Study Title: Mobile Contingency Management for Concurrent Abstinence from Cannabis and Cigarette Smoking: A Pilot Study

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Background

Cannabis is the most widely used illicit drug in the United States, with 19.8 million current users (Substance Abuse Mental Health Services Administration, 2014). Population-based data indicate that almost all cannabis users (90%) have a lifetime history of tobacco smoking (Agrawal, Budney, & Lynskey, 2012), and the majority (74%) currently smoke tobacco (Richter et al., 2004; Richter, Ahulwalia, Mosier, Nazir, & Ahulwalia, 2002). While cannabis use alone is associated with significant adverse health effects (Hall & Degenhardt, 2009; Hall, Degenhardt, & Lynskey, 2001), tobacco smoking is the number one preventable cause of illness and death in the U.S. (Centers for Disease Control and Prevention, 2010). This is especially true for illicit drug users, for whom the tobacco-related mortality rate is twice that of the general population (Hurt et al., 1996). Among cannabis users, smoking tobacco is associated with increased frequency of cannabis use (Richter et al., 2004), increased morbidity (Peters, Budney, & Carroll, 2012; Taylor et al., 2002), and poorer cannabis cessation outcomes (de Dios, Vaughan, Stanton, & Niaura, 2009; Gray et al., 2011). Treatment among dual users is complicated, as the cessation of one substance is often associated with increased utilization of the other (Akre, Michaud, Berchtold, & Suris, 2010; Copersino et al., 2006; Allsop et al., 2014). There is a surprising lack of research, however, focused on addressing cessation of both substances simultaneously (Agrawal et al., 2012; Peters et al., 2012; Becker, Haug, Sullivan, & Schaub, 2014). Few preliminary studies have targeted both behaviors concurrently. Preliminary studies include two small open trials (Hill et al., 2013) and a web-based intervention aimed at increased readiness to quit both substances (Becker et al., 2014). Hill and colleagues (2013) enrolled 12 adults with cannabis use disorder (CUD) and nicotine dependence in an open trial that included 10 treatment sessions. Forty-two percent of participants dropped out before the end of treatment; of those who remained, tobacco smoking was reduced (number of daily cigarettes smoked); however, no change was observed in cannabis use. Becker and colleagues (2014) demonstrated that brief web-based interventions (psychoeducation, personalized normative feedback; motivational interviewing) can increase readiness to quit tobacco and cannabis, suggesting that dual users are interested in quitting both substances, but effective treatments are not available. Thus, more intensive and innovative interventions are needed to reduce dual use of cannabis and tobacco.

Contingency management (CM) is an intensive behavioral therapy that provides positive reinforcers (e.g., vouchers, money) to individuals misusing substances, contingent upon bioverification of abstinence from drug use. The efficacy of CM has been established for a broad range of problematic behaviors. In particular, CM has well-established efficacy for smoking cessation (Dallery, Raiff, & Grabinksi, 2013), and several trials also support the efficacy of CM in treating CUD (Higgins & Petry, 1999). Further, CM has demonstrated effect sizes in excess of other behavioral treatments in several substance use trials (Dutra et al., 2008). In a small open trial (n=6) of computer-assisted cognitive behavioral treatment (CBT) for CUD paired with CM to reduce cannabis use, 5 of 6 participants achieved abstinence from marijuana. Although all 6 participants attempted to reduce tobacco use during treatment, none successfully quit smoking tobacco (Lee et al., 2014). No studies to date have targeted cannabis and tobacco smoking simultaneously with CM.

While the implementation of CM approaches is gaining acceptance (Pilling, Strang, & Gerada, 2007; Petry, DePhillips, Rash, Drapkin, & McKay, 2014), widespread implementation of CM has largely been

limited to inpatient and day treatment programs because of the burdensome need to verify abstinence multiple times daily. CM approaches for smoking cessation typically monitor patients 2-4 times per day with a clinic-based carbon monoxide (CO) monitor. As a result of relying on clinic-based monitoring, only a small fraction of those who could benefit from CM for substance use receive this highly effective intervention. We have developed a smartphone application that allows patients to video-record themselves several times daily while using a small CO monitor and to transmit the data to a secure server. This mobile contingency management (mCM) innovation has made the use of CM for reducing smoking portable and feasible. We expect that mobile technology can be used to implement CM to reduce cannabis use as well. This will provide a cost-effective way to implement and improve reach of intensive CM treatment.

While CM alone may be insufficient for increasing long-term abstinence, there is little debate that CM helps retain difficult-to-treat populations in treatment, and is effective in enabling them to achieve initial abstinence. We expect that pairing CM with another evidence-based treatment that includes relapse prevention skills will maximize long-term abstinence. With this model in mind, the ideal strategy is to integrate CM with evidence-based CBT for substance misuse relapse prevention. There are relatively few studies aimed at evaluating multi-component substance use interventions that integrate CM with evidence-based CBT. CBT includes teaching coping skills, relapse prevention training and home practice that encourage generalization of skills to the naturalistic environment, contributing to the durability of treatment effects on substance use outcomes (Carroll et al., 2000; Carroll et al., 1994; O'Malley et al., 1996).

We have previously demonstrated that patients will video themselves multiple times daily using a CO monitor in order to verify tobacco smoking abstinence; however, verification of cannabis abstinence for CM is more complex. Like tobacco, smoking cannabis is associated with significant elevations in CO levels measured in both blood carboxyhemoglobin (Tashkin et al., 1991; Wu, Taskin, Dhajed, & Rose, 1988) and *via* expired air CO (Azorlosa, Greenwald, & Stitzer, 1995; Chait, Russ, & Griffiths, 1985; Cooper & Haney, 2009). Measurement of expired CO can be used to provide a quantitative index of inhaled cannabis smoke similar to tobacco smoke (Chait, Russ, & Griffiths, 1985). The use of expired CO alone to detect use of cannabis is limited, however, as expired CO is not elevated if the drug is ingested. Similarly, the recent development of cannabis vaporization systems (i.e., vaping) has facilitated delivery of the drug without associated increases in expired CO (Abrams et al., 2007). The standard in the field for detection of cannabis use has been urinalysis examining excretion of the cannabis metabolite 11-nor-Δ9-tetrahydrocannabinolic acid (THC-COOH) *via* immunoassay completed in a clinic setting (Budney et al., 2015). In our view, there are several drawbacks to this approach for CM treatment. While multiple factors affect detection times for cannabis use *via* urine screening (e.g., frequency of use, dosage, individual metabolism), THC-COOH levels are typically significantly elevated in regular cannabis users (e.g., background levels above 1,000 ng/ml). As a result, a washout period (1-2 weeks or longer) is needed between cessation of use and submission of negative urine samples to verify recent abstinence. This washout period delays potential reinforcement of abstinence using CM at a critical juncture (i.e., time surrounding the quit date and early abstinence). To date, implementation of CM for CUD has been discouraged in large health care settings like VHA because this lag-time between cessation of use and submission of negative samples makes CM more complicated to administer (Petry et al., 2014). Following a washout period, the detection window for

single use of cannabis is typically 3-4 days (based on a 50 ng/mL cutoff level) or up to 7 days (based on a 20 ng/mL cutoff for cannabinoids) using urinalysis (Huestis, Mitchell, & Cone, 1996). Thus most previous CM approaches for CUD require clinic-based monitoring at least twice a week to verify abstinence. Clinic-based urine testing is burdensome, as participants must travel to attend clinic sessions.

In contrast to traditional urine- or blood-based drug testing approaches, saliva (oral fluid, or OF) testing is a relatively new form of drug testing. OF testing is non-invasive and has the benefits of directly observable sample collection methods (reducing potential for sample adulteration), lower biohazard risk during collection, ease of multiple sample collections, and stronger correlation with blood than urine concentrations (Lee & Huestis, 2014). In contrast to urinalysis, which detects cannabis metabolites, the majority of current OF devices directly measure Δ9-tetrahydrocannabinol (THC). The reliability and validity of OF drug testing has improved significantly over the past decade (Lee & Huestis, 2014). There is currently an FDA-approved saliva testing method (Oratect® AOT-06 Oral Fluid Drug Screen Device) that can be used to detect THC use (40 ng/mL) in the past 6-12 hours. To date, no studies have examined the feasibility of using OF testing methods for CM to treat CUD.

The use of OF testing methods would eliminate the need for a long washout period before abstinence could be reinforced *via* CM. We expect that the combination of CO monitoring and saliva testing can significantly increase the feasibility of CM for CUD. We expect that verification of abstinence without the necessity of clinic visits is possible using mobile technology, expired CO and saliva testing. We will examine the feasibility of using both random saliva screens (assessing cannabis use in last 6-12 hours) administered at high risk use times and CO (assessing smoked cannabis use in the last 3 hours).

Our long-term goal is the reduction of morbidity associated with cannabis and smoking through the implementation of cost-effective, evidence-based interventions that maximize recovery. The purpose of this **pilot** project is to evaluate feasibility of treatment, recruitment, and abstinence bioverification methods for a combined cannabis and tobacco smoking tele-health mCM intervention that will effectively treat both disorders. Results from this pilot project will be used in support of an NIH grant to further develop the treatment and evaluate its feasibility and acceptability on a larger scale.

Preliminary Data

We developed and tested the mCM smoking app in combination with telephone CBT and used them in an initial validation study of 22 smokers with posttraumatic stress disorder (PTSD; Hertzberg et al., 2013). In this study, participants were randomized to 4 weeks of mCM plus CBT or to CBT plus yoked non-contingent reinforcement condition (i.e., compensation was based on earnings of participant matched from the other condition). Participant adherence to the protocol of submitting two on-time valid video readings daily was excellent (92%). Three-month self-reported 7-day point-prevalence quit rates were 18% in the yoked group and 50% in the mCM group. These preliminary results suggest that the tele-health mCM intervention is feasible and may lead to a longer duration of abstinence when CBT complements mCM in a multi-component intervention.

