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Risks associated with mid-level cannabis use among people treated for alcohol use disorder

Meenakshi S. Subbaraman, PhD[1,*], **Sarah Beth Barnett, PhD**[1], and **Katherine J. Karriker-Jaffe, PhD**[1]

[1]Alcohol Research Group, 6001 Shellmound Ave, Suite 450, Emeryville, CA 94608, USA

Abstract

Objective: To examine the relationships between cannabis use frequency with alcohol use, alcohol-related harms and persistent AUD in a general population subsample of individuals previously treated for AUD.

Methods: Secondary analyses of the 2005, 2010, and 2015 U.S. National Alcohol Surveys, a nationwide general population sample of individuals ages 18+. The analytic subsample (N=772) reported 3+ lifetime DSM-IV alcohol dependence criteria and prior AUD treatment. Primary exposure was past 12-month frequency of cannabis use (weekly or more, or "heavy"; more than monthly/less than weekly or "mid-level"; less than monthly or "light"; none). Primary outcomes were past 12-month total volume, average frequency of 5+ drinks/month, past 12-month alcohol-related harms, and past 12-month DSM-IV alcohol dependence.

Results: Multivariable negative binomial and logistic regressions showed that the only cannabis users who consistently differed significantly from cannabis abstainers were mid-level users; specifically, more than monthly/less than weekly cannabis users drank 2.83 times as many drinks (95% CI: 1.43, 5.60); had 2.83 as many 5+ occasions (95% CI: 1.38, 5.79); had 6.82 times the odds of experiencing any harms (95% CI: 2.29, 20.33); and had 6.53 times the odds of persistent AUD as cannabis abstainers (95% CI: 2.66, 16.02; all *P*s <0.05). The relationship between mid-level cannabis use and harms remained significant after adjustment for volume and frequency of 5+ (OR = 6.18, 95% CI: 1.35, 28.37).

Conclusions: Among those with lifetime AUD who have been to treatment, only more than monthly/less than weekly cannabis use is related to more alcohol-related harms and persistent AUD compared to cannabis abstinence. Heavier and lighter cannabis use are not related to worse alcohol outcomes compared to cannabis abstinence.

Keywords

Alcohol; cannabis; marijuana; alcohol-related problems; alcohol use disorder; treatment

[*]Corresponding author: Phone: (510) 898-5854, msubbaraman@arg.org.

INTRODUCTION

Second to tobacco, cannabis is the most commonly used drug among people with alcohol use disorder (AUD), with almost a quarter of people with lifetime AUD reporting past-year cannabis use Weinberger, 2016. A growing literature suggests the relationship between cannabis/alcohol co-use and deleterious outcomes may depend on the nature of co-use (concurrent versus simultaneous), the subpopulation examined (general population versus treatment sample) and/or the way cannabis use is measured (any versus frequency of use) (Subbaraman, 2016).

General population studies show adults and adolescents who co-use cannabis and alcohol are at increased risk of heavy episodic drinking and AUD (Brière et al., 2011; Midanik et al., 2007). While many studies do not distinguish between concurrent (use of both substances, but separately) and simultaneous use (use of both substances at the same time such that effects overlap), one study using nationally-representative data found the prevalence of simultaneous use was almost twice that of concurrent use among cannabis/alcohol co-users (Subbaraman and Kerr, 2015). This finding suggests that among those who co-use, most use the substances together, which carries higher risks than the use of either substance alone (Volkow et al., 2014).

Distinguishing between any cannabis use and the frequency of cannabis use is crucial in the study of co-use. In the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), any use of cannabis in the past 12 months at baseline increased the odds of prevalent and incident AUD, cannabis use disorder and other substance use disorders (SUD) three years later (Blanco et al., 2016). However, the middle frequency group (more than 1x/year but less than 1x/month) were at highest risk (Blanco et al., 2016). Frequency of cannabis use was also associated with alcohol abstinence among people in AUD treatment who participated in a randomized controlled trial of combinations of medication and behavioral therapies (Subbaraman et al., 2017). Compared to no cannabis use during treatment, any use was related to fewer alcohol-abstinent days at the end of treatment. However, when examining frequency of cannabis use, only those who used cannabis 1–2x/month during treatment had fewer abstinent days compared to those with no cannabis use. Importantly, the lowest and highest levels of cannabis use were not associated with alcohol outcomes (Subbaraman et al., 2017).

