The association between regular marijuana use and adult mental health outcomes

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Abstract

Objective

The present study is a prospective examination of the relationship between regular marijuana use from adolescence through young adulthood and mental health outcomes at age 33.

Methods

Data came from a gender-balanced, ethnically diverse longitudinal panel of 808 participants from Seattle, Washington. Outcomes included symptom counts for six mental health disorders. Regular marijuana use was tracked during adolescence and young adulthood. Regression analyses controlled for demographics and early environment, behaviors, and individual risk factors.

Results

Nonusers of marijuana reported fewer symptoms of alcohol use disorder, nicotine dependence, and generalized anxiety disorder than any category of marijuana users. More persistent regular marijuana use in young adulthood was positively related to more symptoms of cannabis use disorder, alcohol use disorder, and nicotine dependence at age 33.

Conclusions

Findings highlight the importance of avoiding regular marijuana use, especially chronic use in young adulthood. Comprehensive prevention and intervention efforts focusing on marijuana and other substance use might be particularly important in the context of recent legalization of recreational marijuana use in Washington and other U.S. states.

Keywords: regular marijuana use, cannabis, persistence, adult mental health

1. Introduction

Marijuana is the third most frequently used substance—after tobacco and alcohol—that causes addiction (Caulkins, 2016; Compton et al., 2004). However, evidence from prospective studies regarding the long-term effects of regular marijuana use on other psychiatric disorders remains limited and mixed. The present study uses data from a longitudinal project to examine the relationship between regular marijuana use from age 14 to 30 and mental health outcomes at age 33.

There is some evidence that heavy and persistent marijuana use is associated with negative long-term health consequences, including cognitive deficits and physical and mental health problems (for reviews, see Hall, 2015; Volkow et al., 2014)). These associations are most salient for substance use disorders with more frequent marijuana use predicting higher likelihood and more symptoms of drug use disorder (e.g., Hall and Degenhardt, 2009). However, reports of the association between marijuana use and other mental health disorders, such as depression and anxiety, are more mixed (for reviews, see Crippa et al., 2009; Hall, 2015; Lev-Ran et al., 2014; Moore et al., 2007; Yurasek and Hadley, 2016). Specifically, while there is some evidence that heavy (i.e., at least weekly) marijuana use predicts increased likelihood of developing depression when compared to occasional use and nonuse (Lev-Ran et al., 2014), the mechanisms that account for this association are unclear and longitudinal studies that account for confounding factors are needed (Crippa et al., 2009; Hall, 2015; Lev-Ran et al., 2014; Yurasek and Hadley, 2016).

Adolescent marijuana use has a special prominence in studies examining the adverse effects of marijuana use. Regular marijuana use by adolescents has been associated with comorbid use of other substances and an increased risk of later drug abuse and dependence (e.g., Chen et al., 2005; Perkonigg et al., 2008; Winters and Lee, 2008). Whereas this association might be attributable to the persistence of use or prolonged exposure to marijuana, some researchers have hypothesized that this association may be due to the drug's effects on the developing brain and neurocognitive functioning of adolescents (for review see, e.g., Jacobus et al., 2009; Lisdahl et al., 2014). The association between adolescent marijuana use and other outcomes, including lower academic achievement and educational attainment (e.g., Lynskey and Hall, 2000; Lynskey et al., 2003; Maggs et al., 2015; Silins et al., 2015; Stiby et al., 2015), executive functioning (e.g., Fontes et al., 2011) and interference with the successful transition into adulthood (Brook et al., 2002; Fergusson and Boden, 2008; Lynskey and Hall, 2000; Scholes-Balog et al., 2016), has also been reported. However, there is some recent evidence from twin studies that suggests the association between adolescent marijuana use and deficits in cognitive functioning and academic outcomes may be due to common risk factors, such as other substance use (Mokrysz et al., 2016) and family environment (Jackson et al., 2016).

Indeed, many of the existing studies have been limited in their ability to rule out alternate explanations for the associations between marijuana use and negative outcomes because they lack data on pre-marijuana use functioning or other relevant controls that can confound the relationship between marijuana use and later outcomes. Prospective indicators of early psychopathology should be controlled in models assessing the link between subsequent marijuana use and later psychopathology to account for preexisting vulnerability and selection effects (Griffith-Lendering et al., 2013; Lev-Ran et al., 2014). In fact, some studies have found that once common risk factors such as childhood behavior

problems, socioeconomic disadvantage, life stressors, and deviant peers were accounted for, there was no significant association between marijuana use and later psychopathology, such as depression (e.g., Bechtold et al., 2015; Manrique-Garcia et al., 2012).

