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A Contingency Management Method for 30-Days Abstinence in Non-Treatment Seeking Young Adult Cannabis Users*

Randi Melissa Schuster^{a,b}, Ailish Hanly^a, Jodi Gilman^{a,b}, Alan Budney^c, Ryan Vandrey^d, and **A. Eden Evins^{a,b}**

^aCenter for Addiction Medicine, Department of Psychiatry, Massachusetts General Hospital (MGH) Boston, MA, USA

^bHarvard Medical School, Boston, MA, USA

^cDartmouth College, Geisel School Of Medicine, Lebanon NH, USA

^dJohns Hopkins University School of Medicine, Baltimore, MD, USA

Abstract

Background—Rates of young adult cannabis use are rising, perceived harm is at its historical nadir, and most users do not want to quit. Most studies evaluating effects of cannabis use in young adults are cross-sectional, limiting causal inference. A method to reliably induce abstinence periods in cannabis users would allow assessment of the effects of abstinence and resumption of use on a variety of outcomes in a within subjects, repeated measure design.

Methods—We examined the efficacy and feasibility of a voucher-based contingency management procedure for incentivizing one month of continuous cannabis abstinence among young adults who reported at least weekly cannabis use, volunteered to participate in a laboratory study, and did not express desire to discontinue cannabis use long-term. Continuous cannabis abstinence was reinforced with an escalating incentive schedule, and self-report of abstinence was confirmed by frequent quantitative assays of urine cannabis metabolite (THCCOOH)

Conflict of Interest Statement

Contributors

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Address correspondence to: Randi Melissa Schuster, 60 Staniford Street, Boston, MA 02114; phone: (617) 643-6673; fax: (617) 7243726; rschuster@mgh.harvard.edu.

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concentration. New cannabis use during the abstinence period was determined using an established algorithm of change in creatinine-adjusted cannabis metabolite concentration between study visits.

Results—Thirty-eight young adults, aged 18–25, enrolled and 34 (89.5%) attained biochemically confirmed 30-day abstinence. Among those who attained abstinence, 93.9% resumed regular use within two-weeks of incentive discontinuation.

Conclusion—Findings support the feasibility and efficacy of contingency management to elicit short-term, continuous cannabis abstinence among young adult, non-treatment-seeking, regular cannabis users. Further work should test the effectiveness of this CM procedure for cannabis abstinence periods longer than one month, which may be required to evaluate some effects of abstinence.

Keywords

Contingency management; cannabis; marijuana; young adults; abstinence; methodology

1. INTRODUCTION

Cannabis is the most commonly used substance other than alcohol among young adults in the United States (Johnston et al., 2015; SAMHSA, 2014), with nearly 20% of young adults report using cannabis currently. Widespread policy changes regarding legal access to medical and non-medical cannabis are expected to increase rates of use further. This is concerning given that ongoing brain maturation occurring well into the third decade of life (Giedd et al., 1999) may increase vulnerability to negative consequences associated with regular cannabis exposure. Indeed, frequent use during this developmental period is the best predictor of persistent use in adulthood (Chen and Kandel, 1995; SAMHSA, 2014) and adverse cognitive (Gruber et al., 2012; Jacobus and Tapert, 2014; Lisdahl and Price, 2012; Lisdahl et al., 2014; Solowij et al., 2011), psychosocial (Chadwick et al., 2013; Degenhardt et al., 2013; Hall, 2014; Marmorstein and Iacono, 2011; Palamar et al., 2004; Fergusson et al., 2006; Hurd et al., 2014; Lynskey et al., 2003; Swift et al., 2012), and academic outcomes (Ellickson et al., 2004; Fergusson and Boden, 2008; Maggs et al., 2015; Meier et al., 2015).

Though strong associations have been reported between frequent young adult cannabis exposure and negative outcomes, most studies of the effects of cannabis use are cross sectional, which impedes the ability to draw conclusions about causal effects of cannabis use. Prospective longitudinal trials and experimental manipulations are the gold-standard for determining causality. The former is challenging due to cost and time requirements if initial assessments are to occur before exposure and retains biases associated with the decision to initiate cannabis use prior to adulthood or not, and the latter poses ethical concerns for cannabis-naïve participants. A reliable method that would allow examination of change in clinical, cognitive or other measures in response to cannabis abstinence and resumption of use among young adults who regularly use cannabis may represent a viable strategy to study reversible effects of cannabis on outcomes of interest in this important population.