To further evaluate the tele-health mCM intervention, we enrolled 20 homeless smokers, and they all received the tele-health mCM intervention with CBT and standard smoking pharmacotherapy (Carpenter et al., 2015; Hertzberg et al., 2013). The majority of the sample (70%) had a history of CUD. Adherence to the timing and procedures for uploading videos with the mCM app was excellent during the treatment phase (93%). After 4 weeks of the tele-health mCM intervention, bioverified 7-day point-prevalence abstinence was 50%. Despite removing monetary compensation for abstinence at 4 weeks post-quit, bioverified abstinence in the tele-health mCM group was 55% at a 3-month follow-up assessment, and 45% at a 6-month follow-up assessment (Carpenter et al., 2015).

Methods

Participants

Up to 10 participants with CUD and smoking will be enrolled, with a goal of 5 participants completing the intervention.

Participants will be eligible for inclusion in the study if they meet the following criteria:

- report 40 or more days of cannabis use in the past 90 day;
- have smoked at least seven cigarettes in the past seven days;
- have been smoking for at least the past year;
- can speak and write fluent conversational English;
- are between 18 and 70 years of age; and
- are willing to make an attempt to quit both cannabis and tobacco smoking.

Participants will be excluded for the following:

- expected to have unstable medication regimen during the study;
- currently receiving non-study behavioral treatment for cannabis use disorder or smoking;
- myocardial infarction in past six months;
- contraindication to NRT with no medical clearance;
- use of other forms of nicotine such as cigars, pipes, or chewing tobacco with unwillingness to stop use of these forms;
- current pregnancy;
- primary psychotic disorder or current manic episode;
- substance use disorder (other than mild alcohol use disorder, cannabis use disorder or nicotine use disorder) within the preceding three months; or
- current imprisonment or psychiatric hospitalization.

Recruitment

Participants will be recruited from primary care and substance use clinics at Duke University Medical Center (DUMC). Flyers and brochures will be placed in DUMC clinic areas, and may also be placed in community settings such as local restaurants and grocery stores. We will also advertise in local newspapers and online classified services such as www.craigslist.com. With permission from area

colleges and universities (and their respective IRBs where required), we will post flyers and brochures on area campuses. We will contact administrators and/or clinicians at local area community health centers, including Lincoln Community Health Center. Upon approval by the Durham Veterans Affairs (VA) Medical Center IRB, we will post flyers and brochures at that facility and its community-based outpatient clinics. Any flyer posted at the VA-owned facilities will include the following statement: "This is not VA research, will not be conducted by VA, has not been reviewed by VA's Institutional Review Board, and is not endorsed by VA. VA is not responsible for any costs incurred by a Veteran if the Veteran enters the study as a research subject. The announcement is being provided for information only."

Participants who find the study on clinicaltrials.gov and emails study staff will be sent an email to contact the study coordinator by telephone.

Any participant who contacts by telephone the study coordinator or other study staff regarding the study will be provided more information, and will be interviewed using an IRB-approved telephone screening. We will retain the deidentified telephone screening information for all callers so that we can analyze data regarding telephone screen-outs in order to determine recruitment and inclusion/exclusion feasibility. Participants eligible at the phone screen will be scheduled for a screening visit. An email address will be collected from the participant to send directions and a parking pass for the screening location and send reminders of upcoming study appointments. If a participant does not have access to email or a printer, study staff will collect a mailing address to send directions and a parking pass via FedEx.

Prior to study entry, potential participants will complete a screening visit, including informed consent, diagnostic interview, a saliva sample to assess cannabis and a breath sample to assess CO level, symptom self-report measures, computerized impulsivity tasks, cannabis and smoking history, and sociodemographic data. Urine samples will also be used to screen for other illicit drug use. Because the study drugs are each Category C drugs, urine pregnancy tests will also be completed for women of childbearing potential. We have developed a short interview for female participants; this interview will help us determine which female participants must have a urine pregnancy test, and when the test should be done. Female participants of childbearing potential who are not pregnant must agree to use appropriate contraception during the course of the study, and to notify study staff if they become pregnant during the study. The participants' health information will be evaluated by the study physician, Scott Moore, M.D., Ph.D., who will provide medical clearance to participate in the trial and use smoking cessation pharmacotherapy. Dr. Moore is an experienced psychiatrist and substance abuse researcher with a strong working relationship with the study team.

Procedures

All participants enrolled in the pilot project will receive TELE-HEALTH MOBILE CONTINGENCY MANAGEMENT (mCM) INTERVENTION, a proactive tele-health intervention that combines evidence-based telephone CBT for cannabis and smoking cessation, a tele-medicine clinic for access to nicotine replacement therapy (NRT) and intensive CM therapy administered *via* a smart phone-based

application (mCM) targeting BOTH smoking and cannabis use. Treatment components are separately described herein. Table 1 provides a summary of study visits, procedures, and compensation.

Table 1. Study Procedures

Session	Tasks	Time	Payment
1 (lab)	• Consent • Screening (clinical interview, questionnaires, impulsivity tasks) • Urine sample, breath sample taken • Counseling session 1 • mCM equipment training	30 min 3 ½ hours	$100
2 (phone)	• Counseling session 2	30 mins.	None
3 (phone)	• Counseling session 3 • Begin practice mCM for 1 week • Begin bupropion if using	30 mins.	Up to $49 for monitoring between 3 & 4
4 (phone)	• Quit day • Counseling session 4 • Begin abstinence mCM • Begin NRT	30 mins.	Up to $402.50 for 2 weeks monitoring between 4 & 5
5 (phone; 2 wks post session 4)	• Counseling session 5 • Continue abstinence mCM • Reduce NRT to 14 mg • Continue use of “rescue” NRT PRN	30 mins.	Up to $892.50 for 2 weeks monitoring between 5 & 6
6 (phone; 2 wks post session 5)	• Quick phone check-in • Continue mCM wash-out period • Reduce NRT to 7 mg • Continue use of “rescue” NRT PRN	10 min	Up to $98 for monitoring between 6 & 7
7 (lab; 2 wks post session 6)	• Feasibility interview,questionnaires, impulsivity tasks • Saliva sample, CO reading, and urine drug screen Prompt to return equipment • Cease NRT	1 hour	$35 for returned equipment, $100 for session
8 (lab; 3 month follow-up)	• Questionnaires, impulsivity tasks • Saliva samples, CO readings, and urine drug screens	30 min	$100
9 (lab; 6 month follow-up)	• Questionnaires, impulsivity tasks • Saliva samples, CO readings, and urine drug screens • Cease bupropion	30 min	$100
		TOTAL	**Up to $1,877**

Measures. At the screening visit, participants will provide sociodemographic data on age, gender, education, income, ethnicity, marital and employment status. They will be interviewed using the substance use disorders section and the psychotic and associated symptoms section of the Structured Clinical Interview for DSM-5 (SCID-5; First, Williams, Karg, & Spitzer, 2015). Participants will also

complete the following measures:

1. The Fagerström Test of Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerström, 1991) with additional smoking history questions (e.g., number of cigarettes smoked/day, age of first smoking, number of previous quit attempts);
2. Marijuana Smoking History (Bonn-Miller & Zvolensky, 2005);
3. Motives for Marijuana Use (Simons, Correia, Carey, & Borsari, 1998);
4. Posttraumatic Stress Disorder Checklist (PCL5; Weathers, Litz et al., 2013);
5. Traumatic Life Events Questionnaire (TLEQ), which collects the occurrence and frequency of each of 22 traumatic events (Kubany et al., 2000);
6. Patient Health Questionnaire (PHQ-9; Kroenke, Spitzer, & Williams, 2001);
7. Beck Depression Inventory (BDI; Beck, Steer, & Brown, 1996);
8. Beck Scale for Suicidal Ideation (BSS; Beck & Steer, 1991);
9. Conners' Adult ADHD Rating Scale (CAARS; Conners, Erhardt, & Sparrow, 1998);
10. Cannabis/Tobacco Version of the Stroop Test, computerized (Streeter et al., 2008);
11. Delay Discounting Task, computerized (Richards et al., 1999);
12. Iowa Gambling Task, computerized (Bechara et al., 1994); and
13. Balloon Analogue Risk Task, computerized (Lejuez et al., 2002).

Computerized Tasks. Several computerized measures will be given in order to measure impulsivity. Measures will be purchased as a package from www.millisecond.com. Computerized measures will be given on a Duke-owned laptop that is not connected to the internet. Results will be stored temporarily on the hard drive of that computer. Data will be moved from the laptop to the Duke server (duhsnas-pri\dusom_psych\private\Beckham Logs\Marijuana and Smoking) via encrypted thumbdrive or encrypted DVD. Once data are moved to the Duke server, they will be deleted from the hard drive of the laptop.

mCM Procedures. As part of previous projects (see Duke PRO00031703, PRO00050835, PRO61683, and PRO00062101), we developed a smart phone app that allows CM to be used outside the clinic to address substance misuse. Our programmer has completed adaptation of our existing mCM application to integrate the assessment of cannabis abstinence into the design of the app. Though most of the procedures used in our previous mCM studies are easily applied to CUD, we have made several important changes. We have added a videotaped OF assessment in which participants record themselves self-administering a OF test kit. For each OF video recording, each participant will be asked to 1) begin a recording using the smartphone device; 2) show the unused test strip to the camera; 3) swab his or her cheek while on camera; and 4) place the strip on a flat surface for 5 minutes and 5) show the final result to the camera. Saliva sticks will be numbered so that the number associated with the saliva swab can be ensured to be the number of the swab result. Participants will provide a CO reading and THC OF reading twice daily. Because reinforcers are most effective when delivered immediately after the target behavior is performed (Lattal, 2010), the phone app provides daily feedback on abstinence status, financial amount earned, and how the amount was calculated.