In addition, there is considerable variability in individual patterns of marijuana use over the course of adolescence and adulthood. This variability pertains to both timing and frequency of use. Many users initiate in adolescence, and some progress from occasional to persistent regular use (Substance Abuse and Mental Health Services Administration, 2013), but the associations between different developmental patterns of regular marijuana use over time and mental health outcomes are not well understood (Bechtold et al., 2015). A recent examination of trajectories of marijuana use from adolescence into adulthood using the present sample examined bivariate relationships between four identified patterns of marijuana users (chronic, adolescence-limited, late-onset, and nonusers) and a host of correlates at different developmental periods (Epstein et al., 2015). That study found mean differences in mental health outcomes at age 33; in general, chronic marijuana users had more symptoms of cannabis, alcohol, and tobacco use disorders than other types of users, and more symptoms of anxiety disorder than nonusers of marijuana. However, these analyses were by design descriptive and did not control for potential confounders beyond demographics, thus limiting interpretation of the unique role of marijuana use on subsequent outcomes.

Research has suggested that it may be regular use – i.e., weekly or more frequent use in adolescence (e.g., Silins et al., 2015) and 4+ times per week in adulthood (e.g., Cerdá et al., 2016) – and its persistence over time rather than occasional use that relates more consistently to negative outcomes (Cerdá et al., 2016; Meier et al., 2012). Over the past two decades, a majority of U.S. states loosened their laws related to marijuana and legalized medical marijuana use (e.g., Cambron et al., 2017) and eight states have recently (since 2012) also passed recreational marijuana laws (RML) legalizing recreational marijuana use for adults. Recent nationwide studies have reported that medical marijuana law (MML) implementation was associated with increases in the perceived availability of marijuana and the prevalence of marijuana use among adults in all age groups (Mauro et al., 2017a). MML implementation has also predicted decreases in perceived harm from regular use of marijuana among adults (e.g., Mauro et al., 2017b). While comprehensive studies evaluating the effect of RML implementation on marijuana-related risk factors and adult use are only beginning, it is possible that the continued loosening of the legal and normative context related to recreational marijuana may result in increases in the prevalence of any (or non-regular) use as well as regular use and its persistence over time among adults (e.g., Caulkins, 2017; Caulkins et al., 2012; Pacula et al., 2014). Thus, understanding the relationship between marijuana use (i.e., its different patterns, such as non-regular compared to regular marijuana use, and its persistence in adulthood) and negative consequences, such as mental health problems, is of urgent public health importance.

Although previous studies that have examined mental health outcomes of long-term marijuana use have focused on empirically derived, probabilistic patterns of use over time (e.g., Bechtold et al., 2015; Epstein et al., 2015), they have not focused specifically on *regular* use defined by specific a priori criteria. Furthermore, studies of the effects of *persistent regular* marijuana use (defined as a 5-level variable distinguishing between no use, no regular use, and regular use in 1 through 3 or more assessment points), have been limited to neuropsychological decline (e.g., Meier et al., 2012) and economic and social problems (Cerdá et al., 2016) later in adulthood.

This study distinguished between adolescent- and adult-onset of regular use and its persistence, as well as the non-regular use of marijuana when examining the associations between marijuana use and mental health outcomes. Our research questions were: (1) How do specific patterns of adolescent and young adult regular marijuana use relate to mental health outcomes at age 33? and (2) Is there a relationship between persistence of regular marijuana use in young adulthood and mental health outcomes at age 33? We hypothesized that adolescent onset of regular marijuana use that persists into

adulthood will be associated with the worst mental health outcomes at age 33, and that adult regular users will have worse outcomes when compared to those who do not use marijuana regularly and those who abstain from use. Furthermore, we hypothesized that greater persistence of regular marijuana use in young adulthood will predict worse mental health outcomes at age 33. In order to reduce the potential for reversed causation, we included childhood internalizing and externalizing behavior problems as markers of early psychopathology among the control variables. All models also included behavioral inhibition and disinhibition as markers of the propensity to engage in risky behavior as well as demographic controls and socioeconomic disadvantage. Models that examined substance use outcomes also controlled for adolescent use of that substance.