Contingency management (CM) may be an ideally suited approach for studying the potential consequences of cannabis use. Abstinence-based CM was developed according to basic tenets of behavior analysis and operant conditioning (Budney et al., 2001; Higgins and Petry, 1999; Meredith et al., 2014; Petry, 2000; Stanger and Budney, 2010): reinforcing behaviors increases the likelihood that they will recur (Skinner, 1969). From this perspective, addictive substance use is a learned behavior that is reinforced by desirable drug effects. Abstinence-based CM seeks to alter learned substance use behavior with provision of consistent, competing positive reinforcement (e.g., monetary rewards) for verified abstinence (Bigelow et al., 1981).

CM has well-established efficacy for changing substance use behavior (Higgins et al., 1991; Krishnan-Sarin et al., 2013; Petry et al., 2000; Reynolds et al., 2008; Stitzer et al., 1986), specifically cannabis use among treatment-seeking adults for total days abstinent (Kadden et al., 2007; Litt et al., 2013) and longer duration of continuous abstinence (Budney et al., 2000, 2006; Cooper et al., 2015; Copeland and Swift, 2009; Litt et al., 2013). CM is also efficacious for treatment-seeking adolescent (Kamon et al., 2005; Stanger et al., 2009, 2015; Stewart et al., 2015) and young adult cannabis users (Carroll et al., 2006; Montgomery et al., 2012), particularly when coupled with other psychosocial interventions such as cognitive behavioral therapy (CBT), motivational enhancement therapy (MET), and family therapy (Carroll et al., 2006; Kamon et al., 2005; Stanger et al., 2009, 2015; Stewart et al., 2015). However, participants in previous studies were seeking treatment (Kamon et al., 2005; Stanger et al., 2009) and/or met criteria for a cannabis use disorder (Carroll et al., 2006; Stanger et al., 2015). Although participants in prior trials were not necessarily motivated to stop using cannabis (e.g., Stewart et al., 2015), past findings may still only generalize to the most severely impacted young adult cannabis users given that most individuals do no seek treatment for cannabis use until after age 25 (SAMHSA, 2015), It is not known whether CM can be used to effectively induce a period of continuous cannabis abstinence in young adults who do not use cannabis daily, are not seeking treatment, but who nonetheless may be experiencing reversible effects of cannabis. The purpose of this study was to develop a method to reliably attain abstinence in young adult regular cannabis users for one month so that future studies can assess brain, cognitive, behavioral, and mood changes during four consecutive weeks of abstinence and after resumption of use, using a prospective, withinsubject design that would allow more definitive conclusions regarding potential effects of abstinence in this important population.

2. METHODS

This study was conducted between July and November, 2015. All enrolled participants gave written informed consent to a protocol approved by the Partners' Human Subjects Review Committee.

2.1 Participants

Eligible participants were young adults, aged 18–25, who reported using cannabis at least weekly. They were recruited via peer referral and advertisements in the community that sought potential participants 'who use marijuana and are between age 18 and 25'. Inclusion

criteria included cannabis use in the week prior to the phone screen, English fluency, and willingness to stop using cannabis for 30 days and attend eight study visits over six weeks at the Massachusetts General Hospital (MGH).

2.2 Assessments of Participant Mood and Substance Use

At baseline, current and lifetime diagnoses of Axis I disorders were assessed with the Structured Clinical Interview for DSM-IV (SCID-IV), mood was assessed with the Mood and Anxiety Symptoms Questionnaire (MASQ; Watson et al., 1995), and current and lifetime symptoms of Attention Deficit/Hyperactivity Disorder (ADHD) were assessed with a DSM-IV symptom checklist. At baseline, substance use disorders were assessed using the SCID-IV, the Cannabis Use Disorder Identification Test – Revised (CUDIT-R; Adamson and Sellman, 2003) and Alcohol Use Disorders Identification Test (AUDIT; Saunders et al., 1993). Amount and frequency of substance use was assessed at every study visit using a modified Timeline Follow-Back method (Robinson et al., 2014). Cannabis withdrawal was assessed at every visit using the Cannabis Withdrawal Scale (CWS; Allsop et al., 2011).