Video recordings will be made using a DROID MAXX 2 with an octa-core 1.7 Ghz processor, 2 GB RAM, and 5.5" full HD display. The operating system (OS) being utilized for the smart phones is Android 5.1.1 Lollipop, see FIPS 140-2 certificate 1998. The CO breath monitor, the iCO Smokerlyzer, is a battery

operated instrument that measures CO in ppm (http://www.bedfont.com/shop/smokerlyzer/ico_smokerlyzer). The Bedfont/coVita iCO™ Smokerlyzer® plugs into a smart phone by means of the headphone jack, and communicates with the smart phone app developed by our team. Participants are able to see the CO reading within the app, and the app collects the CO data directly. Data are stored in the same manner as the videorecordings that participants upload (see below and in "Protection From Risks: Data Security" herein).

With regards to FDA device issues, Bedfont/coVita will not be seeking 510k Clearance on the iCO™ Smokerlyzer® because it does not meet the standard/criteria of a medical device. Device manufacturers are required to follow FDA guidance to inform them of when a device necessitates 510k application. Per Jason Aversano at Bedfont/coVita, their regulatory team has determined that this is not necessary primarily because they do not make a medical claim about the device, as it is not designed to diagnose a disease or illness. Simply measuring CO is not diagnosing a disease or illness and Bedfont/coVita makes no medical claim that the iCO™ Smokerlyer® can be used to screen for CO poisoning.

We will compare self-reports to objective measures of cannabis use during the abstinence period. Feasibility of using proposed methods will be based on the observed concordance of self-report, CO readings, and saliva testing in the early abstinence period. If saliva tests taken before bedtime do not coordinate with participants' self-report during early abstinence weeks 1-2, we will modify procedures for subsequent weeks in order to 1) increase frequency of monitoring and 2) have the timing less predictable; e.g., more frequent cannabis readings will occur randomly between 8am-11pm, clustered in the evenings (8pm-11pm) and weekends (Friday-Sunday) (Alessi & Petry, 2013). While potentially more burdensome, this modification will be designed to alarm-prompt readings to occur up to 14 occasions each week to ensure adequate coverage. This procedure is designed to ensure that participants do not know when they will have a long time period between readings that would provide an opportunity for using cannabis that would be metabolized before the next reading. When prompted, participants will have one hour to submit their sample, with a reminder prompt at 30 minutes. Similar procedures have produced good adherence in previous research (Alessi & Petry, 2013). At the end of the monitoring period, qualitative data will be collected assessing bio-verification preferences, barriers, and any attempts to tamper or alter samples.

Participants will receive training on mCM procedures, including use of the mCM app, CO monitor, and saliva kits, by study staff. If equipment is available for loan at the screening visit, participants will be given smartphones with the mCM app, a CO monitor, and numbered saliva kits. If equipment is not immediately available for loan, these things will be mailed to the study participant prior to his/her beginning the mCM monitoring phase of the study. After one week with no mCM activity, they will complete one week of baseline saliva assessments and CO monitoring to ensure that they are expert at using the mHealth technology and can troubleshoot any problems with the assistance of study staff. During the baseline week, participants will be reinforced for completing readings, regardless of abstinence. The baseline monitoring will be followed by four weeks of active mCM. Because an escalating, versus a fixed, reinforcement schedule has produced higher abstinence rates (Heil et al., 2008; Stoops et al., 2009), an escalating schedule will be used in this protocol (identical to our pilot studies). Participants will provide substance use data throughout the mCM phase simply by completing

their readings using the mCM app. After the practice week, monetary reinforcement will be contingent on abstinence from marijuana and tobacco smoking, operationally defined as THC readings that are < 40 ng/mL and CO readings that are < 6 ppm. Following the active CM treatment phase, two weeks of saliva tests and CO monitoring (without contingent reinforcement) will be completed so that we can assess the durability of treatment effects.

During the entire monitoring period, each evening, participants will answer a computerized daily diary (programmed by our mCM app developer) in which they'll be asked to report on cigarette smoking and cannabis use. Participants will be asked 1) if they smoked cigarettes; 2) how many cigarettes they smoked if applicable; 3) if they smoked marijuana and how many if applicable; 4) if they ingested marijuana and how much; and 5) if they vaped marijuana and how much. Participants will be paid $1 per day for completing the diary.

Cognitive Behavioral Therapy for Cannabis Use Disorder and Smoking Cessation. Participants will receive CBT telephone counseling for cannabis and smoking cessation. CBT has been used to concurrently treat cannabis use and smoking and was feasibly implemented and well-tolerated. The CBT will consist of six sessions adapted from the CBT portions of the CUD treatment manual used in previous clinical trials (Litt, Kadden, Stephens, & Marijuana Treatment Project Research Group, 2005; Walker et al., 2011; Marijuana Treatment Research Group, 2004; Steinberg et al., 2002; Walker, Stephens, Towe, Banes, & Roffman, 2015) and our current CBT for smoking cessation protocol used in trials and previous studies (McFall et al., 2010). Counseling will be delivered primarily by phone, and by a counselor with at least a masters' degree in mental health (e.g., psychology, social work). Due to the substantial overlap in treatment procedures and skills acquired in CBT for CUD and smoking, most of each session will be devoted to material that applies to both problems. There are some treatment procedures (e.g., cannabis refusal skills development, managing thoughts about cannabis use) that are unique to CUD treatment, and these will be subsumed within the 60-minute therapy session.

Pharmacotherapy for Smoking Cessation. Participants will receive standard pharmacotherapy for smoking cessation. Study medications will be mailed to participants after the screening visit. Study medications consist of bupropion, an 8-week course of nicotine patch use and up to two rescue methods (e.g., nicotine gum, lozenge). Participants will be screened for suitability for nicotine replacement therapy (NRT) or other smoking cessation medication, and the study physician will determine safety for NRT and bupropion use. Participants will receive tailored amount and delivery type of NRT based on number of cigarettes smoked per day using an established protocol (Bars et al., 2006). Bupropion will be prescribed to start one week prior to their quit day [150 mg/daily for days 1-7 and 300 mg/daily (administered in two daily doses) until the 6-month follow-up. If a participant with a seizure disorder, history of or current hepatitis and/or cirrhosis, renal impairment, and/or uncontrolled diabetes wishes to enroll in the study, he/she will not receive contraindicated medications. If a participant with any of these medical conditions is unwilling to participate in the study without taking bupropion, he/she will be withdrawn from the study.

Follow-Up Visits. Participants will be asked to attend three follow-up visits at end of treatment, 3- and 6-months post-quit. At the follow-up visits, participants will be asked about their experiences with various treatment components. These will include closed ended questions and open-ended interview

questions. In addition, the study coordinator will ask questions about alliance with the study therapist. Participants will be asked to complete symptom self-report measures and computerized impulsivity tasks at each follow-up visit. Participants will be asked about smoking and cannabis use in the period since the quit date. Self-reported abstinence will be bioverified by several means. Self-reported prolonged abstinence from cannabis use will be verified by urine and OF cannabis assessments. Self-reported abstinence from smoking will be verified by saliva cotinine assay and CO reading.

Standard cut-points of 10 ng/ml for cotinine and 50 ng/ml for THC9-carboxylic acid (THC-COOH) will be used to determine abstinence from nicotine and marijuana, respectively. Self-reported and bioverified prolonged abstinence from marijuana, tobacco smoking and dual abstinence at the 6-month follow-up will be the primary end-point. Secondary cannabis use and tobacco smoking outcomes will include 7- and 30-day point prevalence abstinence at each assessment, in which abstinence is defined as no cannabis or tobacco use in the prior 7 or 30 days, respectively. Outcomes will also include cannabis consumption patterns such as standard joints/week and proportion of days abstinent. Participants will also report number of cigarettes smoked each day and days of smoking abstinence. Collection of cannabis and tobacco smoking use data will allow for calculation of dual abstinence days and longest duration of dual abstinence.

Participant Reimbursement. Based on our experience in our previous clinical trials, we are including $100 compensation for completing baseline, end of treatment, and 3- and 6-month follow-up assessments (up to $400). To ensure that participants return the CO monitor and phone, we are providing postage-paid return mailers and adding a $35 incentive for equipment return. Participants can earn up to $1,442for full participation and abstinence for the mCM portion of the study. Total possible payment for participation is $1,877.

Potential Risks

There is a risk of discomfort or distress in answering questions on the study measures. However, distress and discomfort related to questionnaire completion is usually temporary and well-tolerated. Risks also include discomfort related to quitting marijuana and quitting smoking. Symptoms of marijuana withdrawal may include headache, insomnia, sweating, night sweats, anxiety and/or depression, nightmares or vivid dreams, irritability, and cravings for use. Quitting smoking may cause difficulty concentrating, poor sleep, increased appetite, anxious or depressed mood, and craving for cigarettes.

Participants will be offered NRT, and there are risks associated with the use of NRT. Minimal risks associated with wearing a nicotine patch include skin irritation, dizziness, lightheadedness, increased heart rate or blood pressure, nausea or vomiting. If a participant indicates a contraindication to NRT (e.g. uncontrolled hypertension), medical clearance for NRT will be sought from the participant's primary care physician and/or the study physician. If a participant with a seizure disorder, history of or current hepatitis and/or cirrhosis, renal impairment, and/or uncontrolled diabetes wishes to enroll in the study, he/she will not receive contraindicated medications.

Participants who are medically eligible will also be prescribed bupropion SR. Risks of bupropion use include dry mouth, insomnia, nausea, constipation, headache, shakiness or jitteriness, skin rash, sweating, allergic reaction, change in appetite, weight loss, dizziness, tremor, thinking abnormally, hot flashes, worsening depression or suicidal thoughts and behavior, and ringing in the ears. At the highest dosage of bupropion to be used in this study, seizures occurred in 1 out of every 1000 (0.1%) who took this drug. Participants are informed that they are not required to take bupropion, and will be allowed to participate in the study if they refuse to do so.

