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Cannabis use disorder and male sex predict medical cannabis card status in a sample of high risk adolescents

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Abstract

Objective—To examine if a substance use disorder (SUD), especially cannabis use disorder in adolescence, predicts future medical cannabis card status among high-risk youth.

Methods—Data collection occurred in Denver and San Diego. We recruited adolescents, with or at high risk for SUD and conduct problems (hereafter probands) and their siblings (n=654). Baseline (Wave 1) assessments took place between 1999 and 2008, and follow-up (Wave 2) took place between 2010 and 2013. In initial bivariate analyses, we examined whether baseline DSM-IV cannabis abuse/dependence (along with other potential predictors) was associated with possessing a medical cannabis card in young adulthood (Wave 2). Significant predictors were then included in a multiple binomial regression. Self-reported general physical health was also evaluated at both time points. Finally, within Wave 2, we tested whether card status was associated with concurrent substance dependence.

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Author Disclosures

Conflicts of Interest

Marilyn Coors is the spouse of the Chairman of the MolsonCoorsBrewing Company, and the company has not contributed any funds nor had any influence on this project. The authors have no conflicts of interest to disclose.

Contributors

Kim contributed towards the design, analysis, data interpretation, and manuscript. Coors contributed towards the data interpretation and manuscript. Young contributed towards the analysis, data interpretation, and manuscript. Raymond contributed towards the data interpretation, and manuscript. Hopfer contributed towards the design, data interpretation, and manuscript. Wall contributed towards the data interpretation and manuscript. Corley contributed towards the data interpretation and manuscript. Brown contributed towards the data interpretation, and manuscript. Sakai contributed towards the design, analysis, data interpretation, and manuscript. Drs. Hopfer, Wall, and Brown served as PIs of the grants, which funded collection of this longitudinal sample and designed the original study. All authors approved of the final manuscript before submission.

Results—About 16% of the sample self-reported having a medical cannabis card at follow-up. Though bivariate analyses demonstrated that multiple predictors were significantly associated with Wave 2 card status, in our multiple binomial regression only cannabis abuse/dependence and male sex remained significant. At Wave 2, those with a medical cannabis card were significantly more likely to endorse criteria for concurrent cannabis dependence. There was no significant difference in self-reported general physical health.

Conclusions—Cannabis abuse/dependence and male sex positively predicted future medical cannabis card holder status among a sample of high risk adolescents. Physicians conducting evaluations for medical cannabis cards should carefully evaluate and consider past and concurrent cannabis addiction.

Keywords

medical marijuana; marijuana; adolescents; substance use disorder

1. Introduction

In recent decades, there has been a shift in the legal perspective in the United States regarding cannabis use. In 1996, California enacted the Compassionate Use Act, becoming the first state to legalize medical cannabis (People of the State of California, 1996). Many states followed suit, including Colorado with passage of Amendment 20 to the state constitution in 2000, and as of August 2017, 29 states and D.C. have medical cannabis laws (MMLs; ProCon, 2017). However, individuals in these states can still be charged for cannabis-related crimes under federal law because the Drug Enforcement Agency schedules cannabis as a Class I substance and because Federal law considers possession and distribution of cannabis a crime (USDEA, 2016). Between 2001 and 2008 medical cannabis participation was “relatively low and flat” (Fairman, 2016). But in 2009, the Department of Justice issued the Ogden Memorandum, which stopped the Federal prosecution of “individuals whose actions are in clear and unambiguous compliance with existing state laws providing for the medical use of cannabis” (Ogden, 2009). Starting in 2009, some states experienced rapid growth of their medical cannabis registries (Fairman, 2016; Schuermeyer et al., 2014). For example, in Colorado between 2001–2008 a total of only 6,704 new patients applied for a medical cannabis card (The Colorado Medical Marijuana Registry, 2009). In 2009, Colorado saw a dramatic increase in the number of cardholders and by the end of 2010, 116,198 people held medical cannabis cards (The Colorado Medical Marijuana Registry, 2010). Unfortunately, some states do not release state registry data or do not require registration (e.g., California’s medical cannabis registry is voluntary; Bowles, 2012), making monitoring of prevalence of medical cannabis participation challenging. In 2012, Colorado legalized recreational cannabis use for adults, though the first recreational sales did not begin until January of 2014. As of August 2017, eight states, including California, have legalized recreational cannabis (NORML, 2016). Thus studying medical cannabis card status during years 2010–2013 in Colorado and California, as we do here, allows examining a period which comes after the issuance of the Ogden-Memo but is prior to the initiation of legal recreational cannabis sales in either state.