2.3 Assessment of Cannabis Metabolites

Participants provided urine specimens at each session. Urine samples were shipped overnight to Dominion Diagnostics (Kingstown, RI, USA) to quantify 11-nor-9-carboxy- 9-tetrahydrocannabinol (THCCOOH) levels, a non-psychoactive metabolite of 9-tetrahydrocannabinol (THC) and the standard urine biomarker for cannabis use, using liquid chromatography/tandem mass spectrometry (LC-MS/MS). The lower limit of quantification (LOQ) was 5ng/mL and the maximum value quantified by the LC-MS/MS method was 500ng/mL. Samples with THCCOOH values 500ng/mL were further analyzed for THC using enzyme immunoassay (EIA), which had an upper LOQ of 900ng/mL.

Urine creatinine concentration was quantified and used to correct THCCOOH concentration for individual differences in hydration (Lafolie et al., 1991). The THCCOOH to creatinine concentrations ratio (CN-THCCOOH) was calculated by dividing the urinary THCCOOH concentration (ng/mL) by urine creatinine concentration (mg/mL), yielding ng THCCOOH/mg creatinine.

2.4 Contingency Management (CM) Procedure

The CM procedure consisted of a four-week abstinence-based incentive program consisting of seven study visits over 4 weeks, and a two-week follow-up visit. The first four visits occurred in the first week of the study, followed by three weekly visits. See Figure 1 for detailed visit schedule. In order to better ensure initial abstinence requirements were being met, more frequent visits were conducted during Week 1. This allowed for more frequent quantitative assessment of cannabinoid metabolites during early abstinence when CN-THCCOOH reductions are greatest (Budney et al., 2003). More frequent testing initially helps differentiate abstinence from reduction in severity of use and also provides better reinforcement of initial abstinence behavior (Schwilke et al., 2011; Stitzer and Vandrey, 2008). At the baseline visit, all participants completed an abstinence contract with a study staff member that clearly delineated the behavior to be monitored, schedule of monitoring, and contingencies (Budney and Higgins, 1998; Petry, 2000). Participants were then

instructed to refrain from using cannabis for the next month (Visits 2–7). After Visit 7, abstinence was no longer reinforced, and participants were assessed two weeks later (Visit 8). Participants were asked to refrain from using illicit drugs and alcohol on the day of study visits.

Participants earned incentives based on a two-track system for attendance and abstinence. Please see Table 1 for incentive schedule. The value of incentives for both attendance and abstinence escalated incrementally to encourage both study retention and achievement of longer periods of continuous abstinence (Roll and Howard, 2008; Roll and Shoptaw, 2006). Participants were told that they would revert to the initial attendance payment level (\$5) following a missed study visit and that they would be discontinued from the study if abstinence was not confirmed. At the two-week follow-up visit (Visit 8), participants were compensated for attendance only. Participants abstinent for 30 days with full attendance earned \$585 (\$405 for continuous abstinence and \$180 for full attendance). Incentives were provided on reloadable credit cards through Clinical Trials Payer (CT Payer), a secure webbased platform that facilitates HIPAA and HITECH safe clinical trial and study-related payments. Incentives for attendance were made available for use 15 minutes after each study visit. Incentives for abstinence were provided upon receipt of the quantitative urinalysis results (described below), typically about four days after specimen collection. Incentive payments for verified abstinence were added to the credit cards remotely between study visits (see Figure 1). Study staff called participants as soon as lab results were received to inform them of the results and the value added to their cards.

2.5 Determination of Cannabis Abstinence at Each Study Visit

Residual cannabinoid excretion was differentiated from new cannabis exposure using a statistical model developed by Schwilke and colleagues (2011). This model was empirically derived from urine CN-THCCOOH concentration ratios of consecutively collected specimen pairs (current specimen/prior specimen). This model takes into account the time between collection of specimens, which enhances the accuracy of prediction of new cannabis use (Smith et al., 2009). This formula yields an expected CN-THCCOOH ratio associated with specimen pairs during abstinence, and observed ratios that exceed this expected value are interpreted as new cannabis use.

Model parameters are specific to the CN-THCCOOH concentration of the first specimen collected in each pair as well as the desired level of specificity. For this study, we used a 95% level of certainty, which allows for a 2.5% probability that an observed CN-THCCOOH concentration ratio of specimen pairs would exceed the expected ratio and be falsely interpreted as new cannabis use (see supplementary information¹ for additional model details and an example application of this formula in the current study). As sensitivity analyses, new use determinations with 80, 90, and 99% specificity are reported. New use determinations are also reported with the cutoff of 0.5 and 1.5 ratio in specimen pairs, widely used methods for determining new cannabis use in non-daily cannabis users originally recommended by Huestis and colleagues (1998). The former cutoff for new use

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(0.5) yields very low false positive rates, and the latter (1.5) allows some increase in metabolite concentration that could be consistent with no new use.

