Cost Effectiveness of Combined Contingency Management and Cognitive Behavioral Therapy for Alcohol Use Disorder

NCT03987581

Study Protocol and Statistical Analysis Plan

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A. SPECIFIC AIMS

Alcohol contributes to 88,000 deaths (Centers for Disease Control and Prevention) and costs an estimated $223 billion annually in the United States. Alcohol use disorder (AUD) is highly prevalent in veterans; estimates of the number of veterans meeting diagnostic criteria for AUD range from 32% (Lan et al., 2016) to 40% (Fuehrlein et al., 2016). Early patient attrition from substance abuse interventions is a major barrier to positive outcomes and is highly prevalent (e.g., 30%-50%; Mennis & Stahler, 2016). Behavioral incentives could increase treatment retention and increase abstinence among veterans with AUD. Contingency management (CM) is an intensive behavioral therapy that provides incentives (e.g., money, vouchers) to individuals misusing substances. Rewards are contingent upon confirmed abstinence from drug use. CM has demonstrated effect sizes beyond that of other behavioral treatments across multiple drugs of abuse (Dutra et al., 2008), including a trial in veterans with AUD (Petry, Martin, Cooney & Kranzler, 2000). This trial demonstrated that CM increased both treatment retention and completion rates, and was associated with increased abstinenence from alcohol compared to standard treatment.

The Veterans Health Administration (VHA) is the largest integrated health care system in the U.S. and provides care to over 9 million veterans. The VHA has launched the largest implementation of CM in history, resulting in over 100 VA substance use disorder (SUD) specialty clinics who now provide CM as an adjunct to existing SUD treatments (DePhilippis, Petry, Bonn-Miller, Rosenbach, & McKay, 2018). To date, however, implementation of CM interventions in VHA has largely focused on stimulant use disorders (e.g., cocaine; methamphetamine) due to the diffculty of bioverifying abstinence from alcohol, which requires daily monitoring. Thus, despite demonstrated efficacy (Petry, Martin, Cooney & Kranzler, 2000), CM aproaches for treatment of AUD are not currently available to veterans. The use of mobile health (mHealth) technology could significantly increase the feasibliity of monitoring daily abstinence from alcohol. Our group has developed a mobile smart-phone application that allows patients to video themselves using a small FDA-approved alcohol breath monitor and transmit the encrypted data to a secure server. This innovation has made the use of CM for outpatient AUD treatment feasible. Our pilot data suggest that veterans will perform mobile-monitoring of breath alcohol and that this approach is associated with high rates of abstinence and reduction in heavy drinking days at 6-month follow-up when paired with CBT. The innovative use of mHealth technology removes several barriers to daily alcohol monitoring and significantly increases the implementation potential of CM for AUD.

Our long-term goal is to implement cost-effective treatments that reduce the morbidity and mortality associated with alcohol and substance misuse. VA has widely implemented evidence-based cognitive-behavioral therapy (CBT) for treatment of subtance abuse disorders (Karlin & Cross, 2014). The primary goal of the current study is to evaluate the clinical effectiveness and cost effectiveness of CM as an adjunct to CBT for AUD. The trial will also explore the potential utilty of a long-term abstinence incentive on treatment utilization and alcohol outcomes. We plan to conduct a comparative effectiveness trial with a 2 x 2 factorial design in which 140 veterans with AUD will be proactively recruited and randomized to receive either CM as an adjunct to state-of-the-art evidence-based CBT, or receive CBT alone; and to one of two long-term incentive conditions (i.e., receipt of a monetery incentive for abstinence/low-risk drinking at 6-months vs. no incentive). *Specific aims* include:

AIM 1: To evaluate the effectiveness of mobile contingency management, as an augment to evidence-based CBT for AUD, on (1) treatment engagement and retention, and (2) reduction in heavy drinking days and abstinence from alcohol at post-treatment, 6-month and 12-month follow-ups.

Hypothesis 1a: Mobile contingency management for AUD will be associated with greater treatment engagement and treatment completion.

Hypothesis 1b: Mobile contingency management for AUD will be associated with decreased self-reported heavy drinking days and increased rates of abstinence from alcohol at each follow-up.

AIM 2: To evaluate the cost effectiveness of CM as an adjunct to evidence-based CBT for SUD in quality adjusted life years (QALY).

Hypothesis 2: CM paired with CBT will result in greater cost-effectiveness compared to the CBT alone as measured by the incremental cost-effectiveness ratio.

AIM 3: To explore the effects of a long-term (six-month) abstinence incentive on (1) treatment utilization and (2) alcohol outcomes at the 6-month and 12-month follow-ups.

Hypothesis 3**:** A long-term abstinence incentive will (1) increase utilization of AUD aftercare and (2) be associated with reduced heavy drinking days and increased abstinence rates.

VHA has implemented CM for treatment other substances (Petry, DePhilippis, Rash, Drapkin, & McKay, 2014; Ruan, Bullock, & Reger, 2017), but CM for AUD has not been implemented due to difficulty monitoring abstinence from alcohol. This project addresses this barrier and will provide highly needed cost-effectiveness data on the use of behavioral incentives as an adjunct to CBT for the treatment of AUD.

B. RESEARCH STRATEGY: SIGNIFICANCE

The positive public health impact of reducing heavy drinking among veterans with AUD would prevent significant medical morbidity and mortality. We expect that targeting AUD with mobile CM (mCM) paired with evidence-based CBT will significantly improve long-term abstinence rates and reduction in heavy drinking days among veterans with AUD. As described in detail below, the scientific premise of the proposed project is built solidly upon evidence that intensive CM can reduce substance misuse and alcohol dependence. Despite widespread implementation of CM in VA specialty SUD clinics, CM is not currently widely available for AUD due to the barriers of daily alcohol monitoring. *To date, no studies have examined the cost-effectiveness of CM approaches in VHA*. Among psychosocial treatments for SUDs, CM has the largest effect of any single intervention (Davis et al., 2016). An even larger effect, particularly for long-term abstinence, has been observed in the few studies that have combined CM with CBT (Davis et al., 2015; Cooper, Chatters, Kaltenthaler, & Wong, 2015). Several studies have demonstrated that achieving early abstinence is predictive of long-term outcomes. Further, increases in self-efficacy through achieving early abstinence are associated with long-term abstinence (Kadden, Litt, Kabela-Cormier, & Petry, 2007; Litt, Kadden, & Petry, 2013). Our pilot data provide additional evidence to support the premise and feasibility of the proposed work. Note that:

- AUD is highly prevalent in VHA. As many as 40% of veterans meet criteria for an AUD (Fuehrlein et al., 2016). Though ICD-9 codes underestimate the true prevalence of AUD, 10% of veterans have a current AUD diagnosis in VA.
- AUD is the third leading cause of preventable death. Relative to veterans without AUD, veterans with AUD die 15 years prematurely (Fudalej et al., 2010).
- The annual cost of excessive drinking in the U.S. is $249 billion with $27 billion in direct healthcare costs (Centers for Disease Control and Prevention, 2016). Costs associated with AUD and other mental illness in veterans is 2.7 times the cost of an average veteran (Watkins et al., 2011).

