



Published in final edited form as:

J Neuroimmune Pharmacol. 2018 December ; 13(4): 479–487. doi:10.1007/s11481-018-9813-6.

Reduction in Cannabis Use and Functional Status in Physical Health, Mental Health, and Cognition

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Abstract

Treatment for substance use disorders has traditionally been abstinence-oriented, but evaluating the merits of low-level cannabis use as potential treatment endpoint may identify benefits that are clinically relevant for treatment-seeking individuals who do not attain abstinence. This study explores if reduction in cannabis use to a lower level of use is related to improved physical health, mental health, and perceived cognitive functions. Study participants with a history of problematic cannabis use (n=111) completed assessments. Regression models were used to explore the relationship between past 30-day cannabis use levels (abstinent [57%], low use [22%] defined as less than or equal to 3 days per week, and heavy use [22%] defined as 4 or more days of use per week) and functional status in physical health, mental health, and cognition. Compared to heavy users, both abstinent and low-use individuals were similarly associated with better global health, appetite, and depression outcomes. Abstinent users also reported improved sleep, anxiety, and self-reported cognitive functioning relative to heavy users. Thus, reduction in cannabis use to lower levels is associated with beneficial outcomes important to health and other areas of functioning in individuals with problematic cannabis use.

Keywords

cannabis use; functional outcomes; health; mental health; cognition

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Conflict of Interest: All authors report no financial or possible conflicts of interest.

Compliance with Ethical Standards

Ethical approval: procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

Introduction

Evaluations of treatments for substance use disorders (SUD) have predominantly focused on abstinence-based primary outcomes. The SUD field has increasingly recognized that this approach does not capture the functional status of patients who may reduce drug use and experience improvements in health and other important clinical outcomes. In clinical trials of alcohol use disorder treatments, the Food and Drug Administration (FDA) has moved from total abstinence to no heavy drinking as the primary treatment outcome (Falk et al. 2010; Food and Drug Administration 2006; Kline Simon et al. 2017); no heavy drinking includes low-risk drinking in addition to abstinence. Cannabis is the most commonly used drug worldwide (United Nations Office on Drug and Crime 2017; World Health Organization 2014), and approximately 3 out of 10 users in the United States (U.S.) develop cannabis use disorder (CUD) (Hasin et al. 2015). Applying a similar low-risk concept in alcohol research to cannabis use is of great interest since individuals with CUD may have use reduction, rather than abstinence as a treatment goal, or may reduce use for periods of time before achieving abstinence. However, the question of whether reduction in cannabis use is associated with improvement in health and other areas of functioning has not been adequately examined. The present study aims to explore potential functional outcomes (e.g. physical health, psychiatric symptoms, and cognitive abilities) that may be improved with reduction in cannabis use.

Few studies have directly examined functional improvements associated with cannabis use reduction, but recent work suggests improvements in quality of life with abstinence and lower use frequency (Brezing et al. 2018). Based on secondary analyses of a medication trial for CUD, we (Hser et al. 2017) have previously reported findings showing improvements in anxiety, depression, and sleep among participants who reduced cannabis use over the 12-week trial. Regular cannabis use has been associated with increased risk of depression and anxiety symptoms, improvements in short-term sleep outcomes, and worsening of sleep during periods of withdrawal in prior studies (National Academies of Science, Engineering and Medicine 2017; Volkow et al. 2014). Cannabis users report elevated rates of respiratory symptoms (Owen et al. 2014). However, studies investigating the relationship between reduced cannabis use and respiratory functioning are lacking. Though cannabis use is known to acutely stimulate appetite, the relationship between use and body weight is not well studied, but the majority of studies indicate an inverse association between cannabis use and body mass index (Warren et al. 2005; Le Strat and Le Fall 2011). Cognitive impairments have been observed in cannabis users, particularly in the areas of memory, attention, and executive function; these deficits have been associated with amount, frequency and duration of use in some studies (Crean et al. 2011). In the current study, we extend this research by examining individuals recruited from specialty SUD treatment facilities and the general community to complete assessments on potential functional outcomes across multiple domains. We examined the likelihood that compared to heavy cannabis users, low-use and abstinent individuals would have better functional outcomes in physical health, mental health, and cognition.

