be included in the analysis. Covariates modeled as time-varying included the following: anxiety, recent incarceration, recent homelessness, recent cigarette smoking, SIP and SIP-DU scores, use of more than one substance other than marijuana and any medical comorbidities. Preliminary crude analyses were performed that included only marijuana use, time, and randomization group. A full multivariable model was then fit including all potential confounders as well as time of outcome assessment (3, 6, or 12 months) and interval of time between assessments of marijuana use and outcome assessment. To minimize the potential for collinearity, we verified that no pairs of independent variables were highly correlated (> 0.50). Odds ratios and 95% confidence intervals are reported for each model. The odds ratios are used as effect sizes to quantify the magnitude of difference between groups.

For the secondary, confirmatory analysis of abstinence at 6 months based on biochemical testing, we used univariate logistic regression and the same covariates as main model. For comparison, we tested the same association in the same sample with self-report as the outcome using univariate logistic regression and the same covariates. Secondary analyses were conducted to explore whether substance dependence type (alcohol only; drug only; both) was a potential effect modifier of the relationship between marijuana use and abstinence from drug (i.e., opioid and stimulant) and heavy alcohol use. An interaction term between substance dependence type and marijuana use was included in the full multivariable

models described above (excluding SIP and SIP-DU due to high correlation with substance dependence type) and stratified analyses were conducted if interactions were significant. In post-hoc analyses we tested the interaction between marijuana use and time, described the association between marijuana use at each timepoint and abstinence at the subsequent timepoint, and assessed the association between frequency of marijuana use (number of days used in the past month: 0; 1–4 days; 5–30 days) and self-reported subsequent abstinence using GEE logistic regression. A (two-sided) significance level of 0.10 was used for the test of interaction due to a potential lack of power for this secondary analysis and because of the exploratory and hypothesis-generating (rather than confirmatory) nature of the analysis. All other analyses were conducted using two-sided tests and a significance level of 0.05. Analyses were performed using SAS software (version 9.1; SAS Institute, Cary, NC).

3. RESULTS

Between 2006 and 2008, 2,029 individuals were screened for trial eligibility, 655 were eligible, 569 (87%) provided informed consent and 563 were enrolled. Of the 563 participants enrolled, 553 (98%) completed at least one follow-up assessment. Of those, 535/553(97%) had at least one pair of consecutive assessments and thus were included in the analyses. Most follow-up assessments were done in person, 4.6% by phone. Participant demographics and substance use characteristics at study entry are shown in Table 1. They were mostly male, middle-aged, diverse in terms of race and ethnicity, majority homeless and with recent incarceration history. Most had both alcohol and other drug dependence. Substantial proportions had medical comorbidity, depression and anxiety symptoms, smoked cigarettes, and had use of more than one substance other than marijuana.

Almost half (48%) reported past 30-day marijuana use at study entry. Those who reported marijuana use were younger, more likely to report homelessness, meet criteria for drug dependence, use more than one substance other than marijuana, smoke cigarettes, and have greater drug use severity and consequences.

The 535 participants contributed a total of 1429 observations to the analysis. Among the 1429 observations, 36% reported marijuana use (the exposure of interest) and 38% reported abstinence from drug (i.e., opioid and stimulant) and heavy alcohol use (the primary outcome). The observed proportions with marijuana use at study entry, 3 and 6 months were 48%, 30%, and 29%, respectively. For abstinence from drug (i.e. opioid and stimulant) and heavy alcohol use, the observed proportions were 35%, 34%, and 43% at 3, 6, and 12 months, respectively.

In the crude longitudinal regression model, adjusted for only time and randomization group, marijuana use was significantly associated with a lower likelihood of abstinence (adjusted odds ratio (AOR), 0.52[95% confidence interval (CI), 0.40–0.67]). In the fully adjusted models, marijuana use remained statistically significant and was associated with a 27% reduction in the odds of subsequent abstinence from drug (i.e. opioid and stimulant) and heavy alcohol use (AOR,0.73 [95% CI,0.56–0.97]); adjusted proportions 36% vs. 43% for those with and without marijuana use, respectively). Of note, use of more than one substance was also significantly associated with a lower odds of abstinence. There was no significant

interaction between marijuana use and use of more than one substance other than marijuana (P=0.78). Table 2 displays the results for abstinence and covariates from the multivariable regression model.

