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Treatment Models for Targeting Tobacco Use During Treatment for Cannabis Use Disorder: Case Series

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Abstract

Approximately 50% of individuals seeking treatment for cannabis use disorders (CUD) also smoke tobacco, and tobacco smoking is a predictor of poor outcomes for those in treatment for CUD. Quitting tobacco is associated with long-term abstinence from alcohol and illicit drugs, yet there are no established treatments for CUD that also target tobacco smoking. This report highlights issues related to cannabis and tobacco co-use and discusses potential treatment approaches targeting both substances. Data is shared from the first six participants enrolled in an intervention designed to simultaneously target tobacco use in individuals seeking treatment for CUD. The twelve-week program comprised computer-assisted delivery of Motivational Enhancement Therapy, Cognitive-Behavioral Therapy, and Contingency Management, i.e., abstinence-based incentives for CUD. In addition, participants were encouraged to complete an optional tobacco intervention consisting of nicotine-replacement therapy and computer-assisted delivery of a behavioral treatment tailored for tobacco and cannabis users. All participants completed the cannabis intervention and at least a portion of the tobacco intervention: all completed at least one tobacco computer module (mean = 2.5 modules) and 50% initiated nicotine replacement therapy. Five of six participants achieved abstinence from cannabis. The number of tobacco quit attempts was lower than expected, however all participants attempted to reduce tobacco use during treatment. Simultaneously targeting tobacco during treatment for CUD did not

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Contributors: AJB and CS designed the study, wrote the protocols, and directed the study. DCL assisted with management of the study, conducted the descriptive analyses of the data, and wrote the initial draft of the manuscript. MB contributed to study design, and managed NRT dosing schedules and side-effects reports. JRH and JFE assisted in the design of the tobacco intervention and development of the computer modules. All authors contributed to the writing and have approved the final manuscript.

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negatively impact cannabis outcomes. Participation in the tobacco intervention was high, but cessation outcomes were poor suggesting that alternative strategies might be needed to more effectively prompt quit attempts and enhance quit rates.

Keywords

Tobacco; Cannabis; Dependence; Co-Use; Behavior; Treatment

1. Introduction

Cannabis users frequently report concurrent tobacco use. National Household Survey on Drug use and Health (2012) indicates that over 60% of individuals 18 or older who reported current (past month) cannabis use also reported current tobacco use. In addition, approximately 50% of individuals in treatment for cannabis use disorders (CUD) report concurrent tobacco use, and over a third of individuals with CUD meet criteria for nicotine dependence (Agrawal, Budney, & Lynskey, 2012; Moore & Budney, 2001). This high rate of concurrent tobacco use in cannabis users raises much concern, particularly given the ubiquitous negative-health related effects of tobacco smoking [Center for Disease Control and Prevention (CDC), 2008]. The present report: 1) highlights clinical issues related to the co-use of cannabis and tobacco, 2) describes potential treatment approaches targeting both substances, and 3) provides illustrative data from the first six pilot cases that have completed treatment and are informing the development of an intervention that integrates a tobacco cessation intervention with an evidence-based treatment for CUD.

1.1 Impact of co-use

Studies examining mechanisms of tobacco and cannabis co-use have identified multiple risk factors common to both substances that increase vulnerability for use and development of use disorders. First, behavioral genetic studies suggest common and reciprocal pathways to use and dependence (Agrawal et al., 2012). Second, neurobiological studies indicate that the endocannabinoid system enhances the reinforcing effects of nicotine, and antagonizing CB1 receptors can block these effects, suggesting that the endocannabinoid system is a mechanism of action for the reinforcing effects of nicotine (Castañé, Berrendero, & Maldonado, 2005; Cohen, Kodas, & Griebel, 2005). Third, cannabis users frequently engage in concurrent and simultaneous use of both substances, either by smoking a mixture of tobacco and cannabis (e.g., blunts, spliffs) or by closely following cannabis use with tobacco smoking (i.e., chasing), and some report that combining the substances results in enhanced pleasurable effects (Amos, Wiltshire, Bostock, Haw, & McNeill, 2004; Cooper & Haney, 2009; Penetar et al., 2005; Ream, Benoit, Johnson, & Dunlap, 2008). Last, tobacco and cannabis frequently share the same route of administration, i.e., inhalation by smoking, which likely increases the probability of one substance prompting initiation or interfering with cessation of the other due to conditioning and learning factors (e.g. conditioned smoking cues signaling reinforcement availability associated with the other substance; for review on cue-reactivity see Carter & Tiffany, 1999). Reciprocal enhancement of reinforcing effects and learned associations between substances may strengthen behavior for

using both substances increasing the risk for ongoing use and the development of use disorders.

