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Feasibility and preliminary effectiveness of varenicline for treating co-occurring cannabis and tobacco use

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Abstract

Few studies have evaluated treatment for co-occurring cannabis and tobacco use. The objective of this pilot study was to evaluate the feasibility and preliminary effectiveness of varenicline for co-occurring cannabis and tobacco use. Participants who reported cannabis use on ≥ 5 days per week were recruited from an urban, outpatient opioid treatment program (OTP). Participants were randomized to either four weeks of standard OTP clinical care (SCC; medication assisted treatment for opioid use disorder and individual behavioral counseling), followed by four weeks of SCC plus varenicline (SCC+VT), or to four weeks of SCC+VT followed by four weeks of SCC. All participants contributed feasibility and outcome data during both study phases. Of 193 persons screened, 7 were enrolled. Retention at eight weeks was 100%. No adverse effects prompted varenicline discontinuation. Participants reported lower cannabis craving during the SCC+VT phase compared to baseline, and lower frequencies and quantities of cannabis use compared to both baseline and the SCC alone phase. In the SCC+VT phase, participants also reported fewer cigarettes per day. Among persons with co-occurring cannabis and tobacco use, varenicline is well-tolerated and may reduce cannabis craving, cannabis use, and tobacco use.

Keywords

Varenicline; cannabis; tobacco; concurrent use; feasibility

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Introduction

Cannabis is the most commonly used illicit drug in the U.S., with 26.2% of adults reporting past-month use (Center for Behavioral Health Statistics and Quality 2015). Despite widespread perceptions that cannabis use is benign, an estimated 3.5 million persons meet diagnostic criteria for past-year cannabis use disorder (CUD) (Center for Behavioral Health Statistics and Quality 2015). In addition to risks of abuse and dependence, long-term effects of CUD also include impaired brain development, and increased risk of chronic psychosis (Volkow et al. 2014). Behavioral treatments are the mainstay of treatment for CUD, but in addition to having limited effects, are resource intensive to implement. A number of medications have been evaluated for CUD, but none have had robust effects on cannabis abstinence compared to placebo among adults (Marshall et al. 2014).

Varenicline has demonstrated efficacy treating tobacco dependence (Anthenelli et al. 2016; Gonzales et al. 2006; Jorenby et al. 2006), which is highly prevalent among individuals with CUD (Belanger et al. 2011; Ramo & Prochaska 2012; Schauer et al. 2016). Varenicline is also a promising therapeutic candidate for CUD because it has activity at α7 nicotinic acetylcholine receptors, to which tetrahydrocannabinol, the psychoactive agent in cannabis, binds (Mihalak, Carroll & Luetje 2006; Solinas et al. 2007). In addition, varenicline has been shown to decrease both rewarding effects and use of both alcohol and cocaine (Mitchell et al. 2012; Plebani 2012; Plebani et al. 2013). The only published data on varenicline's effectiveness for CUD are from a case series of five cannabis and tobacco users. In that study, participants reported a reduction in cannabis enjoyment and cannabis use (Newcombe et al. 2015). However, adverse effects were common, and no participants completed the 12-week treatment course.

Because there are no efficacious, FDA-approved medications for adult CUD, one promising strategy is to treat CUD along with other co-morbid conditions, such as tobacco dependence (Budney et al. 2007; Rabin & George 2015). Co-occurring cannabis and tobacco use is highly prevalent, with 75% of current cannabis users reporting current tobacco use (Schauer et al. 2016), and 20–50% of tobacco smokers reporting current cannabis use (Belanger et al. 2011; Ramo & Prochaska 2012; Schauer et al. 2016). Because cannabis and tobacco have common routes of administration, smoking tobacco may act as a behavioral cue to cannabis use (Agrawal & Lynskey 2009). Tobacco use is implicated in continued cannabis use, escalation of cannabis use over time, and relapse to cannabis use following abstinence (de Dios et al. 2009; Haney et al. 2013; Moore & Budney 2001; Penetar et al. 2005). Similarly, cannabis use increases the risks of tobacco use, progression to daily tobacco use, and nicotine dependence (Agrawal et al. 2008; Patton et al. 2005; Timberlake et al. 2007). Treating co-occurring cannabis and tobacco use disorders might reduce the health burdens associated with both substances. However, few studies have evaluated pharmacological interventions, in combination with behavioral treatment, to address co-occurring cannabis and tobacco use; these are limited by high participant attrition, poor adherence to interventions, and lack of controls (Becker et al. 2015; Hill et al. 2013; Lee et al. 2014; Newcombe et al. 2015).