In an analysis that included dependence type (alcohol only, drugs only, or both) and an interaction term between marijuana use and dependence type the interaction was not statistically significant (P=0.31). In the same model without the interaction term (but retaining dependence type) the effect of marijuana use on abstinence remained significant (AOR, 0.70, [95% CI, 0.53–0.92], P=0.01). In total, 339 subjects had a 3 month assessment and 6 month biochemical testing. The logistic regression for biochemical abstinence at 6 months yielded an AOR 0.69 (CI 0.28, 1.72), p=0.43. For self-report abstinence at 6 months using the same sample as the biochemical analysis AOR was 0.76 (CI 0.37, 1.56), P=0.45. These effect sizes are of similar magnitude though the effects lose statistical significance, possibly due to decreased sample size and increased variability (and therefore decreased power) from utilizing fewer observations in this analysis where the outcome is assessed only at a single time point.

In post-hoc analyses, AOR for the association between marijuana use at study entry and abstinence at 3-month assessment was 0.84 (95% CI 0.55, 1.27)(n=446), for marijuana use at 3 months and abstinence at 6 months 0.50 (95% CI 0.30, 0.82)(n=446), and for marijuana use at 6 months and abstinence at 12 months, 0.84 (95% CI 0.54, 1.32)(n=466). A test of the interaction between marijuana use and time was not statistically significant (P=0.17). In analyses evaluating the association between frequency of marijuana (number of days of use in past month) use and self-reported abstinence, the results were: AOR 0.90 1–4 days use vs. none (95% CI 0.66, 1.24); AOR 0.54 for 5 or more days vs. none (95% CI 0.37, 0.79); and AOR 0.60 for 5 or more days vs. 1–4 days (95% CI 0.39, 0.92), suggesting the association between marijuana use and abstinence may be stronger with more days of use.

4. DISCUSSION

In adjusted analyses, marijuana use was significantly associated with a of subsequent abstinence from other substances (opioids, stimulants and heavy alcohol use) among alcohol and drug dependent adults, who were not necessarily seeking treatment for their dependence. The association between marijuana use and abstinence appeared stronger at 6 months, however there was no significant interaction between marijuana use and time. The association was also present in analyses adjusting for dependence type (alcohol only, other drug only or both). That association did not appear to be simply an effect of multiple substance use—the effect of marijuana use was independent of the effect of using more than one substance (which was also significantly associated with less abstinence). Analyses also suggest that a greater frequency of marijuana use is associated with less abstinence, though these were post-hoc tests; those results should be viewed as hypothesis generating.

Marijuana use could theoretically have helpful or harmful influence on achieving abstinence. Substituting a possibly less harmful drug might help achievement of abstinence from alcohol, stimulants or opioids when they are the focus of treatment. On the other hand, continuing to use an addictive drug, such as marijuana, could interfere with efforts to

achieve abstinence from other drugs. Or it may have no effect (Budney et al., 1998; Hill et al., 2013; Church et al., 2001; Epstein and Preston, 2003; Nirenberg et al., 1996; Saxon et al., 1993; Alessi et al., 2011; Budney et al., 1996; Darke et al., 2006). Prior studies lend some support for each of these possibilities and hence findings among previously published studies are inconsistent. A recent study found that pre-treatment marijuana use favorably influenced abstinence in cocaine users treated with contingency management for cocaine use, compared to no pre-treatment marijuana use (Alessi et al., 2011). Other studies have shown that marijuana use is associated with worse treatment outcomes in patients undergoing opioid agonist treatment (Aharonovich et al., 2005; Wasserman et al., 1998). Of note, those two studies were prospective whereas many of the studies not finding effects were smaller and retrospective.