2.6 Data Analysis

All statistical analyses were performed using Stata 13.1. The ratio of CN-THCCOOH concentrations of each consecutive specimen pair was the primary outcome measure, and was used to assess cannabis abstinence for each participant at each time point. Specimens in which the THCCOOH concentration exceeded the upper LOQ could not be adjusted for creatinine and were excluded from analyses. When possible, the THCCOOH concentration from Visit 2 or Visit 3 was substituted for baseline THCCOOH concentrations that exceeded the upper LOQ. To determine change in CN-THCCOOH across 30 days of abstinence, a non-parametric Friedman test of differences among repeated measures was conducted, with pairwise comparisons evaluated using Wilcoxon Signed Ranks Test. Alpha was set at 0.05 for all statistical tests.

3. RESULTS

3.1 Participants

Fifty-six people were screened for participation and 38 were enrolled. No subject failed the screen due to unwillingness to stop using cannabis for 30 days. Seven declined to enroll due to not wanting to commit to eight study visits; four did not meet current substance use criteria; three no longer lived in the greater Boston area; and four were older than 25 years of age. Participant age range was 18 to 25, a majority was in or had completed some college, and nearly half had a lifetime psychiatric diagnosis. See Table 2. Participants reported an average age of onset of cannabis use at least once per week on most weeks of 17.7 years, and an average use of cannabis on 19.7 of the last 30 days. Over 58% met criteria for possible Cannabis Use Disorder on the CUDIT-R. See Table 3 for participant substance use characteristics.

3.2 Abstinence Outcomes

Of the total number of urine specimens collected (N = 293), 8.5% were above the upper LOQ of 500ng/mL (10 samples at Visit 1, five samples at Visit 2, four samples at Visit 3, two samples at Visit 4, and four samples at Visit 8). There was wide inter-subject variability in the CN-THCCOOH concentrations in the first urine specimen. After removal of the samples with the greatest THCCOOH concentrations (>500ng/mL), the 73% of participants with quantifiable baseline THCCOOH concentrations had a median CN-THCCOOH concentration of 29.4ng/mL (IQR= 17.6, 85.6).

Thirty-day abstinence was confirmed in 89.5% of the sample (n = 34 of 38 enrolled), with 95% certainty (Schwilke et al., 2011). See Table 4. These participants completed all seven visits of the active CM protocol. Table 4 also highlights the percent new-use determination in this sample according to alternative upper prediction limits stipulated by Schwilke and colleagues (2011) and Huestis and Cone (1998). Of the four participants who did not achieve 30 days of abstinence, two were lost to follow-up (one after Visit 2 and one after Visit 6, and thus presumed to be non-abstinent), and two reported using cannabis one time

between Visits 5 and 6 and were accurately classified as non-abstinent by the Schwilke algorithm at 80%, 90% and 95% accuracy as well as by the Huestis 0.5 and 1.5 ratio guidelines.

Thirty-day abstinence with CM was associated with reduction in consecutive CN-THCCOOH concentrations ($X^2 = 83.9$, p<0.0001). All pairwise comparisons between CN-THCCOOH values were significant (p-values < 0.0007), with the exception of Visit 6 and Visit 7 (p = 0.12) which were both close to zero. See Figure 2.

3.3 Resumption of Cannabis Use Two-Weeks Following End of CM

Among the 34 30-day abstinent participants, 97.1% (n=33) completed the two-week followup assessment (Visit 8), at which time 93.9% (n=31) had resumed using cannabis. CN-THCCOOH values at this visit were comparable to baseline levels among those who resumed use and whose THCCOOH levels were quantifiable (Baseline: Med=44.2, IQR= 20.4, 85.6; 2-Week Follow-Up: Med=43.9, IQR= 3.4, 99.9). See Figure 2.

4. DISCUSSION

This study aimed to examine the effectiveness of a modified CM approach for four weeks of continuous cannabis abstinence in non-treatment seeking young adults with a range of cannabis dependence scores. Here we show that CM can be used to induce short-term cannabis abstinence in non-treatment seeking young adults who report using cannabis weekly or more. This CM manipulation may serve as a useful methodological approach for examining the effects of cannabis abstinence on various brain, cognitive, behavior and psychiatric outcomes, which are more commonly investigated using cross sectional designs in this population. Policy changes have made investigation of the effect of cannabis use on these outcomes urgent, particularly among adolescents and young adults who may be differentially impacted by early cannabis exposure due to ongoing brain development.