The primary objective of this pilot study was to evaluate the feasibility and preliminary effectiveness of varenicline for treatment of cannabis use among frequent cannabis users. We also examined its impact on tobacco use outcomes.

Methods

Setting and Participants

Participants were recruited from an urban, outpatient substance abuse treatment program that offers both intensive behavioral counseling and medication-assisted treatment (MAT) for opioid use disorder. We selected these clinical sites because we have successfully recruited and retained participants from these sites in prior clinical trials, and anticipated we would find a high prevalence of persons with frequent cannabis use. Eligible participants provided informed consent, and were: ≥18 years; English-speaking; reporting cannabis use on ≥5 of the past 7 days; with a urine toxicology test positive for cannabinoids; not taking varenicline in the past 30 days; not pregnant, trying to conceive, or breastfeeding; and without unstable medical or psychiatric illness. Participants were current or former tobacco smokers; for former smokers, duration of tobacco abstinence was not specified. Interest in quitting cannabis or tobacco was not a criterion for inclusion. We initially recruited from the behavioral counseling program, excluding persons taking methadone or buprenorphine for opioid use disorders, but later revised eligibility criteria to facilitate recruitment. All participants in the final sample were receiving MAT. Psychiatric eligibility was evaluated with structured psychiatric interviews (Posner et al. 2007; Sheehan et al. 1998). The Albert Einstein College of Medicine Institutional Review Board approved the protocol.

Study Design

This was an 8-week pilot study with a within-subject cross-over design. There were two, open-label treatment phases: four weeks of MAT with standard clinical care (SCC), and four weeks of MAT with standard clinical care plus varenicline therapy (SCC+VT). We selected this design over a conventional between-subjects design to facilitate efficient, controlled examination of preliminary varenicline effects even with a limited sample size. MAT includes individual counseling that uses motivational and cognitive behavioral strategies, may address cannabis or tobacco use, and is delivered by trained substance abuse counselors. Counseling content was not controlled or standardized. Varenicline therapy (VT) included a one month supply of standard doses: 0.5 mg for the first 3 days, 0.5 mg twice a day for the following 4 days, and 1 mg twice a day for the remaining 21 days. To prevent contamination of varenicline effects, participants were randomly assigned to the sequence of therapy, i.e., first SCC followed by SCC+VT, or first SCC+VT followed by SCC. We conducted research visits at baseline and at weeks 2, 4, 6, and 8. Participants were compensated with $15 for each completed visit, which was divided to facilitate pill count adherence measures. Participants received $10 for completing study interviews and $5 for bringing varenicline for pill counts.

Study Measures

Feasibility—We examined enrollment and recruitment rates, participant retention, medication adherence and varenicline tolerability. We determined enrollment rate by the

proportion of screened participants eligible and willing to participate, and retention as the proportion of completed study visits. We measured adherence by pill count at each 2-week visit during the SCC+VT phase, calculated as the proportion of pills taken as prescribed. Finally, we based medication tolerability on adverse effects and incident psychiatric symptoms reported by participants while in the SCC+VT phase. To assess psychiatric symptoms, we used the Mini International Neuropsychiatric Interview (M.I.N.I.) and the Columbia Suicide Severity Rating Scale (Posner et al. 2007; Sheehan et al. 1998).

Varenicline Effectiveness

Cannabis Use: Baseline cannabis measures included: cannabis craving, measured by the Marijuana Craving Questionnaire (Heishman, Singleton & Liguori 2001); cannabis withdrawal, measured by the Marijuana Withdrawal Checklist (Budney, Novy & Hughes 1999); past 90-day cannabis use, using the timeline follow-back (TLFB) method; interest, perceived importance of and confidence in quitting cannabis; and cannabis abuse and dependence, measured using the M.I.N.I. Cannabis outcome measures were assessed at weeks 2, 4, 6, and 8, and included: craving; withdrawal; past two-week cannabis use quantity and frequency; and abstinence, defined as past two-week self-reported abstinence using TLFB and negative cannabinoid urine toxicology results (via qualitative tests, using a <50 nanograms per milliliter cut-off). Urine samples were analyzed at a commercial laboratory.