Some researchers have suggested that marijuana could be used as a substitute for some other substances when becoming abstinent from them. In one example from Brazil, crack cocaine addicts who reported using marijuana to ease their withdrawal symptoms also reported reduced craving for cocaine (Labigalini et al., 1999). In another study, within a subgroup of daily marijuana users with past alcohol problems, the results demonstrated that alcohol consumption increased in those who became abstinent from marijuana use, suggesting a substitution effect (Peters and Hughes, 2010). However, Kadden et al. (2009) found alcohol and marijuana use to be independent of one another. In a large cohort study, Darke et al. (2006) were interested in understanding the association between reduced heroin use and other drug use among 615 Australian heroin users; marijuana and alcohol use were not related to heroin use. Our findings might help clarify this issue. For example, it is possible that marijuana use is a marker for more severe addiction although this seems an unlikely explanation since the findings in our study persisted essentially unchanged despite adjustments for severity. An alternative explanation is that these findings could be a consequence of drugs of abuse influencing the brain via similar common pathways, leading to craving or desire for drug use. This would be consistent with findings in which cannabis cues activate brain areas, patterns associated with poor addiction outcomes (e.g., continued use and relapse; Cousijn et al., 2013). Hence, it is plausible that marijuana exposure could lead to worse outcomes with regards to other substance use.

Limitations should be considered when interpreting the results of this study. One limitation is that chronic disease management could confound the results, as could other potential confounders. Thus we included randomization group and other covariates in the analyses (and group assignment was not significantly associated with the outcome). Also, due to the observational nature of the data, we cannot definitively conclude there is a causal relationship between marijuana use and abstinence. The study may also have been underpowered to detect an interaction between marijuana use and substance dependence type. We did not have biochemical verification of abstinence at every follow-up time point. However, we did have it at one time point and analysis of those data revealed an odds ratio consistent with the main analytic findings although the results did not meet statistical significance, we believe, due to decreased sample size (339 versus 1429) and increased variability. Nonetheless, the lack of statistical significance observed in the biochemical analyses could be viewed as a limitation of the study. It is possible that self-report was

biased though the direction of that bias is uncertain and the true association could be stronger or weaker than the one we observed.

Generalizability is another potential limitation—study results may not be applicable beyond urban adults with low socioeconomic status. However, the directions of the associations observed in covariates such as drug problems, use of more than one drug, and cigarette smoking, even if not statistically significant, were all in the expected direction, suggesting that our findings are not likely unique to this sample.

In sum, we found a significant association between marijuana use and less abstinence from drug and heavy alcohol use. Post-hoc analyses of the associations at varying frequencies of marijuana use were consistent with the overall findings. These analyses suggested the findings that marijuana use was associated with a lower odds of abstinence may be stronger for marijuana use at 3 and abstinence at 6 months, however there was no significant interaction between marijuana use and time.

Our study was among the largest to address this question, was prospective, included users of various drugs, used longitudinal analyses, had little loss to follow-up, examined self-report gathered with validated tools for the main predictor and outcome, and employed hair, saliva and carbohydrate deficient transferrin testing results. Marijuana use was associated with a lower odds of subsequent abstinence from opioid, stimulant and heavy alcohol use among substance dependent persons across time. While the findings do not mean addressing marijuana use during addiction treatment will improve treatment outcomes, they do suggest that possibility. It seems reasonable to consider addressing marijuana use in substance dependent people and in their treatment.

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Table 1

Demographic and Substance Use Characteristics of 535 Adults with Alcohol and/or Other Drug Dependence at study entry