- The majority of AUD treatment occurs in outpatient settings. Unfortunately, drop-out rates are extremely high (e.g., over 40%) which negative impacts efficacy (Mennis & Stahler, 2016). CM has been shown to increase treatment retention in AUD treatment among veterans (Petry et al., 2000).
- CM is an evidence-based treatment for SUDs including AUD (Petry et al., 2000). Despite widespread implementation of CM in VA specialty SUD clinics, CM is not widely available for AUD due to the barriers of daily alcohol monitoring. The use of mHealth technology as a platform to provide CM overcomes this limitation.

C. PRELIMINARY DATA

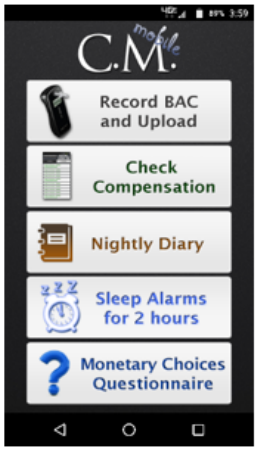
C.1. Expertise in CM and CBT for Addictions

Our research team has conducted research on SUDs for more than a decade. Our laboratory has extensive experience with the proposed methods of identifying and recruiting veterans with SUDs, including our recently completed pilot study on veterans with AUDs. Drs. Calhoun and Beckham have conducted health services research sponsored by NIH and the VA to examine the comparative effectiveness of CM approaches for smoking in a number of difficult to treat populations including rural and homeless veterans (R01CA196304; HSRD Merit Review 5I01HX00132; RR&D Merit Review 1I01RX001301). Drs. Dedert and Calhoun are experienced in treatment development and conducting clinical trials targeting CM for AUD (R34AA023877). Drs. Beckham and Calhoun have each conducted multiple clinical trials in veteran populations (CSR&D Merit Review; K24DA016388; R01CA081595; R21CA128965). Our preliminary studies (described below) strongly suggests that 1) our team can effectively recruit and conduct research with veterans with AUDs, and 2) CM can significantly reduce alcohol use in veterans with AUD.

C.2. Mobile App Technology

We believe there is great promise in mHealth technologies to promote alcohol abstinence monitoring. Our group has been involved in the development of several mobile applications targeted at reducing substance misuse in collaboration with the VA Office of Public Health Policy and the National Center for PTSD including a relapse prevention application for PTSD smokers. Most pertinent to the current application, we have developed a mHealth method to make daily abstinence monitoring feasible (Carpenter et al., 2015; Hertzberg et al., 2013) and have now demonstrated its utility for alcohol monitoring in an open pilot trial and our ongoing project that targets smoking and AUD (R34AA023877).

Figure 1. Screen Shot of Mobile Monitoring CM app



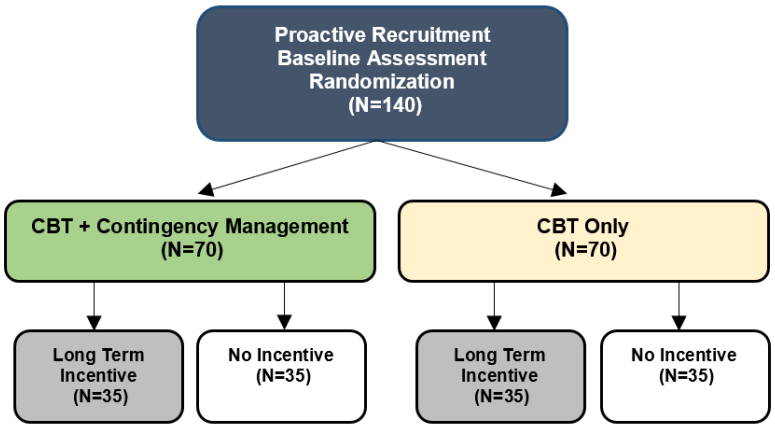
The mHealth app (see screenshot in Figure 1) is the platform through which we provide intensive behavioral therapy, i.e., CM. participants are able to generate a side-profile video recording of themselves breathing into a small FDA-approved breath alcohol monitor. The app uploads the video recordings via encrypted network connections. Subsequently, the participant can receive reinforcement information and receive scratch-offs all through a mobile application on a smart-phone or tablet. We are currently using server space provided by InMotion Hosting, Inc. and use Transport Layer Security (TLS) protocols to ensure all video uploads and participant data are transferred through encrypted network connections. The web application has been checked for vulnerabilities including SQL injection, Code Injection, XSS, and RFI vulnerabilities and has passed. The site is accessible only to participant and study staff via 512-bit SHA-2 hashed passwords.

D. RESEARCH DESIGN AND METHODS

D.1. Study Design

As shown in Figure 3, proposed is a 2X2 factorial randomized clinical effectiveness trial testing the effects of combining CM as an adjunct to state-of-the-art, evidence-based CBT (CBT + CM vs. CBT only) and the effects of a single, long-term incentive for bioverified abstinence/no heavy drinking at 6-months follow-up (Long Term Incentive vs. No Incentive). All patients will be referred to standard aftercare and encouraged to participate in 12-step programs following the intervention. Use of aftercare and other health care utilization will be collected based on objective measures (VA electronic medical record) and participant report. Health-related quality of life will be collected at each follow-up. The primary endpoint (AIM 1) will be number of heavy drinking days in the past 30 days at the 6-month follow-up. Cost effectiveness analysis (AIM 2) will be performed using quality-adjusted life years (QALY) as the outcome. The utility of a long-term incentive (AIM 3) will be tested by examining use of aftercare and other alcohol-related treatment and heavy drinking days in the past 30 days at the 6 and 12-month follow-ups.

Figure 3. Trial Design



D.2. Patient Identification, Eligibility, and Recruitment

Patients will be identified from the Durham VA Health Care System (DVAHCS) using the hospital's computerized medical record. Records will be screened for AUD. After mailing introductory materials with an opt-out number, we will contact those who do not opt out via telephone to explain the study and recruit them for participation. If necessary, in order to reach female veterans, we can oversample women for the screening mailouts.

We will also utilize reactive recruitment methods as needed to reach potentially eligible veterans. For example, we will seek referrals from the DVAHCS Substance Use Disorders Clinic. In order to reach female veterans, we will seek referrals from the Women's Health Clinic. In addition, we will post IRB-approved flyers and brochures throughout the DVAHCS catchment area, especially in clinic areas and Vet Centers. In addition, we will post, if necessary, flyers and brochures in the community, in local restaurants, laundromats, university student centers, etc. We will also use online classified advertisements such as Craigslist.com to reach potential participants.

