Research Protocol: Abstinence Reinforcement Therapy (ART) for Homeless Veteran Smokers
Principal Investigator: Jean C. Beckham, Ph.D.

Cigarette smoking is the most lethal substance use disorder in the United States in terms of morbidity and mortality (Centers for Disease Control and Prevention, 2008, Mokdad, et al., 2004). Unfortunately, smoking cessation treatment including smoking cessation aids such as nicotine replacement therapy (NRT) are greatly underutilized (National Institute of Health, 2006). Veterans who are homeless, along with those who have mental health or substance abuse problems, are at the highest risk for nicotine dependence (Tsai, et al., 2011). Prevalence estimates for smoking among homeless Veterans are 80% (Tsai & Rosenheck, 2012). Thus, homeless Veterans are at tremendous risk for smoking related morbidity and mortality.

Risks associated with smoking among homeless Veterans are also increased because of the high rates of HIV prevalence among persons who are homeless (Reynolds, 2009; Robertson et al., 2004; Culhane et al., 2001) and homeless Veterans specifically (100,000 Homes, 2011). Evidence suggests that there are substantial health implications for smoking among persons living with HIV/AIDS (PLWHA; Reynolds, 2009). For example, PLWHA who smoke compared to those who don't smoke are at increased risk of developing an AIDS-related condition (Crothers et al., 2005). To our knowledge, the impact of smoking cessation on disease progression among homeless Veterans who are living with HIV/AIDS has not been examined.

Smoking cessation efforts among homeless Veterans to date have been largely ineffective. Even among 754 homeless Veterans enrolled in mental health, primary care and supported housing at 11 U.S. sites (3/4 of whom had discussed their smoking with a health care professional), smoking was not decreased over a one year period. Taken together, this information suggests that smoking needs to be targeted specifically among this high risk population of smokers (Tsai & Rosenheck, 2012).

The addition of contingency management (CM) to existing evidence-based tele-health smoking cessation interventions is expected to be a cost-effective way to increase the reach of intensive smoking cessation treatment. CM is a behavioral therapy that provides positive reinforcers (e.g., money, vouchers) to individuals misusing substances contingent upon objective evidence of abstinence from drug use. Implementation of CM has been limited because of the need to verify abstinence multiple times daily with a clinic-based carbon monoxide (CO) monitor. As a result, CM has largely been relegated to inpatient and day treatment programs. The application of emerging smart phone technology, however, can overcome this barrier, and may be particularly well suited to homeless Veterans, most of who use cell phones. We have developed a smart phone application which allows a participant to video themselves several times daily while using a small CO monitor and to transmit the data to a secure server. This innovation has made the use of CM for outpatient smoking cessation portable and feasible, i.e., mobile CM (mCM). The goal of the current study is to evaluate the effectiveness of a combined tele-health and mCM intervention that we are calling Abstinence Reinforcement Therapy (ART). Proposed is a comparative effectiveness trial with a two-group design in which 165 homeless Veteran smokers will be screened and 126 will be randomized to either:

ABSTINENCE REINFORCEMENT THERAPY (ART), a tele-health intervention that combines guideline-based cognitive-behavioral telephone (CBT) counseling, a tele-medicine clinic for access to smoking cessation aids including choice of pharmacotherapy, and intensive behavioral therapy through mCM.

VA SPECIALTY SMOKING CESSATION TREATMENT *control,* which includes all the elements associated with enrollment in a VA specialty smoking cessation clinic including group counseling, individual telephone counseling, self-help materials, and smoking cessation aids including choice of pharmacotherapy.

Both of the proposed interventions are designed in accordance with national smoking cessation guidelines. Tele-health smoking cessation interventions are typically less intensive than clinic-based specialty care, but increase reach of services through bypassing barriers to participation such as transportation. The addition of mCM to an evidence-based tele-health smoking intervention will significantly increase the intensity of the intervention and is predicted to increase efficacy. If cessation programs are to have significant impact (Impact = Reach X Efficacy) (Abrams, et al., 1996) on changing health behavior at the population level, we must identify new and innovative strategies to increase treatment intensity, access, and participation. Specific aims are to:

AIM 1: Evaluate the impact of ART on rates of abstinence from cigarettes as measured by bio-verified, self-reported prolonged abstinence at post-treatment, and 3-month, 6-month, and 12-month post-randomization follow-ups.

Hypothesis 1: Abstinence rates will be significantly higher among homeless Veterans randomized to the ART intervention than among those randomized to the VA specialty smoking cessation intervention (primary end-point will be self-reported and bio-verified prolonged abstinence at the 6-month follow-up).

AIM 2: Evaluate the relative cost-effectiveness of the ART intervention in quality adjusted life years (QALY).

Hypothesis 2: ART will result in greater cost-effectiveness compared to the control condition as measured by the incremental cost-effectiveness ratio.

AIM 3: Evaluate potential treatment mediators including self-efficacy-related mechanisms.

Hypothesis 3: Increased abstinence associated with ART will be partially mediated by increased self-efficacy compared to the VA specialty smoking cessation care condition.

Supplementary AIM 1: To evaluate the impact of psychiatric (i.e., PTSD, depression and alcohol abuse) symptoms on treatment outcome across the two conditions.

Supplementary AIM 2: To evaluate the impact of smoking status on HIV disease progression (presence of AIDS-related illnesses) and disease progression markers (CD4 T-cell count, viral load).

The funding source for the study is a VA Rehabilitation Research and Development Merit Review awarded to Dr. Jean Beckham. Portions of the salaries of Dr. Beckham's study team are funded by this grant.

METHODS

Participants

We anticipate consenting and screening 165 homeless male and female adult Veterans in order to reach our goal of randomizing 126 participants. Based on the following conservative assumptions, we expect to be able to recruit approximately 165 Veterans in the 36 month enrollment period; we anticipate more than 35 screen outs at the screening visit. There are currently over 67,000 Veterans enrolled at the Durham VAMC and approximately 33% of these Veterans are current smokers. There are currently at least 1,231 homeless Veterans with co-morbid nicotine dependence enrolled at the DVAMC. If we enroll only 11% of eligible homeless smokers we expect to achieve our recruitment goal of 126 eligible Veterans within a 36 months recruitment window. Based on our previous studies, we expect that 10-15% of our participants will be female, and 40% will be minorities. See Table 1 for a summary of the study's inclusion and exclusion criteria.

Table 1. Inclusion/Exclusion Criteria

Veterans must meet **all** inclusion criteria:	Veterans who meet **any** one of the exclusion criteria will be excluded:
• Homeless • Enrolled in the Durham VA for ongoing care • Current smokers (at least 10 cigarettes or equivalent daily) • Willing to quit smoking in the next 30 days	• Has current uncontrolled substance use disorder (other than nicotine dependence) that would interfere with his/her ability to perform study procedures • Uncontrolled psychotic symptoms • Severely impaired hearing or speech (Veterans must be able to respond to phone calls.) • Lack of interest in participating in telephone care • Pregnancy

There are multiple competing definitions for "homeless." We will use the definition followed in the most recent VA congressional report (Perl, 2012) that defines homelessness as one of the following: 1) living in a shelter; 2) living in an institution that provides temporary residence; 3) a public or private place not designed for regular sleeping accommodation for human beings; 4) imminent loss of housing; and 5) other federal definitions including a) experienced a long term period without permanent house; b) instability as evidenced by frequent moves; or c) can be expected to continue in unstable housing due to factors such as chronic disabilities.

Recruitment

Study staff will identify potential eligible Veterans using several different means. First, potentially eligible Veterans may be identified through data pulls from DVAMC's electronic medical record using Fileman. The study staff will also work closely with staff in the DVAMC's Healthcare for Homeless Veterans program to identify potentially eligible Veterans. Flyers, informational business cards and brochures that have been approved by DVAMC's Institutional Review Board (IRB) will be posted on research bulletin boards, program offices, and clinic areas, including the VA's Infectious Disease Clinic. In addition, study staff members will visit local housing facilities (e.g., shelters, transitional housing developments) to identify potential participants, and flyers and brochures will be placed in those community settings. We will also advertise via the closed circuit television system within the VA Medical Center. We will post ads in local newspapers and online classified advertisement services, including Craigslist.com. Also, upon approval from the Public Affairs officer, we will host informational tables in the medical center. At these informational tables, IRB-approved recruitment materials from the study (and from other studies run in the Traumatic Stress and Health Research Laboratory) will be made available to interested veterans, and study staff members may be on site to answer questions about the research studies. No participants will be consented or screened at these public locations.

If a Veteran is identified from the electronic medical record, he/she will be sent an introductory letter signed by the PI that describes the study and informs them that they will be called or contacted regarding participation. If the electronic medical record reveals that the Veteran has an upcoming appointment at the medical center, that Veteran will be sent a special letter indicating that the study coordinator may be available to meet them at their scheduled appointment. The study coordinator will contact via encrypted email the scheduled provider to notify the provider that the Veteran is potentially eligible, and ask him/her to mention the study and provide basic information (if willing). The clinician will be asked to introduce the potentially eligible Veteran to the study coordinator in person. The study coordinator would then describe the study,

stress the voluntary nature of the study, and if possible, determine basic eligibility using the IRB-approved telephone screen. If a clinician does not wish to assist recruitment in this manner, he/she will also be given the option of providing a direct referral via a paper form; see following paragraph. If the clinician indicates unwillingness to assist with recruitment, the study coordinator will not solicit help from him/her. In both versions of the recruitment letter, potential participants will be given an "opt-out" number to call in order to decline participation and/or further contact regarding participation. Study staff members will perform random spot-checks of names and addresses on 20% of all letters prior to mailing. This will capture any sorting error that may have occurred during the preparatory procedures. Seven business days after the mailing, Veterans who have not called the toll free number to decline participation may be called by a study staff member to request their participation in the research study. In the telephone contact, the study staff member will inform the Veteran that he/she was contacted for recruitment because he/she is a homeless Veteran who smokes and is registered for care at DVAMC. Any Veteran who contacts or is contacted by study staff will be told that their participation is voluntary, and they may choose not to answer any questions that they find too sensitive. Also, Veterans will be told that their participation will not affect their care at the VA. The study staff member will explain the study in detail, including compensation. No study procedures will begin until formal, written informed consent has been obtained.