With nearly 90% of the sample able to achieve 30-day cannabis abstinence, this study provides strong preliminary support for the feasibility of this CM protocol to study abstinence associated change in outcomes of interest. This high rate of abstinence is consistent with prior studies demonstrating the efficacy of CM in treatment-seeking and cannabis-dependent populations (Carroll et al., 2006; Kamon et al., 2005; Stanger et al., 2009, 2015). Young adulthood is a critical time to examine the effects of cannabis given that this is the peak developmental period for use (1 in 5 18 to 25 year olds are current cannabis users; SAMHSA, 2014) and use during this time is the best predictor of related problems (Chen and Kandel, 1995). Further, this study supports the efficacy of CM among cannabis users with psychiatric co-morbidities, as 48.6% of our sample met criteria for a lifetime Axis I psychiatric diagnosis, and 89.5% and 47.4% used alcohol and tobacco in the last week, respectively. While many studies restrict their samples to cannabis-dependent individuals and/or systematically exclude for co-morbid conditions, it has also become essential to elucidate cannabis' residual effects among the "average" young adult cannabis user who may not use cannabis daily, is not seeking treatment, and presents with other drug use and psychiatric co-morbidities.

There are several aspects of the CM approach that merit discussion. Our protocol delivered CM alone, suggesting that CM without complimentary manualized treatments may be sufficient in incentivizing non-treatment seeking young adult cannabis users with a range of dependence scores to abstain from use for 30 days. Additionally, participants achieved nearly a 90% verified abstinence rate using delayed (rather than immediate) monetary rewards for abstinence. The quantitative urine drug testing utilized to monitor abstinence in the days immediately following the point of discontinued use took about four days for results, and therefore this approach required a delayed delivery of rewards for confirmed abstinence. Importantly, this approach eliminated the need for the "washout" period used in prior trials because most frequent cannabis users will test positive for cannabis several days to weeks after their last use (Goodwin et al., 2008; Hawks and Chiang, 1986) due to the storage and subsequent release of THC and THCCOOH in fat and relatively long half-life (Hunt and Jones, 1980; Lowe et al., 2009). The primary benefit of the present approach is that requiring a "washout" period may result in the systematic exclusion of individuals who are not able to achieve early continuous abstinence without more immediate contingent incentives to motivate abstinence efforts. Finally, despite the positive effect of CM in this sample, more than 90% of participants resumed use within two weeks of CM termination, consistent with other studies that show poor maintenance of gains post-treatment (Stanger et al., 2009, 2015). Future studies are needed that evaluate the benefit of alternative positive reinforcement strategies (e.g., increased magnitude of reinforcers, longer duration of intervention) as well as adding brief interventions (e.g., motivational interviewing) prior to the removal of the abstinence contingencies to promote continued abstinence.

Limitations of this study warrant consideration. A limitation includes the small sample size, precluding identification of predictors of abstinence. There is also no control group against which to evaluate the specificity of CM's efficacy on cannabis abstinence. Additionally, a large proportion of this sample had a high level of education (>73% had completed at least some college coursework) and a major minority had a psychiatric co-morbidity, which may limit generalizability of findings to young adults with similar background characteristics. Finally, although the amount of compensation provided to participants was commensurate with other studies (e.g., Kamon et al., 2005; Stanger et al., 2015) and the use of contingencies for abstinence may actually increase the cost-effectiveness of clinical interventions (e.g., López-Núñez, et al., 2016), the high cost of conducting a protocol such of this may reduce its ability to be utilized when research budgets are modest.

Despite these limitations, this study provides important support for the use of CM as a tool to examine change in various outcomes of interest during four weeks of continuous cannabis abstinence. A checklist is provided as a resource for investigators interested to setting up a research study using a similar CM approach (Figure 3). From a clinical perspective, establishing the efficacy of CM in this population is critical given that current cannabis use is disproportionately represented among young adults yet this population is among the lowest to access treatment for use. Additionally, young adults are especially poised to experience greater consequences from early exposure due to ongoing brain development. CM may be a viable avenue for active secondary prevention that targets young people at an early stage of their cannabis-use. Early prevention among this vulnerable group, particularly during a time of rapid policy change surrounding cannabis' legal status, may help to

minimize problematic use, promote problem recognition, and facilitate informed choice regarding cannabis use and its potential consequences.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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	Highlights
•	Contingency management may be useful for studying the effects of cannabis in youth.
•	Nearly 90% of the sample attained biochemically confirmed 30-day abstinence.
•	Abstinence was associated with reduction in concentrations of cannabis metabolites.