There has been keen interest in understanding whether this shifting legal landscape may lead to changes in cannabis use patterns and cannabis use disorder prevalence among adolescents and adults in the general population (Cerdá et al., 2012; Hasin et al., 2017; Hasin et al., 2015; Martins et al., 2016; Wall et al., 2011; Wen et al., 2015). Similarly, there has been interest in understanding whether use of medical cannabis is related to high prevalence of substance use disorders and non-cannabis substance use. For example, Grella et al. (2014) found that about half of their sample of medical cannabis users had engaged in risky alcohol use and about 20% had used illicit drugs in the past 30 days. Zaller et al. (2015) report that one-fifth of their medical cannabis patient sample reported previous treatment for drug/alcohol dependence. In contrast, several other studies have found that medical cannabis users have similar or lower rates of other drug use (Reinarman et al., 2011; Roy-Byrne et al., 2015), though relative levels of course depend on the identified comparison group and various comparison groups have been utilized in studies of medical cannabis patients (Bohnert et al., 2014; Haug et al., 2017; Ilgen et al., 2013; Lankenau et al., 2017). One criticism of the current literature is that studies to date have generally utilized cross sectional designs, mainly recruiting subjects from a single (e.g., Haug et al., 2017; Ilgen et al., 2013) or multiple medical cannabis dispensaries (Kepple et al., 2016; Reinarman et al., 2011), through chain referral sampling (Lankenau et al., 2016) or through health care settings (Davis et al., 2016; Richmond et al., 2015; Roy-Byrne et al., 2015). While some work supports that recruitment from dispensaries does not introduce substantive sampling or respondent biases (Thomas and Freisthler, 2016), others have suggested that asking medical cannabis users about other substance use in the context of recruitment at a medical cannabis assessment center might encourage under-reporting of other drug use (Reinarman et al., 2011). Concurrent assessment of other drug use after ascertainment at dispensaries might also potentially cause under-reporting because medical cannabis users are concerned with, and commonly experience, high levels of stigma (Satterlund et al., 2015). In addition, cross-section designs cannot disentangle temporal relationships (e.g., early cannabis use predicts later medical cannabis use or vice versa). One possibility that has not yet been well investigated, is that medical cannabis may serve as a convenient way for those with a cannabis addiction to access cannabis. Here we utilized a longitudinal sample, with baseline assessments in 2008 and prior years, and Wave 2 assessments in 2010–2013. We hypothesized that those with a cannabis use disorder at baseline assessment would be more likely to have a medical cannabis card at follow up. Mirroring the approach of prior studies (Grella et al., 2014; Reinarman et al., 2011), we additionally utilized Wave 2 cross-sectional data to assess whether those accessing medical cannabis have relatively high rates of concurrent substance use disorders.

One confound of testing the relationship between early cannabis use disorder and later medical cannabis use is that at baseline cannabis might have been used to mitigate general medical or mental health concerns. In other words, early health concerns might drive both early cannabis use and future medical cannabis use. There is currently moderate quality evidence supporting that cannabinoids benefit spasticity and chronic neuropathic or cancer-related pain, but evidence for other indications is of low quality (Whiting et al., 2015). One recent review also found limited evidence that cannabinoids used for medical concerns improve functioning and health-related quality of life, in part again because of limited high

quality data (Goldberg et al., 2017). The available literature on the promise of cannabinoids for various medical issues can be interpreted very differently by prominent and well-informed researchers e.g., (Haney and Evins, 2016), suggesting the importance of continued research in this area. Still, many patients use cannabis to help with various general medical and mental health concerns, including anxiety disorders, depression, and attention-deficit/hyperactivity disorder (Lucas and Walsh, 2017; Park and Wu, 2017), and report substituting medical cannabis for prescribed medications (Lucas and Walsh, 2017; Zaller et al., 2015). Although many medical cannabis users report past-year psychological distress (Grella et al., 2017) and adverse events from cannabinoids are common (McGriff et al., 2016; Whiting et al., 2015), many users also endorse subjective improvement in their symptoms from cannabis use (Grella et al., 2014; McGriff et al., 2016; Reinarman et al., 2011 Zaller et al., 2015) and report that side effects experienced are less than with prior trials of prescribed medications (Zaller et al., 2015). Thus, any study examining the longitudinal relationship between early cannabis use disorder diagnosis and later medical cannabis use, must also consider possible contributions from general medical and mental health concerns.

2. Methods

2.1 Sample

Subjects were recruited as part of a multi-site study on the genetic linkage of substance use disorders (SUDs) and conduct disorder (CD; Derringer et al., 2015). Data was collected both in Denver and San Diego and focused on adolescents, 13–19 years of age, with or at high risk for substance and conduct-related problems (hereafter referred to as probands) and their close-age siblings. In Denver, investigators recruited probands from (1) a University-based adolescent treatment program for youth with serious substance and conduct problems and (2) adjudicated youth from the Colorado criminal justice system. In San Diego, investigators recruited participants from (1) treatment programs and (2) high schools for behaviorally troubled youth.

Participants were excluded if they 1) presented with signs of psychosis, 2) obvious intoxication, 3) imminent dangerousness (i.e., current risk of suicide, violence or fire setting), or 4) exhibited insufficient English skills for assenting/consenting to the interview or completing the interview.

Baseline (Wave 1) assessments were completed between 1999 and 2008, and follow-up (Wave 2) assessments were conducted between 2009 and 2013. Questions regarding medical cannabis card status were added to the battery in 2010 and only those participants with this data (n=654) were utilized in these analyses. The mean age of participants utilized in this study at Wave 1 was 17.3 years (SD = 3.1) and at Wave 2 was 24.1 years (SD = 2.5).

2.2 Attrition Analysis

We compared the sample used in these analyses and those that were excluded from these analyses (i.e., some individuals targeted for follow up were not able to be seen at Wave 2 or were seen prior to the addition of the Medical Cannabis questions in 2010). Attrition

analyses (see Table 1) indicated that both groups, those included in these analyses and those that were not, were similar in all measures except for the years the participants were tested.

