Mobile Contingency Management for Concurrent Abstinence From Alcohol and Smoking

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Study Protocol and Statistical Analysis Plan

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Background:

Alcohol and nicotine are the most frequently used drugs in the United States (Kandel, Chen, Warner, Kessler, & Grant, 1997) and each results in substantial morbidity, mortality, and functional impairment. While the rate of smoking is only 19% in the general U.S. population, an estimated 60% of those with an alcohol use disorder (AUD) smoke (Falk, Yi, & Hiller-Sturmhofel, 2006). Similarly, daily smokers have approximately three to four times the risk of alcohol misuse, while former smokers have risk levels near that of those who had never smoked (Chiolero, Wietlisbach, Ruffieux, Paccaud, & Cornuz, 2006; Grant, Hasin, Chou, Stinson, & Dawson, 2004; McKee, Falba, O'Malley, Sindelar, & O'Connor, 2007). Naturalistic studies of persons who both smoke and consume alcohol suggest that smoking and consumption of alcohol tend to occur on the same occasions (Gulliver et al., 1995; Lisha, Carmody, Humfleet, & Delucchi, 2014). In addition, the pattern of relapse risk across time is similar for smoking and alcohol, following a log-logistic function in which the first days carry the highest risk followed by decelerated risk with increased time of abstinence (Kirshenbaum, Johnson, Schwarz, & Jackson, 2009). Several studies have observed substantial decrease in alcohol consumption in former smokers (Chiolero et al., 2006; McKee et al., 2007; Morabia, Curtin, & Bernstein, 1999), and treatment research has found successful smoking cessation to be related to subsequent decreases in alcohol consumption (Friend & Pagano, 2005). Despite the lethality of these problems and the potential for synergistic effects of addressing both AUD and smoking, there is a lack of validated treatment approaches for achieving concurrent abstinence (Holt, Litt, & Cooney, 2012).

As chronic, relapsing conditions, AUD and smoking are well-suited to intensive behavioral treatments that intervene frequently in the early stages of achieving abstinence (McFall et al., 2010; Willenbring, 2013). Unfortunately, inpatient substance use disorder treatment is very costly, and episodic outpatient treatment is often insufficient for achieving abstinence (Willenbring, 2013). One especially efficacious treatment for AUD is contingency management (CM), an intensive behavioral treatment that frequently provides monetary reinforcement of abstinence from substances. Among psychosocial treatments for substance use disorders generally, CM has the largest effect of any single intervention, but an even larger effect has been observed in the few studies that have combined CM with CBT (Dutra et al., 2008). Unfortunately, the burdensome requirement of clinic based assessment multiple times each day has largely limited the widespread use of CM.

While there is a large body of evidence to support the short-term efficacy of CM approaches for treatment of both AUD and smoking independently, the proposed pilot

intervention will be the first to utilize CM as part of a concurrent treatment of AUD and smoking. Because successful smoking cessation alone is expected to reduce relapse to alcohol, the advantages of concurrent treatment go beyond the notable benefit of also promoting smoking cessation. Recent efforts have attempted to expand the reach of intensive CM approaches through internet based paradigms (Dallery & Raiff, 2011) which overcome the need for clinic monitoring and have been found to be helpful in reducing smoking among difficult-to-treat populations (e.g. adolescents and rural populations; (Dallery, Meredith, & Glenn, 2008; Reynolds, Dallery, Shroff, Patak, & Leraas, 2008). Building upon web-based paradigms (Dallery & Raiff, 2011), we have developed a smart-phone based application and website that significantly reduce the labor intensity of CM and increase portability even beyond web-based approaches. The innovative use of mHealth technology removes several barriers to the widespread implementation of CM approaches including the need to travel to verify abstinence and the automation of complex reinforcement strategies. In addition to the application of innovative mHealth technology and concurrent treatment of both AUD and tobacco use, the proposed research is particularly novel, in our opinion, because it will be the first evaluation of smart phone based mobile CM in conjunction with evidence-based CBT for AUD and smoking cessation, which is expected to significantly increase relapse prevention.

Despite established short-term efficacy, CM has not been widely adopted to treat either AUD or smoking. One prominent concern is the long-term impact of CM after contingencies are removed. However, follow-up abstinence rates for CM treatments have been improved by the integration of CBT into CM (Carpenter et al., 2014; R. M. Kadden, Litt, Kabela-Cormier, & Petry, 2007). CM-induced abstinence could provide advantages to CBT alone, as it gives the individual a positive early experience with abstinence that 1) increases self-efficacy, 2) increases engagement in CBT, 3) provides the opportunity to practice CBT skills in time to acquire and utilize the coping skills provided by CBT, and 4) provides time for people to develop alternative reinforcers to substance use, and 5) engages people in CBT intervention that includes coping skills acquisition and home practice that encourages generalization of skills to the naturalistic environment, which likely contributes to the durability of CBT effects on substance use outcomes (Carroll et al., 2000; Carroll et al., 1994; O'Malley et al., 1996). There is evidence that CM can be used to treat comorbid substance use disorders, as a trial targeting only cocaine use in those who used both cocaine and opioids produced large and unexpected reductions in opioid use (Silverman et al., 1998). In addition, previous research has found that using CM can be effective in increasing simultaneous abstinence from multiple substances (Piotrowski et al., 1999).

There is a surprising lack of research aimed at evaluating multi-component interventions that integrate CM with evidence-based CBT and pharmacotherapy. The addition of CBT is critical because CM interventions alone have been limited in their ability to maintain behavior change after the removal of the contingency (Dallery & Raiff, 2012). With the inclusion of evidence-based CBT and a tele-health clinic for NRT, we will be able to

evaluate whether the tele-health mCM intervention keeps participants engaged in treatment, improves NRT adherence, reduces delay discounting (i.e., decreased subjective valuing of rewards that are temporally distant), and increases self-efficacy, all of which have been predictive of long term abstinence from both alcohol and tobacco.