1.2 Treatment Challenges and Approaches

These ubiquitous associations between cannabis and tobacco use pose difficult challenges to those who desire to quit using one or both substances. Tobacco use has been observed as a predictor of poor outcomes during treatment for CUD (Peters, Budney, & Carroll, 2012), and cessation of cannabis may lead to increases in legal psychoactive substances for some individuals (Copersino et al., 2006; Peters & Hughes, 2010). Moreover, cannabis use among tobacco smokers predicts continued long-term tobacco use and may be associated with poor tobacco-cessation outcomes (Amos et al., 2004; Ford, Vu, & Anthony, 2002).

Despite these concerns, only one published study has focused on developing interventions targeting both substances (Hill et al., 2013; reviewed below). Interventions targeting tobacco cessation during treatment for substances other than cannabis generally report decreases in tobacco use with no concomitant adverse effects on outcomes for the other substances (for review see: Sullivan & Covey, 2002; Baca & Yahne, 2009). A meta-analysis of 19 controlled trials evaluating tobacco interventions for substance-abuse problems found that smoking interventions were associated with a 25% increased likelihood of long-term abstinence from alcohol and illicit drugs (Prochaska, Delucchi, & Hall, 2004), although this finding is not unequivocal (see Joseph, Willenbring, Nugent, & Nelson, 2004).

Both simultaneous and sequential approaches to treatment of concurrent tobacco and other substance use (including alcohol and illicit drugs) have been evaluated, with both approaches showing success with decreasing concurrent use of both drugs (Kalman, Kim, DiGirolamo, Smelson, & Ziedonis, 2009; Nieva, Ortega, Mondon, Ballbe, & Gual, 2010; Prochaska et al., 2004). The advantage of a simultaneous approach is that both drugs can be targeted during a single treatment program, which decreases the resources required for treatment (Kalman et al., 2009). Since cannabis users frequently report using tobacco and cannabis in close proximity (i.e. cannabis rolled in cigar wraps, chasing cannabis with tobacco), and conditioned cues associated with tobacco or cannabis may generalize to the other drug, a simultaneous rather than sequential treatment would appear optimal.

1.3 Efficacious Treatments

Effective treatments for CUD include Motivational Enhancement Therapy (MET), Cognitive Behavioral Therapy (CBT), Contingency Management (CM) and their combination (Budney, Roffman, Stephens, & Walker, 2007; Danovitch & Gorelick, 2012). The bulk of the evidence suggests that the combination intervention, MET/CBT/CM, engenders the highest rates of abstinence (Budney, Moore, Rocha, & Higgins, 2006; Budney, Higgins, Radonovich, & Novy, 2000; Carroll et al., 2006, 2012; Kadden, Litt, Kabela-Cormier, & Petry, 2007; Litt, Kadden, & Petry, 2013). Moreover, recent studies report that computer-assisted delivery of these interventions produce comparable outcomes to therapist-delivered approaches at a decreased cost (Budney et al., 2011, Kay-Lambkin, Baker, Kelly, & Lewin, 2011; Kay-Lambkin, Baker, Lewin, & Carr, 2009), making implementation by community clinics more likely.