Because Traumatic Stress and Health Research Laboratory has many studies that are currently enrolling participants, we will utilize a centralized recruitment strategy in order to "triage" participants into the correct studies. We have created a centralized recruitment phone screen and flowchart that reflects our current studies. When any potential participant contacts our centralized recruitment telephone number, the study team member answering the VA phone line will use the centralized phone screen to determine potential eligibility. The study team member will then pass along any potential participants' information to the study coordinator for the appropriate study. That study coordinator will use his/her study-specific phone script to further determine eligibility.

In conversations with clinicians from several clinics in DVAMC, we have been provided the feedback that they strongly prefer to provide potential participants' names and contact information. Clinicians have reported that they Veterans often indicate that they prefer that their names and contact information be provided directly to study staff. We'd like to make it easy for interested Veterans to get involved in research, while protected the privacy of those Veterans who are not interested in research. Towards that end, we have developed a system whereby clinicians can more directly identify potentially eligible participants. We will ask that the clinician or provider provide basic information about the study to potentially eligible Veterans; clinicians will be provided IRB-approved recruitment materials to assist this patient education. If the Veteran is interested in learning more about participation, the clinician or provider will provide a "Contact Me" information sheet to the Veteran for him/her to complete. We will request that all "Contact Me" sheets will be completed by the Veteran, not by the provider. The information sheet includes options for contact by the study staff (e.g., send me information, call me, send me information and call me). If any Veteran prefers to receive information by mail, he/she will be sent the IRB-approved recruitment letter. Any Veteran who prefers to receive information by phone will be contacted using the IRB-approved telephone script. This information sheet will provide "…written documentation that the subject is willing to be contacted by telephone about the study," as outlined in VHA Handbook 1200.5. "Contact Me" sheets will be delivered to study staff members via secured means (e.g., internal VA snail mail, encrypted Outlook emails with pdf attachments, personal delivery). Any sheets sent via internal VA mail will be placed inside a sealed and addressed envelope that is THEN put into the snail mail envelope. This plan has been reviewed with local privacy and information security officers. Similar to VA consults, if any clinician finds use of the "Contact Me" sheets to be too onerous, he/she can refer

a participant directly to our clinic by adding the study PI or study coordinator as a co-signer to a note in CPRS in which the clinician has documented that the participant wishes to be contacted about participation.

In order to reach a wider range of homeless Veterans, we will plan to use a recruitment method referred to as respondent-driven sampling, or "seed recruitment" (Christina Meade, Ph.D., personal communication). Seed recruitment is suitable for sampling "hidden populations" of participants who are best known by their own peers (Heckathorn, 1997). It includes providing incentives to participants for referral of other eligible participants. In our model, each participant, or seed, will receive six coupons to recruit other Veterans in his/her social networks. The recruitment coupons will provide a brief description of the survey and a phone number for contacting the study coordinator. The coupon will be marked with a unique identification number (not the study identification number) so that when the coupons are returned to us, the ID number can be used to provide a small payment ($25) to the participant who made the referral. The key connecting the participant's study ID number with the seed ID number will be kept in a database separate from other PHI, creating two layers of separation between the seed ID and the already-participating Veterans' identifying information. Any Veteran who does not wish to recruit in this manner will not be required to do so.

There is evidence suggesting that research study branding may be helpful for recruitment and retention of research participants, especially those with low incomes (Nicholson et al., 2011). In order to enhance recruitment and retention, we'd like to use branded recruitment materials and provide branded materials to participants. Branded materials may include banners, tote bags, and plastic bracelets. Of course, any participant who does not wish to use the branded materials such as the tote bag will not be required to do so.

Study Procedures

Table 2 depicts a summary of study procedures for control group participants; Table 3 depicts a summary of study procedures for ART group participants.

Table 2. Control Group Study Procedures

Session	Tasks	Time	Payment
1 (lab)	• Consent • Screening (clinical interview, questionnaires) • Urine sample, breath sample taken • Referral to VA specialty smoking cessation • Seed recruitment coupon distribution	30 min 3.5 to 4 hours	$50 $10 for coupon return
7 (phone; about 9 weeks after enrollment)	• Quick phone check-in	10 min	None
8 (lab; 3 month follow-up)	• Questionnaires • Saliva sample & urine drug screen requested	20 min	$25 for survey; $75 for returned saliva sample; potentially $100 for abstinence
9 (phone; 6 month follow-up)	• Questionnaires • Saliva sample & urine drug screen requested	20 min	$25 for survey; $75 for returned saliva sample
10 (phone; 12 month follow-up)	• Questionnaires • Saliva sample & urine drug screen requested	20 min	$25 for survey; $75 for returned saliva sample
		TOTAL	**Up to $460**

Session 1. All participants will complete an initial screening visit. At the beginning of the visit lasting approximately five hours, participants will meet with a senior staff member. The study will be explained in detail and informed consent with HIPAA authorization will be obtained. The participant will then provide a breath sample in order to assess CO level. Urine will be collected for drug screening to corroborate participants' self report. Because a substance use disorder that would impact ability

to participate in study procedures, not any drug use, is an exclusion criterion for this study, any participant whose urine drug screen is positive will not necessarily be excluded from participation. Exclusion will be based on psychiatric interview results, with drug screen results serving as corroborating evidence for reported abstinence where applicable. Any woman who is of child-bearing age and/or potential will be given a urine pregnancy test. Pregnant women will be excluded from participation.

Participants who continue to be potentially eligible will be interviewed using the Structured Clinical Interview for DSM IV Diagnosis (SCID; First, Spitzer, Gibbon, & Williams, 1994) in order to further determine participant eligibility. If during the SCID interview a participant endorses risk for suicidal or homicidal ideation, staff members will follow policy set out in the Traumatic Stress and Health Research Laboratory's Psychiatric Emergency Standards of Practice.

Table 3. ART Group Study Procedures

Session	Tasks	Time	Payment
1 (lab)	• Consent • Screening (clinical interview, questionnaires) • Urine sample, breath sample taken • Seed recruitment coupon distribution	30 min 4-4.5 hours	$50 $10 for coupon return
2 (phone)	• Counseling session 1 • Set target quit date (midnight before session 4)	30 mins.	None
Training call (phone)	• mCM equipment training	15 mins	None
3 (phone)	• Counseling session 2 • Begin practice mCM for 1 week • Begin bupropion if using	30 mins.	Up to $14 for monitoring between 3 & 4
4 (phone)	• Quit day • Counseling session 3 • Begin abstinence mCM • Begin NRT	30 mins.	Up to $132.50 for monitoring between 4 & 5
5 (phone; 2 wks post session 4)	• Counseling session 4 • Continue abstinence mCM • Reduce NRT to 14 mg • Continue use of "rescue" NRT PRN	30 mins.	Up to $333.50 for monitoring between 5 & 6
6 (phone; 2 wks post session 5)	• Counseling session 5 • Continue mCM wash-out period • Reduce NRT to 7 mg • Continue use of "rescue" NRT PRN	10 min	Up to $48 for monitoring between 6 & 7
7 (phone; 2 wks post session 6)	• Quick phone check-in • Prompt to return equipment • Cease NRT	10 min	$50 for returned equipment
8 (lab ; 3 month follow-up)	• Questionnaires • Saliva sample & urine drug screen requested	20 min	$25 for survey; $75 for returned saliva sample; potentially $100 for abstinence
9 (phone and/or lab; 6 month follow-up)	• Questionnaires • Saliva sample & urine drug screen requested	20 min	$25 for survey; $75 for returned saliva sample
10 (phone and/or lab; 12 month follow-up)	• Questionnaires • Saliva sample & urine drug screen requested	20 min	$25 for survey; $75 for returned saliva sample
		TOTAL	**Up to $1038**

Participants will meet with a study staff member to complete study measures using a REDCap survey in which participants are "interviewed" for survey answers. We have chosen this method of collection of baseline measures because it most closely matches the collection of questionnaire data in the telephone follow-up sessions. The baseline survey will include the following measures:

1. A demographics measure inquiring about age, race, gender, marital status, education, employment status, travel time, cell and smart phone use, and homelessness status/definition information (Perl, 2012);
2. The Fagerström Test of Nicotine Dependence [FTND; (Heatherton, et al., 1991)] and a general smoking history questionnaire (e.g., number of cigarettes smoked/day, age of first smoking, living with a smoker);
3. A brief checklist asking about contraindications to NRT and bupropion;
4. PTSD Checklist for DSM-5 [PCL-5; (Weathers, et al., 2013)];
5. Patient Health Questionnaire [PHQ-9*;* (Spitzer, et al., 1999)];
6. Three-item AUDIT-C (Bush, et al., 1998);
7. A single item to assess global self-efficacy to quit smoking: "How confident are you that you will be able to quit smoking?" [1= Not at all confident to 4= Very confident; (Shiffman, et al., 2000)];
8. Quality of life will be measured using the EuroQol 5D (The EuroQol Group, 1990). The EuroQol includes questions designed to measure quality of life across five domains: mobility, self care, usual activities, pain/discomfort, and anxiety/depression. This measure is required for computing quality-adjusted life years.
9. Several questions designed to measure electronic cigarette use;
10. Several questions designed to evaluate efficacy of CO readings and recording as an indication of abstinence (at 3-month follow-up only);
11. The Smoking Abstinence Questionnaire (Hendricks et al., 2011), which is a measure of expectancies related to quitting smoking;
12. An alcohol use assessment designed by National Institute on Alcohol Abuse and Alcoholism (NIAAA; from http://www.niaaa.nih.gov/research/guidelines-and-resources/recommended-alcohol-questions;
13. A marijuana use measure, including items related to marijuana smoking history (Bonn-Miller & Zvolensky, 2005) and motives for marijuana use (Simons, Correia, Carey, & Borsari, 1998);
14. A mobile technology use questionnaire (Erbes et al., 2014) that has been modified to include questions regarding texting;
15. The revised Helping Alliance Questionnaire (HAQ), which measures participant alliance with the therapy and the individual therapist. Therapeutic alliance has been shown to be an important construct that predicts positive outcome in therapy (Horvath & Luborsky, 1993);
16. The Role Functioning Scale, which measures adult functioning in four domains: working productivity, independent living and self care, and both immediate and extended social network relationships (Goodman, Sewell, Cooley, & Leavitt, 1993);
17. The Social Disconnectedness Scale and Perceived Isolation Scale, which measure two aspects of social isolation: social disconnectedness, or lack of contact with others, and social isolation, or a lack of social resources for relationship-building (Cornwell & Waite, 2009a; Cornwell & Waite, 2009b); and
18. Self Efficacy to Overcome Personal Barriers to Cessation, which is a 9-item scale designed to identify those circumstances in which a person feels tempted to smoke.

At this first session, eligible participants will be randomized to one of the two treatment groups. Any Veteran who is randomized to the control condition will be informed that a consult will be placed for smoking cessation at this facility's specialty smoking clinic. Participants will be told that he/she will contacted approximately nine weeks later, and at, 3, 6, and 12-month follow-up sessions, and that they may be contacted briefly prior to these follow-up sessions for a check-in by study staff.

Any Veteran who is randomized to the ART group will be offered up to a 12-week course of NRT in the form of nicotine patches and up to two rescue methods (e.g., nicotine lozenge). Participants will be screened for

suitability for NRT or other smoking cessation aids (SCA), including bupropion. Veterans will receive tailored amount and delivery type of NRT based on number of cigarettes smoked per day [using an established protocol (Bars, et al., 2006)]. All participants who are medically eligible may also be prescribed bupropion. Any eligible participants will be prescribed sustained-release bupropion, 150 mg/daily for days 1 to 3 and 300 mg/daily (administered in two daily doses) for the remaining study period. Participants will be allowed to continue bupropion through the 6 month follow up visit or their final study visit (if they drop out earlier).

NRT will be provided via mail. Should the Veteran want NRT or other smoking cessation aid that is not available over the counter, an appointment will be made for him/her in the medication clinic. Dr. Moore will write the NRT prescriptions and both Dr. Moore and the study coordinator will work with patient's primary VA physician to discuss contraindications. In those cases in which a participant reports contraindications to NRT (e.g., high blood pressure not controlled by medication) or other contraindications to bupropion, the study coordinator or Dr. Moore will contact the participant's primary VA physician in order to obtain authorization to use the study medications. In order to determine eligibility to use SCA, study staff will review participants' self-report measures and available CPRS records for any relevant health information. This will include, but is not limited to, liver function tests where available, because bupropion use is contraindicated in persons with renal impairment, hepatitis, cirrhosis, seizure disorder, and/or uncontrolled diabetes. If a participant with a seizure disorder, history of or current hepatitis and/or cirrhosis, renal impairment, and/or uncontrolled diabetes wishes to enroll in the study, he/she will not receive contraindicated medications. If a participant with any of these medical conditions is unwilling to participate in the study without taking bupropion, he/she will be withdrawn from the study. In addition, any participant who has not had a recent liver function test will be asked to either participate without taking bupropion or have a blood test (to examine liver function) within three months of beginning bupropion. Study medications will be administered and delivered through the standard VA pharmacy rather than the research VA pharmacy, as all Veterans are eligible for NRT through the VA pharmacy, and the NRT prescribed is not the focus of the study and does not differ from that offered in the Stop Smoking Clinic, of which Dr. Moore is the prescribing physician.

Participants will be prescribed nicotine skin patches delivering up to 21 mg/24 hours. Most smokers will be prescribed an initial dose of 21 mg patches; smokers reporting light smoking may be asked to use a lower dose patch in consultation with the study physician. Participants will be provided with detailed information and education regarding the use of the nicotine skin patches. This educational component will include a rationale for using the patches, proper placement of the patch, when to use them, possible side effects, and how to report side effects to research staff as they may occur in the course of the study. Dosage of NRT will be reduced at two week intervals after it is begun. If a participant indicates any negative side effects of NRT use, dose may be adjusted downward based on the physician's recommendations. All doses will be logged for later analysis. Beginning on the identified quit date, participants will be allowed to choose one acute administration "rescue method" of NRT from the following: nicotine gum, nicotine lozenge, nicotine inhaler, or nicotine nasal spray. This rescue method will be used PRN to reduce cravings during the post-quit period. All medications will be mailed to participants.

After randomization, ART participants will receive study equipment, including the smart phone equipped with the study app, and CO monitor. Participants will be provided with a manual that summarizes payment information and provides instructions on use of the equipment. The CO breath monitor is a hand-held battery operated instrument that measures CO in ppm, and provides an LED reading of CO levels. The smart phone provided to participants will be the Droid Razr Maxx (Motorola Mobility Inc, Libertyville, IL) or an iPhone 5C. The Razr Maxx is a FIPS 140-2 compliant device with a dual-core 1.2 Ghz processor, I GB DDR2 RAM, and 4.3" gHD display. The operating system (OS) being utilized for the smart phones is Android 4.1.2, see FIPS 140-2

certificate 1998. The iPhone 5C is a FIPS 140-2 compliant device with 2.4 GHz processor, 4" Retina display. The OS being used for the iPhones is iOS 7.1 in FIPS 140-2 encrypted mode; see FIPS 140-2 certificate 2021. In the event that the Droid Razr Maxx or iPhone 5C are not available in the future, another FIPS-140-2 compliant device may be used upon written approval by the facility's Information Security Officer (ISO). This policy has been developed in conjunction with the ISO. Both phones will be run off the Verizon 4G LTE network because Verizon has the best coverage in North Carolina. It is assumed that most participants will only achieve 3G speeds and the methods proposed in this project are based on 3G speed availability. For each video recording, participants will be asked to 1) begin a recording using the smart phone; 2) show the initial zero CO reading to the camera; 3) video record him/herself holding his/her breath during the monitor's countdown; 4) blow into the carbon monoxide monitor while on camera; and 5) show the final CO reading to the camera. Any video recordings taken with the phone remain on the phone until the phone undergoes a hard reset (i.e., upon return to the lab). It is important for this data to remain on the phone because if technical difficulties prevent participants from uploading a viewable video, the study's technical developer can manually remove the videos from the phone to the web-server. This is important because the readings are crucial to the study's primary intervention, and are therefore crucial to gathering reliable and valid data. Study coordinators can monitor validity and compliance on a daily basis and offer feedback to ongoing participants regarding compensation. Participants will receive training by telephone on how to use the study equipment to perform monitoring; this training session will occur at some time point between sessions 1 and 3, depending on the participant's chosen smoking quit date. Participants will not begin actual monitoring until after Session 3. If a participant is lost to contact after he/she should have begun home monitoring (defined as two weeks of no contact and no video recordings loaded), we will disable the telephone and telephone service, and will only reinstate service if the participant contacts the laboratory. In order to enhance ability to reach participants easily, to encourage full participation, and to limit losing contact with participants, all participants assigned to ART will be allowed to use the study smart phone to make calls to persons other than study staff and to use the phone for text messaging to persons other than study staff. An ORD ISO reviewed this procedure, and indicated to the facility ISO that we have covered information security well enough to allow participants to use the texting feature on the smart phones.

After Session 1 has been completed, the study coordinator, in conjunction with the study physician, will perform a medical chart review to determine HIV status. For those participants who are HIV positive, a medical record abstraction form will be used to collect baseline information regarding HIV treatment, lab results, presence of AIDS-defining illnesses, and medication regimen.

Session 2 (ART participants only). Participants randomized to ART will receive CBT telephone smoking cessation counseling. The treatment manual and participant workbook were adapted from the treatment manual developed as part of VA Cooperative Studies Program #519 on which Dr. Beckham was a co-investigator (McFall, et al., 2010), and are consistent with the Public Health Service Clinical Practice Guide (Fiore, et al., 2000). During this session, participants will set a smoking quit date to occur the day of Session 4. The telephone counseling intervention will be provided by trained clinicians; see "Staff Training" for a description of training activities.

Session 3 (ART participants only). At session 3, participants will receive session two of five of the CBT smoking cessation counseling. At this session, any participants who will be using Bupropion will be prompted to begin the study medication. They will also be prompted to begin the practice week of mCM. Participants will be asked to provide fourteen CO samples prior to Session 4. They will be instructed to take two readings per 24-hour period, with at least eight hours between each sample. For the first week of monitoring, participants

will be reimbursed $1 per reading for each CO sample that they provide, regardless of the CO reading itself; that is, reimbursement is not based on abstinence for the first week of readings. The purpose of this week of monitoring is to ensure that there are no difficulties with taking the readings and video, and uploading the video to the website. Beginning at Week 2 of mCM, all compensation will be for uploading videos that suggest an abstinent CO reading. Participants will receive monetary compensation based on their own reduced CO readings; see Table 4 for the abstinence-based payment schedule.