There is a potential risk associated with the loss of confidentiality of study data. Specifically, collection and transfer of videotaped carbon-monoxide monitoring have risks with regards to privacy and confidentiality. Please see "Protection From Risk: Data Security" for details on reduction of risk with regards to the proposed videotaping.

Protection From Risk: Data Security

While participants may benefit from quitting smoking and marijuana use, there are no guaranteed benefits to the individual participant and no immediate benefits of the proposed research to others. There are potential benefits to others from the information generated that potentially will be helpful in developing new combined treatments for smoking and marijuana use. In our opinion, the anticipated benefits of this study outweigh the potential risks. The study is completely voluntary and participants are informed that they are free to refuse to answer any items on the questionnaires or questions from the interview. They are also informed that they are free to decline participation in procedures and can withdraw from the study at any time.

Potential risks will be minimized by carefully screening potential participants according to the inclusion/exclusion criteria, closely monitoring symptom levels, and following established laboratory procedures associated with participant safety.

If at the screening or follow-up visit(s), the participant reports marijuana use within the past three hours or seems impaired, we will advise the participant not to drive home. We will encourage him/her to use the local bus system, call for someone to pick him/her up, or call a taxi. The study coordinator will help the participant to make these telephone calls. However, due to budgetary limitations, the study will not provide monetary assistance to these participants who require alternative transportation methods. If a participant is unwilling to arrange alternate transportation, we will encourage him/her to remain at the medical center for a period of time until he/she is no longer impaired. If a patient does not wish to remain at the medical center, and voices intent to drive a vehicle while under the influence of marijuana, we will notify the Duke police.

We will be providing the study phones to participants for the course of the monitoring period and will retrieve them at the conclusion of monitoring. We will restrict access to the following applications: internet browsers, installation of apps, deletion of apps, and in-app purchases. We will prevent access to music, podcasts, movies, TV shows, apps, and other websites. We will prevent ability to change the following: accounts, cellular data use, background app updates, location services, contacts, calendars, reminders, photos, Bluetooth sharing, microphone, Twitter, Facebook, and advertising. We will have

the ability to remote wipe the phones if they are not returned. We will encourage participants via consent to only enter information on the phone that they are comfortable with sharing with the entities listed below.

Regarding mobile information security, we have taken care in previous projects using similar methods and technology to develop procedures to limit the risk of breach of confidentiality and privacy. For example, the smart phone is programmed such that a staff member will set up the telephone and enter the participant's code into the phone. When uploading a video, participants upload directly from the phone to an approved website that has been vetted by Duke's information security officers, and the phone programming ensures that the video is uploaded into the correct participant's area of the website. This ensures that study participants' data is stored in the correct place, and that study participants cannot view any other participants' data. Participants are asked to review their videos before posting, and they can choose not to upload any video that they don't wish to upload for any reason. In previous studies that have been run using this methodology, we have had no participant complaints regarding issues of privacy and confidentiality related to use of the smart phone videotaping procedures. In order to enhance participants' privacy, we will restrict access to several of the telephone's ancillary applications, and we have the ability to remotely delete data from any phones that are not returned to the study team.

For the study's website, we will use shared server space provided by InMotion Hosting, Inc (website www.Calhounlab.com). We will be using AES-256-CBC encryption with SHAI for message authentication and RSA as the key exchange mechanism. The video recordings will be collected on devices that are FIPS-140-2 compliant. The data at rest at InMotion Hosting is AES-256 encrypted at rest, and the data being transferred are encrypted at transfer (AES-256). Data will be unencrypted only by study staff members who have access to the secured server at InMotion Hosting; the encryption key is held only by our staff. This will ensure all video uploads and data that the participant sends over the internet via their phones will only be transferred over encrypted network connections, essentially nullifying the possibility of someone gaining access to the video before it reaches our server. InMotion also runs audits regularly of the websites hosted within their shared servers to prevent scriptside vulnerabilities, as well as having a 24/7 support team monitoring their servers. The web application written for this study has been checked for SQL injection, Code Injection, XSS, and RFI vulnerabilities and has passed. The site will only be accessible by the study participants and the study coordinators via 512-bit SHA-2 hashed passwords.

In previous studies using this methodology that have been run in the Traumatic Stress and Health Research Laboratory, we have had no participant complaints regarding issues of privacy and confidentiality related to use of the smart phone videotaping procedures. As security controls have not been validated for InMotion Hosting, we will include a statement in the informed consent that the data/videos voluntarily submitted will be sent to InMotion and are no longer covered by Duke privacy protections.

No "key personnel outside Duke" will have access to identifying information on subjects. There will be only one key personnel member outside Duke. Jeffrey Hertzberg, the smart phone app developer and website developer/maintainer, will have access to coded data as he provides telephone and/or website

support. He will not have access to PHI. Data that links participants to information collected in the course of a given study will be kept separately from identifying information in an electronic, password-protected MS Access database stored at duhsnas-pri\dusom_psych\private\Beckham Logs\Marijuana and Smoking; the key connecting identifying information and data will be stored here as well. Hard copy paper records will be stored in a locked filing cabinet in the study coordinator's locked office, within Dr. Beckham's laboratory space at Duke University Medical Center South. Information from the interview and/or questionnaires may be entered into a computerized database that will be stored on the DUMC server at duhsnas-pri\dusom_psych\private\Beckham Logs\Marijuana and Smoking in a password-protected database separate from the "logbook" of identifying information. This database is accessible only by Dr. Beckham and study staff. Any staff members who leave the study for any reason will have access to study resources, including data, removed immediately.

The study's safety monitoring plan is based on long-term clinical and research experience with patients with psychiatric illness, and is explained in more detail in the "Data and Safety Monitoring Plan" section. All project staff will complete educational units required by Duke's IRB, including CITI training and DHRT training.

Protection From Risk: Certificate of Confidentiality

In order for us to further protect the privacy of research participants, we have obtained a Certificate of Confidentiality (CoC) from the National Institutes of Health, certificate CC-DA-16-150. With this Certificate, we cannot be forced (for example by court subpoena) to disclose research information that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes. Participants are informed in the informed consent process that study investigators will use the Certificate to resist any demands for information that would identify them, except as follows:

1. A CoC does not prevent the participant or a member of his/her family from voluntarily releasing information about the participant.
2. If an insurer or employer learns about a participant's participation, and obtains consent to receive research information, then we may not use the CoC to withhold this information.
3. If a participant reveals current intent to harm him/herself or someone else, we may be required to take action in accordance with our laboratory's existing Psychiatric Emergencies SOP.
4. If a participant reveals anything that gives cause to suspect abuse or neglect of any child, elderly adult, or person with a disability, we are required by federal law to report the suspected abuse to the local Department of Social Services.

Data and Safety Monitoring Plan

Quitting smoking and marijuana use should enhance rather than jeopardize health status, and potential serious adverse events (SAEs) for participants in this project are not expected. Regardless, we will minimize potential risk by careful screening of potential participants (e.g., medical clearance by their primary care provider if there are contraindications to smoking cessation pharmacotherapy).

The individuals responsible for data safety and monitoring will be the PI, the project manager, and the Study Physician. The Study Physician for this trial will be Scott Moore, M.D., Ph.D. Dr. Moore is a board certified general psychiatrist, and is the treating physician of the local VA Medical Center's specialty smoking cessation clinic. As the Study Physician, Dr. Moore will ensure participants are medically cleared to participate in this trial and will review all reports of adverse events (AEs) sent by the study coordinator and evaluate the patient as necessary to determine whether there is any corrective action needed.

Further data safety and monitoring will be provided by the PI. There will be several ongoing mechanisms for monitoring and reporting of AEs: 1) ongoing participant contact via study personnel, 2) a toll-free number provided to participants to report concerns related to study participation; 3) weekly meetings between the PIs and study personnel.

The PI will meet at least weekly with study personnel to discuss participants' reactions to the intervention, proper delivery of the intervention, and any adverse events or unanticipated problems. Regular meetings between investigators and the project manager will allow for ongoing progress reports, including the number of participants currently involved in the study groups, attrition rates, and scheduled data collection from participants, as well as notification and review of any AEs. Safety monitoring for AEs will be conducted in real time by the PI and/or project manager. The following information about adverse events will be collected: 1) the onset and resolution of the AE, 2) an assessment of the severity or intensity (use existing grading scales whenever possible), 3) an assessment of the relationship of the event to the study (definitely, probably, possibly or not related), and 4) action taken (e.g., none, referral to physician, start or increase concomitant medication). The PI will determine the severity of the event, will assign attribution to the event, and will monitor the event until its resolution. Any adverse events will be reported to the IRB in accordance with the IRB guidelines.

Plans for Responding to a Participant Who Expresses Suicidal Ideation

Our research laboratory has established standards of practice for the evaluation of risk of suicide and homicide; these standards have been previously approved by the DUMC IRB. The policy includes a thorough risk assessment including evaluation of risk factors and protective factors associated with both suicide and homicide. Also included in the policy are differential recommendations for action based on determinations of low, moderate, or high risk. Any staff member conducting an interview in which moderate or high risk is determined will contact a senior staff person with clinical expertise in risk assessment.

Data Analyses

Descriptive statistics will be used to summarize all study variables. For continuous variables, means, standard deviations, percentiles, ranges, box plots and histograms will be generated. For categorical variables, frequencies and proportions will be generated. We will examine all variables to determine if parametric distributional assumptions (e.g. normality for the continuous variables) are valid. Variables not meeting distributional assumptions will either be transformed or modeled using nonparametric or

semi-parametric methods (e.g. quasi-likelihood methods; McCullagh & Nelder, 1989). In planning a full RCT of the tele-health mCM intervention for CUD and smoking, it is important to evaluate study feasibility and treatment procedures, as well as gaining information about effects on proposed outcome variables. To remain consistent with guidelines for designing and evaluating pilot studies, analyses will be primarily descriptive (Thabane et al., 2010) and aimed at informing feasibility and needed modifications rather than detecting statistically significant between-group differences (Leon, Davis, & Kraemer, 2011). However, to best utilize participant data to optimally design the treatment, we have established several objectives to indicate whether the planned trial is feasible.