2. Methods

2.1. Sample

Data came from The Seattle Social Development Project, a longitudinal study that followed 808 youth from elementary school to adulthood to understand prosocial and antisocial development across the lifespan. In the fall of 1985, all 1,053 fifth-grade students in 18 Seattle public elementary schools serving high-crime areas were invited to participate in the study; 808 (77%) of the eligible students and their parents consented to participate in the longitudinal study. Consenting participants were assessed in the fall of 1985 and spring of 1986. Thereafter, they were surveyed annually through 10th grade, again in the 12th grade, and then every 3 years until age 33. The annual retention rate was relatively high; 92% (n=721) of those still living (784 participants) completed the age 33 assessment in 2008. There were few differences between those who participated at the age 33 assessment and those who did not. Those who participated were more likely to be female, less likely to be eligible for free or reduced price lunch in childhood, less likely to be Black, and reported lower levels of childhood internalizing and externalizing behavior problems. These variables were included in the final regression models. Those lost to attrition, compared to those who participated in the age 33 assessment, did not differ significantly on any of the other covariates. The Human Subjects Review Committee at the University of Washington approved the procedures and measures. Table 1 shows the sample demographics as well as the distribution of the variables included in the present study.

Table 1

Descriptive statistics for the full sample and by the regular marijuana use groups

		Total sample[#]	% non-missing	Adolescent onset of persistent regular use (n=38)	Adult onset of persistent regular use (n=66)	Adolescence-limited regular use (n=53)	Non-regular use (n=358)	(n
Demographics	Male	51.0%	100.0	78.9%	68.2%	66%	48.3%	
	White	47.2%	100.0	47.4%	51.5%	35.8%	57%	
	Black	25.6%	100.0	39.5%	36.4%	50.9%	20.9%	
	Native	5.3%	100.0	7.9%	3%	9.4%	6.4%	
	Asian	21.9%	100.0	5.3%	9.1%	3.8%	15.6%	
	Free lunch	52.4%	100.0	63.2%	51.5%	73.6%	45.5%	
Predictors	Regular marijuana use in adolescence	11.4%	99.0	100%	NA	100%	NA	
	Persistence of regular marijuana use in YA	NA	97.8	2.61 (0.79)	2.56 (0.79)	NA	NA	
Early environmental risk	General community risk	1.50 (1.12)	79.6	2.00 (1.02)	1.69 (1.21)	1.86 (1.00)	1.45 (1.14)	
	Substance use related community risk	1.50 (1.12)	97.3	1.94 (1.12)	1.59 (1.18)	2.12 (1.02)	1.67 (1.08)	
	General peer risk	1.50 (1.12)	97.4	2.14 (0.99)	1.75 (1.02)	2.31 (1.02)	1.67 (1.04)	
	Substance use related peer risk	1.46 (1.15)	73.0	1.93 (0.81)	1.43 (1.12)	2.28 (1.00)	1.63 (1.15)	

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Notes:

[#]the sample size is based on the total sample of original participants n=808. Because of some missing data, the actual sample size for each variable is the % nonmissing times 808 (e.g., the n for Cannabis use disorder SC is 85.6% times 808=692); SD = standard deviation; NA = Not Applicable; YA = young adulthood; SC = symptom count.

2.2. Measures

2.2.1. Outcomes

The outcomes in this study involved substance use and other mental health problems assessed by the short form of the Diagnostic Interview Schedule (DIS; Robbins, 1981) at age 33. Participants reported on their symptoms of alcohol, cannabis, nicotine, anxiety, depression, and social phobia disorders in the last year. The symptoms reported for alcohol abuse or dependence and cannabis abuse or dependence (termed henceforth alcohol use and cannabis use disorders, respectively), nicotine dependence, generalized anxiety disorder, major depression, and social phobia disorders were based on the DSM-IV diagnostic criteria (American Psychiatric Association, 1994) and summed into symptom count indices. The measures ranged from 0 to 10 criteria for the cannabis use disorder, 0 to 11 for the alcohol use disorder, 0 to 6 for the nicotine dependence and the generalized anxiety disorder, 0 to 9 for the major depressive disorder, and 0 to 5 for the social phobia disorder. Table 1 shows the mean and standard deviation for each – in the full sample as well as by the marijuana use groups.