Tobacco Use: At baseline, we evaluated cigarettes smoked/day, using a 90-day TLFB calendar, and confidence in and importance of quitting tobacco. At each follow up visit, we assessed cigarettes smoked/day and seven-day point prevalence tobacco abstinence using the TLFB method. We biochemically verified tobacco abstinence with an expired carbon monoxide of <8 p.p.m. (Bedfont Smokerlyzer).

Results

Enrollment and Participant Characteristics

Of 193 persons screened, 186 were ineligible (Figure 1). Cannabis use was infrequent: 129 individuals reported no cannabis use in the prior 30 days, and only 17 met criteria for frequent use (≥5 days per week). A total of 7 participants met inclusion criteria and enrolled in the study.

Enrolled participants (Table 1) had a mean age of 47 years, were mostly male (n=6), and mostly identified as Hispanic (n=4) or Black (n=2). Eligible participants were comparable to ineligible participants with respect to age and race/ethnicity. Four participants reported a pain condition and three reported HIV infection. All seven participants met criteria for cannabis abuse, cocaine dependence, and opioid dependence. Participants were stable in MAT; all had been in MAT for at least three months (with a median of three years), and none had undergone a change in methadone or buprenorphine dose in the two weeks prior to study initiation. Our sample included one former tobacco smoker (with self-reported abstinence for 20 years) and six current tobacco smokers (median 13 cigarettes per day). Using a 10-point scale, mean importance of quitting cannabis was rated as six, and mean importance of

quitting tobacco was rated as ten. Participants completed a median of three counseling visits over the eight-week study period; counseling visits for two participants addressed cannabis use but no visits included documented tobacco use counseling.

Retention, adherence and tolerability

All 7 participants completed 100% of study visits. Because of the crossover design, all participants contributed outcome data during both phases. Overall medication adherence was 62% during the SCC+VT phase. Excluding one participant who did not take any varenicline for the duration of the study, varenicline adherence was 73%. In a deviation from the trial design, one participant completed SCC alone for two weeks, then SCC+VT for four weeks, followed by SCC alone for two weeks. That participant, and three randomized to SCC+VT first followed by SCC, all reported continued use of varenicline during the SCC phase.

Varenicline was well-tolerated; the most frequently reported adverse effects included upset stomach (n=5) and insomnia (n=4). No participants reported stopping varenicline because of adverse effects. One participant met criteria for incident major depressive episode while in the SCC+VT phase. No participants reported suicidal ideation over the study period.

Effectiveness

For all participants, we describe cannabis craving, withdrawal, and use, and tobacco use, at baseline, and compare outcomes at week four of SCC versus week four of SCC+VT (Table 2). Our small sample size precludes statistical testing of outcomes.

Mean cannabis craving and withdrawal scores were lower at week four of both the SCC and SCC+VT treatment phases than at baseline. Cannabis use was reported on 77% of days at baseline, compared to 82% at week four of the SCC phase and 60% at week four of the SCC +VT phase. Mean frequency of cannabis use at baseline was 4 times per day, compared to 3 times per day in the SCC phase and 2 times per day in the SCC+VT phase. Despite the apparent effect of varenicline on decreasing cannabis use, cannabis abstinence was infrequent. One participant achieved cannabis abstinence during both phases. Outcomes were similar when those four participants who took varenicline during the SCC phase were censored (data not shown).

Regarding tobacco use outcomes, participants smoked fewer cigarettes/day in both the SCC (5) and SCC+VT (5) phases than at baseline (13). However, the number of participants who achieved tobacco abstinence did not change during the trial.

Discussion

We found that it was challenging to recruit tobacco-dependent participants with frequent cannabis use from a substance abuse treatment program, but that 100% of enrolled participants were successfully retained. Varenicline treatment was well-tolerated, and overall medication adherence was high. Cannabis craving was lower during the trial than at baseline, and both quantity and frequency of cannabis use was lower at week four during the varenicline (SCC+VT) phase of the trial than at baseline. Similarly, number of cigarettes

smoked/day was lower in both phases than at baseline. However, there was little change in cannabis or tobacco abstinence over the study period.