Effective treatments for tobacco cessation have been established in a wide range of studies and include behavioral and pharmacological treatments, each of which can be used alone or in combination with other treatments. Pharmacotherapies, including varenicline, bupropion, and nicotine replacement therapy (NRT) are equally efficacious pharmacological treatment options (Eisenberg et al., 2008; Stapleton et al., 2008). Behavioral treatments such as brief counseling and readily available internet-based tobacco interventions have also been established as effective strategies to reduce tobacco use (Civljak, Sheikh, Stead, & Car, 2010; Herman & Sofuoglu, 2010; Strecher et al., 2005). More intensive behavioral treatments using CM have also been effective at increasing tobacco abstinence in high-risk populations (Donatelle, Prows, Champeau, & Hudson, 2000; Heil et al., 2008; Shoptaw et al., 2002). Interventions that combine pharmacological and behavioral components are generally considered to be most effective (United States Department of Health and Human Services Guidelines, 2008).

The one pilot study that evaluated an integrated treatment for CUD and tobacco provided a ten-week intervention using CBT to simultaneously target both cannabis and tobacco cessation, and NRT (Hill et al., 2013). Findings showed a reduction in cigarettes per day, but no significant improvement in cannabis use, suggesting that this simultaneous approach was feasible, but its efficacy was limited.

Our current project aims to develop and evaluate a treatment program simultaneously targeting CUD and tobacco use combining an established highly efficacious CUD treatment (i.e. MET/CBT/CM) and an effective tobacco intervention (NRT and behavioral therapy). For our initial pilot study, we selected NRT rather than alternative medication for tobacco use such as varenicline or bupropion because both have side-effect profiles that may increase cannabis-related withdrawal symptoms (e.g. irritability, restlessness, depression, insomnia; Haney et al., 2001; Stapleton et al., 2008), and because NRT is available without a prescription making it easier to access. Working hypotheses were: 1) 35-40% of participants would achieve cannabis abstinence (>4 weeks), 2) targeting tobacco use would not negatively impact cannabis outcomes, 3) every participant would participate in at least one tobacco module, 4) a substantial proportion (40%) would initiate NRT, and 5) the tobacco intervention would prompt quit attempts (> 35%) and result in tobacco abstinence (> 2 weeks) during treatment (> 25%).

2. Method

2.1 Participants

The intervention was advertised as a program for those seeking to quit cannabis use who also smoked tobacco. The telephone screening process required participants to have at least some interest in quitting tobacco in the next 6 months (rating of 2 or more on a 5-point interest scale). The first six cases included in this report all indicated a 5, or strong interest in quitting tobacco. Participants had to be at least 18 years of age, meet criteria for a DSM-IV diagnosis of cannabis abuse or dependence assessed by the Substance Use Disorders section of the Structured Clinical Interview for DSM-IV, report use of cannabis on at least 45 of the previous 90 days, and report daily use of tobacco cigarettes, or simultaneous use of cannabis

and tobacco (i.e. blunts or spliffs). Drug use data was assessed using Timeline Followback Questionnaires (TLFB; Form 90; Sobell & Sobell, 1992).

Participants were excluded if they met dependence criteria for alcohol or any drug other than nicotine and cannabis, used non-tobacco nicotine, were currently in treatment for substance abuse, had a medical condition that prevented use of NRT (i.e. current pregnancy, recent heart attack; verified by study physician), or had current, severe psychological distress (i.e. active suicidal plans, psychosis, debilitating panic disorder; assessed by a computerized version of the Structured Clinical Interview for DSM Diagnoses, Axis 1, Research Version (SCID-I RV; First, Spitzer, Gibbon, & Williams, 1995).

Table 1 displays demographic information and baseline cannabis and tobacco use characteristics for each participant. Five out of six participants were male, with a mean age of 39.5 years (range 24-57). All participants met criteria for cannabis dependence. Average age of initiation of cannabis and tobacco use was 16.3 (range 13-22) and 15.5 (range 13-20) years, respectively. Mean reported use rates over the 90 days prior to intake were 3.2 cannabis use occasions per day (range 0.8-4.7) and 13.0 cigarettes per day (range 3.3-25.2). Participants had made an average of 5 (range 1-12) cannabis quit attempts and 3.8 (range 0-12) tobacco quit attempts prior to entering treatment. The Readiness to Change Questionnaire (Heatheron & Honekopp, 2008) indicated that three participants were in the contemplation stage and three were in the action stage of readiness to quit cannabis. The Fagerstrom Test of Nicotine Dependence scores averaged 4.3 (range 1-7; Heatheron, Kozlowski, Frecker, & Fagerstrom, 1991).