Methods

Study Design and Participants

This study recruited adult participants between April 2017 and February 2018 from SUD treatment programs and the community (e.g., Marijuana Anonymous meetings, Craigslist) in Los Angeles. Inclusion criteria were broad with minimal exclusion criteria to increase external validity. Participants were deemed eligible if (1) 18 years old or older, (2) currently or formerly in treatment for cannabis use disorder or who had used cannabis heavily in the past year and reduced their use since then, and (3) able to provide informed consent. Participants were excluded if they were primarily in treatment for any other substance besides cannabis use, had their most recent period of heavy cannabis use more than a year ago, or reported using cannabis at a reduced rate for less than a month. A total of 111 adults provided survey data for the present analysis.

We divided participants into three groups by asking participants to select their frequency of cannabis use in the past 30 days prior to the survey (0, <1, 1, 2–3, 4–5, >5 days/week). Groups were classified as follows: (1) abstinent group, with no cannabis use per week (2) low-use group, with cannabis use less than or equal to 3 days per week, and (3) heavy-use group, with cannabis use 4 or more days per week. This classification was based on results indicating that more than 90% of the study participants used cannabis at least 4 days per week during their heaviest cannabis use period. This classification also allowed the current use level for both abstinent and low-use groups to represent a reduction in cannabis use from their heaviest use period, as opposed to the heavy use group who had not changed their level of cannabis use from their heaviest use period.

Study Procedures

Research assistants explained survey procedures, confirmed study eligibility, and consented participants. Eligible participants filled out questionnaires and assessments about cannabis use patterns and functional outcomes in small group session while being guided with instructions by research assistants. The group session lasted about two hours and participants were compensated for their time. All questionnaires were anonymous.

Main Measures

Survey questions included demographics, cannabis use patterns, history of health and psychiatric conditions, and a wide range of measures of functional outcomes. In the present analyses, cannabis and other substance use frequency was based on number of self-reported days using cannabis and other substances in the past 30 days prior to the survey and during their prior period of heaviest use. Medical and psychiatric history included lifetime history of major physical diseases (e.g., liver disease, kidney disease, chronic pain conditions, and sexually transmitted diseases) and psychiatric conditions (e.g., schizophrenia, depressive disorders, and anxiety disorders). Functional outcomes included physical health (general health, respiratory, sleep, appetite), mental health (depression, anxiety), and perceived cognitive functioning and abilities. We used several short forms of the Patient-Reported Outcomes Measurement Information System (PROMIS) (Cella et al. 2007) which provides norms (relative to the general population in the United States) by converting the total raw

score to a *T*-score metric ranging from 0 to 100, with a mean of 50 and a standard deviation fixed at 10.

PROMIS Global Health-Physical.—We used PROMIS Global Health Scale v1.2 (Hays et al. 2009) to assess participants' self-rated physical health. Participants rated each item on a Likert scale from 1 (poor) to 5 (excellent). Higher scores indicate better perceived physical health. Cronbach's alpha was 0.65 for physical health.

PROMIS Sleep Disturbance (PSD).—We assessed sleep disturbance using eight items from the PROMIS Sleep Disturbance measure, which assessed problems with sleep, difficulty falling asleep, whether sleep was refreshing, and sleep quality over the past 7 days (Buysse et al. 2010). The eight items were rated on a Likert scale, ranging from never (1) to always (5). Higher scores indicate worse symptoms. Cronbach's alpha was 0.88 for sleep quality.

St. George's Respiratory Questionnaire (SGRQ).—The SGRQ version 2.3 is a 17-item self-assessment of respiratory symptoms consisting of two parts (Jones et al. 1991) that assess symptoms, activity, and impacts. We used first 5 items in Part I to assess lung/respiratory symptoms in the past 4 weeks. The first four items were rated on a Likert scale, ranging from almost every day (1) to not at all (5), and the fifth item asked about unpleasant episodes of lung/respiratory problems, ranging from more than three episodes (1) to no episodes (5). Cronbach's alpha was 0.86 for respiratory symptoms.

Simplified Nutritional Appetite Questionnaire (SNAQ).—SNAQ is a 4-item single-domain questionnaire (Wilson et al. 2005), and each item is a Likert scale ranging from 1 to 5 with higher score indicating better appetite, and scores lower than 14 indicating poor appetite. Cronbach's alpha was 0.75 for appetite.

Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith 1983).—HADS is a brief (7 items each), validated self-assessment of anxiety and depression severity (Bjelland et al. 2002). Each item was rated on a four point (0–3) response category with scores ranging from 0 to 21 for both anxiety and depression. A score of greater than or equal to 8 on the two subscales indicates clinically significant depression and anxiety. Three scoring categories included 0–7 for normal, 8–10 for borderline abnormal, and 11–21 for abnormal. Cronbach's alpha was 0.78 for anxiety and 0.77 for depression.

Patient Health Questionnaire-9 (PHQ-9) (Kroenke et al. 2001).—PHQ-9 is a well-validated self-report tool that measures severity and frequency of depressive symptoms, presence of suicidal ideation, and functional impairment related to depression. We included 8 items (excluding the item that assesses suicidal ideation), and higher scores indicate more severe depression. Cronbach's alpha was 0.88 for depression.

PROMIS Cognitive Function Abilities.—We used the 8-item form to assess participants' subjectively experienced cognitive functioning during the prior seven days. Participants rate their responses using a scale ranging from 1 (not at all) to 5 (very much) with regard to cognitive tasks, including the perception of one's cognitive abilities in the

areas of concentration and memory. Higher scores indicate better perceived cognitive function abilities. Cronbach's alpha was 0.96 for cognitive function abilities.

PROMIS Cognitive Function.—We used the 8-item form to assess self-reported cognitive functions in terms of mental acuity, concentration, verbal and nonverbal memory, and verbal fluency. Participants rated these functions on a Likert scale, ranging from very often/several times a day (1) to never (5). Higher scores indicate better perceived cognitive functioning. Cronbach's alpha was 0.93 for cognitive function.

Statistical Analyses

Descriptive statistics are reported by the three cannabis use groups, with group differences tested by chi-square (for categorical variables) or ANOVA (for continuous measures). Pairwise comparisons were conducted for functional outcomes if the overall group difference was significant. Separate linear regression models predicting current functional status in measures of health, mental health, and cognition were conducted to test if the three cannabis use levels are associated with improved functional outcomes controlling for demographics, histories of health and psychiatric conditions, and alcohol, tobacco, and other drug use.

Results

Participant characteristics

The sample was predominantly male (80%), middle-aged (mean age of 36.7, SD=11.5) and consisted of 30% black, 26% white and 24% Hispanics. A quarter of them had college or higher degrees, and only one-third were currently employed with the abstinent group having the lowest level of education and employment among the three groups. More than 90% reported history of SUD treatment, with approximately 64% currently in treatment and highest (89%) among the abstinent group.

Cannabis use and other substance use

Most participants started using cannabis when they were teens (the mean age was 14.6, with the onset of use being older among the low use group at 16.3). Similar across the three groups, the average age during the period of heaviest cannabis use was between 29 and 31. During the heaviest use period, more than 90% used 4 or more days per week and at least 4 times per day. Motivations for cannabis use cited the most included enhancement of positive effects, coping, and social cohesion (Simons et al. 1998). 93% of participants reported using high potency cannabis products, and the most common means of cannabis use (e.g. joint, pipe, vaporizer, bong, wax/dabs) was similar between low and heavy use groups. Only 2 participants reported recent use of synthetic cannabinoids.

Approximately half of the participants across the three groups reported tobacco smoking in the 30 days prior to the survey. Significantly more individuals in the heavy use and low use groups reported alcohol drinking (54% and 42%, vs. 3%) and other drug use (25% and 17%, vs. 3%) than the abstinent group.

History of health and psychiatric conditions

Overall, many participants reported histories of physical conditions (50%) and psychiatric disorders (54%), although none of these conditions differed significantly among the three cannabis use groups. The three most prevalent physical health conditions were sleep disorder (22%), chronic pain conditions (17%), and asthma (15%). The most common psychiatric conditions included anxiety/PTSD/panic disorder (39%), major depressive disorder (23%), bipolar disorder (20%), and ADHD (20%).

Functional status on physical health, mental health, and cognition

We report descriptive statistics on functional status in Table 4 and multiple regression results in Table 5.