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. Participants will not be able to view videos once they have been uploaded to the secured website; they will see only their reinforcement information. Study coordinators can monitor validity and compliance on a daily basis and offer feedback to ongoing participants regarding compensation. Because an escalating versus a fixed reinforcement schedule has produced higher abstinence rates (Heil, et al., 2008, Stoops, et al., 2009), an escalating schedule will be used in this protocol (identical to our pilot study). Participants can check their compensation level at any time through the application. However, they do not receive their final payment until the mCM treatment and two-week follow-up period is completed. Although in general immediate reinforcement is more powerful than distant reinforcement, our pilot data indicate that the proposed procedure results in patient engagement and treatment completion.

Table 4. mCM Reinforcement Schedule

	Days Post Quit	1st CO	2nd CO	Bonus	Total*
Week 1	-1 to -7	$1.00	$1.00		$14.00
Week 2	1	$1.00	$1.25		$16.25
	2	$1.50	$1.75		$19.50
	3	$2.00	$2.25		$23.75
	4	$2.50	$2.75		$29.00
	5	$3.00	$3.25	$5.00	$40.25
	6	$3.50	$3.75		$47.50
	7	$4.00	$4.25		$55.75
Week 3	8	$4.50	$4.75		$65.00
	9	$5.00	$5.25		$75.25
	10	$5.50	$5.75	$5.00	$91.50
	11	$6.00	$6.25		$103.75
	12	$6.50	$6.75		$117.00
	13	$7.00	$7.25		$131.25
	14	$7.50	$7.75		$146.50
Week 4	15	$8.00	$8.25	$5.00	$167.75
	16	$8.50	$8.75		$185.00
	17	$9.00	$9.25		$203.25
	18	$9.50	$9.75		$222.50
	19	$10.00	$10.25		$242.75
	20	$10.50	$10.75	$5.00	$269.00
	21	$11.00	$11.25		$291.25
Week 5	22	$11.50	$11.75		$314.50
	23	$12.00	$12.25		$338.75
	24	$12.50	$12.75		$364.00
	25	$13.00	$13.25	$5.00	$395.25
	26	$13.50	$13.75		$422.50
	27	$14.00	$14.25		$450.75
	28	$14.50	$14.75		$480.00
Week 6	29-35	$1.00	$1.00	$10.00	$504.00
Week 7	36-42	$1.00	$1.00	$10.00	$528.00

***Note. Total column indicates possible cumulative payment amount.**

Session 4 (ART participants only). During Session 4, participants will participate in the third of five CBT counseling sessions, which corresponds to participants' smoking quit day. During this session, participants will be prompted to begin NRT, and to begin abstinence mCM (see Session 3 description above).

Session 5 (ART participants only). During Session 5, which occurs approximately two weeks after Session 4, participants will participate in the fourth CBT counseling session. Participants will continue abstinence mCM.

Any participant using NRT will be prompted to begin using a lower dose patch, and to continue bupropion where applicable.

Session 6 (ART participants only). Session 6 will occur two weeks after Session 5. In this telephone contact, participants will participate in the final CBT counseling session. Participants will be prompted to continue mCM. Beginning at this session, the escalating reinforcement schedule used for the previous four weeks will be discontinued, and participants will enter a "wash-out" period in which they are paid $1 for each reading, regardless of abstinence. Each week, if participants have provided twice daily readings, they will be paid an additional $10 bonus. In session six, any participant using NRT will be prompted to begin using a lower dose patch, and to continue bupropion where applicable.

Session 7 (both control group and ART participants only). Session 7 will be a quick telephone check-in. For ART group participants, this contact will occur two weeks after Session 6. For control group participants, this contact will occur approximately nine weeks after the screening session. In this telephone contact, all participants will be asked to rate the helpfulness of any therapy they received. ART group participants will be prompted to end NRT use and to continue Bupropion use where applicable. ART group participants will be asked return their loaned smart phone and CO monitor, and will be provided a postage-paid mailer for the equipment return, and will be offered $50 as incentive for return of the equipment. Any unreturned equipment will be reported to the Institutional Review Board (IRB), ISO, facility Privacy Officer (PO), and other appropriate personnel as dictated in the Traumatic Stress and Health Research Laboratory's Standard Operating Procedures (SOP) regarding study equipment. This SOP has been previously approved by the facility's ISO, and has been used successfully in by our staff in numerous IRB-approved studies at the Durham VA. In addition, we will report any data security and/or privacy issues to the ISO, PO, IRB, and other agencies immediately, as dictated by our facility's Human Research Protection Program SOP.

Results of our recent research have suggested that abstinence rates may improve at 3-month follow-up visits when participants are offered a $100 reward for abstinence (rather than simply money for providing a saliva sample; see Hertzberg et al., 2013 from IRB #1294 and Carpenter et al., in press from IRB #1666). We would like to examine rates of reported abstinence further. Towards that end, prior to Session 8 (3-month follow-up), all participants (control and active treatment groups) will be randomized to two conditions for abstinence reinforcement and will be informed of their randomization group. Half of all participants will receive $100 for biochemically verified (i.e., salivary cotinine) abstinence at Session 8 (abstinence incentive); half will receive no incentive pay for abstinence at Session 8 (no abstinence incentive).

Following Session 7, the study coordinator will complete a second medical abstraction form for any participant who indicated HIV-positive status at the screening session.

Session 8 (both control group and ART participants). Session 8 will be a 3 month follow-up laboratory visit. In this session, participants will be interviewed regarding general functioning (i.e., Role Functioning Scale), social isolation, current cigarette use, nicotine dependence, self-efficacy for quitting and/or remaining quit, and their use and adherence with SCAs (e.g., nicotine replacement). Medical records will be reviewed to examine and corroborate self-reported SCA use. Veterans in both arms will be asked to evaluate the care they received. Any participant who reports a relapse to smoking will be interviewed to determine approximate date of relapse using the Timeline Follow Back method (Lewis-Esquerre, Colby, Tevyaw et al., 2005). We have recent experience using this method to assess daily smoking behavior. Because smoking relapse often occurs in the context of substance use, we will evaluate alcohol and cocaine use in conjunction with smoking using this procedure. In this session, participants will provide a CO reading and a saliva sample for bio-verification (see

"*Biochemical Verification"* below). Participants will also be asked to provide a urine sample for a urine drug screen. Urine drug screens will only be used as another source of information regarding substance use. If any participant is unwilling or unable to attend an in-lab appointment to complete these study procedures, he/she will be allowed to complete the measures over the phone and to mail in a saliva sample. Participants who cannot come to the lab for the saliva sample will not be asked to provide a urine sample. Participants are sent instructions, saliva vials, a brief tobacco use assessment (that includes use of nicotine replacement therapies in the prior week), and a postage-paid padded envelope for returning the sample to the study coordinator at the VA. The saliva sample will be analyzed for salivary cotinine, a by-product of nicotine. As indicated above, any participant randomized to the "abstinence incentive" group will receive $100 for self-reported and CO-verified abstinence at this session.

Session 9 (both control group and ART participants). Session 9 will be a 6-month follow-up telephone contact. In these sessions, participants will be interviewed regarding general functioning (i.e., Role Functioning Scale), social isolation, current cigarette use, nicotine dependence, self-efficacy for quitting and/or remaining quit, and their use and adherence with SCAs (e.g., nicotine replacement). Medical records will be reviewed to examine and corroborate self-reported SCA use. Veterans in both arms will be asked to evaluate the care they received. Any participant who reports a relapse to smoking will be interviewed to determine approximate date of relapse using the Timeline Follow Back method (Lewis-Esquerre, Colby, Tevyaw et al., 2005). We have recent experience using this method to assess daily smoking behavior. Alcohol and cocaine use will also be assessed using the method. At Session 9, any participant who was assigned to the ART condition and used bupropion as a SCA will be prompted to cease use. Participants will be asked to attend a brief appointment in the Traumatic Stress and Health Research Laboratory. During this visit, participants will provide a saliva sample and urine sample. As stated above, any participant who is unable or unwilling to attend an appointment will be allowed to complete the measures over the phone and to mail in a saliva sample. Only those participants who provide a saliva sample in person will be asked to provide a urine sample.

Session 10 (both control group and ART participants). Session 10 will be a 12-month follow-up telephone contact. In this session, participants will be interviewed regarding current cigarette use, current e-cigarette use, alcohol use, and marijuana use. Participants will be asked to attend a brief appointment in the Traumatic Stress and Health Research Laboratory. During this visit, participants will provide a saliva sample and urine sample. As stated above, any participant who is unable or unwilling to attend an appointment will be allowed to complete the measures over the phone and to mail in a saliva sample. Only those participants who provide a saliva sample in person will be asked to provide a urine sample.

In order to enhance participant retention at the 6-month follow-up, we will mail to participants a Veterans' Day card, birthday card, and a "thank you" card. These strategies have been used by Wisniewski and colleagues (2006) to increase retention.