2.3 Measures

2.3.1 Wave 1 Baseline—At baseline, each participant completed the Composite International Diagnostic Interview Substance Abuse Module (CIDI-SAM), a structured diagnostic interview, which generates DSM-IV substance use disorder diagnoses for 10 drug categories and is validated for use with adolescents (Crowley et al., 2001). Adolescents completed the Diagnostic Interview Schedule for Children (DISC), while adult siblings (18+ years) completed the Diagnostic Interview Schedule (DIS). DISC/DIS are structured diagnostic instruments, which produce DSM-IV mental health diagnoses (Robins et al., 1981; Shaffer et al., 1993). A portion of the sample responded to questions about general health: “In general, how is your health?” and “Do you have to avoid hard physical exercise or games because of your health?”

2.3.2 Wave 2 Follow-up—During Wave 2 investigators asked follow-up subjects “Have you ever used cannabis?” For those subjects reporting lifetime use of cannabis, we asked, “Have you ever been evaluated for Medical Cannabis?” and “Did you obtain a Medical Cannabis Identification Card?” Included in the analysis were only those who responded to the questions above. The same questions used for Wave 1 measures assessed general health in Wave 2. If the participant responded positively for obtaining a medical cannabis card, we added the query: “For what condition did you obtain a Medical Marijuana Card?” Participants filled a text box with their answer. Conditions were then categorized into different medical conditions indicated for medical cannabis. As the approved medical conditions differed slightly between states (California accepted more conditions), we matched the participants’ responses with an indication allowed within their respective state. If the participant listed more than one condition, we used the approved indication for analysis. If the participant listed a condition that was not approved in their state, then this was categorized as “Other.”

2.4 Statistical Analysis

2.4.1 Predictors—The main aim of the current manuscript was to assess whether baseline characteristics (i.e., cannabis use disorder, other non-cannabis substance use disorder and conduct disorder) predicted Wave 2 medical cannabis card status. Investigators selected Wave 1 predictors *a priori*: (1) DSM-IV cannabis abuse or dependence diagnosis, (2) number of cannabis abuse or dependence symptoms, (3) number of non-cannabis substance use disorder diagnoses (range 0–9), and (4) conduct disorder diagnosis. We also examined these potential covariates: (5) baseline age, (6) age at Wave 2, (7) time between Wave 1 and 2 assessments, (8) Hispanic ethnicity, (9) sex, (10) race, (11) family relationship (proband vs. sibling), (12) site of recruitment, (13) calendar year when tested at Wave 1, (14) calendar year when tested at Wave 2, (15) specific substance use disorders, (16) generalized anxiety disorder, (17) major depressive disorder and (18) attention-deficit/hyperactivity disorder. Bivariate analyses were conducted to examine whether those with and without a medical cannabis card at Wave 2 differed in Wave 1 characteristics. For categorical variables (e.g., cannabis abuse or dependence, CD diagnoses) chi-square statistics were utilized. For

continuous variables (e.g., age) t-test was utilized to compare groups (or Mann Whitney U tests when appropriate). Although not part of our original analytical plan, in secondary work we also tested whether cannabis dependence criterion A7 (use despite worsening physical/psychological problems) predicted medical cannabis card status.

Because of the study's complex design (1–5 individuals per family), we utilized a generalized linear model to investigate variables significantly related to medical cannabis card status while accounting for correlation between subjects within a family. Binomial regression was used instead of logistic regression in order to estimate the adjusted relative risk of each predictor variable for an outcome variable that was not rare (15.6% with medical cannabis card at wave 2). Our model included family member status (proband vs. sibling), and site of recruitment (Denver adjudicated, Denver treatment, and San Diego) as covariances and then simultaneously evaluated all significant predictor variables from bivariate analyses to estimate the adjusted contribution for each. These analyses were conducted using SAS Statistics software.

The chi square statistic was used to test whether medical cannabis card status was associated with concurrent substance problems (measured at Wave 2) by analyzing rates of past-year cannabis dependence diagnosis, and separately, the presence of at least one non-cannabis substance dependence diagnosis in the past year against medical card status (all three variables were measured at Wave 2).

3. Results

3.1 Prevalence of Medical Cannabis Card Status at Wave 2

Of the sample of 654 participants, 102 (15.6%) reported that they had obtained a medical cannabis card at Wave 2 assessment.

3.2 Bivariate Analyses (Wave 1 Predictors of Wave 2 Medicinal Card Status)

Table 2 presents analyses testing whether those with and without a medical cannabis card at Wave 2 differed in Wave 1 variables. Baseline variables significantly associated with card status included: being male, race (Caucasian higher among card holders), family relationship (proband>brother>sister), several specific SUDs (cannabis, tobacco, hallucinogen, opioid and amphetamine), greater number of cannabis use disorder symptoms, number of non-cannabis SUD diagnoses (range 0–9), endorsement of cannabis criterion A7, CD and attention-deficit/hyperactivity disorder (ADHD). Multiple notable variables did not differ significantly between groups including: age at Wave 1 and 2, time between Waves 1 and 2 assessments, Hispanic ethnicity, site of recruitment, year tested at Wave 1 and 2, several specific SUDs (alcohol, cocaine inhalant and sedative), generalized anxiety disorder and major depressive disorder. Additionally, there were no significant differences in self-reported general health at baseline between those who did obtain a medical cannabis card and those who did not.

3.3 Multiple Binomial Regression Model Results

Our generalized linear model controlled for study design (i.e., family effects, probands and siblings status, and site of recruitment) and tested whether the relationship between cannabis use disorder and medical cannabis card status remained significant while controlling for site of recruitment, number of non-cannabis SUDs, CD and sex. In these analyses, male sex and cannabis SUD significantly predicted card status in the model (see Table 3).