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References

Abrams, D.I., Vizoso, H.P., Shade, S.B., Jay, C., Kelly, M.E. & Benowitz, N.L. (2007). Vaporization as a smokeless cannabis delivery system: A pilot study. *Clinical Pharmacology & Therapeutics,* 82, 572-8.

Agrawal, A., Budney, A.J. & Lynskey, M.T. (2012). The co-occurring use and misuse of cannabis and tobacco: A review. *Addiction,* 107, 1221-33. PMCID: PMC3397803.

Akre, C., Michaud, P.A., Berchtold, A. & Suris, J.C. (2010). Cannabis and tobacco use: Where are the boundaries? A qualitative study on cannabis consumption modes among adolescents. *Health Education Research,* 25, 74-82.

Alessi, S.M. & Petry, N.M. (2013). A randomized study of cellphone technology to reinforce alcohol abstinence in the natural environment. *Addiction,* 108, 900-9. PMCID: PMC3662495.

Allsop, D.J., Dunlop, A.J., Saddler, C., Rivas, G.R., McGregor, I.S. & Copeland, J. (2014). Changes in cigarette and alcohol use during cannabis abstinence. *Drug and Alcohol Dependence,* 138, 54-60.

Azorlosa, J.L., Greenwald, M.K. & Stitzer, M.L. (1995). Marijuana smoking: Effects of varying puff volume and breathhold duration. *Journal of Pharmacology and Experimental Therapeutics,* 272, 560-9.

Bars, M.P., Banauch, G.I., Appel, D., Andreachi, M., Mouren, P., Kelly, K. & Prezant, D.J. (2006). "Tobacco free with FDNY:" The New York city fire department World Trade Center tobacco cessation study. *Chest,* 129, 979-87.

Bechara A., Damasio A. R., Damasio H., Anderson S. W. (1994). Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition, 50,* 7-15.

Beck, A.T., & Steer, R.A. (1991). *Manual for Beck Scale for Suicide Ideation.* Psychological Corp: San Antonio.

Beck, A.T., Steer, R.A., & Brown, G. (1996). *Beck Depression Inventory-II.* San Antonio, TX: The Psychological Corporation.

Becker, J., Haug, S., Sullivan, R. & Schaub, M.P. (2014). Effectiveness of different web-based interventions to prepare co-smokers of cigarettes and cannabis for double cessation: A three-arm randomized controlled trial. *Journal of Medical Internet Research,* 16, e273. PMCID: PMC4275498.

Becker, J., Hungerbuehler, I., Berg, O., Szamrovicz, M., Haubensack, A., Kormann, A. & Schaub, M.P. (2013). Development of an integrative cessation program for co-smokers of cigarettes and cannabis: Demand analysis, program description, and acceptability. *Substance Abuse Treatment, Prevention, and Policy,* 8, 33. PMCID: PMC3848026.

Bonn-Miller, M.O. & Zvolensky, M.J. (2005). Marijuana Smoking History Questionnaire (version 2). Unpublished measure.Budney, A.J., Stanger, C., Tilford, J.M., Scherer, E.B., Brown, P.C., Li, Z., Li, Z. & Walker, D.D. (2015). Computer-assisted behavioral therapy and contingency management for cannabis use disorder. *Psychology of Addictive Behaviors,* E-pub ahead of print, May 4.

Carpenter, V.L., Hertzberg, J.S., Kirby, A.C., Calhoun, P.S., Moore, S.D., Dennis, M.F., Dennis, P.A., Dedert, E.A., Hair, L.P. & Beckham, J.C. (2015). Multicomponent smoking cessation treatment including mobile contingency management in homeless veterans. *Journal of Clinical Psychiatry,* 76, 959-64. PMCID: PMC4522209.

Carroll, K.M., Nich, C., Ball, S.A., McCance, E., Frankforter, T.L. & Rounsaville, B.J. (2000). One-year follow-up of disulfiram and psychotherapy for cocaine-alcohol users: Sustained effects of treatment. *Addiction,* 95, 1335-49.

Carroll, K.M., Rounsaville, B.J., Nich, C., Gordon, L.T., Wirtz, P.W. & Gawin, F. (1994). One-year follow-up of psychotherapy and pharmacotherapy for cocaine dependence. Delayed emergence of psychotherapy effects. *Archives of General Psychiatry,* 51, 989-97.

Centers for Disease Control and Prevention. (2010). *Tobacco use: Targeting the nation's leading killer*. Atlanta, GA: Centers for Disease Control and Prevention.

Chait, L.D., Russ, N.W. & Griffiths, R.R. (1985). Effects of graded smoke inhalation on subsequent tobacco smoking behavior. *Addictive Behaviors,* 10, 273-80.

Conners, C. K., Erhardt, D., & Sparrow, E. (1999). *Conners' Adult ADHD Rating Scales (CAARS) Technical Manual*. North Tonawanda, NY: Multi-Health Systems, Inc.

Cooper, Z.D. & Haney, M. (2009). Comparison of subjective, pharmacokinetic, and physiological effects of marijuana smoked as joints and blunts. *Drug and Alcohol Dependence,* 103, 107-13. PMCID: PMC2776770.

Copersino, M.L., Boyd, S.J., Tashkin, D.P., Huestis, M.A., Heishman, S.J., Dermand, J.C., Simmons, M.S. & Gorelick, D.A. (2006). Quitting among non-treatment-seeking marijuana users: Reasons and changes in other substance use. *American Journal of Addiction,* 15, 297-302.

Dallery, J., Raiff, B.R. & Grabinski, M.J. (2013). Internet-based contingency management to promote smoking cessation: A randomized controlled study. *Journal of Applied Behavior Analysis,* 46, 750-64.Davis, M.L., Powers, M.B., Handelsman, P., Medina, J.L., Zvolensky, M. & Smits, J.A. (2015). Behavioral therapies for treatment-seeking cannabis users: A meta-analysis of randomized controlled trials. *Evaluation & The Health Professions,* 38, 94-114. PMCID: PMC4429893.

Dang, Q. (2012). NIST Special Publication 800-107: Recommendation for applications using approved hash algorithms. National Institue of Standards and Technology.

de Dios, M.A., Vaughan, E.L., Stanton, C.A. & Niaura, R. (2009). Adolescent tobacco use and substance abuse treatment outcomes. *Journal of Substance Abuse Treatment,* 37, 17-24. PMCID: PMC2735078.

Dutra, L., Stathopoulou, G., Basden, S.L., Leyro, T.M., Powers, M.B. & Otto, M.W. (2008). A meta-analytic review of psychosocial interventions for substance use disorders. *The American Journal of Psychiatry,* 165, 179-87.

First, M.B., Williams, J.B.W., Karg, R.S. & Spitzer, R.L. (2015). *Structured Clinical Interview for DSM-5 (SCID-5 for DSM-5)*. Arlington, VA: American Psychiatric Association.

Gray, K.M., Riggs, P.D., Min, S.J., Mikulich-Gilbertson, S.K., Bandyopadhyay, D. & Winhusen, T. (2011). Cigarette and cannabis use trajectories among adolescents in treatment for attention-deficit/hyperactivity disorder and substance use disorders. *Drug and Alcohol Dependence,* 117, 242-7. PMCID: PMC3128687.Hall, W. & Degenhardt, L. (2009). Adverse health effects of non-medical cannabis use. *Lancet,* 374, 1383-91.

Hall, W., Degenhardt, L. & Lynskey, J. (2001). *The health and psychological effects of cannabis use. National Drug Strategy Monograph No. 25*. Australia: University of New South Wales, National Drug and Alcohol Research.

Heatherton, T. F., Kozlowski, L. T., Frecker, R. C., & Fagerström, K. O. (1991). The Fagerström Test for Nicotine Dependence: A revision of the Fagerström Tolerance Questionnaire. *British Journal of Addiction, 86*, 1119-1127.

Heil, S.H., Higgins, S.T., Berstein, I.M., Solomon, L.J., Rogers, R.E., Thomas, C.S., Badger, G.L. & Lynch, M.E. (2008). Effects of voucher-based incentives on abstinence from cigarette smoking and fetal growth among pregnant women. *Addiction,* 103, 1009-18. PMCID: PMC2731575.

Hertzberg, J.S., Carpenter, V.L., Kirby, A.C., Calhoun, P.S., Moore, S.D., Dennis, M.F., Dennis, P.A., Dedert, E.A. & Beckham, J.C. (2013). Mobile contingency management as an adjunctive smoking cessation treatment for smokers with posttraumatic stress disorder. *Nicotine & Tobacco Research,* 15, 1934-38. PMCID: PMC3790624.

Higgins, S.T. & Petry, N.M. (1999). Contingency management. Incentives for sobriety. *Alcohol Research & Health,* 23, 122-7.

Hill, K.P., Toto, L.H., Lukas, S.E., Weiss, R.D., Trksak, G.H., Rodolico, J.M. & Greenfield, S.F. (2013). Cognitive behavioral therapy and the nicotine transdermal patch for dual nicotine and cannabis dependence: A pilot study. *American Journal on Addictions,* 22, 233-8. PMCID: PMC3641687.

Huestis, M.A., Mitchell, J.M. & Cone, E.J. (1996). Urinary excretion profiles of 11-nor-9-carboxy-delta 9-tetrahydrocannabinol in humans after single smoked doses of marijuana. *Journal of Analytical Toxicology,* 20, 441-52.

Hurt, R.D., Offord, K.P., Croghan, I.T., Gomez-Dahl, L., Kottke, T.E., Morse, R.M. & Melton, L.J., 3rd. (1996). Mortality following inpatient addictions treatment. Role of tobacco use in a community-based cohort. *Journal of American Medical Association,* 275, 1097-103.