We anticipated that recruitment at an outpatient opioid treatment program would yield a high prevalence of persons with frequent cannabis use. However, despite the high prevalence of other drug use, the low prevalence of frequent cannabis use made enrollment challenging. Given the high rates of recent cannabis and tobacco use previously described among methadone patients (Moitra, Anderson & Stein 2013; Richter et al. 2001), this challenge was unanticipated. In our clinical site, many patients are referred for treatment of cannabis use disorder by the child welfare or criminal justice systems, creating potent external contingencies for abstinence that may have reduced the pool of eligible participants. This suggests that future studies may benefit from community-based recruitment. By contrast, our retention rate among enrolled participants was higher than that of previous studies (Hill et al. 2013; Newcombe et al. 2015), and may have been enhanced by recruitment at an opioid treatment program. Coupled with the high medication adherence we observed, our retention and tolerability findings are reassuring and remove safety barriers to further evaluation of varenicline effects among patients with CUD.

Regarding cannabis use outcomes, participants in the varenicline phase had lower cannabis craving and withdrawal symptoms than they reported at baseline, and a lower number of cannabis use days compared to both baseline and to the non-varenicline phase of the trial. Effects observed during the non-varenicline phase may reflect: (1) effects of data collection on reported craving and withdrawal symptoms, or (2) continued varenicline effects, given some participants' continued use of varenicline during the SCC phase. Overall, these findings confirm and extend the findings of reduced cannabis enjoyment and use described in a previous case series of varenicline (Newcombe et al. 2015). Despite this, varenicline was not associated with complete cannabis abstinence. While it is possible that varenicline is ineffective, other factors may have contributed to lack of cannabis abstinence. First, participants were only moderately interested in cannabis cessation. Second, psychosocial interventions were minimal, and relied on outpatient standard clinical care which may not have addressed marijuana use. Finally, the short varenicline treatment duration may have been insufficient to promote abstinence. Our findings and others among concurrent cannabis and tobacco users (Newcombe et al. 2015) suggest that varenicline may need to be targeted to persons motivated to quit, coupled with cannabis use counseling or need a longer treatment duration to be most effective.

Regarding tobacco use outcomes, participants in the varenicline phase reported smoking fewer cigarettes/day compared to baseline. One participant was a former smoker at the beginning of the study, and one participant achieved tobacco abstinence during the trial. Though participants reported fewer cigarettes per day, CO was not reduced in either the SCC or SCC+VT phase. This may reflect inaccurate self-report of cigarettes smoked per day, or, alternately, proximity of cigarette smoking prior to research assessments. The limited tobacco abstinence we observed is consistent with data showing low rates of early tobacco cessation among smokers with substance use disorders (de Dios et al. 2014; Nahvi et al. 2014), and may be partially attributable to the short varenicline treatment course. Further, these tobacco abstinence rates are consistent with the modest cessation observed among

smokers with opioid and other substance use disorders treated with varenicline (Nahvi et al. 2014; Rohsenow et al. 2017; Stein et al. 2013). Finally, counseling on smoking cessation was limited. We hypothesized that tobacco cessation might mediate varenicline effects on cannabis use, but reductions in the frequency and quantity of marijuana use occurred despite the limited tobacco cessation observed.

This study has limitations. Our small sample size, though consistent with other published studies of interventions to address co-occurring cannabis and tobacco use, precludes statistical testing of outcomes, and limits generalizability. Not all participants met criteria for cannabis dependence, though all reported frequent cannabis use. Participants and research staff were not blinded to treatment condition, and some participants who were randomized to SCC+VT first continued taking varenicline during the SCC phase. Counseling content was not controlled or standardized. There are additional issues that may have attenuated the potential therapeutic effects of varenicline: participants were not required to want to stop cannabis or tobacco; all participants were opioid- and cocaine-dependent; and the duration of varenicline treatment was brief. Though it did facilitate retention, our recruitment of a convenience sample of patients at an opioid treatment program may have impacted results and limited generalizability.

Varenicline was well-tolerated, did not increase the risk of incident mental illness, and lowered the quantity and frequency of cannabis use relative to baseline levels and standard clinical care. Participants in both treatment phases smoked fewer cigarettes/day than at baseline. Overall, augmenting standard clinical care with varenicline is feasible, could be of benefit for concurrent cannabis and tobacco smokers, and warrants investigation in a controlled clinical trial.