3.4 Bivariate Analyses (Within Wave 2) and Reported Indication for Medicinal Cannabis

Wave 2 analysis showed that those with a medical cannabis card were about twice as likely to have met a cannabis dependence diagnosis in the past year (see Table 4). They were also significantly more likely to have met criteria for any non-cannabis substance dependence diagnosis, but this result appears mainly driven by group differences in tobacco dependence. No significant difference was found in reported general health at Wave 2 between medical cannabis card holders and non-card holders. Amongst card holders, the most commonly reported condition for obtaining a medical cannabis card was for severe or chronic pain (75.5%), followed by “Other” (medical conditions that were not listed by the state; 12.75%), and then muscle spasms (3.92%; see Table 5). This supports that 1:8 of our subjects (77/654) reported using medical cannabis for severe or chronic pain (see Table 5), though <2% of our sample reported poor health at Waves 1 and 2 (see Tables 2 and 4).

4. Discussion

The study has three main findings. First, we report relatively high rates of medical cannabis card status in longitudinal follow up of a sample of high-risk adolescents and their siblings. Second, we attempted to understand what Wave 1 factors predicted Wave 2 medical cannabis card status. Our bivariate analyses identified several factors that were associated medical cannabis card status in this sample but our mulitvariate model supported that most of this predictive power is explained by cannabis use disorder diagnosis in adolescence and male sex. We found no significant difference in general health status between those with medical cannabis cards and those without at either Wave 1 or Wave 2 assessment. Several factors surprisingly failed to predict medical cannabis card status in our bivariate or multiple binomial regression model. These included several specific substance use disorders, major depression, ADHD, and generalized anxiety disorder. Third, those with a medical cannabis card at Wave 2 were more likely to concurrently meet cannabis dependence criteria compared to those without a medical cannabis card.

4.1 Relatively High Rates of Medical Cannabis Card Status

One recent review utilizing data from multiple states found a “national average [of] around 7.6 per 1000 adults” are registered for medical cannabis participation (Fairman, 2016). However, there is state-to-state and temporal variability. In Colorado, ~3% of the general adult population had obtained a medical cannabis card by late 2010 (Fairman, 2016; Schuermeyer et al., 2014). In California, because registration is voluntary, registry information (CDPH, 2017a) likely provides gross under-estimates of that state’s medical cannabis population (Fairman, 2016; Ryan-Ibarra et al., 2015). In contrast to available estimates, ~16% of this study sample reported having a medical cannabis card at Wave 2.

We should exercise some caution in directly comparing prevalence rates from this study against the Colorado state registry because our sample consisted of young adults at Wave 2 and substance use disorder prevalence is often higher in young adult populations compared to older adults (SAMHSA, 2014). Still, data available from our Wave 2 time period support that the mean age of medical cannabis card holders in Colorado was approximately 40 years (Bowles, 2012). While noting this caveat, that our sample consisted of young adults at Wave 2, our results suggest a relatively high prevalence of medical cannabis cards in this sample. This finding is in some ways expected. Probands in this sample recruited from treatment or high risk schools already had, or were at high risk for a substance use disorder and conduct problems. Siblings also were at higher risk than general population youths (albeit with lower rates than probands; Kendler et al., 1997) both because substance use disorders aggregate in families and because siblings have similar genetic and environmental backgrounds to probands, which increases their risk for drug use problems (Meyers and Dick, 2010). One conclusion that may be drawn from our study, however, is that youth with, or at high-risk for, substance use disorders were over-represented among early adopters of medical cannabis and were likely to obtain a medical cannabis card when they reached young adulthood.

4.2 Predicting Wave 2 Medical Cannabis Card Status from Wave 1 factors

In our multiple binomial regression model, male sex and adolescent cannabis use disorder diagnosis predicted Wave 2 medical cannabis card status. It is not surprising that male sex was a significant predictor. Some medical cannabis registries record and report information on sex, and those data support that about two thirds of registered persons are male (Bowles, 2012; Fairman, 2016), though the strength of such sex differences may be lessening in recent years (Fariman, 2016). Several factors might explain why males were more likely to be early adopters of medical cannabis. For example, SUDs are more prevalent in males than females (Brady and Randall, 1999) and SUD might drive such results. Alternatively, sex differences in other factors, such as unintentional injuries (Chandran et al., 2010), sensation seeking and risk taking (Cross et al., 2011) or other domains might instead drive the observed sex differences in medical cannabis card status. Our analyses cannot explain the reasons for this association.

Adolescent cannabis use disorder predicted Wave 2 medical cannabis card status. It seems logical that those with a prior cannabis abuse or dependence diagnosis in adolescence might be attracted to the medical cannabis industry in young adulthood. Our study, however, cannot fully explain why those youths obtained a card. It is possible that individuals obtained medical cannabis cards as a way to allow them to use cannabis without the usual potential legal repercussions. Alternatively, it is also possible that youth with cannabis abuse and dependence were more likely to have a medical reason to pursue medicinal cannabis. However, our analyses show that only a very small portion of this young sample (both at Wave 1 and Wave 2) reported poor health (i.e., less than about 2%). Still we cannot rule out that baseline cannabis use mitigated substantial health concerns allowing reports of good health in this group. While cannabis may be used by some individuals to help with symptoms of depression and anxiety (Walsh et al., 2013), baseline psychiatric disorders were not predictive of having a medical cannabis card at Wave 2 in our generalized linear

model. Cannabis dependence criterion A7 was more often endorsed at Wave 1 by those with a medical cannabis card at Wave 2. This criterion asks whether the individual continued to use cannabis even though it was causing or worsening a physical or psychological problem. These results are inconsistent with the hypothesis that these youths used cannabis to mitigate psychological or physical complaints. These findings instead support the hypothesis that medical cannabis may be utilized by those with a cannabis use disorder to conveniently access cannabis.