2.2.2. Predictors The primary predictor variable was regular marijuana use, which was assessed prospectively via self-report starting at age 14. Regular use was operationalized, based on previous research (i.e., Cerdá et al., 2016; Meier et al., 2012; Silins et al., 2015), as weekly use at any wave in adolescence (through age 18), and using 4+ days a week at any wave in adulthood (ages 21+). To answer the first research question about different patterns of regular marijuana use, the *frequency of use* variables over time were combined to create a set of five mutually exclusive dummy variables: (1) adolescent onset of regular use that persisted into adulthood (n = 38), (2) adult onset of regular use (n = 66), (3) adolescence-limited regular use (n = 53), (4) non-regular use (n = 358) in adolescence and/or adulthood, and (5) nonuse (n = 269) in adolescence and adulthood.

In the second set of analyses that addressed the second research question, persistent regular marijuana use in adulthood was quantified based on the number of waves in adulthood (ages 21, 24, 27, and 30) that the adult regular users engaged in regular marijuana use. This variable ranged from 1 to 3 (1 = regular use in one adult wave, 2 = regular use in two adult waves; and 3 = regular use in three or more adult waves (Cerdá et al., 2016). Table 1 presents the average number of waves of regular use for the two groups of adult regular marijuana users (i.e., those who onsetted regular use in adolescence that persisted into adulthood and those who onsetted regular use in adulthood). This three-level variable was entered into the models while controlling for any regular use in adolescence (weekly use at or before age 18).

2.2.3. Control Variables Control variables included demographic characteristics: gender (coded male = 1, female = 0), ethnicity (dummy variables for African American or Black, Asian American, Native American, and "Other" ethnicity, with White as the referent group), and childhood poverty defined as eligibility for participation in the National School Lunch/Breakfast program collected from participants' school records (coded as 1 = eligible, 0 = not eligible between the ages 10 and 12). Other control variables included the average frequency of tobacco and alcohol use during adolescence, for which self-reports of use of each substance were averaged across adolescence (ages 11 through 18); these were used in the models testing the nicotine dependence and alcohol use disorder outcomes, respectively. Analyses also included controls for early environmental and individual risk (see below).

2.2.3.1. *Early Environmental Risk* was assessed between ages 10 and 14 by general and substance use-related risk factors in three domains: peer, family, and community. All items were standardized and averaged within age, and then averaged across available ages to create six composite measures assessing exposure to risk within the domain; resulting scales were then divided into quartiles (Lee et al., 2012). General peer environment risk included items about youth's association with antisocial peers (39 items, average α = 0.67; for description of items and coding, see Lee et al., 2012); general family risk tapped into family conflict, management, and bonding (55 items across grades, α = 0.73); community risk included items on neighborhood disorganization, such as crime and gang activity (10 items, α = 0.70). In addition, children and parents reported on parents' norms about alcohol use, and parents reported on their own and their live-in partner's binge drinking (5 or more drinks per occasion),

which comprised the substance use-related family risk factor (20 items across ages, $\alpha = 0.77$). Substance use-related peer risk was assessed by participants' report of alcohol-related behavior of their three or four best friends (13 items across ages, $\alpha = 0.79$; see Lee et al., 2012). Substance use-related neighborhood risk was assessed by participant report of alcohol use and norms in their community (3 items, $\alpha = 0.79$).

2.2.3.2. Early Individual Risk included five variables: baseline symptoms of psychopathology measured by the internalizing (affective disorder and anxiety problems) and externalizing (conduct problems and other problems related to under-control of emotion and behavior) scales from the Teacher Report Form of the Child Behavior Checklist (Achenbach, 1991), averaged between ages 10 and 14; academic achievement measured as an average of students' grades and achievement scores based on student report and school records from ages 10 through 14 (see Guttmannova et al., 2012); and behavioral inhibition and disinhibition, denoting relatively stable individual difference characteristics related to trait anxiety and propensity to engage in risky behaviors, respectively, assessed via self-report at age 14 (for items, see Hill et al., 2010).

A part of this sample participated in a preventive intervention during elementary school (see Hawkins et al., 1999 for a description and analysis of the intervention and effects). While differences in prevalence rates and means have been observed between intervention and control groups, prior analyses have shown few differences in the relationships among variables related to the etiology of substance use and the covariance structures of the groups (e.g., Huang et al., 2001). Analyses for this report were based on the full sample after determining that there were no substantial group differences in the relationships of the predictors with adult mental health outcomes. As a sensitivity check, all of the final models were also estimated with a variable indicating early intervention group status (experimental or control), and the results remained analogous.