Kroenke, K., Spitzer, R.L., & Williams, J.B. (2001). The PHQ-9: Validity of a brief depression severity measure. *Journal of General Internal Medicine, 16*, 606-613.

Kubany, E.S., Haynes, S.N., Leisen, M.B. et al. (2000). Development and preliminary validation of a brief broad-spectrum measure of trauma exposure: The traumatic life events questionnaire. *Psychological Assessment*, *12,* 210-24.Moore, B.A. & Budney, A.J. (2001). Tobacco smoking in marijuana-dependent outpatients. *Journal of Substance Abuse,* 13, 583-96.

Lattal, K.A. (2010). Delayed reinforcement of operant behavior. *Journal of the Experimental Analysis of Behavior*, 93, 129-139. PMCID: PMC2801538.

Lee, D.C., Budney, A.J., Brunette, M.F., Hughes, J.R., Etter, J.F. & Stanger, C. (2014). Treatment models for targeting tobacco use during treatment for cannabis use disorder: Case series. *Addictive Behaviors,* 39, 1224-30. PMCID: PMC4066896.

Lee, D. & Huestis, M.A. (2014). Current knowledge on cannabinoids in oral fluid. *Drug Testing and Analysis,* 6, 88-111. PMCID: PMC4532432.

Lejuez, C. W., Read, J. P., Kahler, C. W., Richards, J. B., Ramsey, S. E., Stuart, G. L., Strong, D. R., & Brown, R. A. (2002). Evaluation of a behavioral measure of risk-taking: The Balloon Analogue Risk Task (BART). *Journal of Experimental Psychology: Applied, 8,* 75-84.

Leon, A.C., Davis, L.L. & Kraemer, H.C. (2011). The role and interpretation of pilot studies in clinical research. *Journal of Psychiatry Research,* 45, 626-9. PMCID: PMC3081994.

Litt, M.D., Kadden, R.M., Stephens, R.S. & Marijuana Treatment Project Research Group. (2005). Coping and self-efficacy in marijuana treatment: Results from the marijuana treatment project. *Journal of Consulting & Clinical Psychology,* 73, 1015-25.

Marijuana Treatment Project Research Group. (2004). Brief treatments for cannabis dependence: Findings from a randomized multisite trial. *Consulting and Clinical Psychology,* 72, 455-66.

McCullagh, P. & Nelder, J.A. (1989). *Generalized Linear Models*. 2nd ed. London: Chapman & Hall.

McFall, M., Saxon, A., Malte, C., Chow, B., Bailey, S., Baker, D., Beckham, J., Boardman, K.D., Carmody, T.P., Joseph, A., Smith, M.W., Shih, M., Lu, J., Holodniy, M. & Lavori, P.W. (2010). Integrating tobacco cessation into mental health care for posttraumatic stress disorder: A randomized controlled trial. *Journal of the American Medical Association,* 304, 2485-93.

O'Malley, S.S., Jaffe, A.J., Chang, G., Rode, S., Schottenfeld, R., Meyer, R.E. & Rounsaville, B. (1996). Six-month follow-up of naltrexone and psychotherapy for alcohol dependence. *Archives of General Psychiatry,* 53, 217-24.

Peters, E.N., Budney, A.J. & Carroll, K.M. (2012). Clinical correlates of co-occurring cannabis and tobacco use: A systematic review. *Addiction,* 107, 1404-17. PMCID: PMC3377777.

Petry, N.M., DePhilippis, D., Rash, C.J., Drapkin, M. & McKay, J.R. (2014). Nationwide dissemination of contingency management: The Veterans Administration initiative. *The American Journal on Addictions,* 23, 205-10. PMCID: PMC3986725.

Pilling, S., Strang, J. & Gerada, C. (2007). Psychosocial interventions and opioid detoxification for drug misuse: summary of NICE guidance. *British Medical Journal,* 335, 203-05. PMCID: PMC1934496.

Richards, J. B., Zhang, L., Mitchell, S. H., De Wit, H. (1999). Delay or probability discounting in a model of impulsive behavior: Effect of alcohol. *Journal of the Experimental Analysis of Behavior, 71,* 121-143.

Richter, K.P., Ahluwalia, H.K., Mosier, M.C., Nazir, N. & Ahluwalia, J.S. (2002). A population-based study of cigarette smoking among illicit drug users in the United States. *Addiction,* 97, 861-9.

Richter, K.P., Kaur, H., Resnicow, K., Nazir, N., Mosier, M.C. & Ahluwalia, J.S. (2004). Cigarette smoking among marijuana users in the United States. *Substance Abuse,* 25, 35-43.

Shein-Chung, C. & Chang, M. (2011). *Adaptive design methods in clinical trials*. Boca Raton, FL: CRC Press.

Simons, J., Correia, C. J., Carey, K. B., & Borsari, B. E. (1998). Validating a five-factor motives measure: Relations with use, problems and alcohol motives. *Journal of Counseling Psychology, 45*, 265–273.

Steinberg, K.L., Roffman, R.A., Carroll, K.M., Kabela, E., Kadden, R., Miller, M., Duresky, D. & Marijuana Treatment Project Research Group. (2002). Tailoring cannabis dependence treatment for a diverse population. *Addiction,* 97 Suppl 1, 135-42.

Stoops, W.W., Dallery, J., Fields, N.M., Nuzzo, P.A., Schoenberg, N.E., Martin, C.A., Casey, B. & Wong, C.J. (2009). An internet-based abstinence reinforcement smoking cessation intervention in rural smokers. *Drug and Alcohol Dependence,* 105, 56-62. PMCID: PMC2743786.

Streeter, C.C., Terhune, D.B., Whitfield, T.H., Gruber, S., Sarid-Segal, O., Silveri, M.M., et al. (2008). Performance on the Stroop predicts treatment compliance in cocaine-dependent individuals. *Neuropsychopharmacology, 33*, 827–836

Substance Abuse Mental Health Services Administration. (2014). National Survey of Substance Abuse Treatment Services (N-SSATS): 2013. Data on Substance Abuse Treatment Facilities. Rockville, MD.

Tashkin, D.P., Gliederer, F., Rose, J., Change, P., Hui, K.K., Yu, J.L. & Wu, T.C. (1991). Effects of varying marijuana smoking profile on deposition of tar and absorption of CO and delta-9-THC. *Pharmacological Biochemical Behavior,* 40, 651-6.

Thabane, L., Ma, J., Chu, R., Cheng, J., Ismaila, A., Rios, L., Robson, R., Thabane, M., Giangregorio, L. & Goldsmith, C.H. (2010). A tutorial on pilot studies: the what, why and how. *BMC Medical Research Methodology,* 10, 1-10.

Taylor, D.R., Fergusson, D.M., Milne, B.J., Horwood, L.J., Moffitt, T.E., Sears, M.R. & Poulton, R. (2002). A longitudinal study of the effects of tobacco and cannabis exposure on lung function in young adults. *Addiction,* 97, 1055-61.

Walker, D.D., Stephens, R., Roffman, R., Demarce, J., Lozano, B., Towe, S. & Berg, B. (2011). Randomized controlled trial of motivational enhancement therapy with nontreatment-seeking adolescent cannabis users: A further test of the teen marijuana check-up. *Psychology of Addictive Behaviors,* 25, 474-84. PMCID: PMC3177997.

Walker, D.D., Stephens, R.S., Towe, S., Banes, K. & Roffman, R. (2015). Maintenance check-ups following treatment for cannabis dependence. *Journal of Substance Abuse Treatment,* 56, 11-5. PMCID: PMC4519423.

Weathers, F.W., Litz, B.T., Keane, T.M., Palmieri, P. A., Marx, B. P., & Schnurr, P.P. (2013). *The PTSD Checklist for DSM-5 (PCL-5)*. Scale available from the National Center for PTSD at www.ptsd.va.gov.

Wu, T.C., Taskin, D.P., Dhajed, B. & Rose, J.E. (1988). Respiratory hazards of smoking marijuana as compared to tobacco. *New England Journal of Medicine,* 318, 347-51.

Zhang, Y. & Wildermuth, B.M. Qualitative analysis of content. In: Wildemuth, B., ed. *Applications of social research methods to questions in information and library science*. Westport, CT: Libraries Unlimited; 2009:308-19.

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DUKE UNIVERSITY HEALTH SYSTEM

Consent to Participate in a Research Study
Mobile Contingency Management for Concurrent Abstinence from Cannabis and Cigarette Smoking: A Pilot Study

You are being asked to take part in this research study because you use marijuana and smoke cigarettes. Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, discomforts, and other important information about the study are listed below.

Please tell the study doctor or study staff if you are taking part in another research study.

Dr. Jean Beckham will conduct the study and it is funded by Duke University Medical Center departmental funds. Portions of Dr. Beckham's salary will be paid for by this grant. The study physician will be Scott Moore, MD, PhD.

WHO WILL BE MY DOCTOR ON THIS STUDY?
If you decide to participate, Drs. Moore and Beckham will be your doctors for the study. They will be in contact with your regular health care provider throughout the time that you are in the study and afterwards, if needed.

WHY IS THIS STUDY BEING DONE?
The purpose of this study is to learn more about ways to help people quit using marijuana and stop smoking cigarettes at the same time. This study is looking specifically at the use of monetary rewards and a smart phone application (App), for helping stop smoking and using marijuana.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
Approximately 10 people will take part in this study at Duke.

WHAT IS INVOLVED IN THE STUDY?
The study involves three laboratory visits and a few telephone visits.

If you agree to be in this study, you will be asked to sign and date this consent form. We will ask you to do the following tests and procedures to make sure that you are eligible:

- provide a breath sample by blowing into a device that measures the amount of carbon monoxide (CO, a gas found in your breath) in your breath, which will indicate how much you are smoking;
- participate in an interview about your substance use;
- provide a saliva (spit) sample so we can measure any recent marijuana use; and
- provide a urine sample so that we can test for substances such as cocaine, heroin, and amphetamines. If you are a woman of child-bearing age and/or potential, we will also use this urine to perform a pregnancy test.