In terms of adolescent substance use disorders, examination of Table 2 supports that rates of Wave 1 SUD were generally relatively high for those with a medical cannabis card at Wave 2. But in several instances, these differences did not achieve statistical significance. This is likely related to low prevalence for some drug categories (i.e., inhalants and sedatives) reducing power to achieve statistical significance. For alcohol and cocaine, the lack of group differences cannot be attributed to low prevalence in this sample. Adolescents with these two specific SUDs do not appear to have been more likely to obtain a medical cannabis card at follow up. Of course, in our generalized linear model, baseline number of non-cannabis substance use disorder diagnoses did not predict medical cannabis card status at Wave 2.

4.3 Medical Cannabis Card Associated With Concurrent Cannabis Use Disorder

Similar to several prior studies (Grella et al., 2014; Reinarman et al., 2011), we tested whether those with a medical cannabis card at Wave 2 were more likely to have a concurrent substance use disorder (see Table 4). About one in five of those with a medical cannabis card, met criteria for a cannabis dependence diagnosis in the past year at Wave 2. This rate was about double that of other respondents. Medical cannabis card holders were also more likely to have a past-year tobacco dependence diagnosis. But no group differences were seen for other specific substance dependence diagnoses tested. As mentioned previously, cross-sectional analyses cannot disentangle temporal relationships (e.g., cannot answer the question, did the cannabis dependence come first and lead to the medical cannabis card or vice versa?) However, we can also consider our Wave 1 results, which show 76% of those who had a medical cannabis card at Wave 2 met criteria for a cannabis use disorder at Wave 1. This suggests that medical cannabis was unlikely the cause of cannabis addiction seen at Wave 2 in this sample. Instead cannabis addiction likely predated obtaining a medical cannabis card in many instances here.

5. Conclusions and Future Directions

Adolescent cannabis abuse and dependence and male sex positively predicted future medical cannabis card holder status in this high-risk adolescent sample. Future cannabis policies should consider high-risk adolescent populations as they may be more impacted than the general population. Medical cannabis programs may also attract individuals with a history of (and concurrent) addiction to cannabis. Physicians who conduct screenings for medical cannabis recommendations have a responsibility to appropriately screen for prior and concurrent cannabis addiction in consideration of appropriateness of medical cannabis recommendations. In addition, 1 in 4 of our Wave 2 medical cannabis card holders met criteria for a past-year alcohol dependence diagnosis and 1 in 2 tobacco dependence.

Providers helping medical cannabis patients may be well positioned to intervene with approaches to mitigate other substance use, such as motivational interviewing and screening brief intervention and referral to treatment.

5.1 Strengths and Limitations

This study has several limitations in addition to those discussed previously. The sample used in this study is not generalizable to the general population but rather, provides information on high risk participants. Furthermore, questions in the survey relied on recall, possibly biasing the results. However, this would have been consistent across all groups. Information about medical conditions relied on participants' response and did not include a formal assessment to determine whether a clear indication for medical cannabis use was present. Additionally, this study cannot determine causality, only that there is a temporal relationship between sex and cannabis abuse and dependence in adolescence and future medical cannabis card status.

Attrition analyses support that the sample utilized here is very similar to subjects not included in these analyses (e.g., lost to follow up at Wave 2) in terms of baseline characteristics. The only difference demonstrated related to the calendar year seen at baseline. Those not included in the analyses were likely to have been seen earlier at Wave 1. If a participant was seen earlier at baseline, then they were more likely to have been assessed earlier in Wave 2. Though Wave 2 data collection started in 2009, questions regarding medical cannabis cards were not added until 2010. Therefore, the earliest participants seen in Wave 2 were excluded from the sample used in this manuscript. It is unclear how this might have biased our results, but remains important to recognize.

Finally, we conduct a number of statistical tests in our bivariate analyses (see Table 2) which raises the potential for false positive results. However, our study hypothesis focused on the relationship between baseline cannabis use disorder, other substance use disorders, conduct disorder and follow up medical cannabis card status (see our bivariate results; Table 2). Given the strong association among these clinical diagnoses, we conducted *post hoc* multiple binomial regression model (Table 3) to examine which, if any, of these adolescent characteristics remained as significant predictors of medical cannabis card status after controlling for the others. For these reasons, corrections to the p-values were not utilized.

Strengths of the study include the longitudinal data collection and the historical timeline. Wave 2 occurred in an important window just after the Ogden Memorandum but prior to legal recreational cannabis becoming available in Colorado. In addition, we focus attention on a population often neglected when considering the effects of shifts in policy and laws regarding cannabis, those with or at high risk for SUDs in adolescence. More work is needed focusing on this important group.