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References

Agrawal A, Lynskey M. Tobacco and cannabis co-occurrence: does route of administration matter? Drug and Alcohol Dependence. 2009; 99:240–247. [PubMed: 18926646]

Agrawal A, Madden P, Bucholz K, Heath A, Lynskey M. Transitions to regular smoking and to nicotine dependence in women using cannabis. Drug and Alcohol Dependence. 2008; 95:107–114. [PubMed: 18325694]

Anthenelli RM, Benowitz NL, West R, St Aubin L, McRae T, Lawrence D, Ascher J, Russ C, Krishen A, Evins AE. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. Lancet. 2016; 387(10037):2507–20. [PubMed: 27116918]

Becker J, Haug S, Kraemer T, Schaub MP. Feasibility of a group cessation program for co-smokers of cannabis and tobacco. Drug Alcohol Rev. 2015; 34(4):418–26. [PubMed: 25676414]

Belanger R, Akre C, Kuntsche E, Gmel G, Suris JC. Adding tobacco to cannabis-its frequency and likely implications. Nicotine Tob Res. 2011; 13:746–750. [PubMed: 21454910]

Budney A, Roffman R, Stephens R, Walker D. Marijuana dependence and its treatment. Addict Sci Clin Pract. 2007; 4:4–16. [PubMed: 18292704]

Budney AJ, Novy PL, Hughes JR. Marijuana withdrawal among adults seeking treatment for marijuana dependence. Addiction. 1999; 94(9):1311–1322. [PubMed: 10615717]

Center for Behavioral Health Statistics and Quality. HHS Publication No. SMA 154927, NSDUH Series H50. 2015. Behavioral health trends in the United States: Results from the 2014 National Survey on Drug Use and Health.

de Dios MA, Anderson BJ, Caviness CM, Stein MD. Early Quit Days Among Methadone-Maintained Smokers in a Smoking Cessation Trial. Nicotine & Tobacco Research. 2014; 16(11):1463–9. [PubMed: 24951495]

de Dios MA, Vaughan EL, Stanton CA, Niaura R. Adolescent tobacco use and substance abuse treatment outcomes. Journal of Substance Abuse Treatment. 2009; 37(1):17–24. [PubMed: 19004603]

Gonzales D, Rennard SI, Nides M, Oncken C, Azoulay S, Billing CB, Watsky EJ, Gong J, Williams KE, Reeves KR. for the Varenicline Phase 3 Study G. Varenicline, an alpha4beta2 Nicotinic Acetylcholine Receptor Partial Agonist, vs Sustained-Release Bupropion and Placebo for Smoking Cessation: A Randomized Controlled Trial. JAMA. 2006; 296(1):47–55. [PubMed: 16820546]

Haney M, Bedi G, Cooper ZD, Glass A, Vosburg SK, Comer SD, Foltin RW. Predictors of Marijuana Relapse in the Human Laboratory: Robust Impact of Tobacco Cigarette Smoking Status. Biological Psychiatry. 2013; 73(3):242–248. [PubMed: 22939992]

Heishman SJ, Singleton EG, Liguori A. Marijuana Craving Questionnaire: development and initial validation of a self-report instrument. Addiction. 2001; 96(7):1023–1034. [PubMed: 11440613]

Hill KP, Toto LH, Lukas SE, Weiss RD, Trksak GH, Rodolico JM, Greenfield SF. Cognitive Behavioral Therapy and the Nicotine Transdermal Patch for Dual Nicotine and Cannabis Dependence: A Pilot Study. The American Journal on Addictions. 2013; 22(3):233–238. [PubMed: 23617864]

Jorenby D, Hays JT, Rigotti NA, Azoulay S, Watsky EJ, Williams KE, Billing CB, Gong J, Reeves KR. for the Varenicline Phase 3 Study G. Efficacy of Varenicline, an alpha4beta2 Nicotinic Acetylcholine Receptor Partial Agonist, vs Placebo or Sustained-Release Bupropion for Smoking Cessation: A Randomized Controlled Trial. JAMA. 2006; 296(1):56–63. [PubMed: 16820547]

Lee DC, Budney AJ, Brunette MF, Hughes JR, Etter JF, Stanger C. Treatment models for targeting tobacco use during treatment for cannabis use disorder: case series. Addict Behav. 2014; 39(8): 1224–30. [PubMed: 24813547]

Marshall K, Gowing L, Ali R, Le Foll B. Pharmacotherapies for cannabis dependence. Cochrane Database Syst Rev. 2014; 12:CD008940.