Objectives:

The purpose of this pilot project is to gather feasibility data to support grant development for a combined alcohol and smoking tele-health mCM intervention that will effectively treat both disorders. The study will be undertaken with the following objectives:

1) Develop a multi-component alcohol and smoking tele-health mCM intervention in two successive cohorts of five participants. The first cohort of treatment completers (n = 5) will provide qualitative data from participants and therapists, which will be utilized to modify the treatment components including the therapist manual, mCM apps, and data collection procedures. The second cohort (n = 5) will yield qualitative and quantitative data to refine the intervention and in preparation for a pilot trial.
2) Evaluate the feasibility and acceptability (e.g., mCM app reliability, mCM app procedures completion, patient satisfaction) of a tele-health mCM intervention; relative to a comparison group receiving a tele-health intervention without mCM, This will be evaluated in a third cohort that will include a pilot trial randomizing participants to telehealth with mCM (n = 30) or to a comparison group receiving the same phone counseling (Cognitive Behavioral Therapy; CBT) and tele-medicine without mCM (n = 15).

Methods:

Study Design

A successive cohort design will be used to refine the intervention, resulting in three cohorts of participants with AUD and cigarette use. The first two cohorts will focus on treatment refinement, followed by a third cohort participating in a pilot trial.

Successive Cohort Design Stage 1: Feasibility

The successive cohort design (SCD; Epstein et al., 2007) is an iterative process designed to systematically refine and modify behavioral treatments in the early stage of development. The SCD model is a good fit for Stage 1 research, which is designed to generate or modify existing protocols and conduct preliminary testing before initiating larger efficacy trials (Stage II) and effectiveness research (Stage III).

The first cohort of five participants will complete the tele-health mCM intervention and provide evaluative feedback during an in-depth interview administered at the end of the study, and described in the Measures section below. A coding scheme will be developed for categorizing comments made during the interview based on the study components (e.g., mCM procedures, CBT, interface with smart phone app), subcomponents (e.g., mCM feasibility, CBT burden), and the evaluations drawn (e.g., CBT session too long, video upload still unclear after mCM training).

Successive Cohort Design Stage 2: Treatment Refinement

After the intervention and study have been modified based on information learned from the first cohort, we will treat a second cohort (*n* = 5). Though qualitative data will be evaluated and utilized using methods similar to those of the first cohort, the second cohort will more closely evaluate quantitative data. We will explore relationships of sociodemographic, baseline substance use, and psychiatric comorbidity variables with treatment retention and outcomes. This will identify treatment components to modify or enhance to maximize treatment effectiveness.

Successive Cohort Design Stage 3: Pilot Trial

After treatment modifications from cohort 2, we will conduct a pilot randomized controlled clinical trial. The primary goal of the trial is to evaluate the efficacy of a combined tele-health mCM intervention. The pilot trial will use a two-group design in which 45 participants with an AUD who smoke regularly will be randomized to either:

TELE-HEALTH MOBILE CONTINGENCY MANAGEMENT (mCM) INTERVENTION, a proactive tele-health intervention that combines evidence-based telephone CBT for alcohol 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 (CM).

OR

TELE-HEALTH FOR ALCOHOL AND SMOKING CESSATION, a proactive tele-health intervention that will provide controls for therapist, medication, time and attention effects. The tele-health intervention provides the same evidence-based telephone CBT for alcohol and smoking cessation, and tele-medicine clinic for access to smoking cessation pharmacotherapy as in the mCM intervention, but does not include mCM. Instead, participants will receive monetary compensation for each assessment, regardless of abstinence ($3.00 for breathalyzer, $1.00 for CO). No escalating or reset contingencies will be used to alter monetary compensation amounts in this group. Mobile assessments of abstinence will occur on the same schedule as the tele-health mCM condition.

C.9.2. Participant Recruitment, Eligibility, and Screening

A total of 55 participants with AUD and smoking will be enrolled across the three cohorts. Participants will be recruited from primary care and substance abuse clinics at

Duke University. We will also post flyers at local hospitals and in community settings. To allow more detailed analysis of the tele-health mCM intervention that is the focus of this study, the pilot trial conducted with the third cohort will randomize 30 participants to the tele-health mCM intervention, and 15 to the tele-health smoking cessation comparison condition.

Completers of the proposed tele-health mCM intervention will provide self-report data and evaluative feedback during an in-depth interview administered at the end of treatment, and described in the Assessments section below. Content analysis of the resulting data will evaluate study components (i.e., mCM procedures, CBT, interface with smart phone app, NRT utility and adherence) and subcomponents (e.g., mCM feasibility, CBT burden) that they address and the evaluations drawn (e.g., CBT session too long, video upload still unclear after mCM training). We will explore sociodemographic, substance use, and psychiatric comorbidity variables to examine the magnitudes of their associations with treatment retention and outcomes. This will identify areas of the treatment potentially in need of modification or enhancement to maximize its effectiveness. A summary of the findings will be evaluated by our team of clinical researchers (Drs. Dedert, Beckham, Calhoun), all of whom are experienced in treatment development and trial design, will evaluate a summary of the findings and determine changes to make to the intervention.

Recruitment

Participants will be adult men and women with mild to moderate AUD who smoke cigarettes. We aim to enroll 55 participants in the study. In order to reach this enrollment goal, we anticipate that 70 participants will sign consent forms. 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.craisglist.com and www.dukelist.duke.edu. We will also utilize Duke IRB-approved recruitment services such as ResearchMatch and the Duke Clinical Research Unit Research Volunteer Registry to invite patients who have indicated interest in research to participate in this study. Finally, Duke providers who would like to invite potentially eligible patients to participate in this study will send an invitational letter with a basic study description and contact information for study staff. This letter asks patients to let the provider know if they do not wish to be contacted about the study. For the remaining patients, after waiting at least 10 days, the provider will deliver contact information by secure Duke email to study staff. Study staff will then contact patients to discuss the study and invite the patient to screen if the patient is potentially eligible. An example of the type of letter providers will send is included for IRB review. However, please note that providers will be free to write their own letters or modify this letter according to their clinical judgment of the type of information that will be most useful for informing their patients.