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. If any participant contacts the email associated with the Facebook page (TSHRLab@dm.duke.edu, he/she will be sent an automatic email response.

Based on our previous studies, we expect to screen 250 participants to enroll and randomize 140. Eligibility criteria for the current trial include:

- are an enrolled veteran at the DVAHCS for primary care,
- can read/write/speak fluent conversational English,
- have current AUD (meeting past month DSM-5 criteria), and
- are willing to make a quit attempt and/or reduce alcohol use to low risk levels.

Exclusion criteria are:

- have fewer than 3 days of abstinence,
- have a history of clinically significant alcohol withdrawal, as indicated by 1) a score of 10 or more on the Clinical Institute Withdrawal Assessment of Alcohol (CIWA), 2) past medical alcohol detoxification, or 3) a history of seizures or hallucinations during alcohol withdrawal.
- is current imprisoned or hospitalized on an inpatient psychiatric unit,
- have had a seizure as an adult (e.g., child febrile seizures not exclusionary),
- is unwilling to sign a VA consent form to retrieve medical records, or
- is currently receiving professional behavioral treatment for AUD.

Veterans with a history of clinically significant withdrawal will not be eligible to participate, and will be referred to their providers for evaluation of medical management of clinical detoxification.

D.3. Study Screening Session and Randomization

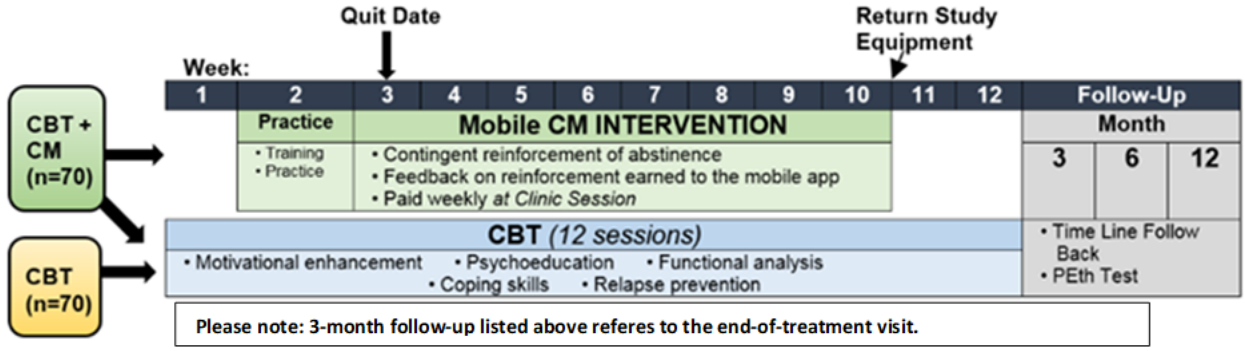
Potential participants who discuss the study with study personnel will complete a brief phone screen to assess potential eligibility. Veterans who are potentially eligible will attend a screening session where they will complete diagnostic interviews, self-report measures, urine drug screen and alcohol breathalyzer to determine inclusion. Participants who screen in will be randomized at the first treatment session to one of two treatment conditions (CBT+mCM vs. CBT alone) and to one of two long term incentive conditions (abstinence incentive at 6 months vs. No incentive). Stratified permuted block randomization assignments will be performed using a computerized sequence generated by the study statistician before the study starts. The sequence will be password-protected so that only the statistician and other study staff who do not have patient contact will have access to the sequence. We will stratify on the presence of comorbid non-tobacco SUD.

D.4. Interventions

D.4.1. Cognitive-Behavioral Therapy for Substance Use Disorders

We will use the VA CBT for SUD protocol (DeMarce, Gnys, Raffa, & Karlin, 2014) to provide in-person treatment in both study arms. CBT will be provided by a therapist with at least a Master's degree in mental health (e.g., psychology, social work) who has reviewed CBT for SUD training materials. To prevent confounding from therapist effects, study therapists will treat cases in both study arms. CBT sessions will be weekly over 12 weeks as shown in Figure 3. Following the standard of care for AUDs, all participants will be referred to aftercare and encouraged to participate in 12-step programs following completion of the 12-session CBT intervention (Proctor & Herschman, 2014).

Figure 3. Timeline for Intervention and Follow-Ups



D.4.2. Mobile Contingency Management for AUD Procedures

As shown in Figure 3, participants will begin one week of practice mCM monitoring at session two of CBT so they can troubleshoot any difficulties they have using the app. The beginning of contingent reinforcement (i.e., the target quit date) is scheduled for the same date as session three of CBT (week 3), which will provide eight weeks of mCM before the end of CBT. Patients who attend all weekly appointments will have two sessions of CBT occurring after mCM ends to assist in preventing relapse when monetary reinforcement is removed.

Table 2. Virtual Scratch-Off Lottery Ticket Reinforcement Amounts

Number of Possible Prizes	Size of Prize	Odds per Ticket	Cost per Ticket	Number Expected per Week*
500	$0	2:1	$0.00	20
239	$1	4:1	$0.24	10
125	$2	8:1	$0.25	5
65	$5	15:1	$0.33	2.7
40	$10	25:1	$0.40	1.6
30	$20	33:1	$0.60	1.2
1	$100	1000:1	$0.10	<1
			Total cost per ticket = $1.92	
			*Expected cost for CM per patient = $601	

Note *assumes perfect adherence. Participants with perfect adherence can earn up to 34 tickets in week 1 of CM with a maximum of 40 tickets for weeks 2-8 (maximum of 314 tickets over 8 weeks). The intermittent reinforcement schedule follows principles designed by Petry and is designed to ensure that participants can earn at least one “large” ($20) prize per week for demonstrated abstinence.

We will reinforce abstinence using an intermittent reinforcement schedule that has demonstrated efficacy and has been widely implemented in VHA (DePhilippis et al., 2018). For each BAC reading that tests negative, the participant will earn virtual scratch-off lottery tickets (scratch-offs) that contains 1000 potential values (see Table 2). Participants will be provided one scratch-off for their first bioverified negative BAC reading, and the number of scratch-offs will increase by one, up to a maximum of four, for each consecutive bioverifed negative BAC reading. The number of tickets will be reset to one for any positive (BAC > 0.02) or missed BAC reading. This reinforcement structure is designed to result in an average of $1.91 of reinforcement per ticket. Adding in the average of $11 for the practice week, there is an expected total possible of $611 in abstinent-contingent reinforcement.

Based on procedures used in our mCM for AUD pilot study, participants will be prompted an average of ten times weekly during waking hours to provide video bioverfication of BAC within the next 60 minutes. Though prompts are programmed to occur at unpredictable intervals throughout the day, prompts will be scheduled to occur on at least five identified high-risk time periods per week, which are typically the five hours preceding bedtime. At least one prompt will be scheduled for the first two hours of scheduled waking to assess the previous night's drinking.