The SCID-I-RV was used to assess for Axis I disorders. Participant 03 had a history of depressive episode and alcohol dependence, Participant 04 had past history of depressive episode, and Participant 06 had a history of depressive episode, current generalized anxiety disorder, and reported a history of visual and auditory hallucinations, but did not meet criteria for a psychotic disorder. Participant 03 was currently prescribed bupropion and aripiprazole, and Participant 06 was currently on bupropion and Fluoxetine.

2.2 Intervention

A 12-week, 9 session computer-assisted version of MET/CBT/CM for CUD (Budney et al., 2011), was combined with a tobacco intervention that comprised five computer modules tailored for this program and NRT.

2.2.1 CUD Intervention—The computer assisted MET/CBT/CM for CUD is described in detail in Budney et al. (2011). Briefly, it comprised: a) nine computer-delivered MET/CBT modules, b) three supportive counseling sessions with a therapist, and c) an abstinence-based CM program. Computer modules 1 and 2 delivered MET, which involved an interactive review of a personalized feedback report generated from assessment information, and goal-setting exercises, including setting a quit date. Computer modules 3–8 (CBT) involved developing an effective social support system, understanding use patterns, coping with craving, managing thoughts about using, problem solving, refusal skills, coping with lapses, managing moods, assertiveness skills, and a lifestyle goal-setting exercise. The last

module encouraged participants to revisit helpful computer modules, and to remotely access the relapse prevention module in the future.

Participants were assigned a therapist and scheduled for three sessions (15-30 min each). The first occurred immediately prior to the first computer module, and involved discussion of motivation for initiating treatment, and provision of information about the treatment program. Subsequent sessions occurred in weeks 4 and 12, and reviewed progress, issues with the computer, need for clinical assistance, and encouragement to access their program remotely.

An abstinence-based incentive CM program was used to motivate and reinforce cannabis abstinence (Budney et al., 2006, 2011). Participants provided urine specimens twice weekly. Weeks 1-2 were considered a washout phase, and participants received \$5 incentives for clinic attendance, independent of test results, to reinforce participation and to allow time for cannabinoid levels to drop below the detection cutoff level. During Weeks 3–12, participants could earn incentives contingent on negative urine tests. The first negative specimen earned \$1.50, and values for each subsequent consecutive negative specimen increase by \$1.50. Participants earned a \$10 bonus for each week of abstinence. Positive tests reset the value to \$1.50, and the value for negative tests escalated again according to the same schedule. Participants remaining continuously abstinent during weeks 3–12 earned incentives worth \$435. Earnings were remotely deposited into a prepaid MasterCard.

2.2.2 Tobacco Intervention—The tobacco intervention comprised NRT plus five computer-delivered psychoeducation and behavioral therapy modules, developed for this program based on previous internet-based tobacco interventions (i.e. Etter, 2005; 2009) and tailored to address issues of co-use of cannabis and tobacco. The first module focused on issues related to the pros and cons of smoking, and participants completed a personalized assessment using a web-based tobacco intervention (Stop Tabac; Etter, 2005, 2009). Participants were encouraged to set a tobacco quit date, if interested. Module 2 provided information about co-use of cannabis and tobacco, including potential additive health risks of cannabis and tobacco co-use, difficulties associated with quitting one substance while continuing to smoke the other, planning to stop use of both substances, and roadblocks to quitting both. Module 3 provided NRT education and instruction. Participants were required to complete this module prior to starting NRT. Module 4 focused on planning for change and setting a quit date. Module 5 provided reduction strategies for those interested in reducing rather than quitting at the present time.

Participants were prompted by research staff to complete the first tobacco module during the second visit, and to complete additional modules throughout the program. The general approach of staff was to remind and encourage participants to complete tobacco modules in concert with their tobacco status and stated goals at each visit. However, it was always made clear that the tobacco intervention was optional and participants could complete any of the tobacco modules and use NRT at any time during the program.

Participants were offered free NRT each week by the research staff, which could be initiated at the beginning of the first week of treatment. NRT options included the patch, gum,

lozenge, or a combination following standard guidelines for dosing (Stead et al., 2012). Research staff provided a supply of NRT weekly, and monitored adverse effects at each visit.