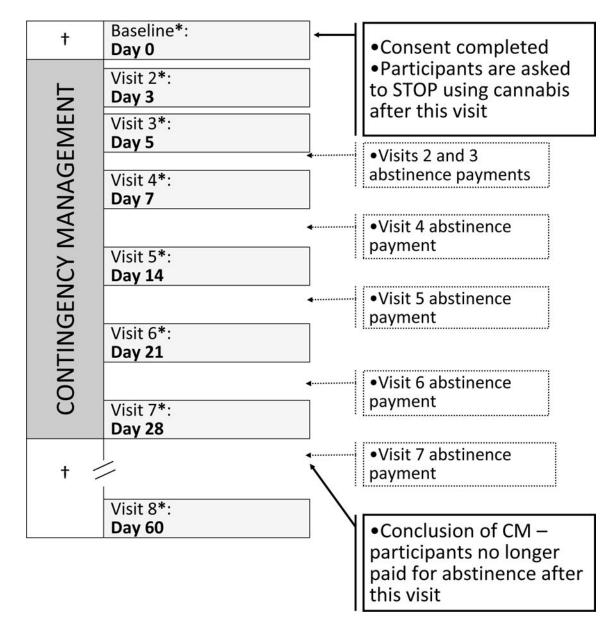


Figure 1.

Participants were assessed 8 times over the course of approximately six weeks. Abstinence was reinforced between Visits 2 and 7. Visits 4, 5, 6, 7, and 8 had a scheduling window of ± 2 days

†Participants using cannabis as usual

* Delivery of attendance payments

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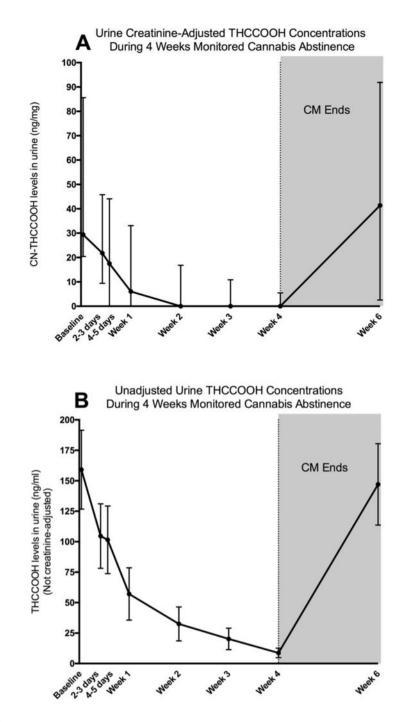


Figure 2.

A. Urine creatinine-adjusted THCCOOH concentrations declined during four weeks of monitored cannabis abstinence. All values represent medians and interquartile ranges. Values are only presented for the participants who provided urine samples with THCCOOH values under the limit of detection (500ng/mL). **B.** Unadjusted THCCOOH concentrations declined during four weeks of monitored cannabis abstinence. All values represent means and standard errors. Values are coded as "501" for participants with urine THCCOOH values over the limit of detection (500ng/mL).

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The target behavior should be objectively quantified.
 Abstinence: Continuous non-use for a designated period of time Abstinence: Continuous non-use for a designated period of time Reduction in use: Use fewer days per week, times per day, or amount per day compared to baseline levels Clinic attendance, compliance with treatment plans, clinic behaviors (if treatment seeking)
Define how the target behavior will be monitored
Quantitative drug testing: Indicates the amount of detectable THC or secondary metabolites in urine or blood
 Benefits: Most reliable method for determining early abstinence; prevents the need for a "washout period" Concerns: Expensive, delay in results which leads to delay in reward administration; sample validity needs to be ensured by checking temperature, dilution and/or pH Cost: \$20 to \$50 per sample, depending on the lab and assay method
Qualitative drug testing: Indicates whether there is any measureable concentration of cannabis in urine or blood above the minimum detectable threshold of the test
 Benefits: Rapid results, which allows for immediate delivery of reward or punishment; ease of use Concerns: High lower limit of quantification for THC (typically 50 ng/mL) which may result in false negatives; inability to confirm abstinence in the weeks immediately following cessation of use and therefore requires use of a "washout period;" possible false negatives in light users; sample validity needs to be ensured by checking temperature, dilution and/or pH Cost: \$3 to \$5 a test
Self-report (e.g., via a Timeline Follow-Back Calendar)
 Benefits: Useful, low-burden tool that may be best used <u>only</u> in conjunction with biological verification of abstinence/reduction Concerns: Inaccuracy in recall; dishonesty; difficult to estimate amount of substance used (i.e. grams of marijuana) Cost: None