Our study team will use social media to reach potentially eligible participants. We have developed a Facebook page for posting IRB-approved study flyers and information for this and other studies in the Traumatic Stress and Health Research Laboratory, https://www.facebook.com/Duke-Traumatic-Stress-and-Health-Research-Lab-379366159145563/. We plan to place pictures of our study flyers on the Facebook page, and use Facebook's post boost to draw attention to the post. The post itself will say "Enroll now!" or "Now enrolling!" We will also plan to use Facebook ads to target potential participants within a 50-mile radius of Duke. The proposed Facebook ad photos and text have been uploaded to the recruitment materials section of the eIRB space. If any participant contacts the email associated with the Facebook page (TSHRLab@dm.duke.edu, he/she will be sent an automatic email response. Potential participants will also be allowed to indicate that they would like to be contacted by the study coordinator by completing a "Contact Me" RedCap survey that gathers their name and contact information.. We have attached a screenshot of the RedCap survey with this IRB submission, and here is the link to the RedCap Survey: https://redcap.duke.edu/redcap/surveys/?s=DCAJXYDCEY. Any participant who completes the RedCap survey will be contacted by the study coordinator using the IRB-approved telephone script.

If any potential participant contacts the PI or study coordinator by email via clinicaltrials.gov, we will send him/her a secured email response asking that he/she contact the study coordinator by phone. 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.

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 or traditional mail. Some of our participants strongly prefer email communication re: appointments, so we will plan to use secured emails re: appointments, etc. for those participants who prefer it.

Three study visits (screening visit, end-of-treatment, and six-month follow-up) will occur at Duke-leased space at Hock Plaza, and the others will occur via telephone. Once a participant reports to the laboratory to begin the study, the study staff member obtaining consent will explain the study in detail, provide the participant with an IRB-approved written consent form explaining the procedures and risks, and answer any questions. The initial consent process and documentation takes place in a quiet, private office at Hock Plaza, and participants are given the chance to thoroughly read the consent prior to participation. Participants are given a copy of the signed informed consent form, and are given phone numbers to call if they have additional questions about the consent form or the research, if they have any problems during the study, or

if they have questions about participating in research studies in general. No study procedures will begin until informed consent has been obtained.

Participants

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

- currently meet criteria for DSM-5 alcohol use disorder (meeting 2-8 criteria for AUD)
- have been engaging in hazardous drinking over the past month, defined as either exceeding a mean of 14 standard drinks/wk for men, 7 drinks/wk for women; or by consuming ≥5 on at least one occasion in the last month for men, ≥4 drinks on at least one occasion in the last month for women
- currently smoke at least 7 cigarettes per week
- can speak and write fluent conversational English
- are between 18-80 years of age
- are willing to make an attempt to quit both alcohol and smoking

Participants will be excluded from the study for the following:

- are expected to have unstable medication regimen during the study
- are currently receiving non-study behavioral treatment for alcohol use disorder or smoking
- have alcohol use disorder that exceeds our severity threshold of 8 symptoms or exhibit significant risk for alcohol withdrawal.
- have AUD that is in early remission, with no symptoms evident over the past month
- have experienced myocardial infarction in past 6 months
- contraindication to nicotine replacement therapy with no medical clearance to participate in the study
- use other forms of nicotine such as cigars, pipes, or chewing tobacco
- are currently pregnant
- have a primary psychotic disorder or current manic episode
- have had substance use disorder (other than alcohol or nicotine) in the preceding 3 months
- are currently imprisoned or in psychiatric hospitalization

Table 1. Study Procedures

Session #	Location of Visit	Procedures	Payment
1	Lab	Consent; psychiatric interview; questionnaires; urine drug screen and pregnancy test; carbon monoxide and breath alcohol readings	$50

1-3 weeks			
2	Phone	Counseling session 1 of 4	n/a
1 week			
3	Phone	Counseling session 2 of 4; begin practice mCM monitoring, begin bupropion if eligible	Up to $34 for monitoring
1 week			
4	Phone	QUIT DATE; counseling session 3 of 4; begin active mCM monitoring OR active mobile monitoring (MM); begin nicotine replacement therapy (NRT)	n/a
2 weeks			
5	Phone	Counseling session 4 of 4; continue active mCM monitoring OR active mobile monitoring	n/a
1 week			
6	Phone	Final week of abstinence induction in mCM group; MM group continues monitoring; questionnaires	Up to $702 (mCM) OR $132 (MM) for active monitoring; $50 for assessment
2 weeks			
7	Lab	End thinning (mCM group) OR mobile monitoring (MM group); return equipment; questionnaires; end NRT and bupropion; saliva sample; interview about treatment	Up to $400 (mCM) OR $88 (MM) for continuing monitoring; $35 for equipment return; $50 for assessment; $50 for saliva sample
6 months after Session 4			
8	Lab	Questionnaires; saliva sample; blood spot collection	$50 for assessment and $50 for saliva sample; $50 for blood spot test
TOTAL COMPENSATION POSSIBLE:		**mCM Group** **Mobile Monitoring**	**$1521*** **$639***

*because compensation depends partly on the number of alcohol breathalyzer prompts, it is possible that the total compensation will vary slightly.

Consent and Screening Procedures

Prior to study entry, potential participants will complete a screening visit, including informed consent, the diagnostic interview, breath samples to assess alcohol and CO level, symptom self-report measures, alcohol and smoking history, mental health treatment history, and sociodemographic data. Participants will complete the Structured Clinical Interview for DSM-IV (First, Spitzer, Gibbon, & Williams, 1994) to diagnose AUD and psychiatric comorbidities. Urine samples will be obtained to screen for illicit drug use. Because urine drug screen results are not exclusionary, but rather provide descriptive information about the study population, any participant may refuse to provide a urine sample for drug screen purposes. We have not added this caveat to the informed consent form because we want to encourage participants to provide the urine samples. At any time, if a participant refuses to provide a urine sample, this will be documented as a protocol deviation. Of note, to date we have had no participants in studies in the Traumatic Stress and Health Research Laboratory refuse to provide a urine sample for drug screening. Urine drug screen results are collected on the participants' screening cover sheet in their research folder, and then are entered into a password protected database that is stored on the Duke psychiatry protected server; this database contains only deidentified data. 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. Breath alcohol level (BrAC) will be assessed and must be 0.0 to continue with the screening.