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Highlights

- Adolescent cannabis use disorder and male sex predict medical cannabis (med) card
- Neither self-reported mental illness nor general health predicted med card status
- Young adults with med cards had higher rates concurrent cannabis use disorder
- High-risk adolescents have high participation in med card programs as young adults
- Suggests benefits of screening for substance use disorders in med card evaluations

Table 1

Attrition Analysis.[1]

		Not in analysis (% or standard deviation); n=969	In analysis (% or standard deviation); n=654	Test statistic; p-value
Demographics and sample characteristics				
	Age at Wave 1 testing mean (sd)[a]	17.2 (2.42)	17.3 (2.48)	MW p=0.76
	Hispanic ethnicity[b]	274 (28.5%)	179 (27.4%)	χ^2=0.26; p=0.61
	Male sex	637 (65.7%)	394 (60.2%)	χ^2=5.09; p=0.02
Race[c]				
	Caucasian race	488 (50.8%)	331 (50.7%)	LRT=7.31; p=0.29
	Unknown/Not reported	253 (26.4%)	159 (24.3%)	
	More than one race	111 (11.6%)	78 (11.9%)	
	Black/African American	74 (7.7%)	70 (10.7%)	
	American Indian/Alaskan Native	18 (1.9%)	9 (1.4%)	
	Native Hawaiian/Pacific Islander	8 (0.8%)	4 (0.6%)	
	Asian	8 (0.8%)	2 (0.3%)	
Family/Relationship				
	Proband	488 (50.4%)	310 (47.4%)	χ^2=4.80; p=0.09
	Brother	262 (27.0%)	165 (25.2%)	
	Sister	219 (22.6%)	179 (27.4%)	
Site/Recruitment				
	Denver Treatment	420 (43.3%)	310 (47.4%)	χ^2=2.69; p=0.26
	Denver Adjudicated	245 (25.3%)	150 (22.9%)	
	San Diego	304 (31.4%)	194 (29.7%)	
Year tested in Wave 1 (range 1999–2008)[a]				
	1999	0 (0.0%)	2 (0.3%)	LRT=82.80; p<0.001
	2000	42 (4.4%)	10 (1.5%)	
	2001	92 (9.6%)	37 (5.7%)	
	2002	159 (16.5%)	62 (9.5%)	
	2003	188 (19.6%)	105 (16.1%)	
	2004	185 (19.3%)	109 (16.7%)	
	2005	144 (15.0%)	149 (22.8%)	
	2006	87 (9.1%)	88 (13.5%)	
	2007	56 (5.8%)	77 (11.8%)	
	2008	8 (0.8%)	15 (2.3%)	
Lifetime Substance Use Disorder (DSM-IV abuse or dependence) from the CIDI-SAM[2] measured at Wave 1[a]				
	Cannabis use disorder	536 (55.8%)	352 (53.8%)	χ^2=0.60; p=0.44
	Alcohol use disorder	510 (53.1%)	328 (50.2%)	χ^2=1.33; p=0.25

		Not in analysis (% or standard deviation); n=969	In analysis (% or standard deviation); n=654	Test statistic; p-value
	Tobacco use disorder	410 (42.7%)	295 (45.1%)	χ^2=0.94; p=0.33
	Amphetamine use disorder	134 (13.9%)	96 (14.7%)	χ^2=0.17; p=0.68
	Cocaine use disorder	113 (11.8%)	68 (10.4%)	χ^2=0.72; p=0.40
	Hallucinogen use disorder	89 (9.3%)	55 (8.4%)	χ^2=0.35 p=0.56
	Opioid use disorder	31(3.2%)	27 (4.1%)	χ^2=0.92; p=0.34
	Sedative use disorder	25 (2.6%)	17 (2.6%)	χ^2<0.001; p=0.99
	Inhalant use disorder	12 (1.2%)	10 (1.5%)	χ^2=0.23; p=0.63
Mental Health Diagnoses (lifetime) measured by DIS or DISC at Wave 1[3]				
	Conduct disorder[d]	557 (58.1%)	356 (54.4%)	χ^2=2.18; p=0.14
	Major depression[c]	178 (18.6%)	130 (19.9%)	χ^2=0.44; p=0.51
	Attention-deficit/hyperactivity disorder[e]	119 (12.4%)	75 (11.5%)	χ^2=0.34; p=0.56
	Generalized anxiety disorder[b]	70 (7.3%)	61 (9.3%)	χ^2=2.16; p=0.14

[1]There were 1,623 subjects who were targeted for follow up at study Wave 2.

[2]CIDI-SAM is the Composite International Diagnostic Interview – Substance Abuse Module.

[3]DIS/DISC are the Diagnostic Interview Scheduled/Diagnostic Interview Schedule for Children

Of those, 654 are utilized in these analyses. Some subjects not utilized in these analyses were seen at study Wave 2 (e.g., not lost to follow up) but were seen prior to addition of the relevant medical cannabis questions (i.e., those were added to the battery in 2010 but wave 2 data collection began in 2009).

[a]sample size is 1615;

[b]sample size is 1614;

[c]sample size is 1613;

[d]sample size is 1612;

[e]sample size is 1611.

MW = Mann Whitney U test. LRT = Likelihood Ratio test.

Table 2

Bivariate analyses examining Wave 1 demographics, sample characteristics, CIDI-SAM[1] and DIS/DISC[2] data as predictors of Wave 2 medical cannabis card status. Mean (standard deviation) or n (column percent) presented.