- Define the type of reward (e.g., vouchers, cash, reloadable debit cards, etc.)
- Define the monitoring schedule (i.e., consistency and frequency of reward delivery)
- Reinforcers should be delivered in close temporal proximity to the incident of the target behavior, as subjective values of rewards diminish with time.
- Define whether rewards escalate in value

1. Define the target behavior that will be monitored

 Escalating schedules of reinforcement typically yield better outcomes than static schedules of reinforcement (Roll et al., 1996; Roll & Higgins, 2000).

4. Define the consequences for failure to achieve the target behavior

Explicitly outline what are the negative consequences for failure to achieve target behavior

• If a participant fails to follow the agreed upon protocol, the most common consequence is either withdrawal from the study or, if it occurs in the early stages of the protocol, resetting the payment/reward scale back to baseline.

5. Create a behavioral contract

Detail the above information in a behavioral contract that the participant and a study staff member sign

Be specific!

Specify the exact behaviors, how they will be monitored and over what period of time, when and how they will be reinforced
 The contract should include expectations of the participant, what rewards will be dispensed upon confirmation of achievement of the target behavior, when the rewards will be provided (i.e. if there is any anticipated delay between obtaining the sample and receiving the results), what the consequences of failure to achieve target behavior will be, and how long the protocol will last for.

· The participant should retain a copy of this contract to keep.

Figure 3.

Key considerations for setting up a CM-based research protocol are delineated in checklist format.

Table 1

Contingency Management Payment Schedule

	Visit Number	Attendance	Abstinence
1	Baseline	\$5	-
2	3 days	\$10	\$30
3	4 days	\$15	\$45
4	1 week	\$20	\$60
5	2 weeks	\$25	\$75
6	3 weeks	\$30	\$90
7	4 weeks	\$35	\$105
8	2 week follow-up	\$40	-
	Max Subtotal	\$180	\$405
	Max Total	\$5	85

Table 2

Baseline Participant Characteristics

Baseline Participant Characteristics (N=38)	
Demographics	
Sex, % Male	57.9%
Age	21.1 (1.7) (range: 18–25)
Ethnicity, % Hispanic or Latino	13.2%
Race	
% White	68.4%
% Black	13.2%
% Other	18.4%
Highest Level of Education	
% High school diploma or less	5.3%
% Some college/in college currently	73.7%
% 4-year college diploma or more	21.0%
Intellectual/Academic Functioning	
Predicted full scale IQ (WTAR)	106.1 (9.2)
Grade point average (on a 4.0 scale)	3.2 (0.5)
Psychopathology	
% Lifetime SCID-IV diagnosis (excluding substance use)	48.6%
Major Depressive Disorder:	
% Lifetime	45.9%
% Current	5.4%
Anxiety disorder (GAD, PTSD, Panic, Phobia)	
% Lifetime	21.6%
% Current	16.2%
Bipolar Disorder	
% Lifetime	2.7%
% Current	2.7%
Eating Disorder	
% Lifetime	2.7%
% Current	2.7%
% ADHD (Self-Report)	23.7%
Concomitant Psychotropic Medications	
% Currently taking any psychotropic medication	26.3%
% currently taking antidepressants	7.9%
% currently taking anxiolytics	2.6%
% currently taking mood stabilizers	5.3%
% currently taking stimulants	10.5%
Psychiatric Symptoms	
Childhood ADHD symptoms (max=9)*	
Inattention	3.3 (2.8)

Baseline Participant Characteristics (N=38)	
Hyperactivity	4.2 (2.9)
Current ADHD symptoms (max=9)*	
Inattention	3.6 (2.8)
Hyperactivity	3.7 (2.6)
MASQ	
General Distress Anxious Symptoms	21.7 (7.2)
Anxious Arousal	25.2 (7.7)
General Distress Depressive Symptoms	25.3 (9.9)
Anhedonic Depression	57.1 (13.5)