Mihalak KB, Carroll FI, Luetje CW. Varenicline Is a Partial Agonist at α4β2 and a Full Agonist at α7 Neuronal Nicotinic Receptors. Molecular Pharmacology. 2006; 70(3):801–805. [PubMed: 16766716]

Mitchell JM, Teague CH, Kayser AS, Bartlett SE, Fields HL. Varenicline decreases alcohol consumption in heavy-drinking smokers. Psychopharmacology (Berl). 2012; 223(3):299–306. [PubMed: 22547331]

Moitra E, Anderson BJ, Stein MD. Perceived stress and substance use in methadone-maintained smokers. Drug Alcohol Depend. 2013; 133(2):785–8. [PubMed: 24011853]

Moore B, Budney A. Tobacco smoking in marijuana-dependent outpatients. Journal of Substance Abuse. 2001; 13:583–596. [PubMed: 11775084]

Nahvi S, Ning Y, Segal KS, Richter KP, Arnsten JH. Varenicline efficacy and safety among methadone maintained smokers: a randomized placebo-controlled trial. Addiction. 2014; 109(9):1554–1563. [PubMed: 24862167]

Newcombe DA, Walker N, Sheridan J, Galea S. The Effect of Varenicline Administration on Cannabis and Tobacco Use in Cannabis and Nicotine Dependent Individuals - A Case Series. Journal of Addiction Research & Therapy. 2015; 6(2):1–5. [PubMed: 26925299]

Patton G, Coffey C, Carlin J, Sawyer S, Lynskey M. Reverse gateways? Frequent cannabis use as a predictor of tobacco initiation and nicotine dependence. Addiction. 2005; 100:1518–1525. [PubMed: 16185213]

Penetar DM, Kouri EM, Gross MM, McCarthy EM, Rhee CK, Peters EN, Lukas SE. Transdermal nicotine alters some of marihuana's effects in male and female volunteers. Drug and Alcohol Dependence. 2005; 79(2):211–223. [PubMed: 16002030]

Plebani JG. Results of an initial clinical trial of varenicline for the treatment of cocaine dependence. Drug and Alcohol Dependence. 2012; 121(1–2):163–166. [PubMed: 21925806]

Plebani JG, Lynch KG, Rennert L, Pettinati HM, O'Brien CP, Kampman KM. Results from a pilot clinical trial of varenicline for the treatment of alcohol dependence. Drug and Alcohol Dependence. 2013; 133(2):754–758. [PubMed: 23916324]

Posner K, Oquendo MA, Gould M, Stanley B, Davies M. Columbia Classification Algorithm of Suicide Assessment (C-CASA): Classification of Suicidal Events in the FDA's Pediatric Suicidal Risk Analysis of Antidepressants. Am J Psychiatry. 2007; 164(7):1035–1043. [PubMed: 17606655]

Rabin RA, George TP. A review of co-morbid tobacco and cannabis use disorders: possible mechanisms to explain high rates of co-use. Am J Addict. 2015; 24(2):105–16. [PubMed: 25662704]

Ramo D, Prochaska J. Prevalence and co-use of marijuana among young adult cigarette smokers: An anonymous online national survey. Addiction Science & Clinical Practice. 2012; 7(1):5. [PubMed: 23186143]

Richter KP, Gibson CA, Ahluwalia JS, Schmelzle KH. Tobacco use and quit attempts among methadone maintenance clients. American Journal of Public Health. 2001; 91(2):296–299. [PubMed: 11211643]

Rohsenow DJ, Tidey JW, Martin RA, Colby SM, Swift RM, Leggio L, Monti PM. Varenicline versus Nicotine Patch with Brief Advice for Smokers with Substance Use Disorders with or without Depression: Effects on Smoking, Substance Use and Depressive Symptoms. Addiction. 2017; 112(10):1808–1820. [PubMed: 28498504]

Schauer GL, Berg CJ, Kegler MC, Donovan DM, Windle M. Differences in Tobacco Product Use Among Past Month Adult Marijuana Users and Nonusers: Findings From the 2003–2012 National Survey on Drug Use and Health. Nicotine Tob Res. 2016; 18(3):281–8. [PubMed: 26009578]

Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, Hergueta T, Baker R, Dunbar GC. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. Journal of Clinical Psychiatry. 1998; 59(Suppl 20):22–33. quiz 34–57.