Videos bioverifying alcohol abstinence will be reviewed by study staff to verify the participant's identity and alcohol abstinence. Study staff will write notes to the participant through the app to provide feedback on how the bioverification results translate into virtual scratch-off lottery tickets (scratch-offs). At that point, participants will use the app to reveal the scratch-offs and find out what level of reinforcement they have received. At the beginning of each session of CM+CBT, therapists will review the essential elements of CM as indicated on the Contingency Management Competence Scale (Petry, 2010). Essential elements include feedback and review of how bioverification results resulted in reinforcement draws, discussion of the mean number draws that could be earned if the participant is bioverified abstinent over the upcoming week, praise of the participant's efforts toward abstinence, communication of confidence that efforts will yield future success, and general competence ratings. This portion of the session will be rated by an independent fidelity rater using the Contingency Management Competence Scale. Therapists will be trained on the essential elements of CM during a half-day training. The CM portion of CM+CBT sessions will be videorecorded and rated by an independent fidelity rater.

Participants will be asked not to initiate any new treatments for AUD during the study treatment period. Following the active treatment period, participants will be encouraged to become involved with local 12-step programs and other aftercare.

D.4.3 Long Term Incentive

Participants randomized to the long-term incentive condition will receive $300 for self-reported and bioverified 30-day abstinence from heavy drinking at the follow-up scheduled for 6-months after the initial quit date. Bioverification will be based on PEth test.

D.5. Rationale for CM Parameters

The structure of CM interventions has varied considerably across studies in duration, frequency, and magnitude of reinforcement, providing valuable information in designing the proposed intervention. Reviews have found that the following components of monetary reinforcement schedules increase effectiveness: 1) an *escalating reinforcement schedule* in which each subsequent behavior verification is reinforced with a greater amount of money; and 2) a *reset contingency* in which substance use or missed reading will result in reinforcement levels being reset to their initial amount (Lynagh, Sanson-Fisher, & Bonevski, 2013). These design features reliably improve substance use outcomes (Heil et al., 2008) and will be used in the proposed intervention. To match CM procedures currently implemented in VHA specialty SUD clinics, we will use an intermittent reinforcement system that reinforces bioverified substance abstinence with an escalating number of virtual scratch off lottery tickets that contain various levels of monetary reinforcement (as shown in Table 2). Intermittent reinforcement (as opposed to a continuous schedule of reinforcment) reduces the cost of abstinence incentive interventions and has demonstrated efficacy (DePhilippis et al., 2018).

D.6. Cost Effectiveness

Cost Measurement. Costs to be collected can be grouped into three broad categories: intervention delivery costs, participant time costs, and health care costs. Intervention costs incurred to develop both interventions will be excluded from the analysis as these costs have already been incurred and are thus "sunk" costs. Intervention Delivery Costs for both conditions will be estimated using both standardized estimates and convenience sampling of support staff and our interventionists. The time it takes to prepare for and execute CBT for SUD is specified in the treatment manual but will be assessed through a data tracking system, surveys, and counselor records to validate these estimates. Similar methods will be used to estimate time spent in identifying veterans with AUD, contacting veterans, and training veterans on the use of the mCM smart phone app. To reduce burden, we will not measure every activity for every subject for every occasion. Instead we will collect a convenience sample of observations toward the beginning and the end of the study to account for the fact that there may be a learning curve effect. The size of the convenience sample will depend on the variability we observe in the activity times—the larger the variability the larger the sample we will collect. In addition to labor costs, materials costs, including the cost of the mCM will be included.

Participant Time Costs (i.e., the opportunity costs to participants). This will include the time spent by participants in using the intervention strategies, techniques, or information. As part of the end-of-treatment follow-up, time spent on the intervention materials other than that involved in the treatment sessions will be assessed. In the intervention arm, the number of videos submitted will be used to assess the time involved in providing bioverification as part of mCM. We will derive participant time cost estimates for each group by combining the time estimates with standard wage estimates adjusted for age, gender, and if possible race, derived from the Statistical Abstract of the United States. Because we chose to conduct the cost-effectiveness analysis from the societal perspective, the use of mean wage rates has higher generalizability and validity than self-reported wages by the subjects. *Health care costs* will be obtained from VA medical records for outpatient, inpatient and medication use one year prior to trial enrollment and through the final follow-up.

Cost and Effectiveness Measurement. Our primary cost effectiveness outcome measure will be the incremental cost-effectiveness ratio (ICER), with costs as the numerator and effectiveness as measured by QALYs as the denominator. Costs will include: intervention delivery costs, participant time costs and health care costs as described above. The QALY is a standardized effectiveness measure, based on the EuroQol (EQ-5D5L), that allows for the comparison of the value of a particular intervention to a broad range of other potential health care investments. Differences in reduction in heavy drinking days and secondary drinking outcomes (e.g., abstinence) among veterans in the mCM+CBT and the CBT comparison group will allow us to identify changes in the QALY effectiveness measure across groups. To estimate the QALYs, we will employ the methods and estimates developed by Barbosa and colleagues (2010), who used a Markov model to assign utility weights to a range of drinking patterns for medical morbidity and mortality, adjusted for health-related quality of life. Incremental costs and effectiveness of mCM+CBT will be compared to those of the CBT comparison group.

D.7. Optional Study Procedure

One of our study therapists, Madison Tobin, is seeking licensure as a Licensed Professional Counselor, and as part of her supervision, needs to provide video recordings of therapy sessions to her supervisor, Ms. Courtney White, MS, LPCS for review. Data will be shared with Ms. White as view only in a Duke Box folder to which only Ms. Tobin, Ms. White, and Dr. Dedert have access. Data will be shared in accordance with a data agreement facilitated by Duke's Office of Research Contracts, and signed by Ms. White and Dr. Dedert. This study procedure is fully optional, and is indicated as such during the informed consent process.

D.8. Measures

Participants will complete measures at primary assessment time points (baseline, post-treatment, 6 months post-quit date, and 12 months post-quit date), as well as reporting on alcohol at each CBT session. Follow-ups will be completed in-person.

D.8.1. Diagnostic Assessment and Psychiatric Symptom Measures. We will assess AUD and other major psychiatric disorders with the Structured Clinical Interview for DSM-5 (SCID-5). Our group has trained diagnostic interviewers for our studies using training videos, observation of live interviews, and monthly meetings to prevent rater drift. Inter-rater reliability across previous interviewers has been excellent (kappa = .96). We will administer the Clinical Institute Withdrawal Assessment to assess past alcohol withdrawal symptoms. Due to the high comorbidity with AUD, we will measure severity of PTSD symptoms with the PTSD Checklist-5 and measure depressive symptoms with the Patient Health Questionnaire-9. At each session, participants will be asked four questions regarding suicidality. The items will be used to examine how the co-occurring mental health problem of suicidal thoughts and behaviors impacts the progression of AUD treatment, as well as the extent to which this treatment simultaneously reduces alcohol use and the occurrence of suicide-related phenomena.