Participants will be screened for good health via self-report. If any participant indicates that he/she has a primary care provider and/or other treating physician, and the participant endorses contraindications to medications our study physician plans to prescribe for smoking cessation, medical clearance to take those medications will be obtained from that care provider (see letter to physician). If the request is denied, potential participants will be excluded from taking any contraindicated medications. If the request is not returned within two weeks, the study physician will determine eligibility for study medications. We are seeking medical clearance rather than excluding participants from taking smoking cessation medications to ensure that we are not prematurely ruling out participants who may benefit from smoking cessation pharmacotherapy. We are consulting with their primary physician to determine if the use of nicotine replacement therapy is appropriate and safe given their current physical status and medication regimen. All participants who are medically eligible will also be prescribed bupropion. 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 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.

Telehealth Mobile Contingency Management (mCM) Intervention

All enrolled participants will receive a tele-health intervention that combines evidence-based telephone CBT for alcohol and smoking cessation, access to nicotine replacement therapy (NRT), and intensive CM therapy administered via a smart-phone based application (mCM). The treatment components are separately described below. After the baseline assessments to determine eligibility, participants who screen into the study will be given smart phones with the mCM app. Participants will also receive a breathalyzer and CO monitor. Participants will receive training on mCM procedures by study staff. They will then be asked to start submitting practice alcohol and CO monitoring videos the day after the screening to provide more time to become expert at the mHealth technology and troubleshoot any problems with the assistance of the study staff.

Once any necessary approvals for study medications have been provided by the participant's treating physician, participants will advance to the practice week, in which participants will be reinforced for completing readings, not contingent on abstinence. The practice monitoring will be followed by 3 weeks of Abstinence Induction mCM in which monetary reinforcement is provided for every scheduled video, contingent on alcohol and smoking abstinence. This will be followed by two weeks of Thinning mCM in which the monetary reinforcement remains contingent on alcohol and smoking abstinence, but the reinforcement is provided once weekly for providing videos bioverifying alcohol and/or smoking abstinence throughout that week. Participants can earn $200 for the week if they bioverify abstinence from both alcohol and cigarette smoking throughout the week, and must submit at least 90% of weekly videos. If participants bioverify abstinence from only one substance throughout the week, they will be reinforced $50. The frequency of monetary reinforcement is being reduced in the Thinning mCM phase to assist participants in transitioning from intensive monetary reinforcement toward managing triggers with infrequent reinforcement. This is designed to prevent relapse and promote long-term abstinence from alcohol and cigarette smoking. Target quit dates will be set for the end of the practice week. Participants will provide substance use data throughout the mCM phase by completing their readings using the mCM app. They will complete interview and self-report measure outcome assessments at 3 weeks post-quit date (end of Abstinence Induction), at 5 weeks post-quit date (end of Thinning mCM), and at 6-month follow-up.

Mobile CM Procedures

As part of a previous project, we developed a smart phone app that allows CM to be used outside the clinic to address substance misuse (screenshot shown in Figure 1). On this app, individuals can generate a videorecording of themselves breathing into 2 small monitoring devices. The breathalyzer and CO monitor are both hand-held battery

operated instruments that measure alcohol in g/dL and CO in ppm, providing lightemitting diode (LED) readings that are visible from the phone's video recorder.

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 video recordings 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 we make no medical claim on the iCO™ Smokerlyer® that it can be used to screen for CO poisoning.

For each video recording, participants will be asked to 1) begin a recording using the smartphone device; 2) show the pre-assessment zero breathalyzer reading to the camera; 3) expel air from lungs into the breathalyzer while being video-recorded; 4) show the final reading to the camera; and 5) log in to a secure website through the app interface on the Google Android operating system that includes pages tailored to each participant, and upload the video recordings using encrypted network connections. Immediately after completing a breathalyzer reading, participants will provide a CO reading following the same procedures. Participants will receive a chart with descriptions detailing the rules for earning incentives. Because reinforcers are most effective when delivered immediately after the target behavior is performed (Lattal, 2010), the phone app is designed to allow therapists to provide quick feedback on abstinence status, financial amount earned, and how the amount was calculated. Participants will be informed that results are pending video review from the study coordinator to confirm validity. Based on a previously published protocol using mobile CM for alcohol, the alcohol assessments for our study will occur from awakening until the participant goes to sleep at night, with a higher probability of assessment occurring during high-risk alcohol consumption times during the day (Alessi & Petry, 2013). High-risk consumption times will be based on alcohol consumption patterns, rather than smoking patterns, because alcohol is eliminated from body more quickly than CO from smoking. The alarm algorithm targets a mean of 10 readings each week, with a variable number of alarms across weeks. This will ensure that there are no times in which participants are aware that there will be no more assessments for the week. The app is designed to alarm-prompt assessments that could potentially occur at any point during

waking hours, occurring on at least five high-risk periods each week, and twice in the same evening on at least two evenings each week. This procedure is designed to ensure that participants do not know when they will have a long period of time between readings that would provide an opportunity for drinking alcohol that would be metabolized before the next reading. When prompted, participants will have one hour to submit their reading, with reminder prompt at 30 minutes. Similar procedures have been employed with good adherence and have been well-tolerated in one published study (Alessi & Petry, 2013). Participants will be allowed to opt out of alarms for one hour if there are circumstances that would prevent them from safely or conveniently responding to an alarm (e.g., while driving, at a meeting, etc.). When participants are alarm-prompted to submit an alcohol reading, they will also receive a text message sent to their personal phone number informing them that they have an alcohol reading due for submission. The text message will read "A research alarm has gone off. Please upload a video by xxxx!" Nothing in the text message to participants will give away the nature of this study. This text message is designed to assist participants who are in loud areas or will not be near enough to the study-provided phone to hear the prompt. This additional informational procedure is based on qualitative feedback from participants in our first two cohorts, who wanted to adhere to monitoring but did not always hear the study phone prompts. Participants who prefer not to receive text messages on their personal phones will be able to opt out of text messages from the study at any time.