2.3. Analysis

For both research questions, we ran a series of negative binomial regression models to predict the DSM-IV symptom count for the three substance use disorders and three other mental health disorders. All analyses were conducted with Mplus 7.11 (Muthén and Muthén, 1998–2013). To reduce potential bias due to some missing data, full information maximum likelihood estimation (FIML; e.g., Graham, 2009) using the maximum likelihood estimator with robust standard errors and Monte Carlo integration was implemented in all analyses. The predictors were entered in a series of steps. First, we entered the marijuana use variables (the categories of marijuana use in the first set of analyses, and adolescent regular marijuana use and persistence of adult regular use in the second set; Model 1). Then we added demographics (Model 2), then the early environmental risk variables (Model 3), and finally the individual risk variables (Model 4). With the exception of nicotine dependence, the results remained similar across model specifications, and for brevity we present results from Model 1 and then the fully controlled model (Model 4).

For the first research question, the models were first run to compare the nonusers to all other groups of users (i.e., the nonusers were specified as the referent group). The referent group was subsequently switched in order to examine whether non-regular users differed from regular users and whether adolescent-onset regular users differed from adult-onset regular users. For the cannabis use disorder outcome, we started with non-regular users as the referent group and the nonusers were excluded from the analyses. We applied the Benjamini-Hochberg procedure to adjust the statistical significance level for multiple pairwise statistical comparisons (e.g., Benjamini and Hochberg, 1995; Keselman et al., 2002). This procedure provides a reasonable balance between Type I and Type II errors (e.g., Hochberg and Benjamini, 1990).

3. Results

3.1. Research Question 1: How do different patterns of adolescent and young adult regular marijuana use relate to mental health outcomes at age 33?

Table 2 presents the predicted mean symptom count for each group for the baseline models (Model 1; see Table 1 for observed means for each group) as well the predicted mean symptom counts adjusted for covariates from Model 4 that included all of the control variables. Groups that were statistically different from another are noted with superscripts. We also present the incidence rate ratios (RR) and their 95% confidence intervals to inform about the size of the effect and avoid over-reliance on p-values. These values are presented for the baseline models and the models that included all of the control variables. Coefficients from comparisons that used the first referent group consisting of nonusers of marijuana are presented; the other coefficients can be derived by taking the natural logarithm of the presented incidence rate ratios and subtracting the coefficients of interest from each other before exponentiating them back into incidence rate ratios. However, the main information about group comparisons is presented in the means column.

Table 2

Patterns of regular marijuana use predicting mental health outcomes at age 33.

	CUD			AUD			ND			MDD		
	Means[*]	IRR	95% CI[**]	Means	IRR	95% CI	Means	IRR	95% CI	Means	IRR	95% CI
Model 1: No controls												
Adolescent-onset	1.05[a]	4.52	(1.92; 10.63)	2.07[a]	9.23	(4.45; 19.18)	2.06[a]	4.86	(3.28; 7.21)	1.81	2.20	(1.12 4.33)
Adult-onset	1.09[a]	4.69	(2.49; 8.86)	1.08[a;b]	4.81	(2.44; 9.48)	1.89[a]	4.46	(3.16; 6.30)	1.05	1.27	(0.62 2.63)
Adolescence-limited	0.37[b]	1.60	(0.54; 4.69)	1.34[a;b]	5.97	(2.79; 12.77)	1.06[b]	2.48	(1.48; 4.17)	1.09	1.32	(0.61 2.86)
Non-regular use	0.23[b]	R	R	0.89[b]	3.98	(2.23; 7.09)	1.23[b]	2.89	(2.10; 3.98)	1.32	1.61	(1.06 2.43)
Non-use Model 4: All controls	NA	NA	NA	0.22[c]	R	R	0.42[c]	R	R	0.82	R	R
Adolescent-onset	0.82[a]	6.18	(2.47; 15.46)	1.14[a]	4.72	(2.04; 10.92)	1.28[a;b]	2.70	(1.69; 4.31)	1.28	1.86	(0.72 4.83)
Adult-onset	0.93[a]	7.01	(3.47; 14.18)	0.86[a]	3.57	(1.74; 7.30)	1.54[a]	3.26	(2.21; 4.79)	0.67	0.97	(0.38 2.45)
Adolescence-limited	0.18[b]	1.37	(0.41; 4.64)	0.71[a]	2.96	(1.39; 6.26)	0.65[c]	1.38	(0.81; 2.34)	0.88	1.28	(0.49 3.35)
Non-regular use	0.13[b]	R	R	0.73[a]	3.02	(1.76; 5.16)	1.10[b]	2.33	(1.67; 3.25)	1.14	1.65	(0.99 2.74)
Non-use	NA	NA	NA	0.24[b]	R	R	0.47[c]	R	R	0.69	R	R