Biochemical Verification. Self-reported prolonged abstinence will be verified by cotinine assay after each follow-up session. Our choice of primary and secondary smoking endpoints follows recommendations by the Society of Research on Nicotine and Tobacco (SRNT; Hughes & Brandon, 2003). Self-reported and bio-verified prolonged abstinence at the 6-month follow-up will be the primary end-point. Following definitions used in VA CSP-519 (McFall et al., 2010), we define nonabstinence as smoking (or other tobacco use) for 7 consecutive days or at least once a week for 2 consecutive weeks. Prolonged abstinence will exclude tobacco use in the first two weeks following the quit date (Hughes & Brandon, 2003). Saliva samples will be collected from participants who report prolonged abstinence at each follow-up. This process has been shown to improve the validity of self-report smoking cessation. After saliva samples are collected, they will be sent for analysis to the

University of California at San Francisco Pharmacology Laboratory for analysis. Coded samples will be sent by trained study team members in accordance with the standards of practice outlined in Research Transporting and Shipping Biological Specimens, SRS SOP 202, including samples being mailed by trackable courier. Saliva samples will be analyzed for the presence of cotinine using a standard cut point off 10 ng/ml to determine abstinence. A blind sample of 5% will be run again to assure test accuracy of saliva samples. Secondary smoking outcomes will include 7- and 30-day point prevalence abstinence at each assessment, where abstinence is defined as no tobacco use in the prior 7 or 30 days respectively (McFall et al., 2010). Any participant who provides a saliva sample as requested will be paid $75. We have found in previous IRB approved projects (Calhoun IRB #1415) that participants are unlikely to provide saliva for less money than this, and given that bioverification of abstinence is crucial to the specific aims of the study, we believe this payment is warranted.

Following Sessions 9 and 10, the study coordinator will complete medical abstraction forms for any participant who indicated HIV-positive status at the screening session.

During this study, it is anticipated that participants will miss scheduled telephone contacts. This does not necessarily constitute a protocol deviation. If a no-show or a missed appointment causes interruption in study activities (such as more than 2 days of missed medications), we will report the missed appointments to the IRB as protocol deviations. Otherwise, the missed appointments will be recorded in study databases as necessary. Also, throughout the study, study staff may contact enrolled participants regarding study-related concerns, scheduling/rescheduling appointments, or appointment reminders.

Optional Study Procedures. With subjects' written consent, contact information containing identifying information such as name, address, phone number, and dates of research participation along with diagnostic information will be added into a "Contact Database". The purpose of this database is to re-contact potential subjects about future studies for which they may qualify. Potential participants will only be contacted about future studies under the direction of Dr. Beckham and her staff. Only Dr. Beckham and her research staff will have access to this database, which will be housed on the VA Network's S:\ Drive (path S:\Nicotine Research\Study Information\Study Logbooks).

Diagnostic, demographic, and questionnaire data and other information collected as part of this study will be added to a larger database entitled 'Trauma Database.' Data coding and complete confidentiality of all subject information in the "Trauma Database" will be accomplished in a three-step process. First, information from this study will be coded and will only be linked by an assigned random study number. Second, information collected from other protocols run by Dr. Beckham will be coded and linked by the random study number. Lastly, the information will be merged into the larger "Trauma Database" which will be used for future research. Information collected from many study participants (500 or more) from different studies will then be examined to inform researchers about the topic they are trying to learn more about. Topics of research change over time and for that reason, the development of a combined research database is particularly useful. The purpose of combining information collected from numerous studies is to increase the power of the statistical analysis of genetic, diagnostic, questionnaire and other assessment data. Each study that deposits data into the 'Trauma Database' repository will not include any of the 18 individual identifiers under the Privacy Rule.

Participant Reimbursement. As described in Table 2 above, participants who are randomized to the control group may receive up to $460 for full participation in the study. Participants randomized to the ART condition may receive up to $1038 for full participation. Differential rates of payment for the two conditions are

important, as evaluation of the impact of financial contingencies for smoking cessation is central to the study. Also, participants randomized to ART will devote much more time and effort into study participation, and payment should reflect this additional burden. In each condition, to ensure that patients assigned to the ART group return the CO monitor and phone, we are providing postage paid return mailers and adding a $50 incentive for each equipment return. In order to enhance rates of equipment return, any participant who doesn't return loaned study equipment will have their final payment decreased by $100.

In our previous studies, the follow-up rates for surveys have been consistently less than 75%. We suspect that subjects who continue to smoke are less likely to complete the follow-up surveys. Based on our experience in our previous HSR&D smoking projects, we are adding a $25 incentive for completing each follow-up survey. We have used these incentives in other studies with success (McBride, Bastian, Halabi et al., 2002). If participants report abstinence at the 3, 6, and 12 month follow-ups, they will be paid $75 to provide a saliva sample.

We will present the overall payment information in the informed consent document; however, rather than describe in detail in the informed consent form the payment details for mCM in the ART condition, participants assigned to that condition will be provided information about details of payment in the instruction manual "mCM: Mobile Contingency Management Manual." We believe that the payment information is detailed and thorough, and that this detailed information would not be useful to provide to all participants. Rather, we believe that the information is really only relevant to participants in the ART condition.

Payment will be issued to participants via check, as has been consistent with other telephone-based care studies run by our study team. Checks for payment will be issued through VA Financial Services. VA has recently changed payment options such that Veterans who have a bank account are paid through direct deposit into their account. Study staff members are required to complete a "Vendorizing Coversheet" with participants, which includes bank account information. Participants will be informed that payment will be received approximately 4 to 6 weeks after it is requested.

For those study visits that occur in the research laboratory, participants in both arms may be provided with local bus passes in order to facilitate transportation.

Staff Training. Of the study measures utilized, only the SCID requires specific training or skills for administration (above a BA degree). As in our other studies, multiple 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 interview meetings, and consultation is provided regularly to interviewers.

All clinicians who will be providing the smoking cessation counseling intervention will attend a half-day training meeting during which they will be trained by Drs. Calhoun & Beckham, both clinical psychologists who have extensive clinical and research experience providing cognitive-behavioral interventions for smoking cessation. After training, counselors will role-play each counseling session with another staff member. These sessions will be videotaped and rated for fidelity and competence by Dr. Calhoun using the Yale Adherence

and Competence Scale system [YACS; (Carroll, 2000)]. Counselors will not be allowed to provide the intervention to live participants until they have demonstrated 100% competence and adherence with the required elements of each treatment session. During the study, a random selection of twenty percent of all counseling sessions will be audio-recorded, using a VA approved audio recorder, and Dr. Calhoun will rate counselor treatment fidelity/adherence using the YACS (Carroll, 2000). Only the therapist portion of the interaction will be recorded, therefore voice print of the participants will not be collected during these fidelity checks. The therapist will ensure that the phone is not being used on speaker, and we will ask therapists not to use any names or other identifiers while talking to the participant. At present, VA records control requirements do not require us toretain audiorecordings that are collected for the purpose of establishing treatment fidelity. Therefore, audiorecordings will be deleted from the approved audio recorder after fidelity has been established. The system includes checklists for measuring critical treatment elements. Fidelity feedback will be provided to the counselors. In order to protect against drift, the frequency of fidelity review will occur equally across the beginning, middle, and end of the intervention period. Counselors will attend weekly supervision meetings to review critical points in counseling sessions and receive ongoing consultation.

Rationale for Using and Description of VA Specialty Care as a Control Comparison. We considered using primary care based smoking cessation care or telephone counseling as the control comparison. Although national clinical practice guidelines (CPG) suggest that intensive interventions associated with specialty care are "more effective than less intensive interventions and should be used whenever possible," (Fiore, et al., 2000) there is significant disagreement in the tobacco control field regarding how smoking cessation care should be structured (Sherman, et al., 2006). Many experts emphasize treatment in specialty clinics has been shown to be most efficacious (Fiore, et al., 2000) as well as most cost effective (Cromwell, et al., 1997). Others, citing low enrollment rates in specialty care, argue that primary care approaches should be emphasized (Stead & Lancaster, 2002). Sherman and colleagues (Sherman, et al., 2006) assessed the institutional approach to implementing tobacco CPG among 40 VA facilities. Results suggest that most sites emphasized a specialty approach and some restricted medications to those attending a specialty clinic. Thus, our decision to compare the ART intervention to specialty care was based both on recommendations from the CPG and evidence suggesting that it is currently the preferred approach among VA facilities (Sherman, et al., 2006).

The DVAMC has a long history of providing state-of-the-science specialty smoking cessation care. The specialty Smoking Cessation clinic currently employs the QuitSmart Program (Shipley et al., 1999), which was developed locally and is now used extensively throughout the VA system. The clinic provides group treatment and telephone counseling provided by doctoral-level psychologists and medication management provided by psychiatry. Patients receive three group counseling sessions provided over 6 weeks, a telephone counseling session following their quit date, NRT (up to three forms), bupropion and potentially varenicline (if multiple quit attempts with NRT and bupropion have failed). The treatment is manualized, which will allow us to easily measure which aspects of the intervention were administered to the patient by a review of medical records.

Cost-Effectiveness Measures

Smoking cessation counseling alone or in combination with NRT has been shown to be highly cost effective (Song, et al., 2002). We will estimate the cost and cost-effectiveness of the ART and VA specialty care. Approaches to accounting for costs and outcomes in cost analyses can vary widely. One important variable is the perspective taken in the analysis, i.e., the standpoint from which costs and benefits are realized. Consistent with previous work in this area and with expert panel recommendations (Gold, et al., 1996), we have chosen to take a broad societal perspective as opposed to the unique perspective of the patient, VHA, or other third-party payer. We considered the measurement of future resource utilization costs as an outcome variable, e.g., differences between groups in the costs associated with the number of outpatient and inpatient

visits in the year following the intervention. It is unlikely, however, that groups will differ in smoking-related illness visits in the year following the intervention. Thus, consistent with the Public Health Service (PHS) task force guidelines (Gold, et al., 1996) we propose to use quality adjusted life year (QALY) as the primary outcome. Additionally, we made decisions regarding cost measurement outcomes. Proposed costs will include both intervention delivery costs and participant costs. Costs associated with the development of the interventions will be excluded from the analyses as these costs have already been incurred and are thus "sunk" costs.