	All Subjects at Study Entry (n=535)	Subjects with Past 30-day Marijuana Use (n=261)	Subjects with No Past 30-day Marijuana Use (n=274)	*P* Value
Age (years)				
Mean (SD)	38.4 (10.2)	36.9 (10.0)	39.7 (10.2)	<0.001
Sex (% Male)	391 (73.1%)	190 (72.8%)	201 (73.4%)	0.88
Race (%)				
White	248 (46.4%)	110 (42.1%)	138 (50.4%)	0.23
Black	172 (32.1%)	94 (36.0%)	78 (28.5%)	
Hispanic	72 (13.5%)	36 (13.8%)	36 (13.1%)	
Other	43 (8.0%)	21 (8.1%)	22 (8.0%)	
Dependence & Recent Use [a] (%)				
Alcohol Only	92 (17.2%)	26 (10.0%)	66 (24.1%)	<0.001
Drug Only	140 (26.2%)	60 (23.0%)	80 (29.2%)	
Alcohol & Drug	303 (56.6%)	175 (67.0%)	128 (46.7%)	
Depression [b] (%)	444(83.5%)	219 (84.6%	225 (82.4%)	0.51
Anxiety [c] (%)				
Mild	207 (39.7%)	97 (38.3%)	110 (40.9%)	0.69
Moderate	156 (29.9%)	80 (31.6%)	76 (28.3%)	
Severe	159 (30.5%)	76 (30.0%)	83 (30.9%)	
Incarceration (%)	417 (77.9%)	208 (79.7%)	209 (76.3%)	0.34
Homelessness (%)	313 (58.5%)	173 (66.3%)	140 (51.1%)	<0.001
Alcohol Addiction Severity [d]				
Median (IQR)	0.5 (0.1, 0.8)	0.6 (0.2, 0.8)	0.5 (0.1, 0.8)	0.33
Drug Addiction Severity [d]				
Mean (SD)	0.3 (0.2)	0.3 (0.1)	0.2 (0.2)	<0.001
SIP Score [e]				
Mean (SD)	19.6 (15.3)	20.1 (15.0)	19.1 (15.5)	0.36
SIP-DU Score [e]				
Mean (SD)	28.1 (14.3)	30.6 (12.2)	25.7 (15.6)	<0.001
Medical Comorbidity [f](%)	221 (45.5%)	111 (47.2%)	110 (43.8%)	0.45

	All Subjects at Study Entry (n=535)	Subjects with Past 30-day Marijuana Use (n=261)	Subjects with No Past 30-day Marijuana Use (n=274)	*P* Value
Use of More than 1 Substance Other than Marijuana [g] (%)	430 (80.4%)	238 (91.2%)	192 (70.1%)	<0.001
Heavy Alcohol Use [h] (%)	418 (78.1%)	216 (82.8%)	202 (73.7%)	0.0015
Cocaine Use (%)	362 (67.7%)	199 (76.3%)	163 (59.5%)	<0.001
Amphetamine Use (%)	24 (4.5%)	17 (6.5%)	7 (2.6%)	0.027
Any Stimulant Use (%)	365 (68.2%)	200 (76.6%)	165 (60.2%)	<0.001
Heroin Use (%)	315 (58.9%)	166 (63.6%)	149 (54.4%)	0.030
Methadone Use (%)	47 (8.8%)	23 (8.8%)	24 (8.8%)	0.98
Opiate/Analgesic Use (%)	193 (36.1%)	116 (44.4%)	77 (28.1%)	<0.001
Any Opioid Use (%)	357 (66.7%)	189 (72.4%)	168 (61.3%)	0.0065
Cigarette Use [i] (%)	470 (87.9%)	245 (93.9%)	225 (82.1%)	<0.001

[a] Dependence & recent use is stratified into 3 categories: (1) subjects with alcohol dependence and recent heavy use only, (2) subjects with drug dependence and recent drug use only, and (3) subjects with both alcohol and drug dependence and recent drug and heavy alcohol use.

[b] Depression here indicates a score of equal or greater than 10 on the PHQ-9 test.

[c] Anxiety is categorized based on severity in the Beck Anxiety Inventory:A score of 0–7is considered ‘minimal’ or no anxiety, 8–15 is considered ‘mild’, 16–25 is considered ‘moderate’, and 26–63 is considered ‘severe’.

[d] Assessed by the Addiction Severity Index (ASI). Scores range 0–1 with higher scores indicating worse severity.

[e] SIP refers to Short Inventory of Problems. For both alcohol (SIP score) and drugs (SIP-DU score), the score range is 0–45 with higher scores indicating more alcohol or drug consequences, respectively.