Rationale for current study

How cannabis use is related to alcohol problems and persistent AUD among individuals who have received AUD treatment remains under-studied. In the current environment of increasingly liberal cannabis laws, those leaving AUD treatment need guidance regarding how cannabis might affect alcohol use. The aim here is to extend prior results by examining relationships of cannabis use frequency with alcohol use, alcohol-related harms, and persistent AUD in a general population subsample of individuals previously treated for AUD.

METHODS

Data

Data came from the 2005 (N=6,919), 2010 (N=7,969), and 2015 (N=7,071) National Alcohol Surveys (NAS), a computer-assisted telephone survey of individuals aged 18+. African Americans and Hispanics are over-sampled. Data were collected using list-assisted random digit dialing. A dual-frame design, including both landline and cellular phones, was implemented in 2010, providing coverage of 97.5% of US households (Blumberg and Luke, 2009). Respondents could be interviewed in either English or Spanish. The Public Health Institute's institutional review board approved the study.

Our analytic subsample (N=772) consisted of participants who reported 3+ lifetime DSM-IV alcohol dependence criteria *and* prior AUD treatment, and had available data regarding cannabis use. Lifetime and past-year dependence were assessed with standard items used in the NAS since 1990 (Caetano and Tam, 1995), and similar to those used in NESARC (based on the Alcohol Use Disorder and Associated Disabilities Interview Schedule (Grant et al., 1995)). Alcohol treatment utilization was determined from the questions, "Did you ever receive treatment from a chemical dependency or substance abuse program for [alcohol]?" and "Have you ever gone to anyone -- a physician, AA, a treatment agency, anyone at all -- for a problem related in any way to your drinking?" The primary exposure was past 12-month frequency of cannabis use. NAS participants were asked "How often have you used marijuana, hash, pot, THC or weed during the last twelve months?" with the possible response categories of 1) every day or nearly every day; 2) once a week; 3) once every 2 or 3 weeks; 4) every month or two months; 5) less often than that; or 6) never. We re-categorized into i) weekly or more (1+2), or "heavy"; ii) more than monthly/less than weekly (3+4), or "mid-level"; iii) less than monthly (5), or "light"; and iv) never (6, referent) to ensure adequate sample sizes within cannabis use subgroups. This re-categorization also allows for more direct comparisons with NESARC findings.

Primary outcomes were *volume* (number of drinks in past 12 months), *frequency of 5+ occasions per month* (number of occasions in past 12 months), *alcohol-related harms* (indicator of any in past 12 months) and *DSM-IV alcohol dependence* in the past 12 months (indicator of symptoms in three or more of seven domains). Volume was measured using graduated quantity-frequency measures that are particularly accurate for estimating consumption among people who occasionally drink heavily (Greenfield, 2000). Alcohol-related harms were assessed using a 6-item scale asking, "Was there ever a time you felt your drinking had a harmful effect on your (i) friendships and social life, (ii) outlook on life, (iii) home life or marriage, (iv) financial position, (v) work and employment opportunities, and (vi) health?" Participants were not asked about past-year alcohol-related harms in 2015, limiting the analytic sample for harms to N=528.

Statistical analyses

The first set of multivariable regressions examined all four primary outcomes. The second set focused on harms and DSM-IV alcohol dependence adjusting for current volume and frequency of 5+ to assess whether cannabis use frequency is related to harms and

dependence when accounting for actual consumption. Negative binomial and logistic regression was used for count and dichotomous outcomes, respectively. Covariates were age, gender, education, employment, marital status, race/ethnicity, tobacco use, lifetime DSM-IV dependence severity, and survey year. Co-varying survey year adjusts for any time trends related to both cannabis and alcohol use, which is important due to possible period effects from combining samples across 2005–2015, especially given changing cannabis laws. All analyses were weighted to adjust for the probability of selection and non-response, and performed using Stata v15.1.