D.8.2. Alcohol-related Measures. Standard self-report and interview-based alcohol-related assessment measures (e.g., severity, craving, consequences; see Table 2) will be used to measure alcohol-related behaviors, perceptions, and attitudes. The Alcohol Purchase Task will be used to provide a behavioral economic measure of the relative reinforcing efficacy of alcohol (Kiselica, Webber, & Bornovalova, 2016).

D.8.3. Self-Efficacy Measures. Attitudes toward behavior change with respect to alcohol will be measured with Alcohol Abstinence Self-Efficacy scale which has demonstrated reliability and validity. Additionally, the Alcohol Readiness to Change will assess motivation to quit alcohol.

Table 3. Measures Administered at Major Study Time Points

Measure	Completer		Time			
		Screen	Txt Session	Post-txt	6-mo. f/u	12-mo. f/u
Diagnostic Assessment						
SCID-5	Study staff	X				
Clinical Institute Withdrawal Assessment	Study staff	X				
Psychiatric Symptom Measures						
PTSD Checklist-5	Participant	X		X	X	X
Patient Health Questionnaire	Participant	X		X	X	X
Suicidality Questions	Study staff	X	X	X	X	X
Alcohol-Related Measures						
AUDIT	Participant	X		X	X	X
BAM	Participant	X		X	X	X
BAM -C	Participant		X			
Penn Craving	Participant	X		X	X	X
Drinker Inventory of Consequences	Participant	X		X	X	X
Alcohol Abstinence Self-Efficacy	Participant	X		X	X	X
NIAAA Alcohol Use Frequency	Participant	X				
Alcohol Readiness to Change	Participant	X		X	X	
Alcohol Purchase Task	Study staff	X		X	X	X
Drinking Norms Rating Form	Participant	X		X	X	X
Alcohol Use, Short Form (PROMIS)	Participant	X		X	X	X
Alcohol Use, Positive Expectancy (PROMIS)	Participant	X		X	X	X
Alcohol Use, Positive Consequences (PROMIS)	Participant	X		X	X	X
Alcohol Use, Negative Expectancy (PROMIS)	Participant	X		X	X	X
Drinking Motives Questionnaire	Participant	X		X	X	X

Alcohol Risk Beliefs	Participant	X		X	X	
Sociodemographic, Clinical, and Process Variables						
Sociodemographic and Military	Participant	X				
DRRI Combat Experiences Scale	Participant	X				
Beck Scale for Suicidal Ideation	Participant	X		X	X	X
Insomnia Severity Index	Participant	X		X	X	X
Dimensions of Anger Reactions	Participant	X		X	X	X
Smoking Exposure Questionnaire	Participant	X		X	X	X
Barratt Impulsivity Scale	Participant	X		X	X	X
Delay Discounting	Participant	X		X	X	X
MOS Social Support	Participant	X		X	X	X
Medical Problems Checklist	Participant	X			X	X
Medications Checklist	Participant	X			X	X
Individual Treatment Alliance	Participant			X		
Working Alliance Inventory	Participant		X*			
Qualitative Interview	Study staff			X		
Satisfaction/Acceptability	Participant			X		
Alcohol Outcome Measures						
Timeline Follow-Back	Study staff	X		X	X	X
Heavy Drinking Days	Study staff	X		X	X	X
% Days Drinking	Study staff	X		X	X	X
Binge Drinking Episodes	Study staff	X		X	X	X
PEth Testing (bioverification)	Study staff				X	X
Addiction Severity Index	Participant	X		X	X	X
Quality of Life, Healthcare Utilization, and Cost Measurement						
EuroQol	Participant	X	X**	X	X	X
Insurance Question	Participant	X				
WHOQOL-BREF	Participant	X		X	X	X
Cost Measurement	Statistical team			X		
Self-Report Healthcare Utilization Measure	Participant	X		X	X	X
Healthcare Utilization	Statistical team	X		X	X	X
* given at CBT sessions 1, 7, and 12 only; ** given at CBT session 7 only						

D.8.4. Socio-demographic Measures*.* Sociodemographic variables will be collected. Social support will be assessed with the MOS social support scale. Impulsivity will be assessed via self-report and through a delay-discounting task (Richards, Zhang, Mitchell, & DeWit, 1999; Garcia-Rodriguez, Secades-Villa, Weidberg, & Yoon, 2013).

D.8.5. Temporary Measures During COVID-19 Pandemic. Given that media outlets are reporting increased rates of alcohol use during COVID19 pandemic, and there is a high incidence of PTSD among the veterans who are enrolled in this study, we would like to ask participants to complete measures related to stress, trauma, and coping strategies during the pandemic. New participants will complete these measures at their first visit, and ongoing participants will complete them at their next study visit. We are adding the CAIR Pandemic Impact Questionnaire (Lang, 2020; https://www.nlm.nih.gov/dr2/CAIR-PIQ_scoring.pdf), and another measure, COVID Core Questions, with variables of interest. If a participant endorses any item marked with an asterisk on the COVID Core Questions measure, we will ask them to complete a PTSD Checklist 5 related to that specific event..

D.8.6. Treatment Process Measures. Protocol adherence will be defined as completing the baseline assessment, post-treatment assessment, and follow-ups at 6, and 12 months. Process measures will include the proportion of abstinence videos uploaded (intervention), the number of counseling sessions completed. We will measure patient satisfaction with questionnaires related to this study's treatment aims and to satisfaction with treatment components. During the one-week follow-up visit, we will perform qualitative interviews with participants to gain information from the participant about his/her/their user experience with the CBT protocol and mobile phone contingency management app. The qualitative interview will be recorded for qualitative analyses.

D.8.7. Treatment Fidelity. Counselors will receive weekly supervision for CBT from Dr. Dedert or another senior clinician. Following procedures recommended by the VA training program, we will utilize the Cognitive Behavioral Therapy for Substance Use Disorders Rating Scale to measure counselor adherence in delivering behavioral treatments for substance abuse disorders (Gnys, DeMarce, Raffa, & Karlin, 2014). A random selection of 10% of the counseling sessions will be rated for fidelity by rater who is otherwise independent of the conduct of the study. Fidelity ratings will be used in supervision to improve counseling. To measure therapeutic alliance, we will use the 16-item Individual Treatment Alliance Scale Revised Short Form, which has a demonstrated relationship with treatment dropout and treatment response in behavioral interventions (Pinsoff, Zinbarg, & Knobloch-Fedders, 2008). This measure will be given at the final treatment session for all participants, including participants who withdraw early from treatment.