Because CO from smoking a cigarette is metabolized more slowly than a drink of alcohol, CO can be assessed less frequently. To take advantage of this feature of CO, and to reduce participant burden, we will ask participants to provide CO assessment videos at two times each day chosen by the participant, as long as the two CO assessments for that day are at least 8 hours apart. By designing the protocol to have CO assessments at times chosen by the participant, we expect to relieve participants of the burden to carry both the alcohol breathalyzer and the CO monitor during the day. This way, only the breathalyzer must be kept with the participant to respond to alarms. For example, participants could choose to complete the CO assessments before leaving the house in the morning and after returning in the evening. Participants will submit videos as needed before the practice week as study staff coordinate approvals for smoking cessation pharmacotherapy with the participants' medical provider. Once the study practice week is initiated, participants will be compensated for practicing this data collection for one week (see contingency table in mCM manual). Through the smart-phone app, participants log-in to a secure website to upload their video recordings and see personalized information regarding their reinforcement information. Study coordinators can monitor validity and compliance on a daily basis and offer feedback to ongoing participants regarding compensation so they are well-practiced at the procedures by the time contingent reinforcement is initiated. During the practice week, participants will be compensated $2.00 for completing a valid alcohol reading, and $1.00 for a valid smoking reading. After the practice week, the MM group will receive $3 for providing a valid on-time Breathalyzer reading and $1.00 for providing a valid on-time CO reading, regardless of whether they are abstinent from the substance. After the

practice week, monetary reinforcement for the mCM group becomes contingent on abstinence, operationally defined as breathalyzer readings that are < 0.02 BrAC and CO readings that are < 6 ppm (after the first week). In the first week of abstinence, smoking cessation compensation will be based not on CO < 6ppm, but on a proportion of participant's baseline CO as defined by Lamb (Lamb, Morral, Kirby, Iguchi, & Galbicka, 2004). 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. If on each day, if a participant submits all required videos, and all videos suggest that they have been abstinent from both alcohol and cigarettes, they will receive a $5 bonus (Sunday through Wednesday) or a $10 bonus (Thursday through Saturday). Participants will be asked to return the monitoring equipment at the end of the monitoring period. To ensure that participants return the breathalyzer, CO monitor, and phone, we are providing postage paid return mailers and adding a $35 incentive for equipment return.

Cognitive Behavioral Therapy for Alcohol Use Disorder and Smoking Cessation
Tele-health mCM treatment will include 4 sessions of CBT telephone counseling for alcohol and smoking cessation, outlined for the therapists in the treatment manual. Though CBT has not been combined with CM in previous AUD treatment, CBT has been used in combination to concurrently treat alcohol use and smoking, and it was feasibly implemented and well-tolerated (Laaksonen, Vuoristo-Myllys, Koski-Jannes, & Alho, 2013). We have developed the CBT manual by drawing on the cognitive-behavioral coping skills therapy portions of the treatment manual generated from Project MATCH (NIAAA coping skills manual from Project MATCH, 2003) and the Integrated Care for Smoking Cessation manual (McFall et al., 2010), two treatment with empirical evidence of efficacy (R. Kadden, Carbonar, Litt, Tonigan, & Zweben, 1998). Due to the substantial overlap in treatment procedures and skills acquired in CBT for alcohol and smoking, the first 40 minutes of each session will be devoted to material that applies to both problems. The final 20 minutes of each session will primarily be devoted to CBT for alcohol, as the CBT for alcohol from which our manuals were developed has more total treatment time than the manual from which CBT for smoking was adapted.

Pharmacotherapy for Smoking Cessation
Treatment will include standard pharmacotherapy for smoking cessation. This consists of bupropion, nicotine patch, and an 8-week course of < 2 rescue methods (e.g., nicotine gum, lozenge) in participants for whom these medications are not contraindicated or who receive medical clearance from a physician. Participants will be screened for suitability for NRT or other smoking cessation medication. Participants who report being contraindicated to bupropion or NRT (i.e. high blood pressure not controlled by medication) must obtain authorization from their physician prior to receiving the corresponding medication. If the patient does not have a physician, or the physician does not respond to information requests, Dr. Moore will make determinations about whether to authorize study medications. Dr. Moore will prescribe a tailored amount and delivery type of NRT based on number of cigarettes smoked per

day, quit history, medical conditions, and psychiatric comorbidities. NRT and bupropion will be provided *via* mail. Dr. Moore will write the NRT and/or bupropion prescriptions and work with other study staff and participants' primary care physician to discuss contraindications. Eligible participants will be provided bupropion for eight weeks. Participants will be informed that they can discuss whether or not to continue bupropion use for relapse prevention with their personal physician. At the end of the study's course of bupropion, participants will be reminded to confer with their physician re: continued bupropion use. For participants who relapse to smoking or are unable to quit, Dr. Moore will make decisions about whether to prescribe additional NRT to assist the participant in their continued attempts to stop smoking.

6-Month Follow-Up

All participants will be asked to provide a saliva sample to bioverify smoking abstinence. Alcohol abstinence will be measured by self-report, breathalyzer, and a blood spot sample that measures PEth at the 6-month follow-up. Participants will be encouraged to attend the 6-month follow-up assessment in the lab. However, if participants are unable due to transportation issues or decline to attend the 6-month follow-up, we will administer interview and questionnaire measures by phone and collect saliva samples by mail.

Drinking and smoking will also be monitored by the smart phone app with entries during the day for any drinking and smoking occasions. In addition, before the participants' set bedtime, they will be prompted to estimate their total amount of drinking and smoking during the day. Finally, at the 6-month follow-up, participants will complete a timeline follow-back assessment of alcohol use and smoking, conducted by phone. At the screening session, we will administer a questionnaire developed specifically for this study that asks about beliefs regarding concurrent treatment of substance use disorders. This is called the Concurrent Treatment Questionnaire in Table 2. This will be administered at the screening session, end of monitoring, and 6 month follow up. The NOSIE, Nicotine and Other Substance Interaction Expectancies Questionnaire, will also be administered at these points (Rohsenow, et al. 2005).