RESULTS

Table 1 describes sample demographics and bivariate differences across cannabis use frequency groups. Table 2 displays results from multivariable logistic and negative binomial regressions. Compared to those who did not use cannabis in the past 12 months, light users had 1.90 times as many 5+ drink occasions (95% CI: 1.08, 3.33; $P<0.026$) and 3.51 times the odds of past 12-month DSM-IV alcohol dependence (95% CI: 1.38, 8.89; $P<0.008$), although this relationship was not statistically significant at the traditional 0.05 significance level after adjusting for volume and frequency of 5+ drink occasions (OR=3.53; 95% CI: 0.76, 16.30; $P<0.11$). Mid-level cannabis users had 2.83 times more drinks in the past 12 months (95% CI: 1.43, 5.60; $P<0.003$); 2.83 times as many 5+ drinks occasions (95% CI: 1.38, 5.79; $P<0.004$); 6.82 times the odds of any alcohol-related harms (95% CI: 2.29, 20.33; $P<0.001$); and 6.53 times the odds of DSM-IV alcohol dependence in the past 12 months (95% CI: 2.66, 16.02; $P<0.001$) compared to those who did not use cannabis. Furthermore, the relationship between mid-level cannabis use and any alcohol-related harm remained after adjustment for drink volume and frequency of 5+ occasions (OR=6.18; 95% CI: 1.35, 28.37; $P<0.019$). Compared to those who did not use cannabis in the past 12 months, heavy cannabis users did not differ significantly on any alcohol outcome.

In terms of covariates, there was no consistent pattern. Older age was related to less volume, fewer 5+ occasions, and lower odds of harms and DSM-IV dependence, though only the relationship with harms (not dependence) persisted after adjustment for volume and 5+ occasions. African Americans and Hispanics appeared at elevated risk for both alcohol-related harms and DSM-IV dependence in the models that accounted for volume and 5+ occasions. Frequency of 5+ occasions was related to higher odds of both alcohol-related harms and DSM-IV dependence (Ps<0.05), while volume and lifetime severity were not significantly related to any outcomes.

DISCUSSION

Among those with lifetime AUD who have been to treatment, only more than monthly/less than weekly cannabis use is related to significantly greater past 12-month drinking and related harms compared with cannabis abstinence. Interestingly, the heaviest (weekly or more) cannabis users did not drink significantly more or have higher odds of alcohol-related harms or DSM-IV dependence compared to cannabis abstainers.

This is one of the first studies to examine cannabis use in finer detail than using a dichotomous indicator of any past 12-month use. To our knowledge, the only other study that has examined cannabis use frequency related to AUD in the general population found a similar pattern in that mid-level cannabis users had the highest odds of persistent AUD (Blanco et al., 2016), though significantly increased odds of incident and persistent AUD were also found for other levels of cannabis use. This pattern of mid-level cannabis use (particularly for those using once or twice per month) being most deleterious in terms of fewer alcohol abstinent days was also replicated in the study of individuals undergoing AUD treatment (Subbaraman et al., 2017). Both present and previous findings suggest that rather than any cannabis use, *mid-level cannabis use specifically* is significantly related to negative outcomes. However, the set of findings across studies regarding mid-level use should be interpreted with caution because the definitions of mid-level cannabis use differ. Still, these studies demonstrate the need to even further discriminate levels of use, e.g., specify finer detail beyond basic frequency of co-use while considering motives and event-level data to better understand the relationship between cannabis and alcohol consumption. Additional studies are needed in order to understand how individuals, particularly those at greater risk for SUD, are using cannabis, as well as what other characteristics are related to levels of cannabis use.

We speculate that contexts and motivations of cannabis use differ across cannabis frequency levels. For example, the mid-level users may be using cannabis at parties or during events at which alcohol is also served, while the heavy users may use more often in day-to-day situations that do not involve alcohol. Similarly, mid-level users may be using cannabis recreationally, with intoxication as the primary motivation, whereas the heavy users may be using cannabis medicinally for coping with health issues or past AUD. We will examine how motivation and context vary across levels of cannabis use in future studies.

Possible clinical implications of mid-level cannabis use being related to worst outcomes are complex, and more studies are needed before cannabis can be recommended as a substitute for alcohol (Subbaraman, 2014). In the current sample of previously treated individuals with lifetime AUD, we found that the heaviest cannabis users (weekly or more) did not differ from cannabis abstainers on any alcohol outcome; this finding supports the idea that some heavy cannabis users may be using cannabis as a substitute for alcohol. For example, results from a recent epidemiologic survey of cannabis users in Washington state (N = 991) show that those with medical cannabis recommendations use cannabis significantly more often and drink significantly less and have fewer alcohol-related problems than those without medical recommendations for reasons beyond differences in health (Subbaraman and Kerr, in press). These findings support that those with medical cannabis recommendations might have different motives for cannabis use, e.g., they are using cannabis as medicine and not for intoxication (Subbaraman and Kerr, in press). Therefore, it is possible that there are some heavy, medical cannabis users in the current sample that substitute cannabis for alcohol. However, we are unable to adjust for medical use in these analyses because of inadequate power, and do not have longitudinal data on actual co-use to disentangle how often cannabis and alcohol were being used simultaneously (together) or concurrently (separately). We also did not have information regarding cannabis use quantities, so we do not know whether or how alcohol and cannabis use quantities are related. Without these data, we are unable to

make definitive claims regarding substance substitution. Ongoing studies are collecting daily diary data to address these issues.