D.8.8. Outcome Measurement and Biochemical Verification. At each treatment session, and at post-treatment and follow-ups, we will measure number of heavy drinking days (> 5 drinks in day for men, > 4 drinks in a day for women), binge drinking episodes (heavy drinking within a 2-hour period), number of drinking days, and drinks per drinking day. At follow-ups, we will conduct Timeline Follow-back interviews to improve self-reports of drinking behavior over the previous months. We will ask participants to complete items from the Addiction Severity Index (ASI) to assess the consequences of substance use on functioning in the previous month. Participants will complete all of the items of the Employment subscale, and items 1, 3, 7, 8, 9, 10, 28, 29, 30, 31, 32, and 34 of the Family/Social subscale. Early continuous abstinence will be defined as three consecutive weeks of alcohol abstinence in the first eight weeks after the quit attempt, a threshold that has been predictive of good long-term SUD outcomes (Carroll et al., 2014). We will bioverify self-reports of low risk drinking with fingerstick blood spot samples for PEth testing at 6-month and 12-month follow-ups.

D.8.9. Quality of Life and Health Care Utilization. VA administrative data will be accessed *via* the VA Corporate Data Warehouse to provide objective measures of VA health care utilization. Our team has extensive experience accessing and utilizing VA data (Elhai, Calhoun, & Ford, 2008; Calhoun, Bosworth, Grambow, Dudley, & Beckham, 2002; Calhoun, Bosworth, Stechuchak, Strauss, & Butterfield, 2006). Additionally, we will collect self-reported use of non-VA healthcare and 12-step programs and information about insurance coverage. Health care related quality of life will be assessed with the EuroQol (United Kingdom Alcohol Treatment Trial Team, 2005) at baseline and each of the follow-ups.

D.9. Participant Reimbursement

Participants will be paid as follows:

Project Milestone	Amount
Screening visit	$50
CM abstinence reinforcement	$611
End-of-treatment visit	$50
6-month follow-up	$100
Bioverified abstinence at 6 month follow-up (if randomized to long-term incentive condition)	$300
12-month follow-up	$125
TOTAL	**$1236**

D.10. Potential Challenges and Solutions

One potential challenge to the success of this project is recruitment and retention. Previous AUD trials in veterans indicate lost-to-follow-up rates near 30% at 12 month follow-up (Hagedorn et al., 2013). We have implemented several methods to increase retention in our trials (e.g., pre-alert letters, birthday cards, reminder

calls, thank you notes) and have obtained excellent retention rates (≥80% at 12-months) in substance using populations (e.g., homeless veterans). We will use these methods and have budgeted to provide an incentive to participants to complete each follow-up. Missing data will be treated as indicative of relapse/heavy drinking. Our pilot data and experience in previous trials indicate that proactive recruitment of veterans with AUD is feasible. To augment our proactive recruitment method, we could include reactive recruitment strategies and include referrals from the SUD clinic at DVHCS. Another potential concern is lost/stolen study equipment. We now have extensive experience with providing veterans with a smartphone and monitoring devices to perform mobile monitoring for CM (e.g., R34AA023877; R01CA196304; 1I01HX001109; 1I01RX001301) and have budgeted for anticipated lost/stolen equipment. Costs of lost equipment will be captured and included in cost analyses.

E. DATA AND SAFETY MONITORING

E.1. Risk/Benefit Ratio

E.1.1. Potential Risks. With regards to completing study measures, there is a risk of discomfort or distress in answering questions. However, distress and discomfort related to questionnaire completion and the psychiatric interview are usually temporary and well-tolerated. Participants are informed that they may refuse to answer any questions while completing the questionnaires. Risks also include discomfort related to alcohol withdrawal. 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. There are risks related to participants providing a blood fingerstick. The risks of having a blood puncture includes temporary pain for the needle stick, bruising, and rarely, infection. Some people may experience dizziness, possibly lightheadedness, or rarely, fainting. Finally, there is a potential risk associated with the loss of confidentiality of study data. Because of these risks, the data and safety monitoring plan (DSMP) for this trial focuses on monitoring by the principal investigator (PI), the study physician, and the study coordinator, along with prompt reporting of unexpected and serious adverse events to NIH and to the Institutional Review Board at DUMC.

E.1.2. Potential Benefits. While participants may benefit from quitting or reducing 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 more effective treatment interventions for veterans with AUD.

E.1.3. Protections Against Risk. 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. Finally, all project staff will complete educational units required by DUMC's IRB and Duke Office of Clinical Research.

In accordance with NIH"s recently revised guidelines re: Certificates of Confidentiality (CoC), this study will utilize an NIH CoC. Participants will be informed of the COC during the informed consent process.

With regards to data security, potential risks will be minimized in several ways. Subjects' identifying information will only be available to Dr. Dedert and the research staff at DUMC. Data that links participants to information collected in the course of a given study will be kept separately from identifying information in computerized logbooks maintained at each study site. All study data will be kept in a secured file to which only study investigators will have access. Hard copy paper records will be stored in a locked filing cabinet in the study coordinator's locked offices at Duke-leased space at North Pavilion. Information from the interview and/or questionnaires will be entered into a computerized database. Each password-protected database will be stored on a networked computer on a server that is encrypted, password-protected, and only accessible by Dr. Dedert and study staff, see duhsnas-pri\dusom_psych\private\irb\dedert\CM CBT. Access to these data will be limited to a small number of project staff who have been trained to preserve participant confidentiality. The key linking code numbers and identifying information will be will be maintained in a separate database and stored in the same protected computer environment described above.

Video recordings that are made in the laboratory (i.e., recordings of therapy sessions in order to measure treatment fidelity) will be made using a Duke-owned iPad or iPhone. Recordings will be transferred to a Duke secured server immediately after recording. Regarding the mCM portion of the intervention, we have developed several ways to minimize data security risk. The smart phone used will be any one of four models of Droid phones: 1) Droid Turbo 2 (Motorola Mobility Inc, Libertyville, IL) with a Qualcomm Snapdragon 810 processor, 5.4" Quad HD display; 2)Droid Turbo, with 5.2" Quad HD Super AMOLED™ Corning® Gorilla® Glass 3 Display; 3) Droid MAXX, with a dual-core 1.2 Ghz processor, I GB DDR2 RAM, and 4.3" gHD display; or 4) Droid MAXX 2 DROID MAXX 2 with an octa-core 1.7 Ghz processor, 2 GB RAM, and 5.5" full HD display. Each will be equipped with an Android operating system that is compliant with Federal Information Processing Standard (FIPS) 140-2 standards. Features other than the electronic diary, calling, and texting features will be locked out. The phone will be programmed so that staff can set up the phone by simply entering a participant's code. Encrypted TLS connections will be used to upload data to the server. The study's website will use a Virtual Private Server provided by InMotion Hosting, Inc. The data at InMotion Hosting are Advanced Encryption Standard (AES)-256 encrypted at rest, and the data being transferred are encrypted at transfer AES-256 & Transport Layer Security (TLS). Website properties include TLS 1.0, AES w/ 128 bit encryption (High); Rivest-Shamir-Adleman (RSA) with 2048 bit exchange. 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 to staff via 512-bit SHA-2 hashed passwords.