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Notes: Analytic sample includes all original participants; sample size n=808 for AUD, ND, MDD, GAD, and SPD models, and n=539 (excluding the non-use group) for the CUD models; CUD = Cannabis Use Disorder; AUD = Alcohol Use Disorder; ND = Nicotine Dependence; MDD = Major Depression Disorder; GAD = Generalized Anxiety Disorder; SPD = Social Phobia Disorder; IRR = Incidence Rate Ratio; CI = Confidence Interval; R=referent group for the first set of comparisons; NA=not applicable;

[*]Predicted mean counts of symptoms
[**]95% confidence intervals were computed as the exponentiated endpoints of the confidence intervals in the natural parameter space; within models, predicted mean symptom counts in the same column that do not share superscripts differ at p<.05 after implementing Benjamini Hochberg adjustment for multiple statistical comparisons; because these groups are coded as linear combinations of each other, the incidence rate ratio coefficients presented in the table come from the models where the non-user group served as the referent (except for CUD models where the non-regular use group served as the referent and non-users were excluded); the

coefficients for other comparisons can be derived by taking the natural logarithm of the presented incidence rate ratios and subtracting the relevant coefficients from each other and then exponentiating them again into incidence rate ratios.

In the fully controlled models that assessed the relationship between cannabis use disorder and the various categories of marijuana users, the nonusers of marijuana were excluded from the analyses. Both groups of adult regular users (adolescent-onset and adult-onset) had higher numbers of cannabis disorder symptoms than the non-regular users (the first referent comparisons and the coefficients from these are presented in Table 2), as well as the adolescence-limited users (denoted in superscripts – predicted mean counts of symptoms in the same column that do not share the same superscript differ at $p < 0.05$ after implementing the Benjamini-Hochberg adjustment for multiple statistical comparisons). However, the number of symptoms for the two groups of adult regular users did not differ significantly from each other. For alcohol use disorder, all four marijuana use groups had higher numbers of alcohol use disorder symptoms than those who abstained from marijuana, and the numbers of symptoms among the four use groups were not statistically different from each other. For nicotine dependence, adolescent-onset and adult-onset regular users and non-regular users had higher numbers of nicotine dependence symptoms than both nonusers and adolescence-limited regular users, and no other comparisons were statistically significant. For major depression disorder and social phobia disorder, none of the four use groups were statistically different from nonusers. Similar to the nicotine dependence outcome, the three adult marijuana-using groups (adolescent-onset and adult-onset regular users as well as non-regular users) each reported higher numbers of symptoms of generalized anxiety disorder than nonusers, but did not differ from each other. Adolescence-limited regular users were not statistically different from non-users in their numbers of symptoms of generalized anxiety disorder.

3.2. Research Question 2: Is there a relationship between persistent regular marijuana use in adulthood and mental health outcomes at age 33?

Table 3 summarizes results from the regression models for persistence of regular marijuana use in adulthood predicting mental health outcomes at age 33 among adult regular users. Controlling for adolescent regular use (which—as would be expected based on the results in Table 2—was not statistically significant in any of these models), more persistent regular marijuana use in adulthood was related to significantly higher numbers of symptoms of cannabis use disorder, alcohol use disorder, and nicotine dependence. This pattern of results remained with the inclusion of control variables. Specifically, each 1-unit increase on the ordinal persistence of regular marijuana use in adulthood variable predicted an increase in cannabis use disorder symptoms by a factor of 2.5, an increase in alcohol use disorder symptoms by a factor of 1.6, and an increase in nicotine dependence symptoms by a factor of 1.3. However, more persistent regular marijuana use in adulthood did not predict significantly higher numbers of symptoms of generalized anxiety or social phobia disorders in either model. The persistence of regular marijuana use coefficient, while not statistically significant on a bivariate level for depression disorder (Model 1), became statistically significant in the fully controlled model (IRR = 2.64; 95% CI = 1.24; 5.59).