Table 2: Study Baseline and Outcome Measures

	BL	CBT	PT	EM	FUP
BACKGROUND VARIABLES					
Demographics	X				
AUDIT	X		X	X	X
RAPI	X		X	X	X
Sheehan Disability Scale	X				X
FTND	X		X	X	X
SCID	X				
CIWA	X				
QSU	X		X	X	X
MNWS	X				
Smoking History measure	X				
PANAS	X		X	X	X

AASES	X	X		X	X
RSEQ	X		X	X	
ISI	X		X	X	X
MTSS	X	X	X	X	X
NRT Contraindications	X				
DAR	X		X	X	X
Patient Health Q-9	X			X	X
Alcohol Readiness to Change	X		X	X	X
Delay Discounting task	X		X	X	X
Cigarette Purchase Task	X			X	X
Alcohol Purchase Task	X			X	X
Self-efficacy for Smoking	X	X	X	X	
NSSI checklist	X			X	X
Fidelity ratings		X			
Penn Alcohol Craving Questionnaire	X	X	X	X	X
ITASr-SF			X		
Positive and Negative Expectancies	X	X	X	X	X
Smoking Consequences Questionnaire	X	X	X	X	X
Anxiety Sensitivity Index-Revised 36	X			X	X
OSS	X			X	X
Voils Medical Adherence				X	
Timeline Follow Back					X
PROCESS MEASURES					
Smoking cessation aids			X	X	X
Conners' ADHD Scale	X			X	X
Barratt Impulsivity Scale	X			X	X
Conners CPT	X			X	X
Iowa Gambling Task	X			X	X
Balloon Analogue Risk	X			X	X
Concurrent Treatment Q	X			X	X
NOSIE	X			X	X
Medication Adherence	X			X	X
Qualitative Interview				X	
Treatment feasibility measure				X	
OUTCOME MEASURES					
Efficacy: Prolonged Abstinence; 7-day; 30-day abstinence			X	X	X
Quit Attempts			X	X	X
Tobacco Exposure Questionnaire				X	X
Time-line Follow-Back-Quit Attempts					X

***BL=baseline; CBT= phone counseling sessions, PT=post-treatment/thinning; EM=end of monitoring; FUP= 6-month follow up**

To assist in evaluating potential study exclusion for the alcohol withdrawal criterion, we have adapted the Clinical Institute Withdrawal Assessment for Alcohol to ask about any recent periods of time in which potential participants have abstained from alcohol (Sullivan et al., 1989). This will be administered at the screening session. Demographics information will be collected at the screening session, and the OSS will be administered at the screen, end of monitoring, and 6 month follow up to measure changes in occupation status and household income.

Smoking-Related Measures

The Fagerström Test of Nicotine Dependence (Heatherton, Kozlowski, Frecker, & Fagerström, 1991), Questionnaire on Smoking Urges (Tiffany & Drobes, 1991), the Minnesota Nicotine Withdrawal Scale (Patten & Martin, 1996), and a smoking history questionnaire (e.g., number of cigarettes smoked/day, age of first smoking, number of previous quit attempts) will be used to measure smoking behaviors at baseline. In addition, the FTND, QSU, Dimensions of Anger Reactions, and Patient Health Questionnaire will be administered at the end of Abstinence Induction, end of Thinning mCM, and 6-month follow-up. Participants will also report number of cigarettes smoked each day, and days of smoking abstinence.

Participants will be asked to respond to several questions to determine if the patient is contraindicated to receive NRT. Collection of alcohol and smoking use data will allow calculation of dual abstinence days and longest duration of dual abstinence. The Cigarette Purchase Task will be used to evaluate the behavioral economics of cigarette use (MacKillop et al., 2008), and the Alcohol Purchase Task will evaluate the same for alcohol use (Acuff & Murphy, 2017). At five time points (baseline, quit date, end of abstinence induction, end of treatment, 6 month follow-up), participants will complete the Smoking Consequences Questionnaire, the Penn Alcohol Craving Questionnaire (Flannery et al., 1999), and the Alcohol Expectancies measure (Lee et al., 2015).

Treatment Process Measures

Self-efficacy will be assessed with the Alcohol Abstinence Self-Efficacy Scale for alcohol (DiClemente, Carbonari, Montgomery, & Hughes, 1994) and the Relapse Situation Efficacy Questionnaire for smoking (Gwaltney, 2001). Motivation for smoking cessation will be measured with the Motivation to Stop Scale (Kotz, Brown, & West, 2013). Attitudes toward behavior change with respect to alcohol and smoking behavior will be measured with a brief measure of self-efficacy for quitting alcohol and the Readiness to Change Questionnaire (Heather, Rollnick, & Bell, 1993; Rollnick, Heather, Gold, & Hall, 1992). In addition, confidence to keep from smoking when craving, facing social pressure, or experiencing negative emotion will be measured with the Self Efficacy to Overcome Personal Barriers to Cessation scale (Velicer, DiClemente, Rossi, & Prochaska, 1990). Affective states will be measured with the Positive and Negative Affect Scale (Watson, Clark, & Tellegen, 1988). Sleep disturbance will be measured with the Insomnia Severity Index (Morin, Belleville, Belanger, & Ivers, 2011). These measures will be administered at the baseline visit and administered by phone by study staff at the end of Abstinence Induction mCM, end of Thinning mCM, and 6-month follow-up assessments. At the end of Thinning mCM study session, we will ask participants to report on any problems with CO monitoring, especially regarding the validity of monitoring. All phone counseling sessions will include assessment of alcohol consumption and smoking behavior over the past week, as well as readiness to change and self-efficacy measures for alcohol and smoking.

Process measures will include number of telephone counseling sessions completed and medication adherence. Medication adherence will be defined as using > 80% of prescribed medications, as 80% adherence to NRT has been predictive of doubled abstinence at 6 months (Catz et al., 2011). The primary self-report measure of adherence will be the number of days NRT is used during the study period. Days of NRT use will be recorded at each telephone counseling call. Participants will also be screened for NRT or other smoking cessation aid use at each follow-up. Participants will complete the Voils Medical Adherence Questionnaire to measure adherence to smoking pharmacotherapy. We will measure patient satisfaction with a questionnaire tailored to this study's treatment aims.

At the end-of-treatment visit, each participant will complete a qualitative interview aimed at gathering detailed information on strengths, weaknesses and general user interface components of the intervention. The interview will vary in length, but we expect approximately 30 minutes for participants to provide detailed feedback on the intervention in this interview.