2.3 Outcome Measures

Outcome measures for cannabis included abstinence measured by urinalysis and self-reported days of use [Timeline Followback Questionnaire (TLFB); Sobell & Sobell, 1992). Outcomes for the tobacco included: number of tobacco modules completed, initiation of NRT, number of cigarettes per day, and number of quit or reduction attempts. Self-reported tobacco quit attempts greater than 24 hours were verified using expired carbon monoxide tests.

3. Results

3.1 Cannabis

Five participants achieved abstinence from cannabis during the 12-week treatment averaging more than nine consecutive weeks of abstinence (Figure 1, panels A-F).

3.2 Tobacco

All participants completed the first tobacco module during the first two weeks of treatment. Participants completed a mean of 2.5 of tobacco modules (range 1-4). Three of six participants initiated NRT during treatment. Participant 03 and 06 used a combination patch and lozenge, and Participant 05 used a combination patch and gum. All participants that initiated NRT remained abstinent from cannabis, suggesting that NRT did not interfere with achieving and maintaining cannabis abstinence. However, only participant 03 used NRT throughout the entire program. Participant 05 reported using the patch and gum on 53% and 59% of treatment days, and Participant 06 reported using the patch and lozenge on 73% and 34% of treatment days, respectively. Participant 06 reported moderate to severe insomnia during NRT, which is a common side-effect associated with NRT. In response, the study physician recommended decreasing the dosing plan from a 21 mg patch to a 14 mg patch. No participant discontinued NRT due to negative side-effects.

No participant quit smoking tobacco successfully, but three made quit attempts and five reduced their use. Participant 02 made a quit attempt during the final week of treatment for seven days, and Participant 03 made one during week three for a duration of five days. Participant 05 made two quit attempts, one during week five (duration of two days), and one during week seven (duration of 36 hours). However, all participants had returned to smoking prior to their next clinic visit so CO-verification of quit attempts could not be determined. Five out of six participants made self-reported reduction attempts during treatment (i.e. reduced cigarette use lasting at least 24 hours in duration), with a mean of 4.8 attempts (range 1-8), and cigarettes per day decreased from intake to end of treatment for Participants 01, 02, 03, 05, and 06 (Figure 1). Note that CO was not obtained for reduction attempts, so these were not biologically verified.

4. Discussion

The outcomes from this case series suggest that simultaneously targeting tobacco during treatment for CUD did not negatively impact the initiation of cannabis abstinence; five of six participants achieved long periods of continuous abstinence. Certainly a larger sample and a controlled trial are needed to confirm these observations.

The impact of the intervention on tobacco smoking showed positive signs, but cessation outcomes engendered only moderate enthusiasm for this specific approach. Encouraging indicators that were consistent with our a priori hypotheses included: all participants completed at least one tobacco computer module assessing current tobacco use and motivation to change, and most continued on to participate in additional tobacco modules; three out of six participants initiated NRT, and the majority reduced the number of cigarettes smoked per day, which was similar to the outcomes reported in Hill et al., (2013). Most participants reported repeated reduction attempts, which was consistent with anecdotal staff reports of repeated conversations with participants about their desire and efforts to cut down. However, we expected to observe more tobacco quit attempts and successful periods of cessation.

These initial observations suggest the following. First, offering and encouraging tobacco cessation interventions to those entering CUD treatment does not appear to negatively impact cannabis treatment outcomes. Our tobacco intervention was optional and staff encouraged and prompted engagement in the intervention being careful not to appear coercive or judgmental. Second, the consistent interest of participants in quitting or reducing their tobacco use suggests that alternative strategies might be warranted to obtain more successful tobacco cessation outcomes.