*A score of 5 indicates symptoms consistent with ADHD

Table 3

Participant Substance Use Characteristics

Participant Substance Use Characteristic	s (N=38)
Marijuana (MJ) Use	
Age of first use	15.9 (2)
Age of regular use *	17.7 (2.1)
Recency of last MJ use (in days)	1.9 (2.7)
Frequency of use	
Days used in past 90 days	53.6 (22.0)
Days used in past 30 days	19.7 (7.5)
Times used in past 90 days	103 [50, 164]
Times used in past 30 days	42.5 (32.6)
Amount of use	
Grams consumed in past 90 days	28.3 [11.3, 78.7]
Grams consumed in past 30 days	11.3 [2.6, 31.3]
Severity of use	
MJ Use Disorder (SCID-IV)	
% Lifetime Abuse	45.9%
% Current Abuse	29.7%
% Lifetime Dependence	29.7%
% Current Dependence	18.9%
Baseline CUDIT	14.7 (6.2)
% 8	89.5%
% 12	58.3%
Withdrawal	
Baseline	
Intensity	29.5 [15, 49.75]
Negative Impact	33 [22, 48.5]
Change from Baseline to Week 1	
Intensity	-1 [-11, 5]
Negative Impact	0 [-9, 3]
Change from Baseline to Week 4	
Intensity	-3 [-24.5, 6]
Negative Impact	0 [-16.5, 4]
Alcohol Use	
% Ever used	100%
Age of 1 st use	15.5 (2)
Recency of last use	
% drank in last week	89.5%
% drank in last month	94.7%
% drank in last year	100%
Binge drinking episodes	20 [2.0, 62.5]

Frequency of use	
Days drank in past 90 days	25.1 (14.1)
Days drank in past 30 days	8.4 (5.0)
Amount of use	
Standard drink equivalents in past 90 days	81.8 [54, 152.5]
Standard drink equivalents in past 30 days	30.0 [12.0, 60.5
Severity of use	
Alcohol Use Disorder (SCID-IV)	10.8%
% Lifetime Abuse	0%
% Current Abuse	10.8%
% Lifetime Dependence	0%
% Current Dependence	9.0 (6.3)
Baseline AUDIT	36.8%
% 8	18.4%
% 13 (female) or 15 (male)	
Nicotine Use †	
% Ever used	89.5%
Age of 1 st use	17 (2.5)
Recency of use	
% smoked in last week	47.4%
% smoked in last month	63.2%
% smoked in last year	81.6%
Frequency of use	
Days smoked in past 90 days	2.5 [0, 15.75]
Days smoked in past 30 days	1 [0, 4.5]
Times smoked in past 90 days	2.5 [0, 27.5]
Times smoked in past 30 days	1 [0, 7.0]
Amount of use	
Cigarette equivalents in past 90 days	2.5 [0, 70.5]
Cigarette equivalents in past 30 days	1 [0, 18.0]
Other Drug Use	
% use of any drug >10 times	31.6%
Recency of use	
% use of any drug in past 30 days	26.3%
% use of any drug in past 90 days	68.4%
Severity of use	
Other Drug Use Disorder (SCID-IV)	
% Lifetime Abuse	5.4%
% Current Abuse	0%
% Lifetime Dependence	2.7%
% Current Dependence	0%

* Data available only for 26 participants.

 $^{\dot{7}}$ Includes hookah and mulling

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Table 4

Percent New-Use Determinations Exceeding the Upper Prediction Limits Proposed by Huestis et al., 1998 and Schwilke et al., 2011

		Used in Study		Sei	Sensitivity Analysis	alysis	
Specimen Pairs $N\dot{\tau}$ 95% PI	NŤ	95% PI	80% PI	Id %06	Id %66	80% PI 90% PI 99% PI 0.5 Ratio 1.5 Ratio	1.5 Ratio
Wk 1/Baseline	34	0	0	0	0	0	5.9
Wk 2/Wk 1	35 0	0	0	0	0	2.9	22.9
Wk 3/Wk 2 <i>††</i>	37 5.4	5.4	8.1	5.4	2.8	5.4	35.1
Wk 4/Wk 3	34 0	0	0	0	0	0	25.7

Note.

 $\dot{\tau}$ The number of excluded pairs was as follows: Week 1/Baseline (3 pairs excluded because at least one specimen exceeded the LOQ); Week 2/Week 1 (2 pairs excluded because at least one specimen exceeded the LOQ)

 $\dot{ au}^{\dagger}$ Two participants reported resuming cannabis use after the Week 2 visit, and were therefore not included in subsequent data points.