Univariate analyses consistently showed that individuals who used cannabis heavily demonstrated the worst functional status in all measures among the three groups, except that the group differences in respiratory symptoms and perceived cognitive abilities was not significant. None of the differences between the abstinent and low use groups were statistically significant in pairwise comparisons.

In table 5, compared to the heavy use group, the low use group had higher physical health scores (Global Health - Physical = 8.5, $p < 0.01$; Appetite = 2.3, $p < 0.01$) and lower depression score (PHQ-9 = -4.3, $p < 0.05$). The abstinent group further showed higher functioning in other domains. Compared to the heavy use group, the abstinent group had better physical health (Global Health - Physical = 6.3, $p < 0.05$; Sleep Disturbance = -7.7, $p < 0.01$; Appetite = 2.7, $p < 0.01$) and mental health (HADS-Anxiety = -2.7, $p < 0.05$; HADS-Depression = -3.7, $p < 0.01$; PHQ-9 = -4.9, $p < 0.01$). Also, the abstinent group had higher perceived cognitive function (Cognitive Function = 11.4, $p < 0.01$; Cognitive Function Abilities = 6.0, $p < 0.05$), even after controlling for age at first cannabis use and recent substance use.

Demographic variables were also associated with functional outcomes. Having less than college degree was associated with greater sleep disturbance (difference = 5.6, $p < 0.05$) and lower perceived cognitive function abilities (difference = -5.0, $p < 0.05$). Also, appetite significantly differed by gender and employment status; females had less appetite than males (difference = -2.0, $p < 0.01$), whereas being employed was associated with greater appetite (difference = 1.6, $p < 0.05$).

Discussion

Compared to participants who used cannabis heavily, those who attained abstinence reported significantly better health (global, sleep, appetite), mental health (anxiety, depression), and perceived cognitive functioning outcomes. More importantly, those who used cannabis at a low level did not differ from the abstinent individuals in any of the functional outcome measures in the univariate analyses, and both groups demonstrated in multivariate analyses significantly better outcomes than heavy users in global health, appetite, and depression. Additional improvements in sleep, anxiety, depression (as measured by PHQ-9), and perceived cognitive function and abilities were also reported in the abstinent group relative

to the heavy use group. These findings support the notion that cannabis use reduction to lower levels of use is associated with improved functional outcomes in many important health and other domains.

Study findings are consistent with prior studies demonstrating improvements in depression, anxiety and sleep in individuals with CUD who reduced use over time (Hser et al. 2017), and with improvements in quality of life in treatment-seeking individuals with CUD who reduced or abstained from use (Brezing et al. 2018). Though many individuals report using cannabis to help with insomnia, and cannabis use has been associated with improvements in short-term sleep outcomes (National Academies of Science, Engineering and Medicine 2017), heavy, prolonged cannabis use may have more detrimental effects on sleep quality, particularly during withdrawal which typically subsides within 2 weeks after cessation of use (Budney et al. 2003). In this study, currently abstinent reported significantly improved sleep quality than heavy users. Differences in perceived cognitive functioning between the groups, with heavy users reporting lower perceived abilities, were also consistent with extant literature suggesting deficits in various cognitive domains during cannabis intoxication and after heavier or more prolonged use (Crean et al. 2011; Volkow et al. 2014).

Though cannabis intoxication is known to stimulate appetite, heavy cannabis users in this study reported worse appetite, with a significant proportion at risk of weight loss; those who reduced use to low or abstinent levels reported significantly improved appetite scores. Indeed, cannabis withdrawal symptoms include diminished appetite (Budney et al. 2003), which heavy users may experience between use episodes. Furthermore, individuals with very heavy use may perceive that they require cannabis use to simulate appetite. It is worth noting that female participants reported a lower appetite than males. A possible explanation is that cannabinoids have been shown to exert sex-dependent physiological and behavioral effects, such as food intake and energy (Fattore and Fratta 2010). Lack of significant findings related to respiratory function between the groups were surprising given that regular cannabis use is associated with worse respiratory symptoms and chronic bronchitis (National Academies of Science, Engineering and Medicine 2017); this may be partly related to the relatively younger age of the sample, expected time course to perceive improvement in respiratory functioning, or limitations related to the respiratory assessment, which was developed for individuals with known pulmonary disease.