One potential limitation to the current study was that, relative to the CUD intervention, the tobacco intervention was optional, did not provide incentives for tobacco abstinence, and was composed of fewer modules, which may have limited the potential efficacy of the tobacco intervention. One alternative to the current approach is to provide a parallel incentive program for tobacco abstinence. Such incentive programs have been successful for initiating tobacco abstinence in other high-risk populations (Donatelle et al., 2000; Heil et al., 2008; Shoptaw et al., 2002). Although this approach might increase the initial costs of delivery, increased efficacy may prove cost effective, though more research is needed to address the cost-effectiveness of providing simultaneous incentives for cannabis and tobacco abstinence. It may also be beneficial to provide a more robust behavioral intervention for tobacco, such as adding modules for maintaining tobacco abstinence, and strategies for beginning a new quit attempt following a lapse. Moreover, providing incentives for completing tobacco modules may increase exposure to the intervention. Alternative pharmacotherapies (i.e. varenicline, bupropion) might also be made available to participants, either as a choice at treatment entry, or following NRT if it proves unsuccessful. Participant history and preference might help guide such clinical decisions. Last, a sequential approach that postpones the tobacco intervention until CUD treatment is complete warrants consideration. However, our initial impression is that one need not choose between a simultaneous or sequential approach. Given that the intervention does not

appear to interfere with CUD treatment, it could be offered during as well as following treatment. In our piloting of the current intervention, we continue to offer treatment throughout, and have also made it available at the end of treatment. While most participants continue to be interested and engaged in tobacco reduction efforts up to the end of the program, no participant that declined NRT during treatment was interested in starting it at the end of the intervention.

Additional limitations to the study should be noted. First, we were unable to verify self-reported tobacco quit attempts using CO and/or urine cotinine measurements since all participants who reported making a quit attempt returned to smoking prior to returning for the next session. In addition, using CO to verify quit attempts greater than 24 hours in duration may be problematic since CO is sensitive to recent smoking. Second, although all participants in the study reported daily tobacco use, there was a wide range in reported cigarettes per day between participants (i.e. 3.3 – 25). Enrolling participants that were not regular smokers of at least 10 cigarettes per day may have limited the effectiveness of the tobacco intervention, especially since NRT is typically targeted at heavier tobacco users.

5. Conclusions

Results from this study provide preliminary evidence that supports the safety and feasibility of targeting tobacco use during treatment for CUD. Although tobacco quit rates were lower than anticipated in the current sample, the majority of participants participated in the intervention and showed substantial interest in quitting or reducing tobacco use. Further research is needed in order to better understand potential approaches targeting tobacco use in order to motivate quit attempts and improve quit rates in individuals with CUD that are interested in quitting tobacco.

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Manuscript Highlights

- This intervention targeted tobacco use during treatment for cannabis use disorder
- Simultaneously targeting tobacco use did not negatively impact cannabis abstinence
- All participants completed at least a portion of the tobacco intervention
- Participants reduced tobacco use but quit attempts and abstinence were less common