Participants will complete the computerized delay discounting task for hypothetical monetary values. They will choose between a fixed amount with fixed delay and various monetary amounts available immediately (Garcia-Rodriguez, Secades-Villa, Weidberg, & Yoon, 2013). Delays and monetary options will be presented in ascending order and adjusted with procedures that successively approximate an indifference point. The delay discounting task will be administered by smart phone app at the baseline screening session, the end of Abstinence Induction mCM, end of Thinning mCM, and 6-month follow-up. To assess the impulsivity mechanism more broadly, we will administer two self-report measures of impulsivity and disinhibition at baseline, end of Thinning mCM, and 6-month follow-up: the Conners' Adult ADHD Scale, and the Barratt Impulsivity Scale (BIS-15; Spinella, 2007). We will also administer 3 computerized tasks at office vists occurring at baseline, end of Thinning mCM, and 6-month follow-up: the Conners Continuous Performance Test, the Iowa Gambling Task (Bechara et al., 1994), and the Balloon Analogue Risk Task (Lejuez et al., 2002). Anxiety sensitivity will also be measured at baseline, end of moritoring, and 6-month follow-up using the Anxiety Sensitivity Index-Revised 36 (Taylor & Cox, 1998). Because nonsuicidal self injury (NSSI) is not uncommon in persons with alcohol use disorders, especially those with other comorbid psychiatric diagnoses, we would like to include a brief measure of NSSI at several time points in the study, i.e., baseline and follow-up visits. This measure will be administered to all participants at these time points. Participants can refuse to complete the measure. However, in our laboratory's experience, participants typically do not take issue with completing this brief measure.

Treatment Fidelity and Therapeutic Alliance Measurement

We will utilize a revised version of the Yale Adherence and Competence Scale system to measure counselor adherence in delivering behavioral treatments for substance abuse disorders (Carroll, 2000). The system includes checklists for measuring critical treatment

elements. A random selection of 20% of the counseling sessions will be recorded and rated for counselor fidelity/adherence. Audio recordings of these sessions will be made using an iPad or iPhone (see "Protection Against Risk and Data Security Measures" herein for additional information); only the therapist's voice will be recorded during the conversation. To measure therapeutic alliance, the 16-item Individual Treatment Alliance Scale Revised Short Form (ITASr-SF) will be utilized. The ITASr-SF has been shown to be related to treatment dropout and treatment response in behavioral interventions (Pinsof, Zinbarg, & Knobloch-Fedders, 2008). This will be administered during the end of Abstinence Induction mCM phone session.

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 alcohol withdrawal and quitting smoking. Symptoms of alcohol withdrawal may include headache, insomnia, sweating, shakiness, and rarely, seizures or hallucinations. We will minimize risk of alcohol withdrawal by screening participants at high risk for withdrawal out of the study. However, in case enrolled patients experience alcohol withdrawal that is not reported at the screening visit, we will instruct patients to report symptoms to research staff. The physician prescriber will have the flexibility to adjust medications as needed to account for changes in clinical variables such as withdrawal, craving, and smoking lapse pattern. Participants will be encouraged to utilize emergency resources at Duke as needed to address these symptoms.

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 Against Risk and Data Security Measures" for details on reduction of risk with regards to the proposed videotaping.

Protection Against Risk and Data Security Measures

While participants may benefit from quitting smoking and alcohol 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 alcohol 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 that they do not wish to answer. They are also informed that they are free to decline participation in any procedure 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 any laboratory visit the participant's breathalyzer results are above the legal limit and he/she has driven to the appointment, 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 does not meet legal criteria for intoxication. If a patient does not wish to remain at the medical center, and voices intent to drive a vehicle while intoxicated, 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.

Audio recordings of counseling sessions and qualitative interviews will be made using a Duke-owned iPhone or iPad that is encrypted at levels compliant with FIPS 140-2 standards. The device to be used will be hardened such that only the video recording capability will remain. Recordings will be moved from the device to the Duke shared server (duhsnas-pri\dusom_psych\private\Beckham Research Lab\mCM for Alcohol and Smoking) as soon as possible after the recordings have been made, and will then be deleted from the mobile device. Any device that is not in use will be stored in a locked filing cabinet in Dr. Dedert's office. Recordings of therapy sessions will remain on the Duke shared drive until they are evaluated for fidelity, and recordings of qualitative interviews will remain there until they have been analyzed for content. After this review, recordings will be copied to an encrypted external hard drive for permanent storage. The encrypted hard drive will be stored in a locked file cabinet in Dr. Dedert's lab space at Hock Plaza. Only the key personnel listed on the staff listing will have access to the encryption password and/or the hard drive.

No "key personnel outside Duke" will have access to identifying information on subjects. Two key personnel outside Duke will provide consultation to Dr. Dedert and his study staff. Stephen Maisto, Ph.D., SUNY Upstate Medical University, is a clinical psychologist with expertise in developing evidence-based behavioral interventions for alcohol use disorders and hazardous alcohol use. He has also conducted research into alcohol treatment process and outcome measurement. Dr. Maisto will have primary responsibility for training Dr. Dedert and study staff on the phone counseling portion of the intervention. Daniel Kivlahan, Ph.D. is a clinical psychologist with the Department of Veterans Affairs. He has expertise in clinical research on alcohol and implementation of new treatments for alcohol and substance use disorders. Dr. Kivlahan will provide insight into telephone counseling for alcohol misuse as well as assist in the development and refinement of the treatment, and consult on the measurement of alcohol outcomes.

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 Research Lab\mCM for Alcohol 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 Research Lab\mCM for Alcohol 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 DSRT training.

Staff Training

Of the measures in this study, only the SCID and the qualitative data interview require specific training or skills for administration. As in our other studies, multiple SCID diagnostic raters will be utilized over the data collection period. Each rater will be trained using SCID standardized training (i.e., manual, videotapes, and co-rating training with a trained rater). Interrater reliability for diagnoses based on videotapes of patient interviews across previous studies has been high with a kappa = .96. Additionally, staff providing these diagnostic interviews are trained in use of the Psychiatric Emergency Standards of Practice. Training is completed and supervised by a Master's level clinician with experience in psychiatric diagnosis, or by Ph.D. level clinical psychologists. Regular clinical supervision is provided on a monthly basis in team meetings, and consultation is provided regularly to interviewers.