Solinas M, Scherma M, Fattore L, Stroik J, Wertheim C, Tanda G, Fratta W, Goldberg SR. Nicotinic alpha 7 receptors as a new target for treatment of cannabis abuse. J Neurosci. 2007; 27(21):5615–20. [PubMed: 17522306]

Stein MD, Caviness CM, Kurth ME, Audet D, Olson J, Anderson BJ. Varenicline for smoking cessation among methadone-maintained smokers: A randomized clinical trial. Drug and Alcohol Dependence. 2013; 133(2):486–493. [PubMed: 23953658]

Timberlake DS, Haberstick BC, Hopfer CJ, Bricker J, Sakai JT, Lessem JM, Hewitt JK. Progression from marijuana use to daily smoking and nicotine dependence in a national sample of U.S. adolescents. Drug Alcohol Depend. 2007; 88(2–3):272–81. [PubMed: 17174040]

Volkow ND, Baler RD, Compton WM, Weiss SR. Adverse health effects of marijuana use. N Engl J Med. 2014; 370(23):2219–27. [PubMed: 24897085]

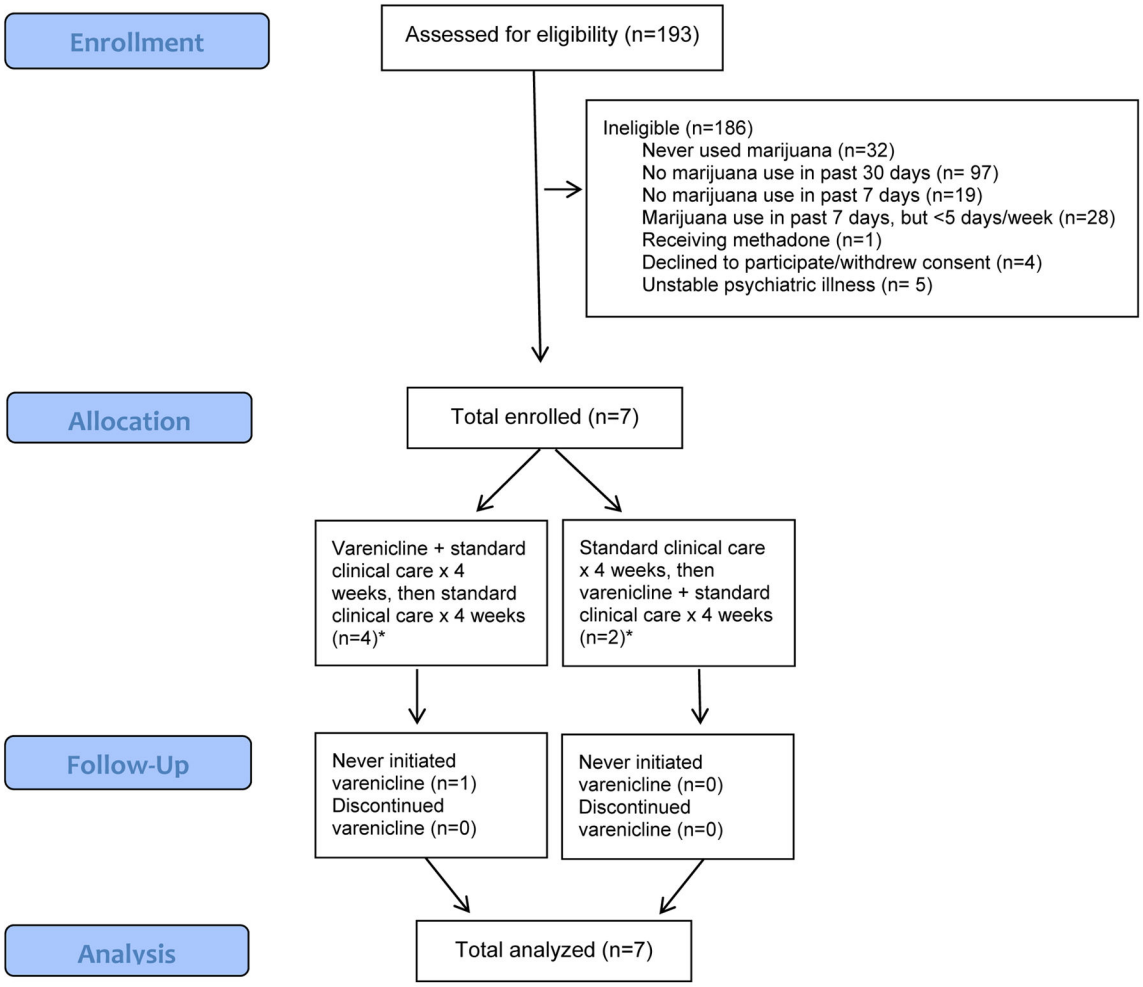

Figure 1.
Flow chart of participant screening, enrollment and follow up

Table 1

Baseline characteristics of enrolled participants

	Enrolled (n=7)
Sociodemographic characteristics	
Age, mean (SD)	49 (10)
Male sex, n	6
Race/ethnicity, n	
Hispanic	4
Black	2
Non-Hispanic White	1
Substance use characteristics	
Interest in quitting cannabis median [interquartile range (IQR)] *	5 (2,10)
Importance of quitting cannabis, median (IQR) †	6 (1,10)
Confidence in quitting cannabis, median (IQR) †	10 (5,10)
Cannabis abuse, n ‡	7
Cannabis dependence, n ‡	4
Baseline positive toxicology test for opioids, n	5
Opioid dependence, on opioid agonist treatment, n	7
Methadone treatment, n	6
Buprenorphine treatment, n	1
Baseline positive toxicology test for cocaine, n	6
Cocaine dependence, n ‡	7
Hazardous alcohol use, n §	0
Tobacco use characteristics	
Current tobacco use, n	6
Cigarettes/day, mean [standard deviation (SD)]	13 (9)
Importance of quitting cigarette smoking, median (IQR) †	10 (6,10)