The study has several limitations. The one-time survey represents a cross-sectional design, with reductions in cannabis use inferred from self-reported changes in use patterns from prior periods of heaviest use to current use levels. Functional outcomes were based on the current status at the time of survey without corresponding measures collected at the time of heaviest use. Nevertheless, an examination of the history of health and psychiatric conditions (Table 3) did not show any differences among the three groups. Future studies may seek to replicate the findings using a prospective design so that changes in cannabis use and functional outcomes can be directly measured and compared over time. Further, the classification of cannabis use group in the present study is limited by sample size and self-reported use data; the varying levels of cannabis use associated with outcomes would ideally include objective verification measures such as urine drug screen and should be further investigated empirically using quantitative levels of cannabis in biological samples

(Schreiner and Dunn 2012). Variability in potency of cannabis products may also affect outcomes; however, 93% of participants reported using high potency cannabis products, and the most common means of cannabis use (e.g. pipe, vaporizer) were similar between low and heavy use groups.

In our study, the proportion of males was significantly higher than females, which may affect generalizability. However, prior studies have reported a higher prevalence of CUD in males compared with females in the general population (Fairman 2016; Hasin et al. 2015). Assessment of cognitive outcomes via self-reported perception of abilities poses another limitation and could be strengthened by corroboration with objective performance on cognitive tasks in future studies; however, the relationship between neurocognitive task performance and practical impairments in functioning has been questioned in prior work (Schreiner and Dunn 2012).

Identification of diverse, clinically relevant outcomes for use in future research may advance treatment development for SUDs. Our study sample represents a population of heavy cannabis users with histories of SUD specialty treatment or 12-step support and many co-occurring conditions. On the other hand, PROMIS provides normative values so that results can also be compared with the general population, and indeed most measures for the abstinent and low-use groups were close to the general population means. Thus, the study findings suggest that reductions in cannabis use to lower levels may confer benefits in improved functioning in treatment-seeking individuals.

Acknowledgements

Support provided through the National Institute on Drug Abuse (DA042280). We are grateful for the dedication of staff at each participating treatment facility in Los Angeles, California: Tarzana Treatment Centers, Los Angeles Centers for Alcohol and Drug Abuse (LA CADA), SHIELDS for Families, Antelope Valley Rehabilitation Centers, UCLA Dual Diagnosis Intensive Outpatient Program, Phoenix House.

Funding: This project has been funded in part with federal funds from the National Institute on Drug Abuse (NIDA) grant# R21DA042280

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Table 1.

Participant Demographics and other Characteristics

	Current use			Total (N=111)
	Abstinent (n=63)	Low use (n=24)	Heavy use (n=24)	
Age, Mean (SD)	37.0 (10.5)	34.6 (10.0)	36.0 (13.7)	36.7 (11.5)
Female (%)	12.7	33.3	26.1	20.4
Race/Ethnicity (%)				
African American	25.4	37.5	33.3	29.7
Asian	3.2	8.3	0	3.6
Hispanic	23.8	16.7	33.3	24.3
White	28.6	25.0	20.8	26.1
Multi-race/Multi-ethnic	15.9	12.5	8.3	13.5
Other	3.2	0	4.2	2.7
College degree or higher, (%)[*]	17.5	50.0	26.1	25.9
Employed (%)^{**}	19.4	54.2	41.7	31.3
Currently in treatment (%)^{**}	88.9	29.2	33.3	63.7

Group comparison based on Chi-square test for categorical variables or ANOVA test for continuous variables

* P<0.05,

** P<0.01

Table 2.