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Session 1: We will ask you to fill out some questionnaires about yourself. These will include questions about your mood, marijuana use, and smoking history. We will also ask you to complete some computerized tasks designed to measure impulsive behavior.

After you have completed the interviews and questionnaires, you will participate in the first of five counseling sessions to help you quit using marijuana and quit smoking. After that, we will train you how to use the study equipment for home monitoring. Equipment will include a CO monitor, some saliva strips, and a mobile telephone. You will use this equipment to monitor yourself taking CO readings and saliva readings twice a day, and upload them to the study team. The mobile telephone has a small video camera. You will be trained how to use the saliva strips and CO monitor, and how to use the telephone to record a video of yourself monitoring your CO and saliva readings. You will also be trained how to upload the video to this study's website using a mobile application (mCM) that will be on the phone you're given. If the equipment is available for loan during this first visit, we will give it to you before you leave. If equipment is not available right away, the study coordinator will mail it to you.

At the end of the study, we will ask you to return the study equipment to the study staff. If you misplace the study equipment, or it is stolen while you have it, we ask you to tell a study staff member immediately. The telephone has tracking software on it, and we may be able to use the software to locate the phone, shut it down, and get all of the data you have stored on it. We will only use the tracking software if you report the telephone as lost or stolen, or you fail to return it to us at the end of the study. If your telephone or other equipment has been misplaced or stolen, and you still need the equipment to continue in the study, we will provide you with a replacement at no cost.

All together, this visit will take about 3 ½ hours to complete. We will pay you $100 for completing this session.

Session 2: In this telephone session, you will participate in a second marijuana/smoking cessation counseling session. You will not be paid for Session 2.

Session 3: In this telephone session, you will participate in the third counseling session. In this counseling session, you will set a smoking/marijuana quit date.

If you are medically eligible, we will give you a medication to begin taking one week before your smoking quit date. The medication is bupropion SR, an antidepressant medication that is FDA approved for treating depression and for helping smokers to stop smoking. You will take 150 mg each day for 7 days and then 300 mg each day. You will continue taking the medication until your 6-month study follow-up visit. Before we give you this medication, though, we will make sure you are medically eligible to take it. Our study physician will review the information you provide to us to determine if it is safe for you to take this medication. If you have ever had seizures or currently have seizures, please tell the study coordinator. You should not take bupropion if you have uncontrolled diabetes, kidney impairment, current or past hepatitis, or current or past cirrhosis. You will still be allowed to participate

in the rest of the study if the study doctor determines you shouldn't take bupropion. You will also be given two forms of nicotine replacement therapy, or NRT. This includes nicotine patches and a "rescue method," like nicotine gum, lozenge, or inhalers. We'll ask you what you prefer. You will be asked to begin using these medications on your quit date.

You will be asked to begin at-home monitoring with the equipment that was loaned to you at Session 1. Starting at Session 2 and lasting until Session 5, you will be asked to record and upload your CO readings twice within a 24-hour period, with at least eight hours between each reading. You will also hear an alarm asking you to do a saliva sample reading twice per day. Also, you'll be asked to answer a few questions each night about your day's use of marijuana and cigarettes. The study's website will include a personalized study area for you. The study area will allow you to see how many readings have been uploaded, and will provide information about monetary rewards for your readings. For the first week of monitoring (between session two and three), you will be paid up to $7 per day for providing all of the readings and doing your diary entry. You will not be paid for Session 3.

If for any reason we lose contact with you for more than two weeks after you start this portion of the study, or you do not load videos, the study coordinator will disable the telephone that you have been loaned and turn off all telephone services. The phone will be unusable until you contact the study coordinator.

Session 4: This telephone session will occur on your marijuana and smoking quit date. You will participate in the fourth counseling session.

You will be asked to start using nicotine patches and your preferred rescue method. Also, you'll be asked to continue home monitoring. Starting at this session, you will receive payment $1 for uploading a video with a CO reading, and $5 for uploading a saliva test strip results video. You will be paid this amount if you upload the readings regardless of whether you have been smoking cigarettes or using marijuana. Also, we will pay you an additional amount if your CO reading indicates you haven't been smoking. You will be paid $1 for the first clean CO reading. After that, 25 cents will be added to each clean CO reading you upload.Similarly, you will be paid an additional amount for uploading the marijuana saliva strip results if the strip indicates you haven't been using marijuana. Similarly, you will be paid $1 for the first clean marijuana saliva reading. After that, 25 cents will be added to each clean reading you upload. If you upload two clean CO readings and two clean marijuana readings in a single day, you will be paid a $1 bonus. The bonus will increase by 50 cents for each day you complete all four readings. If on any day you don't upload a CO reading, you will not receive a money reward for CO, or a bonus. If on any day you don't upload a saliva test reading, you will not receive a money reward marijuana, or a bonus. If you have a positive reading for CO, your rewards will start again after you have another negative CO reading. After you have provided two clean readings for CO, you will be paid for your next clean reading. The amount you are paid for this reading will be the last highest amount you earned. The same is true for marijuana readings. The 25 cents increase per clean readings and 50

increase per bonus will start again. The study coordinator will give you a detailed manual describing how the payments work. Actual payment will be provided after session 7.

You will not be paid for Session 4, but you may be paid for at-home monitoring between sessions 3 and 4.

Session 5: Session 5 will occur about two weeks after session 4. This is a telephone session, and in it, you will participate in your final counseling session. You will not be paid for Session 5.

Session 6: Session 6 is a quick telephone check-in that occurs about two weeks after Session 5. In this session, your payment for continuing home monitoring will go back to up to $7 per day for providing all of the readings and doing your diary entry. You will not be paid for Session 6.

Session 7: Session 7 is an office visit, and it occurs about two weeks after Session 6. You will be asked to return the CO monitor and telephone, and to stop doing at home-monitoring. You will be asked to continue using bupropion, but you will stop NRT. You will complete some questionnaires about your mood symptoms and about your marijuana use and smoking since your quit date. You will also complete some computerized tasks (just like in Session1). We will ask you some questions about your experiences with the at-home monitoring and the telephone counseling. We will also ask you some questions about your experiences with your counselor. If you report that you are still not smoking, we will ask you to provide a saliva (spit) sample and a CO (breath) sample. We will ask you to do a urine drug screen to test for marijuana. If you report that you haven't used marijuana recently, we will ask you to do a marijuana saliva test. You will be paid $100 for Session 7, and you may be paid for at-home monitoring between sessions 3 and 7. We will also pay you $35 for returning the equipment.

Session 8: This session occurs 3 months after your quit date (session 4). In this session, you will complete some questionnaires about your mood symptoms and about your marijuana use and smoking since Session 7. You will be asked to complete some computerized tasks measuring impulsivity. If you report that you are still not smoking, we will ask you to provide a saliva (spit) sample and a CO (breath) sample. We will ask you to do a urine drug screen to test for marijuana. If you report that you haven't used marijuana recently, we will ask you to do a marijuana saliva test. We will pay you $100 for Session 8.

Session 9: This session occurs 3 months after Session 8. In this session, you will complete some questionnaires about your mood symptoms and about your marijuana use and smoking since Session 8. You will be asked to complete the computerized tasks measuring impulsivity. If you report that you are still not smoking, we will ask you to provide a saliva (spit) sample and a CO (breath) sample. We will ask you to do a urine drug screen to test for marijuana. If you report that you haven't used marijuana recently, we will ask you to do a marijuana saliva test. You will stop using bupropion at this time. We will pay you $100 for Session 9.

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The investigational parts of this study are the questionnaires that we ask you to complete, the home monitoring and uploading of videos, and the payments for not smoking and not using marijuana. If you were to go to a doctor for help in stopping smoking or stopping marijuana, you might not be asked to do those parts.

HOW LONG WILL I BE IN THIS STUDY?
Your active participation in this study will last about six weeks. You will have three follow-up sessions at the end of the treatment phase, and at three months and six months after you quit smoking and/or using marijuana. Altogether, your participation will last about 7 ½ months. You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first.

WHAT ARE THE RISKS OF THE STUDY?
As a result of your participation in this study, you are at risk for the following side effects. You should discuss these with the study doctor and your regular health care provider if you choose.

Stopping smoking causes withdrawal symptoms. Symptoms can last for a few days to several weeks. These may include: headaches, dizziness, nausea, anxious or depressed mood, feelings of frustration and anger, trouble sleeping, bad dreams, trouble concentrating, restlessness, tiredness, increased appetite, weight gain, and craving for cigarettes.

Stopping marijuana can cause withdrawal symptoms. Symptoms can last for a few days to several weeks. These may include: headache, trouble sleeping, sweating, night sweats, anxiety and/or depression, nightmares or vivid dreams, irritability, and cravings for use.

There are no known risks associated with completing paper and pencil measures. There is a possible risk of temporary anxiety associated with discussing psychiatric symptoms. There is a potential risk for loss of confidentiality associated with using the mobile application(s).

Using nicotine in the form of patches, gum, inhaler, or lozenge may cause some, all, or none of the side effects listed below.

More likely

- acid or sour stomach
- belching
- coughing
- heartburn
- indigestion
- mouth and throat irritation
- stomach discomfort, upset, or pain
- stuffy nose

Less likely:

- anxiety
- back pain
- change in taste
- diarrhea
- dizziness
- feeling of burning, numbness, tightness, tingling, warmth, or heat
- flu-like symptoms
- general pain
- hiccups
- mental depression
- pain in the jaw and neck
- pain in the muscles
- passing of gas
- problems with teeth
- trouble with sleeping
- unusual tiredness or weakness
- fast or irregular heartbeat
- fever with or without chills
- headache
- nausea with or without vomiting
- runny nose
- shortness of breath
- tightness in the chest, trouble with breathing, or wheezing
- skin rash, itching, or hives
- tearing of the eyes

Nicotine patches may cause skin irritation, increased heart rate, nightmares, and increased blood pressure. Nicotine gum and lozenges may cause a tingling or burning sensation in the mouth. The nicotine inhaler doesn't have any additional risks.