Costs to be collected can be grouped into two broad categories: intervention delivery costs and participant time 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.

Costs for both conditions will be estimated using standardized estimates of support staff and our interventionists. The time it takes to prepare for and execute the intervention used in specialty care is already prescribed in the QuitSmart treatment manual. We will use surveys and counselor record to validate these estimates. Providers will be asked to provide time estimates for sessions associated with a subset of 30 patients randomly chosen to estimate time use (see below). Similar methods will be used to estimate time spent in preparing advanced clinic access letters and scheduling appointments (Specialty Care). The time it takes to prepare for and execute the cognitive-behavioral telephone counseling for the ART intervention is specified in the treatment manual but will be assessed through a data tracking system (time spent on all intervention calls will be recorded using interventionist input). Similar methods will be used to estimate time spent in contacting and training Veterans on the use of the mCM smart phone app. Our study physician will use a similar data tracking system to measure time spent administering NRT and other SCAs to participants. The value of time spent on the intervention will be assessed using VA salary and benefits data, and by applying relevant salary and benefit costs to the quantity of time spent by different study staff. In addition to labor costs, materials costs, including the cost of nicotine lozenge, inhaler, mCM and the smart phone, and costs of compensation to participants will be collected. Dr. Van Houtven's group has experience collecting time logs of activities and has published cost effectiveness studies (Wang, et al., 2012). Her group has built proprietary database collection applications tailored to the various interventions being studied at the Durham HSR&D Center of Excellence.

Evaluation of participant time costs will include the time spent by smokers in using the intervention strategies, techniques, or information. As part of the 3-month follow-up, time spent on the intervention materials other than those involved in the telephone sessions (and attendance to the smoking cessation specialty clinic) will be assessed. In the intervention arm, the number of videos submitted will be used to assess the time involved in providing bio-verification as part of mCM. We will derive participant time cost estimates for individuals in each group by combining the time estimates with standard wage estimates adjusted for age, gender, and if possible, race as derived from the Statistical Abstract of the US. 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 participants.

We propose to estimate participant time by a random sample of participants at key points in the intervention. This is intended to minimize participant burden while collecting reliable measures of participant time use for both ART treatment and comparison participants. Specifically, at randomization, 30 patients (15 in ART and 15 in Specialty Care) will be selected randomly to be a part of the time use study. At three different time periods in the intervention (1 week, 3 weeks and 6 weeks), participants will be asked to answer time use questions for the full range of the intervention tasks in which they engage (e.g. total time spent recording and uploading

readings for ART participants; time spent receiving feedback for ART participants, or time spent on CBT for usual care participants). ART participants will be prompted to answer these questions using their loaned smart phone. Control group participants will be contacted by phone during those weeks to answer time use questions. Randomly selecting 30 patients and varying the dates of data collection will allow the time study to reflect the learning curve of delivering and participating in the intervention by smart phone (and in CBT), yet it will not be announced to patients when the time study will occur so that people do not adjust behavior. The approach for providers will mirror that used for patient time use.

The primary effectiveness outcome measure will be quality-adjusted life years (QALYs) (Fiscella & Franks, 1996). The QALY is a standardized effectiveness measure that allows for the comparison of the value of a particular intervention to a broad range of other potential health care investments. Differences in trial quit rates among Veterans in the ART and control 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 Fiscella and Franks (Fiscella & Franks, 1996), who derived estimates of the increase in QALYs due to smoking cessation from published life expectancy data (Rogers & Powell-Griner, 1991), adjusting for the impact of smoking cessation on health-related quality of life. For analyses, quit rates at the 6-month follow-up will be utilized. Participants who remain abstinent from smoking at the 6-month follow-up will be considered sustained quitters and assigned an age and gender specific increase in QALY.

RISK/BENEFIT ANALYSIS

The clinical interview to establish diagnosis can cause some psychological distress in the form of a temporary increase in anxiety, but any ensuing distress is usually well tolerated. There are no known psychological hazards or risks associated with completing questionnaires. Risks also include discomfort related to quitting smoking. Quitting smoking will cause nicotine withdrawal that may lead to headaches, nausea, irritability, weight gain, difficulty concentrating, poor sleep, increased appetite, anxious or depressed mood, and craving for cigarettes. Participants in the ART condition will be offered NRT, and it is likely that participants in the control condition will also be offered NRT. 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. 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. In both conditions, there is a potential risk associated with the loss of confidentiality of study data.

ART participants have a greater risk of violation of confidentiality and/or privacy in the study. Specifically, collection and transfer of videotaped carbon-monoxide monitoring have risks with regards to privacy and confidentiality. We have limited the likelihood that participant identification will occur by developing a method for training participants to provide only their side profile, as a side profile may not be considered a full-face image, and may limit identifiability. In addition, we allow participants to review any videos prior to uploading them, and participants may choose to delete any video that they feel violates their privacy. 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. Care has been taken to ensure that data collection and transport is in keeping with the most recent VHA Handbook 6500, which addresses information security. Data

is encrypted at rest on the smart phone with encryption that is FIPS 140-2 compliant, and is encrypted upon transport and at rest, as well. These methods are the required methods for collection and transfer of PHI and PII.

The Traumatic Stress and Health Research Laboratory has established, 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 (including the PI, co-investigator(s), and/or the DVAMC's Psychiatric Emergency Clinic or Emergency Room).

Serious adverse events will be promptly reported to the VA IRB as required. All project staff will complete educational units required by the Durham VAMC Human Subjects Committee.

Participants may benefit from this study by stopping smoking.

Protection of Vulnerable Population. The VA has identified persons who are homeless as an "other vulnerable population." It is presumed that one of the primary vulnerabilities of this population is the risk of undue influence from monetary compensation. In designing this research intervention, careful consideration has been given to the risk of undue influence. Divergent with our typical design, which includes compensation for attendance at most or all study sessions, we have designed the study such that compensation is mostly based on obtaining and maintaining abstinence from smoking, especially within the ART condition. Within the control group, more than 55% of the total possible payment is related to smoking abstinence. In the ART condition, more than 70% is related to smoking abstinence. We believe that the risk of undue influence is greatly diminished with this design, and that the potential health benefits of smoking cessation greatly outweigh the risk of influence through compensation for cessation.

DATA SAFETY AND MONITORING

Quitting smoking should enhance rather than jeopardize health status, and potential serious adverse events (SAE) for participants in this project are not expected. Regardless, we will minimize potential risk by careful screening of potential participants. In the ART condition, those with contraindications for NRT will require medical clearance by their primary care provider or the study physician or they will not receive NRT. Similar clearance is often required of Veterans enrolled in DVAMC's specialty smoking cessation clinic.

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 DVAMC'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. Dr. Michael Hertzberg will serve as a backup prescriber.

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

between the PIs and study personnel.

Prior to initiation of any smoking cessation aid, participants will be informed again of the potential risks and side-effects associated with NRT. Participants also will be able to call directly via the study toll-free number to report AEs. This toll-free number, directed to the project manager's phone, will be provided to all participants upon entry into the study.

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 (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 local Human Research Protection Program's Standards of Practice.

DATA MANAGEMENT AND SECURITY

Several types of data will be collected over the course of the study. As described under the Request for Waiver or Alteration of Informed Consent and HIPAA Authorization for Research, PHI to be collected during recruitment activities includes name, address, telephone number, and social security number. Other data to be collected over the course of the study (as described in the HIPAA authorization) include name; address; phone number; social security number; dates of study visits; account numbers (for Veterans who have bank accounts, payment will be issued via direct deposit, which requires a Vendorizing Coversheet that asks for account information and VA Form 10-7078 to be obtained), and images potentially comparable to a full-face image. Sources of health information include medical history and physical exam information, videorecordings, saliva and urine specimens, progress notes in CPRS, laboratory test results, survey responses, alcohol and/or drug use information, and mental health notes. This information will be used for research purposes only.

Any hard copy data collected over the course of the study will be stored in a locked file cabinet in a locked office suite in the Traumatic Stress and Health Research Laboratory at the Durham VA Medical Center. Hard copy data will include, but is not limited to, any information gathered from potential participants during the telephone screening process, participant consent forms and HIPAA authorization forms, laboratory test results, and VA forms 10-3203 and 10-9012.

The study team will develop and maintain two databases for the study. The first will be a computer assisted telephone interviewing system that will facilitate the collection of patient measures at baseline, end of treatment, and 3 and 6-month follow-up. The primary database engine technology underlying this system will be the MySQL database server hosted by the VA Information Resource Center (VIReC). MySQL is a relational database management system. The coded data collected during telephone interviews will be managed using REDCap electronic data capture tools hosted at the Department of Veterans Affairs' VIReC. We have chosen REDCap because it facilitates the easy development, collection and entry of research data, it is available at no

cost, and it is hosted within and only accessible from the VA's intranet. All data collected can be exported into a number of standard formats including SAS, MS Access, and SQL.

Second, the study team will develop a MS Access tracking database that will electronically track participants through all components of the study. This tracking data will contain identifiable data, including the key that links participants to study identification numbers; other data collected in the course of the study will be kept separately from identifying information. This database will be stored on a VA secured computer server (S:\Nicotine Research\Study Information\Study Logbooks) that is encrypted, password-protected, and only accessible by Dr. Beckham and study staff. The key to seed recruitment coupons that connects the participant's study ID number with the seed ID number will be kept in a database separate from other PHI, creating two layers of separation between the seed ID and the already-participating Veterans' identifying information.