Table 3

Persistence of regular marijuana use predicting substance use and mental health outcomes at age 33

	CUD		AUD		ND		MDD		GAD		SPD	
	IRR	95% CI*	IRR	95% CI*	IRR	95% CI*	IRR	95% CI*	IRR	95% CI*	IRR	95% CI*
Model 1: No controls												
Persistence of adult regular use	**1.86**	(1.20; 2.88)	**1.53**	(1.09; 2.15)	1.12	(0.93; 1.34)	1.16	(0.66; 2.05)	0.88	(0.68; 1.14)	1.01	(0.67; 1.51)
Model 4: All controls												
Persistence of adult regular use	**2.47**	(1.36; 4.51)	**1.63**	(1.04; 2.55)	**1.28**	(1.04; 1.57)	**2.64**	(1.24; 5.59)	0.79	(0.60; 1.05)	0.74	(0.46; 1.18)

Notes: Analytic sample excludes those who reported non-regular or no use of marijuana in adulthood; sample size n=124; CUD = Cannabis Use Disorder; AUD = Alcohol Use Disorder; ND = Nicotine Dependence; MDD = Major Depression Disorder; GAD = Generalized Anxiety Disorder; SPD = Social Phobia Disorder; IRR = Incidence Rate Ratio; CI = Confidence Interval; coefficients in **bold** are significant at p<.05.

*95% confidence intervals were computed as the exponentiated endpoints of the confidence intervals in the natural parameter space.

4. Discussion

Understanding the prospective association between regular marijuana use and mental health is important, particularly in the present time when marijuana use for recreational purposes has already been legalized for adults in eight U.S. states and the normative context around marijuana use has been trending toward more positive attitudes about use and lower perception of harm from regular use among young adults (i.e., 18- to 30-year-olds; Johnston et al., 2015). In turn, more favorable attitudes about use and lower perception of harm have been linked to higher prevalence of and more frequent use of marijuana among adolescents (e.g., Fleming et al., 2016) as well as young adults (e.g., Salas-Wright et al., 2015). While the evaluation of the effects of recreational marijuana laws on population increases in marijuana use is currently underway and preliminary findings are mixed (e.g., Cambron et al., 2017; Cerdá et al., 2016; Darnell, 2015), understanding the potential impact of regular marijuana use on adult outcomes is important from public health and prevention perspectives.

The main findings of this study are that all groups of marijuana users—regular and non-regular—reported more symptoms of alcohol use disorder, and all except adolescence-limited regular users reported more symptoms of nicotine dependence and generalized anxiety disorder than those who abstained from marijuana use, even after controlling for salient confounders and early levels of functioning. Importantly, the present study found that more waves of persistent regular marijuana use in young adulthood were related not only to more cannabis use disorder symptoms but also to more

alcohol use disorder and nicotine dependence symptoms at age 33. Thus, our findings highlight the importance of comprehensive prevention and intervention efforts focusing on substance use that include marijuana as well as other substances.

The results regarding regular marijuana use and cannabis use disorder symptoms are consistent with prior research (Compton et al., 2004). Both groups of adult regular users (i.e., those who first used regularly in adolescence and persisted into adulthood and those who first used regularly in adulthood) reported more cannabis use disorder symptoms than adolescence-limited regular users and non-regular users, although they were not different from each other. The finding of no statistically significant difference between those who began using regularly in adolescence and those who began using regularly in adulthood is unexpected in light of studies that find that earlier onset of marijuana use is associated with increased risk for cannabis use disorder [e.g., Winters and Lee (2008); for review, see Gfroerer et al. (2002); Hall and Degenhardt (2009)]. However, the potency of marijuana increased considerably from the early 1990s to the 2000s (Compton et al., 2004; Mehmedic et al., 2010), the years that correspond to adolescence and young adulthood in the SSDP sample. The elevation in marijuana potency could have increased its addictive potential (Compton et al., 2004), and may explain why adults with a relatively shorter career of regular marijuana use experience as many negative symptoms as participants who initiated regular use as adolescents. Future studies with cohorts of youth whose adolescence occurred in more recent years when higher potency of marijuana has become more prevalent and who were followed longitudinally into adulthood should examine this hypothesis explicitly. However, it is also possible that the differential threshold for regular use in adolescence versus in adulthood, while based on previous research and substantively justified (see Cerdá et al., 2016; Silins et al., 2015), could have contributed to the lack of statistically significant difference in outcomes between adolescent- and adult-onset of regular use. In the present sample, only 5% of adolescents engaged in regular marijuana use at the adult threshold (4 or more times in the past week) and, thus, it was not feasible to use that cut-off in adolescence. Studies with samples of at-risk adolescents or clinical samples where higher levels of use are normative should examine the effects of using different definitions of regular use and its persistence.