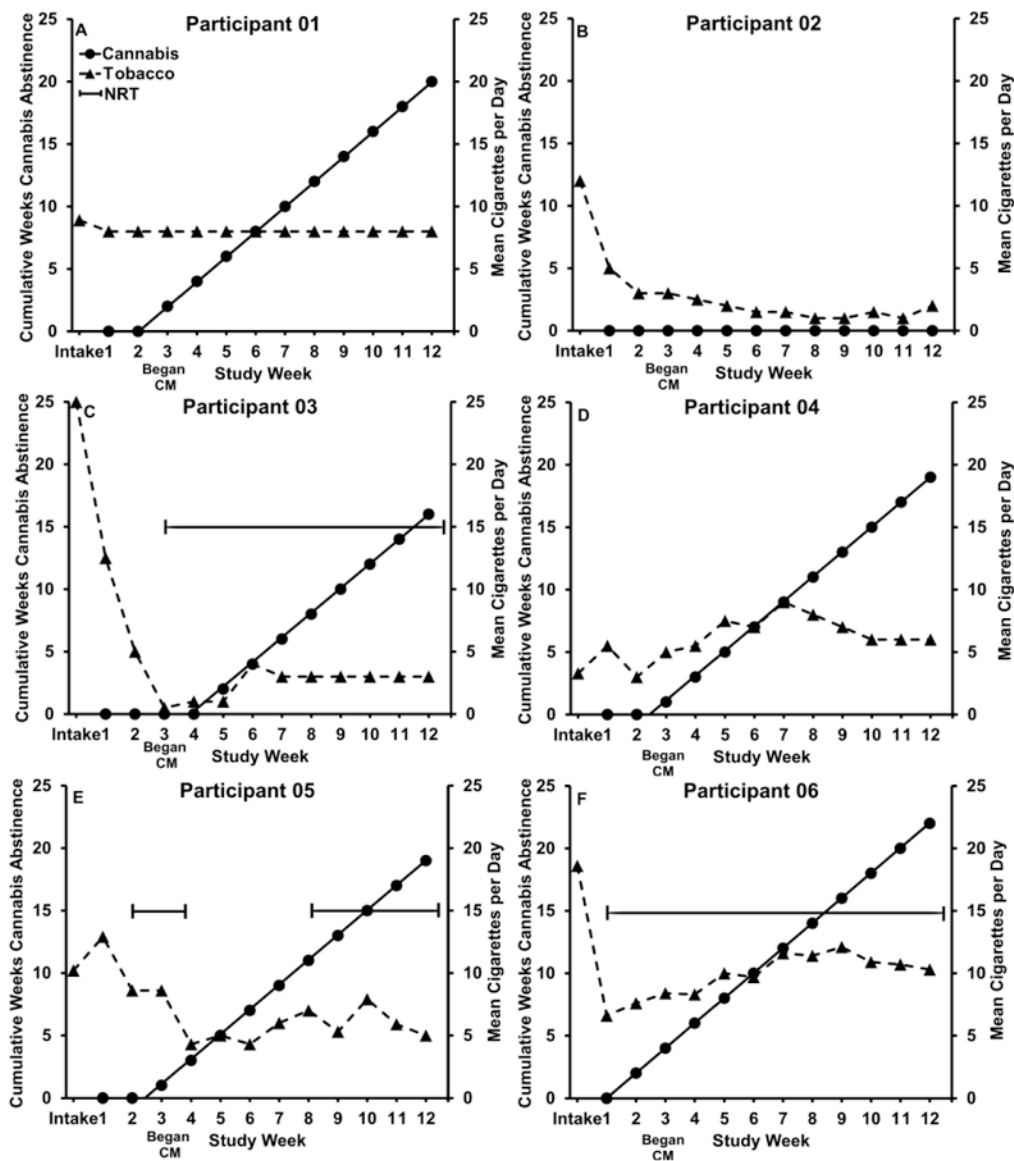


Figure 1. Cumulative cannabis negative test results and average cigarettes per day in each participant across study week. *Note: NRT = nicotine replacement therapy, CM = contingency management*

Table 1
Participant demographics and reported drug use characteristics at intake

| Participant | Sex | Age | Age of Initiation | | Prior Quit Attempts | | | Tobacco Use (cigarettes per day) | Cannabis Use (occasions per day) | Tobacco Use (cigarettes per day) | FTND | RTC Stage | Cannabis |
|-------------|-----|-----|-------------------|---------|---------------------|---------|----------|----------------------------------|----------------------------------|----------------------------------|---------------|---------------|----------|
| | | | Cannabis | Tobacco | Cannabis | Tobacco | Cannabis | | | | | | |
| 01 | M | 42 | 22 | 14 | 10 | 3 | 3.1 | 8.9 | 4 | 4 | Action | Action | |
| 02 | M | 33 | 18 | 20 | 3 | 3 | 5.0 | 12.0 | 5 | 5 | Contemplation | Contemplation | |
| 03 | M | 24 | 18 | 17 | 2 | 3 | 2.6 | 25.2 | 6 | 6 | Contemplation | Contemplation | |
| 04 | F | 28 | 14 | 14 | 1 | 2 | 4.7 | 3.3 | 1 | 1 | Action | Action | |
| 05 | M | 57 | 13 | 15 | 12 | 12 | 0.8 | 10.2 | 3 | 3 | Contemplation | Contemplation | |
| 06 | M | 53 | 13 | 13 | 2 | 0 | 3.2 | 18.6 | 7 | 7 | Action | Action | |

Note: FTND – Fagerstrom Test of Nicotine Dependence; RTC – Readiness to Change Questionnaire