We have used similar methods of data entry in our prior studies, and internal audits show excellent reliability. All data transactions within and between systems will run through controlled, secure transactions to ensure the preservation of database integrity and privacy. Of primary importance in all study activities will be the security and protection of Veterans' private health information (PHI). All staff will complete educational modules designed to improve good clinical practices, improve protection of participant privacy, and promote information security and research compliance. Participants' identifying information will only be available to Dr. Beckham and the research staff at the VA Medical Center. If any staff member leaves the research staff, he/she will be removed from the staff listing, and access to the study's data will be immediately withdrawn. The key and other study data will be kept in accordance with VA records control requirements, and if destruction is required by records control requirements, research data will be destroyed in accordance with VA records control requirements. As mentioned above, audio recordings made for treatment fidelity review will be deleted after review.

Within the ART arm of the study, we have developed several ways to minimize data security risk with video-taping. Participants will be specially trained to provide only partial-face images during the videos, and we ask participants not to speak while making a video so that a voice print is not collected. 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 the participant chooses to upload a video, they upload the video directly from the phone to a secured website (see below for further information about the website), 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. Please see "Study Procedures" for more information about the technology used in the study.

For the study's website, we will use shared server space provided by InMotion Hosting, Inc. The study url is https://www.calhounlab.com. Server space is currently used through a Duke University contract, and is shared with other VA and Duke IRB-approved studies run in the Traumatic Stress and Health Research Laboratory (PIs Dr. Beckham and Calhoun). We will be using AES-256 encryption. 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 is encrypted at transfer (AES-256). Website properties indicate TLS 1.0, AES w/ 128 bit encryption (High); RSA with 2048 bit exchange. Data will be unencrypted only by study staff 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. Data stored on this website are coded in that no direct identifiers are placed on the website. Videos are stored via study ID number, and participants are trained to provide side facial images without voice imprint. 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 order for data analysis to occur using MplusV7 software and SAS software (see "Data Analyses" below), a coded dataset will be sent to VINCI for analysis using VA-owned data analysis software (SAS). In the event that MplusV7 software or appropriate SAS modules for analysis are not available through VINCI, coded data will be moved to Duke University Medical Center for analysis. Any data movement outside the protected VA environment will be accomplished using a VA-issued and owned FIPS-140-2 encrypted thumb drive loaned to a VA study staff member. Data will be stored at Duke on a protected server to which only Dr. Beckham and her study staff have access; data are encrypted at rest.

DATA ANALYSES

The study is a randomized two-arm parallel group, longitudinal trial. The primary analysis will be based on intention to treat principles; the overall intervention effect will be measured for the entire sample assuming participants have followed their randomized assignment. The main conclusions drawn from this trial will be based on the pre-specified hypotheses outlined below and will be tested with two-sided p-values at the standard 0.05 level. Statistical analyses will be performed using SAS (Version 9: SAS Institute Cary NC) and MplusV7.

Missing Data and Attrition Rates. Because the main predictors of interest, treatment group and demographics, are collected at baseline, we do not anticipate much missing data. We do, however, anticipate missing values in the longitudinal outcomes owing to dropout or an inability to reach the patient by phone. The primary analysis will be based on intention to treat principles and will use a missing=smoking approach (treating those who dropped out of the program as current smokers). Although conservative, this approach produces an estimate of the verifiable efficacy of the intervention based on a representative sample rather than a potentially inflated estimate based on an unspecified sub-sample (An, et al., 2009, West, et al., 2005) and is recommended by the SRNT (Hughes, et al., 2003, Hughes, et al., 2004).

Hypothesis 1: Abstinence rates will be significantly higher among Veterans randomized to the ART intervention as compared to those randomized to VA specialty smoking cessation clinic. Rates of abstinence from cigarettes (self-reported prolonged abstinence) will be assessed at post-treatment, 3-months, 6-months, and 12 months follow-up. At each time point, abstinence will be measured as a dichotomous variable (abstinent or not). Self-report of abstinence will be validated with saliva testing of cotinine levels. The primary endpoint is abstinence rate at 6 months. Following the suggestion of a reviewer, we will use logistic regression to test for a between-group difference in the proportion of Veterans with bio-verified abstinence from cigarettes at the primary, 6-month follow-up. This logistic regression model can be written: $\text{Logit}(p_i) = \beta_0 + ART_i * \beta_1$, where p_i represent the probability that patient *i* has abstained from smoking at 6-months of follow-up. In this model, ART_i indicates whether or not patient *i* is in the *ART intervention* group of the study; therefore, β_1 represents the log-odds ratio of smoking abstinence in the ART group as compared to the

Control group. We will first formally test the intervention effect by testing that β_1 differs from zero. We will also explore whether there is a group effect over time using a repeated measures logistic regression model, in which the model parameters are estimated using generalized estimating equations methodology (GEE). GEE methodology allows the relationship between the response and explanatory variables to be modeled separately from the correlations resulting from clustering of repeated measurements within each subject. The regression coefficients from a GEE model have essentially the same interpretation as those from a cross-sectional regression analysis (e.g. logistic regression) but are more appropriate as they properly incorporate the longitudinal structure of the data. The predictors in the model will include intervention arm (a 2-level variable) and a time effect (post-treatment, 3-months and 6-months). Time will be considered as categorical and we will explore whether an exchangeable, unstructured, or AR(1) correlation structure is most appropriate to take into account the within-patient correlation between the repeated measures over time. GEE modeling will be performed using the SAS PROC GENMOD.

As participants are aware that their self-report will be evaluated by biochemical verification, the majority of reports are concordant with test results (> 90% in our current trials). For any discrepancies between self-report and biochemical verification, we plan to determine the sensitivity of model estimates when using results of cotinine assays as the dependent variable.

Hypothesis 2: ART treatment will result in greater cost-effectiveness as measured by the incremental cost-effectiveness ratio. The cost data from the VHA Databases and participant surveys will be utilized to calculate cost-effectiveness. The economic analysis will follow the guidelines developed by the Panel on Cost-Effectiveness in Health and Medicine (Gold, et al., 1996). We will employ the societal perspective (i.e., all costs incurred by and benefits accruing to the society in general, the VA health care system, and the individual participants, including medical, non-medical, productivity), with secondary analyses from the VA health care system perspective. The VA health care system perspective, which is most relevant to VA decision makers, excludes the direct non-medical costs borne by Veterans, such as the costs of their time. Data on the effects and costs of the interventions will be used to estimate the incremental cost-effectiveness, or ICER (US$ per QALY) comparing the ART intervention to VA specialty smoking cessation intervention. The incremental cost-effectiveness ratio R is expressed as: $R = (\mu_{CT} - \mu_{CU}) / (\mu_{ET} - \mu_{EU})$, where μ denotes the estimated mean for CT (cost of ART intervention), CU (cost of specialty smoking cessation intervention), ET (effect of ART), and EU (effect of specialty smoking cessation intervention). Time duration of the economic analysis will be 6 months. To incorporate the uncertainty in the data into the cost-effectiveness analysis, we will develop a decision analytic model and conduct probabilistic sensitivity analysis (2nd order Monte Carlo simulation). Parameter estimate ranges with appropriate distributions will be used for the various intervention and participant times, wage rates, NRT costs, and QALY effectiveness measures in conducting the decision model simulation. We will present our results as means (with CIs), incremental cost-effectiveness analysis scatterplots, cost-effectiveness acceptability curves, and one-way sensitivity analysis of model variables that drive the results (Briggs, et al., 2006, Willan & Briggs, 2006).

Hypothesis 3: The ART treatment effect will be partially mediated by increased self-efficacy compared to the control condition. The self-rating of efficacy collected across study time period will be utilized to evaluate this meditational hypothesis. If there is a significant intervention effect upon smoking cessation at 6-months follow-up, then we also plan to examine whether change in self-efficacy mediates the impact of the intervention. Change will be defined as the difference between baseline and post-treatment. To assess mediation, significance of the indirect effect of the intervention on smoking cessation via change in self-efficacy will be determined using bootstrapping methods. Bootstrapping employs resampling with replacement to generate confidence intervals that adhere to the positive skew inherent to indirect effects.

Relative to conventional tests of mediation, such as Sobel's *z*, which do not account for this skew and therefore inflate the standard error of the indirect effect, bootstrapping methods are quite powerful. Mediation analyses will use standard linear and logistic regression modeling approaches and will be conducted with Mplus v7. Considering that self-efficacy will be measured at four time points—baseline, post-treatment, 3-month follow-up, and 6-month follow-up—we will also examine whether differences by condition in abstinence rates across the study are mediated by changes in self-efficacy from time point to time point. Using linear and logistic GEE models and following mediation procedures for nested data (Krull & MacKinnon, 1999), we will first examine differences in abstinence by condition at time *t* (post-treatment, 3-month follow-up, and 6-month follow-up), controlling for abstinence at time *t*-1 (baseline, post-treatment, and 3-month follow-up). This is equivalent to modeling group differences in change in abstinence rates over the course of the study (Raudenbush & Bryk, 2002). We will then test differences by condition in self-efficacy at time *t*-1 and then test whether the differences by condition in abstinence at time *t* observed in the first model are attenuated with the addition of self-efficacy at time *t*-1.

Supplementary Aim 1 and Exploratory Analyses. To explore the effect of psychiatric symptoms (i.e., PTSD, depression, and alcohol abuse symptoms) on abstinence rates, analyses will be conducted by adding the subgroup variable (psychiatric symptoms vs. none) and its interaction with the intervention indicator to the statistical models described above under hypothesis 1. The interaction term will be tested to determine if the treatment effect is consistent across the levels of the subgroup variable at 3 and 6-month follow-ups.

Supplementary Aim 2: To determine the impact of smoking status on HIV disease progression parameters, presence of AIDS-related illnesses, CD4 T-cell count, and viral load at each time point will be modeled via multilevel modeling as a function of concurrent smoking status.