Finally, while all groups of marijuana users, except for adolescence-limited users, had higher rates of generalized anxiety symptoms than nonusers, the persistence of adult regular use was not related to a higher symptom count. Unlike substance use disorders where a dose-response relationship between persistence of regular marijuana use and severity of disorder was evidenced, anxiety disorder symptoms were equivalently responsive to any regular marijuana use pattern, compared to abstinence. It is plausible that individuals with episodic anxiety problems use marijuana for coping with the negative effects of anxiety (e.g., Bonn-Miller et al., 2008), which might explain why their symptoms of anxiety were higher than that of nonusers despite our controls for early psychopathology. Our findings of the lack of a relationship between marijuana use and depression and social phobia disorders are consistent with other studies that have found no relationship between marijuana use and depression when the relevant confounds were accounted for (Bechtold et al., 2015; Manrique-Garcia et al., 2012), although one study (Buckner et al., 2008) did show a relationship between marijuana dependence and social anxiety disorder.

4.1. Limitations and Strengths

Limitations of the present study should be noted. We assessed frequency of marijuana use but not the amount of use. There may be regular users who use small amounts and less frequent users who use large amounts of marijuana, and those distinctions would be missed by this approach. A similar issue may exist with regard to differences in potency, which is rarely taken into account in marijuana studies and was not assessed here. Future studies could incorporate these dimensions of use to fine-tune the understanding of the relationship between marijuana use and mental health. However, the persistence

of regular use as well as the patterns of marijuana use assessed in this study were strongly related to cannabis use disorder in the expected direction, which provides some evidence of the validity of our approach. In addition, we assessed marijuana use by a single modality as *smoking* marijuana. Edibles and other routes of marijuana administration were less common in 2008 when the age 33 assessment was completed than they are today, given that marijuana-infused products and vaping have proliferated following marijuana legalization in Washington and other states (Schauer et al., 2016). Future studies should assess multiple routes of administration to reflect current trends in marijuana use. As in most other studies, marijuana use was assessed by self-report and may be subject to under-reporting. In addition, as noted above, we used different thresholds for regular use in adolescence and young adulthood, which could have influenced the results. Finally, this sample is geographically limited and may not generalize to other areas of the country.

Despite these limitations, this study had several strengths. The sample was followed prospectively from ages 10 to 33 with high retention rates. In addition, we controlled for several confounding factors predating the onset of marijuana use, which is critical when examining temporal associations between marijuana use and outcomes. Furthermore, our analyses focused on different patterns of *regular* use, a critical consideration when examining marijuana use outcomes.

4.2. Implications

The present study provides evidence that regular marijuana use that persists over time is associated with substance use problems. Moreover, any involvement in marijuana use in adulthood predicted more problems with anxiety than abstaining from marijuana use. The findings from our study contribute to the growing body of evidence that suggests that marijuana use may not be harmless at least in terms of substance use problems. As more states consider legalizing adult marijuana use for recreational purposes, policy, media, and public health outreach needs to include accurate information about the risks associated with marijuana use. This is particularly important if it turns out that legalizing marijuana leads to more regular marijuana use by the general population, an outcome suggested as likely by numerous scientists (e.g., Caulkins, 2017; Caulkins et al., 2012; Pacula et al., 2014).

Highlights

- Abstaining from marijuana predicts fewer symptoms of alcohol use disorder
- Abstaining from marijuana predicts fewer symptoms of nicotine dependence
- Abstaining from marijuana predicts fewer symptoms of generalized anxiety disorder
- Chronic adult marijuana use predicts more symptoms of substance use disorders

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Footnotes

Contributors

Conflict of Interest

The authors have no conflict of interest to declare.

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