E.1.3. Psychiatric Emergencies. As this study includes a novel therapeutic intervention that is behavioral in nature, we do not anticipate study-related SAEs to occur. It is not unanticipated that participants may endorse suicidal or homicidal ideation. We have developed a homicidal (HI) and suicidal (SI) risk assessment checklist based on the currently available research evidence base. All staff members are trained in the use of the assessment instrument, and attend monthly supervision meetings in which HI/SI assessments are regularly reviewed. Our laboratory has a policy regarding SI and HI risk assessment and follow-up. According to the policy, if a participant is deemed at "high" risk of suicide or homicide, the study staff providing the assessment will contact a senior staff member with clinical training who will provide a second opinion. If the senior staff member determines that the participant is in imminent risk of suicide or homicide, that participant will be escorted to the DUMC or DVAHCS emergency room for evaluation for psychiatric hospitalization. If at any time a participant is deemed by our staff to be at imminent risk of harm to self or others, he/she will be immediately withdrawn from the study upon being escorted to the emergency room. If a participant is deemed to be at "low" or "moderate" risk, the study staff member performing the assessment will discuss treatment options with the participant and discuss psychiatric emergency resources that may be available to him or her. Finally, in the case

of moderate SI or HI, study staff will review the assessment with a senior staff member in order to ensure that follow-up has been adequate.

E.1.4. Participant Referrals. Following the standard of care for AUDs, all participants will be referred to aftercare and encouraged to participate in 12-step programs or outpatient relapse prevention treatment in the Durham VA Health Care System or at DUMC following completion of the 12-session CBT intervention. In addition, appropriate referrals will be completed to address any clinically significant increases in symptoms of comorbid psychiatric or medical problems. Referrals will be made first to treatment at DVAHCS, where participants must be enrolled for primary care services. In the event that treatment is not available at DVAHCS or DUMC, referral will be made to a community provider.

E.2. Data and Safety Monitoring Plan

The individuals responsible for data safety and monitoring will be the principal investigator and the project manager. The study physician, Scott Moore, M.D., Ph.D., will serve as a Medical Monitor and in that role, provide additional safety monitoring regarding diagnostic and medical issues in enrollment decisions and any medical questions that arise during treatment. Dr. Moore is a board-certified psychiatrist with 18 years of experience providing pharmacotherapy in clinical research studies and clinics. He is also a psychiatrist in the Durham VA Health Care System, where he serves as a clinician treating substance use disorders. He has collaborated on research with our group over the past 10 years. Dr. Moore has expertise in AUDs and has current and past grant funding from NIH and VA for alcohol-related research. Further data safety and monitoring will be provided by the PI.

As study physician and medical monitor, Dr. Moore will ensure participants are medically cleared to participate in this trial and will review all reports of adverse events sent by the study coordinator and evaluate the patient as necessary to determine whether there is any corrective action needed. The Principal Investigator (PI) will be responsible for executing the DSMP, and complying with reporting requirements.

Further data safety and monitoring will be provided by the PI. There will be several ongoing mechanisms for monitoring and reporting of AEs, including SAEs: 1) ongoing participant contact via study personnel; 2) a telephone number provided to participants to report concerns related to study participation; and 3) weekly meetings between the PIs and study personnel. Any adverse events (AEs) will be reported to the IRB in accordance with the Duke University School of Medicine's Human Research Protection Program.

In order to monitor possible negative effects with regards to treatment, including alcohol withdrawal symptoms, participants will be instructed to report any negative effects as soon as possible to research staff; they will have contact information needed to report these problems to 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. Monthly meetings between the 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 adverse events 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, 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.

F. STATISTICAL ANALYSES AND POWER CONSIDERATIONS

Variables of interest will be examined using means, standard deviations, and distributions (for continuous variables) and their frequencies (for categorical variables). For normally distributed outcome variables, linear statistical models will be used by default. However, examination of residuals and Q-Q plots will be undertaken to determine whether generalized linear modeling may be more appropriate. We will first conduct preliminary analyses to ensure that there are no differences across treatment groups with respect to gender, age, educational history, socioeconomic status, baseline alcohol consumption, PTSD symptoms, and depressive symptoms. In addition, we will evaluate potential effects of psychiatric variables on the treatment response. We do not expect differences to arise on these measures as a result of randomization. Nevertheless, we will potentially use covariate adjustment to address unanticipated differences in baseline variables. We will conduct sensitivity analyses to determine how variability in demographic/baseline variables influence estimates of treatment effects (Thabane et al., 2013).

We plan to ask participants to report both gender and biological sex so that we can evaluate the role of biological sex on study outcomes. The association between sex and outcomes will be evaluated for all three aims. We will conduct sensitivity analyses to determine how variability in demographic/baseline variables influence estimates of treatment effects by analyzing and reporting the effects of randomization on males and females separately.

Multilevel modeling (MLM) will be used to analyze primary treatment outcomes (i.e., number of heavy drinking days; abstinence outcomes). MLM is appropriate for analyzing repeated-measures data; however, unlike ANOVA, MLM can accommodate data missing at random (Searle, Casella, & McCulloch, 1992). Because MLM takes into account the shared variance among observations within a given person, it can be used to leverage repeated measurements of alcohol use to enhance statistical power.

Although we do not anticipate much missing baseline data, we do anticipate missing values at post-treatment and each of the 6- and 12-month follow-ups due to attrition. Given evidence that maximum likelihood (ML) and multiple imputation (MI) provide the least biased results in comparison to lost observation carried forward and worst-case scenario (i.e., missing=relapsed) in alcohol clinical trials under varying missing data assumptions (Hallgren & Witkiewitz, 2013), both approaches will be used here. MLM uses ML estimation; thus, missing values result in casewise—but not listwise—deletion. Consequently, participants with missing data will still be included in the analyses; estimates based on them will simply have a greater level of uncertainty. MI will be used to impute missing data using baseline demographic, clinical, and drinking measures. Regression parameter estimates will be computed for each imputation dataset and then pooled using Rubin's rules (Rubin, 1976). Sensitivity analyses will be conducted to determine how modeled treatment effects may vary by missing-data approach.