		No Card at Wave 2 (n=552)	Med Card at Wave 2 (n=102)	Test statistic; p-value
Demographics and sample characteristics				
	Age at Wave 1 testing	17.3 (2.51)	17.2 (2.33)	MW p=0.56
	Age at Wave 2 testing	24.1 (3.16)	23.8 (2.69)	$t_{156.9}$=0.90 p = 0.37
	Number of years between Wave 1 and Wave 2 testing	6.8 (1.71)	6.7 (1.59)	t_{652}=0.71; p = 0.48
	Hispanic ethnicity	155 (28.1%)	24 (23.5%)	χ^2=0.90; p=0.34
	Male sex	310 (56.2%)	84 (82.4%)	χ^2=24.66; p<0.001
Race				
	Caucasian race	267 (48.5%)	64 (62.7%)	LRT=14.48; p=0.03[3]
	Unknown/Not reported	140 (25.4%)	19 (18.6%)	
	More than one race	68 (12.3%)	10 (9.8%)	
	Black/African American	65 (11.8%)	5 (4.9%)	
	American Indian/Alaskan Native	6 (1.1%)	3 (2.9%)	
	Native Hawaiian/Pacific Islander	4 (0.7%)	0 (0%)	
	Asian	1 (0.2%)	1 (1.0%)	
Family Relationship				
	Proband	246 (44.6%)	64 (62.7%)	χ^2=16.76; p<0.001
	Brother	139 (25.2%)	26 (25.5%)	
	Sister	167 (30.3%)	12 (11.8%)	
Site/recruitment				
	Denver Treatment	252 (45.7%)	58 (56.9%)	χ^2=4.64; p=0.10
	Denver Adjudicated	129 (23.4%)	21 (20.6%)	
	San Diego	171 (31.0%)	23 (22.5%)	
Year tested in Wave 1 (range 1999–2008)				
	1999	2 (0.4%)	0 (0%)	LRT=8.90; p=0.45
	2000	10 (1.8%)	0 (0%)	
	2001	31 (5.6%)	6 (5.9%)	
	2002	55 (10.0%)	7 (6.9%)	
	2003	90 (16.3%)	15 (14.7%)	
	2004	86 (15.6%)	23 (22.5%)	
	2005	127 (23.0%)	22 (21.6%)	
	2006	73 (13.2%)	15 (14.7%)	
	2007	64 (11.6%)	13 (12.7%)	

		No Card at Wave 2 (n=552)	Med Card at Wave 2 (n=102)	Test statistic; p-value
	2008	14 (2.5%)	1 (1.0%)	
Year tested in Wave 2 (range 2010–2013)				
	2010	155 (28.1%)	22 (21.6%)	χ^2=2.39; p=0.50
	2011	212 (38.4%)	46 (45.1%)	
	2012	149 (27.0%)	28 (27.5%)	
	2013	36 (6.5%)	6 (5.9%)	
Lifetime Substance Use Disorder (DSM-IV abuse or dependence) from the CIDI-SAM measured at Wave 1				
	Cannabis use disorder	275 (49.8%)	77 (75.5%)	χ^2=22.8; p<0.001
	Alcohol use disorder	272 (49.3%)	56 (54.9%)	χ^2=1.09; p=0.30
	Tobacco use disorder	239 (43.3%)	56 (54.9%)	χ^2=4.68; p=0.03
	Amphetamine use disorder	72 (13.0%)	24 (23.5%)	χ^2=7.56; p=0.006
	Cocaine use disorder	57 (10.3%)	11 (10.8%)	χ^2=0.02; p=0.89
	Hallucinogen use disorder	36 (6.5%)	19 (18.6%)	χ^2=16.38; p<0.001
	Opioid use disorder	18 (3.3%)	9 (8.8%)	FE p=0.03
	Sedative use disorder	12 (2.2%)	5 (4.9%)	FE p=0.16
	Inhalant use disorder	8 (1.4%)	2 (2.0%)	FE p=0.66
	# cannabis use disorder symptoms	2.98 (3.17)	4.31 (3.12)	t_{652}= 3.92; p<0.001
	Endorsed cannabis dependence criterion 7[4]	261 (47.3%)	64 (62.7%)	χ^2=8.23; p=0.004
Mental Health Diagnoses (lifetime) measured by DIS or DISC at Wave 1				
	Conduct disorder	288 (52.2%)	68 (66.7%)	χ^2=7.29; p=0.007
	Major depression	110 (19.9%)	20 (19.6%)	χ^2=0.01; p=0.94
	Attention-deficit/hyperactivity disorder	55 (10.0%)	20 (19.6%)	χ^2=7.89; p=0.005
	Generalized anxiety disorder	53 (9.6%)	8 (7.8%)	χ^2=0.32; p=0.58
Reported General Physical Health at Wave 1				
General Reported Health[5]	Excellent	51 (13.9%)	10 (13.2%)	χ^2=0.22; p=0.994
	Very Good	116 (31.7%)	23 (30.3%)	
	Good	159 (43.4%)	35(46.1%)	
	Fair	36 (9.8%)	7 (9.2%)	
	Poor	4 (1.1%)	1 (1.3%)	
Avoid hard physical activity due to health[5]		25 (6.8%)	3 (3.9%)	χ^2=0.88; p=0.348

[1] CIDI-SAM is the Composite International Diagnostic Interview – Substance Abuse Module

[2] DIS/DISC are the Diagnostic Interview Scheduled/Diagnostic Interview Schedule for Children

[3] note that Chi square examining Caucasian vs. non-Caucasian (and excluding those with "unknown/not reported" race) yielded a similar result (χ^2=4.61; p=0.03).

[4] "the substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g., current cocaine use despite recognition of cocaine-induced depression, or continued drinking despite recognition that an ulcer was made worse by alcohol consumption)".