Limitations

The harms analyses only cover 2005 and 2010, and do not include the most recent 2015 data set. Given the evolving landscape of cannabis use, products, and regulations, the relationship between cannabis and alcohol might change over time as well. However, our inclusion of survey year in the multivariable regression models partially alleviates this concern by adjusting for differences over time. The NAS is cross-sectional, which limits clinical and etiological conclusions. In addition, the numbers of cannabis users within each frequency category are small relative to the number of abstainers. However, the pattern of findings replicates those found in two longitudinal studies, and extends these previous results by including other clinically important outcomes, like alcohol-related harms. Additional studies with larger samples and more recent data are needed in order to determine whether the pattern of results is stable and consistent across data and other contextual factors. We do not have information regarding type(s) or intensity of AUD treatment received, which likely affects both cannabis and alcohol use; planned studies will collect data on how various types of treatments focused on reducing alcohol use, such as naltrexone, influence co-use with cannabis. We also do not have measures of cannabis-related problems, which may be correlated with alcohol-related problems, and therefore a potential confounder; ongoing studies are collecting data regarding the intersection of cannabis- and alcohol-related problems. We were unable to adjust for use of drugs other than cannabis. Recent work with an untreated sample of drinkers from the 2015 NAS (N=2,813) has shown other drug use to be an important predictor of both drug and alcohol use disorders (Karriker-Jaffe et al., 2016). Other drug use also was a stronger predictor of fewer alcohol abstinent days in comparison to cannabis use as a predictor of fewer alcohol abstinent days in the study of individuals in treatment (Subbaraman et al., 2017). Future analyses should account for other drug use.

Conclusion

Among those with lifetime AUD who have been to treatment, only more than monthly/less than weekly cannabis use is related to more alcohol-related harms and persistent AUD compared to cannabis abstinence. Heavier or lighter cannabis use is not related to worse alcohol outcomes compared to cannabis abstinence.

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Table 1.

Descriptive statistics for general population sample of individuals with lifetime AUD who have been to treatment (N = 772)

	Frequency of cannabis use, past 12 months			
	Never	**< Monthly**	**> Monthly, < Weekly**	**Weekly or more**
Unweighted n	614	44	30	84
Weighted %	75.2	7.0	4.5	13.3
Age (mean(SE))	47.8 (0.7)	43.0 (1.9)*	41.0 (2.7)*	37.7 (2.2)***
Female (%)	31.7	27.7	34.9	27.5
High School graduate (%)	62.9	74.0	43.1	32.9***
Employed (%)	56.0	45.2	60.0	51.9
Married/cohabitating (%)	62.5	46.6	56.3	42.5*
White (%)	74.3	63.1	56.1	81.6
African American (%)	8.0	9.4	17.5	10.1
Hispanic (%)	10.5	12.0	12.3	3.2*
Tobacco use (%)	54.2	87.7***	76.9	85.8***
Past 12-mo volume (mean (SE))	444.2 (64.8)	886.7 (201.5)**	1498.8 (359.9)***	907.0 (199.4)**
Past 30-day freq of 5+ drinks (mean (SE))	0.65 (0.09)	1.89 (0.39)***	2.22 (0.52)***	0.99 (0.33)***
Any alc-related harms[a] (%)	19.1	42.7*	69.8**	34.7
DSM-IV dependence (%)	16.4	44.9***	59.2***	39.1***
Lifetime DSM-IV dependence severity (mean (SE))	5.6 (0.1)	5.7 (0.2)	5.3 (0.4)	5.4 (0.2)

[a]Harms analyses only include n = 528 (442 Never users, 33 < Monthly users, 18 > Monthly, < Weekly users, 35 Weekly or more users) because participants were not asked about harms in 2015

*$P<0.05$

**$P<0.01$

***$P<0.001$ (ref = Never)

Table 2.