Cannabis and other substance use

	Current use			Total (N=111)
	Abstinent (n=63)	Low use (n=24)	Heavy use (n=24)	
Age at first cannabis use, Mean(SD)*	13.8 (3.3)	16.3 (4.3)	15.3 (2.7)	14.6 (3.6)
Age at the heaviest cannabis use, Mean(SD)	31.1 (11.1)	30.5 (9.0)	29.4 (11.7)	31.1 (11.4)
Cannabis use during the heaviest use (%)				
Days per week **				
Less than one day a week	0.0	8.3	0.0	1.8
One day a week	0.0	4.2	0.0	0.9
2-3 days a week	3.2	12.5	0.0	4.4
4-5 days a week	12.7	29.2	16.7	16.8
More than 5 days a week	84.1	45.8	83.3	76.1
Times per day				
Once a day	1.61	4.2	0.0	1.8
2-3 times a day	12.9	33.3	8.3	17.0
4-5 times a day	27.4	25.0	25.0	26.8
6-7 times a day	11.3	12.5	33.3	16.1
More than 7 times a day	46.8	25.0	33.3	38.4
Reduction from heaviest to current use (%)	100	79.2	25.0	79.3
Marijuana Motives Questionnaire (MMQ), Mean (SD)				
Coping	3.3 (1.2)	3.0 (1.2)	3.7 (1.1)	3.3 (1.2)
Social	3.1 (1.2)	2.9 (1.2)	3.1 (1.3)	3.1 (1.2)
Enhancement*	4.0 (1.0)	3.3 (1.1)	3.6 (0.8)	3.8 (1.0)
Conformity	1.8 (1.0)	1.8 (1.0)	1.5 (0.7)	1.7 (1.0)
Expansion	2.7 (1.4)	2.6 (1.2)	3.2 (1.3)	2.8 (1.3)
Use in the past 30 days (%)				
Tobacco	55.6	45.8	50.0	51.3
Alcohol**	3.2	41.7	54.2	22.1
Other drug use**	3.2	16.7	25.0	10.6

Group comparison based on Chi-square test for categorical variables or ANOVA test for continuous variables

* P<0.05,

** P<0.01

Table 3.

History of physical and psychiatric conditions

	Current use			Total (N=111)
	Abstinent (n=63)	Low use (n=24)	Heavy use (n=24)	
Physical comorbidities (%)				
Any physical comorbidity	44.4	62.5	54.2	50.5
Epilepsy or seizure disorder	6.6	4.2	0.0	4.6
Liver disease	4.9	12.5	0.0	5.6
Kidney disease	1.6	0.0	0.0	0.9
Immune disorders	1.6	0.0	4.4	1.9
Heart/cardiovascular conditions	1.6	0.0	0.0	0.9
Asthma	11.5	16.7	21.7	14.8
Other respiratory problems	8.2	12.5	8.7	9.3
Diabetes	3.3	0.0	4.4	2.8
Gastrointestinal disorders	4.8	8.3	4.4	5.5
Chronic pain conditions	11.5	20.8	26.1	16.7
Sexual Dysfunction	1.6	0.0	8.7	2.8
Sexually transmitted diseases	16.4	17.4	17.4	16.8
Sleep disorder	21.0	26.1	21.7	22.2
Psychiatric comorbidities (%)				
Any psychiatric comorbidity	55.6	54.2	50.0	54.1
Schizophrenia	6.6	0.0	0.0	3.7
Major depressive disorder	22.6	26.1	21.7	23.2
Bipolar disorder	18.0	30.4	13.0	19.6
Anxiety/PTSD/Panic disorder	41.9	30.4	39.1	38.9
ADHD	16.1	18.2	30.4	19.6

Group comparison based on Chi-square test

* P<0.05,

** P<0.01

Table 4.

Descriptive statistics on functional outcomes

	Current use			
	Abstinent (n=63)	Low use (n=24)	Heavy use (n=24)	Total (N=111)
Physical Health				
PROMIS Global Health-Physical, Mean (SD) ^{*, ac, bc}	48.3 (9.2)	50.9 (7.4)	42.2 (8.4)	47.4 (9.1)
St. George's Respiratory Questionnaire (SGRQ), Mean (SD)	24.1 (24.8)	24.4 (30.0)	35.0 (32.0)	26.0 (27.7)
PROMIS Sleep Disturbance (PSD), Mean (SD) ^{**, ac}	50.5 (9.4)	54.0 (9.0)	58.6 (11.5)	52.8 (10.3)
Simplified Nutritional Appetite Questionnaire (SNAQ), Mean (SD) ^{**, ac, bc}				
	15.5 (2.8)	15.0 (2.8)	12.5 (3.7)	14.8 (3.2)
High risk of weight loss within 6 months (<=14) (%) ^{**}	25.4	29.2	70.8	35.4
Mental Health				
Hospital Anxiety and Depression Scale (HADS)				
Anxiety, Mean (SD) ^{**, ac}	5.6 (4.3)	7.2 (3.8)	8.2 (4.7)	6.5 (4.4)
Normal (%)	67.2	56.5	45.8	60.9
Borderline abnormal (%)	16.4	21.7	16.7	17.3
Abnormal (%)	16.4	21.7	37.5	21.8
Depression, Mean (SD) ^{**, ac}	5.2 (4.4)	6.5 (3.6)	8.2 (4.3)	5.9 (5.6)
Normal (%)	68.9	60.9	41.7	61.8
Borderline abnormal (%)	16.4	17.4	33.3	20.0
Abnormal (%)	14.8	21.7	25.0	18.2
Patient Health Questionnaire-9 (PHQ-9), Mean (SD) ^{**, ac, bc}				
	4.9 (5.0)	5.2 (3.7)	9.8 (7.2)	5.9 (5.6)
Cognition, Mean (SD)				
PROMIS Cognitive Function (PCS) ^{**, ac}	52.4 (9.4)	47.2 (8.2)	42.4 (12.0)	49.0 (10.5)
PROMIS Cognitive Function Abilities (PCSA)	51.1 (10.5)	50.2 (10.2)	46.1 (9.2)	49.7 (10.2)