[5] n=442

FE=Fisher's Exact test
LRT=Likelihood Ratio test
MW = Mann-Whitney U test

Table 3

Multiple binomial regression model nesting subjects within family: examining predictors of medical marijuana card status[1]

Variables	Adjusted Relative Risk	95% CI	p-value
Sex (female sex=reference group)	2.39	1.47–3.91	0.0005
Hispanic (non-Hispanic)	0.93	0.59–1.44	0.73
Number of non-cannabis substance use disorders (0–9)[2]	1.03	0.91–1.15	0.68
Cannabis abuse or dependence, lifetime (no diagnosis)	2.06	1.21–3.51	0.008
ADHD (no diagnosis)	1.50	0.98–2.30	0.06
Conduct disorder (no diagnosis)	0.98	0.64–1.49	0.91
San Diego (Denver Treatment)	0.81	0.51–1.30	0.39
Denver Adjudicated (Denver Treatment)	0.88	0.56–1.40	0.60
Proband vs. sibling (sibling)	1.11	0.75–1.64	0.60

[1]Examining the adjusted effects of variables predicting medical cannabis card status at Wave 2 (utilizing variables found to be significant in bivariate analyses; n=654) while also controlling for the study design. Note: race (Caucasian vs. non-Caucasian) was also added to the model but a high number of “unknown or not reported” reduced sample size by 159 subjects. That model is not presented but sex (p=0.002) and cannabis abuse and dependence (p=0.02) remained significant predictors, while race was not (p=0.06) significantly associated with Wave 2 medical cannabis card status.

[2]Non cannabis substances include alcohol, tobacco, cocaine, hallucinogens, inhalants, opioids, PCP, sedatives, amphetamines.

Note: reference group for each variable is indicated in parentheses.

Table 4

Bivariate analyses examining Wave 2 CIDI-SAM substance dependence diagnosis and general health status with concurrent Med Card status at Wave 2. N (column percent) presented.

		Without Med Card at Wave 2 (n=552)	With Med Card at Wave 2 (n=102)	Test statistic; p-value
Past-year Substance Dependence	Alcohol	108 (19.6%)	25 (24.5%)	χ^2=1.30; p=0.25
	Tobacco	212 (38.4%)	56 (54.9%)	χ^2=9.69; p=0.002
	Cannabis	56 (10.1%)	20 (19.6%)	χ^2=7.51; p=0.006
	Amphetamine	18 (3.3%)	3 (2.9%)	FE p=0.99
	Cocaine	16 (2.9%)	1 (1%)	FE p=0.49
	Opioid	16 (2.9%)	6 (5.9%)	FE p=0.13
	Club Drug	3 (0.5%)	0 (0.0%)	FE p>0.99
	Hallucinogen	2 (0.4%)	0 (0%)	FE p>0.99
	Sedative	1 (0.2%)	1 (1.0%)	FE p=0.29
	Inhalant	0	0	
	PCP	0	0	
	Any nonTHC	266 (48.2%)	64 (62.7%)	χ^2=7.30; p=0.007
Reported General Physical Health at Wave 2				
General Reported Health[a]	Excellent	125 (23.0%)	18 (18.2%)	χ^2=6.75; p=0.15
	Very Good	169 (31.1%)	25 (25.3%)	
	Good	183 (33.6%)	40 (40.4%)	
	Fair	58 (10.7%)	16 (16.2%)	
	Poor	9 (1.7%)	0 (0.0%)	
Avoid hard physical activity due to health[a]		35 (6.5%)	10 (10.2%)	χ^2=1.75; p=0.19

nonTHC = If subject met criteria for at least one non-cannabis substance dependence diagnosis (including 10 drug categories).

[a] n=643

Table 5

Indications for medical cannabis card per self-report.[1]

Indication[2]	n (%)
Severe/chronic pain	77 (75.5)
Other[3]	13 (12.75)
Muscle Spasms	4 (3.92)
Severe Nausea	3 (2.94)
Migraines[4,5]	2 (1.96)
Seizures	2 (1.96)
Cachexia	1 (0.98)
Anorexia[4]	0 (0)
Arthritis[4,5]	0 (0)
Cancer	0 (0)
Glaucoma	0 (0)
HIV/AIDS	0 (0)

[1] At Wave 2, all subjects with a medical cannabis card were asked, “For what condition did you obtain a Medical Marijuana card?” Subjects filled a text box with their answer. Two physicians and one medical student met and reviewed responses for the 102 subjects with a medical cannabis card at Wave 2 and came to a clinical consensus regarding the subject’s response and alignment with medical indications allowed within that subject’s state. List of approved conditions in California was obtained here: https://www.cdph.ca.gov/programs/MMP/Pages/MMPFAQ.aspx# (CDPH, 2017b) And list of approved conditions in Colorado was obtained here: https://www.colorado.gov/pacific/sites/default/files/MMR%20Qualifying%20Medical%20Conditions.pdf (CDPHE, 2017)

[2] For individuals reporting multiple medical concerns (e.g., “pain and nausea”), the first approved indication listed (in this example, pain) was utilized. If no approved indication was listed (e.g., “anxiety and insomnia”), this was categorized as “Other”.

[3] California includes a broad “any chronic or persistent medical symptom” indication and these are included in “Other” here. In addition, responses such as, “Bullshit-lied to Dr. about something” are also included in this other category.

[4] Migraines, anorexia and arthritis are acceptable indications for medical cannabis only in California.

[5] Coloradans who indicated migraines or arthritis were categorized as having pain.