Bupropion may cause some, all or none of the side-effects listed below.

More likely

- dry mouth
- trouble sleeping
- nausea
- constipation
- headache
- shakiness or jitteriness
- skin rash

- sweating
- change in appetite
- weight loss
- dizziness
- tremor
- hot flashes
- ringing in the ears

Less Likely

- unusual fatigue
- diarrhea or abdominal pain
- muscle or joint aches that last days
- yellowing of your skin
- seizures
- thinking abnormally

You should avoid driving a car or operating heavy machinery until you know how the medications affect you. The Food and Drug Administration (FDA) has recommended that individuals taking certain medications, including bupropion SR, should watch out for worsening depression, or suicidal thoughts and behavior. You should also watch for sudden and severe changes in feelings such as: anxiety, agitation, feelings of panic, irritability, hostility, aggressiveness, impulsivity, severe restlessness, feeling overly excited or hyperactive, or not being able to sleep. In addition, you should tell family members or caregivers to watch out for these symptoms while you are taking the medicine. If you, your family members, or your caregivers notice any of these symptoms, you should notify the study doctor as soon as possible. If you are having suicidal thoughts or behaviors, you should go the nearest hospital emergency room.

If you are a female: Being a part of this study while pregnant may expose the unborn child to significant risks, some of which may be currently unforeseeable. Therefore, pregnant women will be excluded from the study. If you are a woman of childbearing potential, a urine pregnancy test will be done, and it must be negative before you can continue in this study. If sexually active, you must agree to use appropriate contraceptive measures for the duration of the study. Medically acceptable contraceptives include: (1) surgical sterilization (such as a tubal ligation or hysterectomy), (2) approved hormonal contraceptives (such as birth control pills, patches, implants or injections), (3) barrier methods (such as a condom or diaphragm) used with a spermicide, or (4) an intrauterine device (IUD). Contraceptive measures such as Plan B (TM), sold for emergency use after unprotected sex, are not acceptable methods for routine use. If you do become pregnant during this study or if you have unprotected sex, you must inform your study physician immediately.

Drug and Food Interactions: For your safety, you must tell the study doctor or nurse about all the prescribed medical foods and drugs, herbal products, over-the-counter (OTC) drugs, vitamins, natural

remedies, and alcohol that you are taking before you start the study and before starting to take any of these products while you are on the study. While taking bupropion, you should avoid excessive alcohol use since that may increase the likelihood of seizures. If you begin drinking alcohol more frequently than you reported in your first session, please notify the study coordinator. It is important for us to know this so that we can help protect you from the health risks of drinking and taking the medications. If at any point we believe that your alcohol use might be a health risk because of the medications, we will withdraw you from the study or ask you to quit taking the medication(s) that can cause this health risk.

There may be risks, discomforts, drug interactions, or side effects that are not yet known.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
If you agree to take part in this study, there may be direct medical benefit to you. You may benefit from stopping smoking and/or stopping marijuana. However, we cannot guarantee that you will stop smoking or stop using marijuana during this study. We hope that in the future the information learned from this study will benefit other people with your condition.

WHAT ALTERNATIVES ARE THERE TO PARTICIPATION IN THIS STUDY?
Instead of being in this study, you could enroll in another stop smoking or marijuana cessation treatment. There may be other treatment programs available to you in the community. Please talk to your doctor about these and perhaps other options.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?
Study records that identify you will be kept confidential as required by law. Federal Privacy Regulations provide safeguards for privacy, security, and authorized access. Except when required by law, or as outlined below, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of Duke University Health System (DUHS). For records disclosed outside of DUHS, you will be assigned a unique code number. The key to the code will be kept in a password-protected database that is stored on a secured computer in a secured folder to which only study staff members have access. In addition, your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives from the Duke University Health System Institutional Review Board, National Institutes of Health, the Office for Human Research Protections, and/or the Food and Drug Administration. If any of these groups review your research record, they may also need to review your entire medical record. If this information is disclosed to outside reviewers for audit purposes, it may be further disclosed by them and may not be covered by the federal privacy regulations.

The mCM mobile application will upload the videos you take to InMotion Hosting, Inc. When the mCM mobile application is used as directed, the data sent to InMotion Hosting will not contain any information that identifies you. Data stored on your phone is encrypted at rest. As it is being transmitted to InMotion Hosting, it is also encrypted. Finally, it is encrypted at rest while at InMotion Hosting.

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You should not use the phone we loan you for personal use, for example, internet searching, texting, emailing, personal phone calls, taking pictures, downloading mobile apps) during the study. If you use it for non-study related reasons, this could add your personal information onto the device and potentially result in it being sent to unauthorized persons. The device will be preset with security settings. Please do not alter these during the course of the study. When you return the device at the end of the study, the device will be cleaned to remove any of your personal information. If the device is lost or stolen during the course of the study, please contact the study team immediately.

All of the urine and saliva sample studies are being done only because you are in this study. The study results will not be given to you to send OR sent to your physician to include in your medical record.

The study results will be retained in your research record for at least six years after the study is completed. At that time either the research information not already in your medical record will be destroyed or information identifying you will be removed from such study results at DUHS. Any research information in your medical record will be kept indefinitely.

While the information and data resulting from this study may be presented at scientific meetings or published in a scientific journal, your identity will not be revealed.

To help us further protect your privacy, the investigators have obtained a Confidentiality Certificate from the Department of Health and Human Services (DHHS). With this Certificate, the investigators cannot be forced (for example by court subpoena) to disclose research information that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes.

You should understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. Note however, that if an insurer or employer learns about your participation, and obtains your consent to receive research information, then the investigator may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy.

Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others.

If you reveal current intent to harm yourself or someone else, we may be required to escort you or have you escorted to this (or your local) hospital's emergency room for further evaluation. If during the course of the study you discuss or mention anything that gives us cause to suspect abuse or neglect of any child, elderly adult, or person with a disability, we are required by federal law to report the suspected abuse to your local Department of Social Services.

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WHAT ARE THE COSTS?
There will be no additional costs to you as a result of being in this study. However, routine medical care for your condition (care you would have received whether or not you were in this study) will be charged to you or your insurance company. You may wish to contact your insurance company to discuss this further. In order to make sure that tests and studies done solely for research purposes are charged correctly, we will carefully monitor your Duke Hospital and Clinic charges as long as you are participating in this study. These tests and studies are not a part of routine care, and people who are not part of the study do not usually have them performed. Please ask the study coordinator if you would like to know more about which tests and studies are being done solely for research purposes.

Duke University Medical Center will provide the bupropion, NRT and equipment device free of charge for your use in this study. At the conclusion of the study, or if you decide to withdraw from the study, you must return all unused medications to the study coordinator. Dr. Beckham may request that you return for a checkup before you stop your medications if she thinks that stopping them suddenly may harm you. She may also ask you to complete the tests that would ordinarily occur when a person completes the study.

WHAT ABOUT COMPENSATION?
You will be reimbursed up to $400 for attending the screening and follow-up visits ($100 each). You will be reimbursed $35 for returning the study equipment. You will also be compensated up to $1,442 for at-home monitoring. Most people do not earn this much money for at-home monitoring. This compensation is offered as an incentive for you to stop smoking and stop using marijuana. In total, you will be compensated up to $1,877 for participation. If you do not complete the study, you will be given partial compensation for those parts you have completed.

Payment will be given to you in four installments. Payment will be requested for session 1 just after you have completed it. Your second payment (for at-home monitoring) will be requested just after session 7. Payment for sessions 8 and 9 will be requested just after you have completed them.

Payment received as compensation for participation in research is considered taxable income to the research subject. If payment to an individual exceeds $600 in any one calendar year, Duke University is required to report this information to the Internal Revenue Service (IRS). Research subject payments to a non-employee of Duke University exceeding $600 during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to the individual and a copy sent to the IRS.

WHAT ABOUT RESEARCH RELATED INJURIES?
Immediate necessary medical care is available at Duke University Medical Center in the event that you are injured as a result of your participation in this research study. However, there is no commitment by Duke University, Duke University Health System, Inc., or your Duke physicians to provide monetary compensation or free medical care to you in the event of a study-related injury.

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For questions about the study or research-related injury, contact Dr. Beckham at 919-286-0411, ext. 7973 during regular business hours and at 919-286-0411 and ask the operator to contact Dr. Beckham at home after hours and on weekends and holidays.

WHAT ABOUT MY RIGHTS TO DECLINE PARTICIPATION OR WITHDRAW FROM THE STUDY?

You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled, and will not affect your access to health care at Duke. If you do decide to withdraw, we ask that you contact Dr. Beckham in writing and let her know that you are withdrawing from the study. Her mailing address is Jean Beckham, Ph.D., Duke University Medical Center, Box 2969, Durham, NC 27705. You will be asked to return any study equipment you have been loaned.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

Your doctor may decide to take you off this study if your condition gets worse, if you have serious side effects, or if your study doctor determines that it is no longer in your best interest to continue. Reasons why this might occur include failure to follow the instructions of the study staff, inability to complete the study requirements, or inability to attend study visits as scheduled. If this occurs, you will be notified and your study doctor will discuss other options with you.

WHO DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, or if you have problems, concerns, questions or suggestions about the research, contact Dr. Beckham at 919-286-0411, ext. 7973 during regular business hours and at 919-286-0411 and ask the operator to contact Dr. Beckham at home after hours and on weekends and holidays.

For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.

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STATEMENT OF CONSENT

"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told whom to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to obtain information or offer input about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form."

_____	_____	_____
Signature of Subject	Date	Time
_____	_____	_____
Signature of Person Obtaining Consent	Date	Time