[f] Medical comorbidity is defined by having a score greater than 0 on the comorbidity questionnaire (meaning they had at least one or more comorbid medical diagnosis).

[g] Use of more than 1 substanceother than marijuana is defined as the use of more than one substance (as listed in the methods) in the past 30 days at study entry.

[h] Heavy alcohol use is based on the Timeline Follow-Back. For women ≥4 standard drinks and for men ≥5 standard drinks at least once in the past 30 days was considered heavy alcohol use.

[i] Cigarette use is defined as any cigarette smoking in the past 30 days.

Table 2

Association between Marijuana Use and Abstinence from Stimulants, Opioids and Heavy Alcohol Use [a]: Multivariable Longitudinal Regression

	Odds Ratio [95% CI]	*P* Value
Marijuana Use [b]	**0.73 [0.56, 0.97]**	**0.03**
Age[c]		0.70
<33rd percentile	1.00	
33rd – < 67th percentile	0.85 [0.58, 1.24]	
67th percentile +	0.88 [0.59, 1.33]	
Sex		0.94
Male	0.99 [0.71, 1.37]	
Race[d]		0.87
Black	0.87 [0.61, 1.25]	
Hispanic	0.87 [0.57, 1.34]	
Other	0.92 [0.54, 1.58]	
Anxiety[e]		0.14
Moderate	1.34 [0.97, 1.86]	
Severe	1.37 [0.93, 2.03]	
Incarceration	0.90 [0.63, 1.26]	0.53
Homelessness	0.85 [0.65, 1.10]	0.23
SIP score[f]		0.62
<33rd percentile	1.00	
33rd – < 67th percentile	1.13 [0.82, 1.54]	
67th percentile +	0.94 [0.63, 1.40]	
SIP-DU score [f]		0.02
<33rd percentile	1.00	
33rd – < 67th percentile	1.36 [0.97, 1.89]	
67th percentile +	1.74 [1.16, 2.61]	
Use of more than 1 substance other than marijuana [g]	0.25 [0.18, 0.35]	<0.001
Cigarette Use [h]	0.83 [0.56, 1.22]	0.35
Medical Comorbidity [i]	0.73 [0.53, 0.99]	0.04

[a] Heavy alcohol use is based on the Timeline Follow-Back. For women ≥4 standard drinks and for men ≥5 standard drinks at least once in the past 30 days was considered heavy alcohol use.

[b] Marijuana use is based on the ASI. Subjects that reported at least one day of marijuana use at a previous time points were considered marijuana users (Previous time point is study entry for outcomes measured at 3 months; 3 months for outcomes measured at 6 months; 6 months for outcomes measured at 12 months).

[c] Age is categorized into tertiles. The range for the <33rd percentile category is 18.1 – 32.6, the 33rd – < 67th percentile category is 32.9 – 44.1 and the 67th percentile + category is 44.1 – 66.7. The lower tertile is the reference group.

[d] White is the reference group for race.

[e] Anxiety is categorized based on severity in the Beck Anxiety Inventory:A score of 0–7 is considered 'minimal'oe no anxiety, 8–15 is considered 'mild', 16–25 is considered 'moderate', and 26–63 is considered 'severe'. Mild is the reference group.

[f] SIP refers to Short Inventory of Problems. For both alcohol (SIP score) and drugs (SIP-DU score), the score range is 0–45 with higher scores indicating more alcohol or drug consequences, respectively. SIP is categorized into tertiles. The range for the <33rd percentile category is 0–8, the range for the 33rd – < 67th percentile category is 9–30 and the 67th percentile + category is 31–45. SIP-DU is also categorized into tertiles. The range for the <33rd percentile category is 0–25, the 33rd – < 67th percentile category is 26–38 and the 67th percentile + category is 39–45. The lowest tertile is the reference group.

[g] Use of more than 1 substanceother than marijuana is defined as the use of more than one substance (as listed in the methods) in the past 30 days atstudy entry.

[h] Cigarette use is defined as any cigarette smoking in the past 30 days.