Confidence in quitting cigarette smoking, median (IQR) †	10 (1,10)
Carbon monoxide, median (IQR)	9 (4,12)
Medical and psychiatric comorbidity, n	
Diabetes	2
Pain Condition	4
HIV/AIDS	3
Current dronabinol treatment	2
Lifetime major depressive episode	1
Lifetime hypomanic episode	1
Lifetime psychotic disorder	2

[*] Assessed using Ladder of Change, with 5 indicating interest in quitting without specific plans to quit

[†] Assessed using a 10-point Likert scale, with higher scores indicating greater importance/confidence

[‡] Assessed using the Mini International Neuropsychiatric Interview (M.I.N.I.)

[§] Assessed using the Alcohol Use Disorders Identification Test

Table 2

Cannabis and Tobacco Outcomes

	Baseline (n=7)	SCC Week 4 (n=7)	SCC + VT Week 4 (n=7)
Cannabis use outcomes			
Marijuana craving, mean (SD) *	43 (20)	34 (20)	35 (23)
Marijuana withdrawal, mean (SD) †	10 (11)	4 (6)	4 (5)
Marijuana percent days of use ‡§	77	82	60
Frequency of marijuana use per day, mean (SD) ‡	4 (0.5)	3 (0.4)	2 (0.3)
Toxicology-verified cannabis abstinence, n //	1	1	1
Tobacco use outcomes			
Cigarettes per day, mean (SD) ‡	13 (9)	5 (7)	5 (7)
Carbon monoxide-verified tobacco abstinence ¶	1	2	1
Expired carbon monoxide, mean (SD) **	9 (6)	13 (9)	14 (11)

* Assessed using the Marijuana Craving Questionnaire, with total scores ranging from 12–84, and higher scores indicating higher craving

† Assessed using the Marijuana Withdrawal Checklist, with scores ranging from 0–48

‡ Assessed using Timeline follow back (TLFB)

§ Assessed over the prior 90 days (baseline) and prior 14 days (SCC+VT week four, and SCC week four)

// Assessed by both self-reported two-week abstinence by TLFB and urine toxicology tetrahydrocannabinol level < 50 ng/ml

¶ Assessed using TLFB and expired carbon monoxide < 8 p.p.m

** Assessed via Bedfont Smokerlyzer