The qualitative data interview will be administered by an experienced clinical interviewer with an advanced degree (masters or doctoral). Interview sessions will be audio recorded to permit detailed analysis of participant comments and ensure that interviews are conducted skillfully and with respect for participant rights. Audio recordings are made using an encrypted iPad or iPhone; see "Protection Against Risk and Data Security Measures" herein.

Data and Safety Monitoring Plan

Quitting smoking and alcohol 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 phone 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, DUMC IRB-approved standards of practice for the evaluation of risk of suicide and homicide. 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.

Outcome Measurement and Biochemical Verification

Self-reported and bioverified prolonged abstinence from alcohol, smoking, and dual abstinence at the 6-month follow-up will be the primary end-point. Prolonged abstinence will exclude substance use in the first two weeks following the quit date to give participants time to achieve initial abstinence (Hughes et al., 2003). Self-reported prolonged abstinence will be verified by breathalyzer alcohol assessment and assay of cotinine, a metabolite of nicotine in the saliva. Saliva samples will be collected from participants at end of treatment, and at 6-month follow-ups. Deidentified saliva samples will be sent to Salimetrics, and there they will be analyzed for the presence of cotinine using a standard cut point of 10 ng/ml to determine abstinence. A blind sample of 5% will be run again to assure test accuracy of saliva samples. All participants will be asked to provide saliva samples. However if it seems likely that they will have a positive saliva cotinine according to the Tobacco Exposure Questionnaire administered at end of

monitoring at 6-month follow-up, the collected sample may not be sent to Salimetrics for testing.

Participants will also report alcohol consumption patterns such as standard drinks/week, heavy drinking episodes (drinking enough so that BrAC would have reached 0.08g/dL), proportion of days abstinent, and achieving recommended drinking limits ($\leq$14 drinks/wk and <5 drinks/day for men; $\leq$7 drinks/wk and <4 drinks/day for women). Because bioverification of long-term alcohol abstinence is not substantially more reliable than self-report (Babor, Steinberg, Anton, & Del Boca, 2000), alcohol outcomes will primarily be assessed with self-report. Participants will provide breathalyzer verification of alcohol abstinence at the end of Thinning mCM and 6-month follow-up visits. Participants will also report number of cigarettes smoked each day, and days of smoking abstinence. Collection of alcohol and smoking use data will allow for calculation of dual abstinence days and longest duration of dual abstinence. Participants will be asked to submit a saliva sample for biochemical validation. Saliva will be stored in a freezer in a locked office. At the end of the study, the project coordinator will personally mail all saliva samples to the appropriate laboratory to be analyzed for the presence of cotinine. The saliva will only be tested for cotinine, a by-product of nicotine. This method yields response rates that are comparable to in-person collection methods (i.e., 70%). A standard cut-point of 10 ng/ml will be used to discriminate those who are abstaining from those who are continuing smokers.

Prolonged abstinence from alcohol will be assessed using phosphatidylethanol (PEth) as a biomarker at the 6-month follow-up visit. While self-report abstinence has been a proven indicator, bioverification using PEth testing is an effective tool for identifying heavy drinking (Nanau & Neuman, 2015) , and has a 99% sensitivity for detecting excessive alcohol consumption (Aradottir et al., 2006). This will be assessed using a dried blood spot collection, collecting 3 spots (about 3 mL) of blood from the participants' finger. PEth testing has been shown to have. The de-identified test card will be collected by ARCpoint labs of Raleigh Durham for analysis. All sharps and biohazardous material will be collected and disposed of by ARCPoint labs.

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 construct individual and mean trajectory plots of the longitudinal outcome variables to understand their general trends over time (i.e., post-treatment, 6 weeks and 6 months). Differences in treatment outcomes will be tested via generalized linear modeling. In addition, we will explore the variability and correlation structure of longitudinal variables. 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). In planning a full RCT of the tele-health mCM intervention for AUD and smoking, it is important to evaluate study feasibility and treatment procedures, as well as gain information about effects on proposed outcome variables.

Specific Aim 1: Develop a multi-component alcohol and smoking tele-health mCM intervention.

Content analysis of the cohort interviews will yield descriptive data regarding participants' perceptions of specific components of the treatment at each development phase. The first cohort will identify unanticipated problems with treatment procedures and equipment, clarify the change process and potentially identify new variables to examine as treatment mechanisms, and serve as a check on the appropriateness of the selected outcome measures. Participant feedback will also be critical in evaluating the user experience so that the phone app and phone counseling procedures can be enjoyable to the target population. Though the perspective of each participant in the first cohort will be strongly considered, negative feedback about an aspect of the intervention from one participant will be weighed against the feedback from others and the theoretical underpinnings of the treatment before the research team makes changes to the treatment. For example, if any participants note difficulty comprehending a treatment component or message, that component will be modified for clarity, as that does not conflict with the theoretical approach. Similarly, we will consider changes to the sequencing of phone counseling. PIs will meet weekly with the phone counselor to discuss narrative summaries of cases and the strengths and weaknesses of the treatment, as well as ease of manual use.

Specific Aim 2: Evaluate the feasibility and acceptability (e.g., mCM app reliability, mCM app procedures completion, patient satisfaction) of a tele-health mCM intervention; relative to a comparison group receiving a tele-health intervention without mCM.

We will additionally explore differences in alcohol and smoking abstinence outcomes by treatment. Because the tele-health only intervention is expected to have a uniformly small impact on alcohol and smoking outcomes in comparison to the tele-health mCM intervention, implementation of an imbalanced-samples design, with twice as many participants randomized to the tele-health mCM treatment as to the tele-health only treatment, should maximize power for identifying treatment effects. That said, the proposed sample has 80% power to detect a treatment effect equivalent to Cohen's *d* = 0.76. For reference, in our pilot study of 22 smokers with PTSD, tele-health mCM yielded an effect size of Cohen's *d* = 0.79 at the 3-month follow-up. In particular, comparisons by treatment at post-intervention, 6 week follow-up, and 6-month follow-up will be made regarding alcohol consumption (drinks/week, number of heavy drinking episodes, proportion of days abstinent, and achieving recommended drinking limits) and smoking (number of cigarettes smoked each day and number of days of smoking abstinence) *via*

generalized linear modeling, which can accommodate normally and non-normally distributed (e.g., count) variables.

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