Incidence rate ratios (IRR) and odds ratios (OR) with 95% confidence intervals (CI) for alcohol outcomes regressed on cannabis use frequency in a general population sample of individuals with lifetime AUD who have been to treatment (N = 772)

	VOLUME			FREQ 5+[a]			ANY HARMS[b,c]			DSM-IV DEPEND[c]			ANY HARMS[b,d]			DSM-IV DEPEND[d]		
		N=736			N=499			N=499			N=739			N=498			N=498	
	IRR	95% CI		IRR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI		OR	95% CI	
Cannabis use freq (vs. Never)																		
< Monthly	1.40	0.77	2.55	**1.90**	**1.08**	**3.33**	2.27	0.80	6.48	**3.51**	**1.38**	**8.89**	1.45	0.18	11.74	3.53	0.76	16.30
> Monthly, < weekly	**2.83**	**1.43**	**5.60**	**2.83**	**1.38**	**5.79**	**6.82**	**2.29**	**20.33**	**6.53**	**2.66**	**16.02**	**6.18**	**1.35**	**28.37**	6.03	0.65	55.93
Weekly or more	1.37	0.75	2.52	0.95	0.48	1.88	1.51	0.53	4.31	1.86	0.89	3.90	2.50	0.53	11.83	1.63	0.30	8.94
Age	**0.97**	**0.96**	**0.99**	**0.96**	**0.95**	**0.98**	**0.94**	**0.91**	**0.97**	**0.94**	**0.92**	**0.96**	**0.95**	**0.91**	**0.99**	0.95	0.89	1.01
Sex (vs. Female)																		
Male	1.29	0.77	2.16	1.21	0.76	1.93	0.78	0.37	1.65	0.84	0.46	1.54	0.40	0.16	1.03	**0.31**	**0.11**	**0.92**
Education (vs. < High School)																		
High school grad or more	1.70	0.86	3.37	1.33	0.75	2.37	1.41	0.54	3.68	**2.33**	**1.03**	**5.29**	0.93	0.32	2.67	0.92	0.31	3.00
Employment (vs. Unemployed/Retired/etc.)																		
Full- or part-time	1.01	0.59	1.73	0.96	0.60	1.54	0.73	0.35	1.49	0.75	0.42	1.35	**0.39**	**0.15**	**0.99**	0.87	0.33	2.29
Marital staus (vs. Unmarried)																		
Married or cohabitating	0.51	0.33	0.80	0.75	0.50	1.14	0.77	0.40	1.48	0.60	0.34	1.06	1.20	0.48	3.00	1.03	0.41	2.59
Race/ethnic (vs. White)																		
African American	1.32	0.72	2.41	1.15	0.59	2.23	1.88	0.72	4.95	**2.58**	**1.17**	**5.71**	**3.38**	**1.13**	**10.09**	**7.35**	**1.99**	**27.14**
Hispanic	**2.35**	**1.10**	**5.01**	1.18	0.60	2.33	2.41	0.75	7.76	**4.38**	**1.63**	**11.80**	**3.68**	**1.15**	**11.77**	**6.66**	**2.44**	**18.17**
Other/Missing	0.63	0.25	1.58	1.03	0.44	2.42	0.37	0.08	1.79	0.55	0.15	1.99	0.02	0.00	11.60	0.49	0.13	1.83
Tobacco use (vs. No)																		
Yes tobacco	**1.98**	**1.16**	**3.39**	**1.86**	**1.16**	**3.00**	1.52	0.72	3.22	**2.08**	**1.05**	**4.10**	0.59	0.25	1.42	0.72	0.29	1.79
Time	**1.51**	**1.05**	**2.15**	1.30	0.87	1.95	**2.94**	**1.54**	**5.61**	**1.77**	**1.12**	**2.80**	**4.62**	**1.64**	**13.00**	2.13	0.83	5.49
Lifetime DSM-IV dependence severity	1.00	0.85	1.18	0.92	0.80	1.06	0.89	0.72	1.10	1.02	0.85	1.24	0.89	0.68	1.17	1.15	0.85	1.55
Past 12-month alcohol volume	--	--	--	--	--	--	--	--	--	--	--	--	1.00	1.00	1.00	1.00	1.00	1.00
Past 30-day frequency of 5+ *drinks*	--	--	--	--	--	--	--	--	--	--	--	--	**2.91**	**1.73**	**4.91**	**2.60**	**1.36**	**4.95**

Bold signifies $P < 0.05$

[a] Frequency of 5+ drink occasions regression only includes N=499 because only drinkers were asked about frequency of 5+ occasions

[b] Harms regressions only include N=499 because participants were not asked about harms in 2015

[c] Does not adjust for past 12-month alcohol volume or past 30-day frequency of drinks

[d] Adjusts for past 12-month alcohol volume and past 30-day frequency of drinks