Group comparison based on Chi-square test for categorical variables or ANOVA test for continuous variables

* P<0.05,

** P<0.01

Pairwise comparison of mean scores based on the Tukey-Kramer method

a = no use,

b = low use,

c = heavy use

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Table 5.

Multiple linear regression model predicting functional outcome

Parameter	Physical Health				Mental health			Cognition	
	Global Health - Physical	Respiratory Function	Sleep	Appetite	HADS - Anxiety	HADS - Depression	PHQ-9	Cognitive Function	Cognitive Function Abilities
Intercept	42.3 (5.4)**	38.0 (16.6)*	54.8 (6.1)*	12.5 (1.7)**	9.8 (2.7)**	10.9 (2.7)**	9.5 (3.4)**	42.3 (6.1)**	50.1 (5.9)**
Cannabis use (vs. Heavy use)									
Low use	8.5 (2.7)**	-8.6 (8.3)	-3.2 (3.0)	2.3 (0.8)**	-0.5 (1.4)	-1.8 (1.4)	-4.3 (1.7)*	3.5 (3.0)	4.0 (2.9)
Abstinent	6.3 (2.5)*	-15.5 (7.8)	-7.7 (2.9)**	2.7 (0.8)**	-2.7 (1.3)*	-3.7 (1.3)**	-4.9 (1.6)**	11.4 (2.9)**	6.0 (2.8)*
Age at first cannabis use	0.02 (0.3)	-0.3 (0.8)	-0.1 (0.3)	-0.02 (0.1)	-0.1 (0.1)	-0.2 (0.1)	-0.03 (0.2)	0.03 (0.3)	-0.1 (0.3)
Female (vs. Male)	-1.7 (2.4)	-3.1 (7.2)	3.6 (2.6)	-2.0 (0.7)**	0.1 (1.2)	0.3 (1.2)	0.9 (1.5)	-1.1 (2.6)	-2.0 (2.6)
Less than college degree	-1.8 (2.2)	1.8 (6.8)	5.6 (2.5)*	0.1 (0.7)	0.5 (1.1)	0.4 (1.1)	0.3 (1.4)	-3.2 (2.5)	-5.0(2.4)*
Employed	2.9 (2.1)	-5.1 (6.5)	-0.2 (2.4)	1.6 (0.7)*	-0.7 (1.1)	-0.2 (1.1)	-1.7 (1.3)	2.6 (2.4)	2.7 (2.3)
Use in the past 30d									
Tobacco	1.5 (1.8)	9.0 (5.5)	-0.1 (2.0)	0.4 (0.6)	-0.5 (0.9)	-0.3 (0.9)	0.9 (1.1)	2.3 (2.0)	0.9 (2.0)
Alcohol	-1.3 (2.7)	-10.7 (8.2)	1.6 (3.0)	0.9 (0.8)	-0.01 (1.3)	0.1 (1.3)	0.4 (1.7)	2.4 (3.0)	-0.1 (2.9)
Other drug use	1.5 (3.0)	7.1 (9.4)	0.8 (3.4)	-1.1 (0.9)	0.7 (1.6)	-0.5 (1.6)	1.5 (1.9)	-4.0 (3.4)	1.0 (3.3)

* P<0.05,

** P<0.01