Aim 1: To examine the first hypothesis that CM will be associated with greater treatment engagement and treatment completion than the control condition, treatment engagement will be defined as the number of counseling sessions completed, with treatment completion defined as completion of all 12 counseling sessions. Potential group differences in treatment engagement as a function of counseling sessions completed will be examined using independent *t*-tests. Contingency-table analysis will be used to examine whether a greater proportion of the CM participants complete the treatment in comparison to the control group. The second hypothesis is that CM will be associated with higher rates of self-reported abstinence and fewer heavy drinking days at 6 and 12 months. MLM will be used to model each of these outcomes. Specifically, logistic MLM will be

conducted to model abstinence as a function of treatment, time (categorized as end of treatment, 6 months, 12 months), and the interaction between treatment and time. Randomization to long-term abstinence incentive will be covaried. Linear contrasts will be specified at each time point to examine the hypothesis that CM will result in higher abstinence rates than CBT alone at 6 and 12 months. A similar count-based model (e.g., Poisson, negative binomial) will be conducted to analyze number of days of heavy drinking (per 30 days). In addition to modeling the effects of treatment, time, and the interaction between treatment and time, number of days of heavy drinking recorded at baseline and randomization to the long-term abstinence incentive will be covaried. Again, linear contrasts will be derived at each time point to compare treatment effects at 6 and 12 months.

Aim 2: To examine the hypothesis that mCM paired with CBT for SUD will be more cost effective over the lifetime than CBT alone, cost-effectiveness analysis (CEA) will be performed using the incremental cost-effectiveness ratio (ICER), with costs as the numerator and effectiveness as measured by quality-adjusted life years (QALY) as the denominator. QALYs incorporate changes in quality of life (morbidity) using a set of values, one for each possible health state, reflecting the relative desirability of the health state (Drummond et al., 2009). Quality of life ratings, or utilities, will be derived from a prior study of the utility of different drinking states that used the standard gamble technique in a community/clinic sample of 200 individuals (Kraemer et al., 2005). The mean utility values (and standard deviations) calculated for each state were as follows: abstinent 0.93 (0.15), moderate drinking 0.88 (0.22), at-risk drinking 0.82 (0.27), meeting criteria for mild AUD 0.75 (0.29), meeting criteria for severe AUD 0.67 (0.29), and in recovery from alcohol dependence 0.83 (0.24). QALY change will be calculated based on change from baseline to 12-month drinking status. Prior to CEA, CBT alone will be assessed for dominance to determine whether it is both less costly and more effective than combined mCM and CBT. In the absence of dominance, an incremental cost-effectiveness ratio (ICER) will be computed to estimate the additional cost required to achieve one additional QALY. Specifically, the ICER combines the costs of the treatments with the QALY changes, using the cost in the mCM group over and above the control, divided by the incremental QALYs in the mCM group over and above the control. Given likely skewed economic data, nonparametric bootstrap resampling will be used to test the sensitivity of the calculated ICERs and cost-acceptability curves estimated to assess the probability that the mCM intervention is cost-effective at thresholds up to $50,000 or $100,000 per QALY (Willan & Briggs, 2006). Numerous sensitivity analyses will be conducted to evaluate the robustness of these results given varying estimates of abstinence rates, relapse to any heavy drinking, mortality rates, and long-term costs of sustained alcohol use. Cost-effectiveness analysis will be conducted if the primary outcome is significant; otherwise, a cost minimization analysis will be conducted.

Aim 3: To examine the hypothesis that incentivizing long-term abstinence will increase AUD aftercare treatment utilization, enrollment in VA and/or non-VA alcohol treatment programs will be determined both in the first 6 months following randomization and the second 6 months leading up to the 12-month follow-up. Logistic MLM will be used to model treatment utilization during each of these intervals as a function of randomization to the long-term abstinence incentive, time, and the interaction between group and time. Randomization to CM will be covaried. Linear contrasts will be specified at each time point to examine the hypothesis that long-term incentives to promote abstinence will result in greater likelihood of AUD treatment utilization both prior to and following the 6-month incentive. To examine the hypothesis that long-term abstinence incentives will be associated with higher rates of self-reported abstinence and fewer heavy drinking days at 6 and 12 months, MLM analyses similar to those proposed for Aim 1 will conducted. Specifically, logistic MLM will be used to model abstinence as a function of long-term incentive, time (categorized as end of treatment, 6 months, 12 months), and the interaction between incentive and time. Randomization to CM will be covaried. Linear contrasts will be specified at each time point to examine the hypothesis that a long-term incentive for abstinence will result in higher abstinence rates than no incentive at 6 and 12 months. A similar count-based model (e.g., Poisson, negative binomial) will be conducted to analyze number of days of heavy drinking (per 30

days). In addition to modeling the effects of long-term incentive, time, and the interaction between incentive and time, number of days of heavy drinking recorded at baseline and randomization to CM will be covaried. Linear contrasts will compare effects of the incentive at 6 and 12 months.

Power calculations provided below were performed with Power Analysis and Sample Size software (PASS, Version 12: NCSS LLC, Kaysville, Utah). The sample size estimate is based on the first hypothesis that the CM intervention will result in higher overall self-reported abstinence rates and fewer days of heavy drinking at 6-months post-randomization. As described in the analysis section, this hypothesis will be tested via linear contrasts specified within the context of MLM analyses. Because this will be tested using repeated-measures data, statistical power will depend on the effective sample size (ESS). The ESS is the number of statistically independent observations available for this study, which is equivalent to the total number of observations (number of participants x number of data collections) adjusted for within-individual correlations. As the intraindividual, or intra-class, correlation (ICC) decreases, the ESS increases. Given that we found an ICC of .20 for 7-day point prevalence measured at posttreatment, 3 months, and 6 months in an RCT with 218 smokers featuring CM as the experimental treatment (R01 CA196304), we anticipate a similar, if not smaller, figure in this trial, given longer intervals between observations. Using this ICC value, with 140 participants with up to 3 observations each, the ESS would be 300. Even with an unexpectedly high 15% attrition at each observation point, such that only 119 complete treatment, 101 6-month follow-up, and 86 12-month follow-up, the ESS for examining linear contrasts would be 227, which would be sufficient to detect treatment effects as small as Cohen's *d* = 0.43 with 90% power. Because the previous trial examining the effect of CM as an adjunct to behavioral treatment found large effects (Cohen's *d* = 0.92; McDonell et al., 2017) on heavy drinking days, our proposed sample size has sufficient statistical power.

G. PROJECT MANAGEMENT PLAN and TIMELINE

The scheduled project timeline is illustrated in Table 5. Members of this multi-disciplinary research team have experience in one or more key components of the

Table 5. Project Timeline

	Year 1				Year 2				Year 3				Year 4				Year 5			
Activity	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**
Hire/Train Staff																				
Recruitment																				
Intervention																				
Follow-ups: post-txt, 6-and 12-months																				
Data Analysis																				

proposed research that will ensure the successful completion of the project including:

- development and evaluation of alcohol interventions in veterans (Dedert, Calhoun);
- provision of mobile CM for difficult to treat veteran populations (Dedert, Calhoun, Beckham);
- health services research in veterans (Calhoun, Maciejewski, Kimbrel, Dennis, Beckham);
- cost effectiveness design and analysis (Maciejewski, Dennis)
- Medical monitoring of patients with AUD (Moore).

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