Sample Size Considerations. 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; i.e., the ART intervention will result in higher quit rates from cigarettes at 6 months post-randomization and was calculated for a logit-linked logistic regression model with a two-sided type-I error rate of 5%. Six months was chosen as the primary endpoint as it is generally recognized as the standard follow-up duration for reporting data from clinical trials and is consistent with the SRNT recommendations (Hughes, et al., 2003). As described in the analysis section, we are adopting a missing=smoking approach as recommended by the SRNT (Hughes, et al., 2003, 2004) and all randomized patients will be included in the analyses. That is, any participant who is randomized and drops out will be counted as a smoker. Our estimates below reflect this method.

Because homeless smokers are typically excluded from smoking cessation trials, there are few data that directly address potential efficacy of existing smoking cessation interventions in this population. For example, while there is evidence that provider contact and advice is associated with a measurable effect on smoking cessation in non-homeless smokers (Fiore, et al., 2000), physician contact had no impact on smoking rates in a study of 754 homeless persons including homeless Veterans (Tsai & Rosenheck, 2012). Using administrative data we calculated the observed Impact of usual VA specialty care for homeless smokers. In a random sample of homeless smokers (N=100) with an address in Durham county we found that 46% were referred to Specialty Smoking Cessation Care. Of these, 11 homeless Veterans attended at least one session of the intervention resulting in reach defined as 24% (11 of 46). Estimates of attendance rates for VA specialty care in non-homeless Veterans range from 6% to 30% (Sherman, et al., 2005, Yano, et al., 2008) and in our quality improvement evaluation of DVAMC specialty care we found that only 16% of non-homeless Veterans referred to specialty care attend at least one session. Among those accessing care, only 3 completed the program (73%

attrition rate) and only one Veteran quit smoking. Thus, the observed efficacy was 9% (1 of 11 Veterans who received any treatment quit smoking). The resulting impact of specialty care would equal 2% where Impact = Reach (.24) X Efficacy (.09). Note, drop-outs are included in this calculation of efficacy as treatment failures. Even if the efficacy of VA specialty smoking cessation care was as high as the average efficacy rate observed for interventions that combine multiple treatment formats including self-help materials, group counseling, and telephone counseling, i.e., 23% (95% CI, 19.9%-26.6%) among non-homeless smokers (Fiore, et al., 2000), specialty care impact would only approach 5%. Thus, we expect the overall quit rates (impact) of specialty care to fall between 2% and 5%.

Cessation rates for ART are based on our pilot data. Five homeless Veterans were randomized to active mCM in our first pilot examining mCM in Veteran smokers with PTSD and to date 20 have enrolled in our open trial of ART. In the first study of PTSD smokers, the observed efficacy rate was 40% (2 Veterans quit and remained abstinent at 3 months; 1 dropped out of treatment (20% treatment attrition) and did not quit; 2 did not respond to the 3-month follow-up are presumed to be smoking). In the open trial, 3-month efficacy rates among the 20 Veterans are 65%. Collapsing across these trials (n=25), observed 3-month cessation rates are 60%. This rate is consistent with observed short term (end of treatment) quit rates in similar CM interventions with non-homeless populations [e.g., (Alessi, et al., 2004, Roll, et al., 1996)]. We have included a 6-month follow-up in our open trial of homeless smokers and the current bio-verified efficacy rate (missing=smoking) at 6-months is 57% (8 of 14 who are eligible for a 6-month follow-up remain abstinent). We conservatively powered the trial with the expectation that there will be a larger relapse rate between 3 to 6 months than the one we have observed (see Gilpen, et al., 1997, Zhou, et al., 2009); thus we expect the 6-month quit rate for ART will fall between 22%-32%. Based on a 2-sided test, alpha=.05, we would need to enroll between 24 subjects (e.g., 2% vs 32%) or up to 63 subjects (e.g., 5% vs. 22%) in each arm to achieve 80% power to detect expected differences and will randomize a total of 126 subjects to ensure sufficient power at the primary endpoint.

STUDY DISSEMINATION AND ADVISORY BOARD

This study will utilize a Consumer, Family and Expert Provider Advisory Board that will meet annually with the research team to provide guidance to the project, develop goals for consumer involvement, and provide advice on dissemination issues. The board will consist of members representing consumers (e.g., homeless smokers, providers), family members, and content experts in homelessness, and will be led by Dr. Eric Elbogen, Clinical Psychologist for the DVAMC Psychosocial Rehabilitation and Recovery Center (PRRC) Program. At present, the board will include 1) a previously homeless Veteran who has quit smoking; 2) Dennis Culhane, Ph.D., the Director of Research for the National Center on Homelessness Among Veterans; 3) Jeff Doyle, LCSW, VISN 6 Homeless Coordinator; and 4) Lindsey Arledge, LCSW, Supervisor of the Homeless Veterans Program at Durham VA Medical Center.
Table 6 shows a list of planned dissemination activities. Our group has established roles in key partnerships with opinion leaders in the VA responsible for disseminating novel smoking cessation programs that will significantly aid in the dissemination of this work. We include support letters from (1) Dr. Kim Hamlett-Berry, Director of both the VA Public Health National Prevention Program and the VA Smoking and Tobacco Use

Table 6. Dissemination Plan

End Users	Organizations/Network	Activities & Modalities	Dissemination Partner
VA Veterans	**Study participants**	**(1) Letter to participants**	

Scientific Community	**VA MIRECC; VA HSR&D; Society for Research on Nicotine and Tobacco; International Society for Traumatic Stress Studies**	**(1) Newsletters, (2) Websites (3) Presentations (4) Publications**	**Dr. John Fairbank, Director, VISN-6 MIRECC Dr. Patrick Calhoun, Research Associate, HSR&D**
Opinion Leaders	**VA Public Health National Prevention Program**	**(1) Consultation (2) Presentation**	**Dr. Kim Hamlett-Berry, Director**
	SUD QUERI: Tobacco Use Cessation Workgroup		**Dr. Scott Sherman, Chair**
	VA National Center for Health Promotion & Disease Prevention		**Dr. Linda Kinsinger, Director**
	National Center on Homelessness among Veterans		**Vincent Kane, M.S.W., Director**

Director of both the VA Public Health National Prevention Program and the VA Smoking and Tobacco Use Cessation Technical Advisory group, (2) Dr. Scott Sherman, Chair of the Smoking and Tobacco Use Cessation Work Group of the Substance Use Disorders QUERI, (3) Dr. Linda Kinsinger, Director of the VA National Center for Health Promotion, and (4) Vincent Kane, M.S.W., the Director of the National Center on Homelessness among Veterans.

REFERENCES

100,000 Homes (2011). National survey of homeless veterans in 100,000 Homes Campaign communities. Retrieved from http://www.va.gov/HOMELESS/docs/NationalSurveyofHomelessVeterans_FINAL.pdf.

Abrams, D.B., Orleans, C.T., Niaura, R.S., et al. (1996). Integrating individual and public health perspectives for treatment of tobacco dependence under managed health care: A combined stepped care and matching model. *Ann Behav Med*, 18, 290-304.

Alessi, S.M., Badger, G.J. & Higgins, S.T. (2004). An experimental examination of the initial weeks of abstinence in cigarette smokers. *Exp Clin Psychopharmacol*, 12, 276-87.

An, L., Betzner, A., Luxenberg, M.L., et al. (2009). *Measuring quit rates. Quality improvement initiative*. Pheonix, AZ: NAQC.

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

Bonn-Miller, M.O. & Zvolensky, M.J. (2005). Marijuana Smoking History Questionnaire (version 2). Unpublished measure.

Briggs, A.H., Sculpher, M. & Claxton, K. (2006). *Decision Modelling for Health Economic Evaluation*. New York: Oxford University Press.

Bush, K., Kivlahan, D.R., McDonell, M.B., Fihn, S.D. & Bradley, K.A. (1998). The AUDIT alcohol consumption questions (AUDIT-C): An effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). *Arch Intern Med*, 158, 1789-95.

Carpenter, V.L., Hertzberg, J.S., Kirby, A.C., Calhoun, P.S., Moore, S.D., Dennis, M.F., Dennis, P.A., Dedert, E.A., Hair, L.P., & Beckham, J.C. (in press). Multi-component smoking cessation treatment including mobile contingency management for smoking cessation in homeless veteran smokers. *Journal of Clinical Psychiatry.*

Carroll, K.M. (2000). A general system for evaluating therapist adherence and competence in psychotherapy research in the addictions. *Drug Alcohol Depend*, 57, 225-38.

Centers for Disease Control and Prevention. (2008). Smoking-attributable mortality, years of potential life lost, and productivity losses - United States, 2000-2004. *MMWR*, 57, 1226-8.

Cornwell, E.Y., & Waite, L.J. (2009a). Measuring social isolation among older adults using multiple indicators from the NSHAP study. *Journal of Gerontology: Social Sciences, 64B,* i38-146.

Cornwell, E.Y., & Waite, L.J. (2009b). Social disconnectedness, perceived isolation, and health among older adults. *Journal of Health and Social Behavior, 50*, 31-48.

Cromwell, J., Bartosch, W.J., Fiore, M.C., Hasselblad, V. & Baker, T. (1997). Cost-effectiveness of the clinical practice recommendations in the AHCPR guidelines for smoking cessation. *JAMA*, 278, 1759-66.

Crothers, K., Griffith, T.A., McGinnis, K.A., Rodriguez-Barradas, M.C., Leaf, D.A., Weissman, S. et al. (2005). The impact of cigarette smoking on mortality, quality of life, and comorbid illness among HIV-positive veterans. Journal of General Internal Medicine, 20, 1142-1145.

Culhane, D.P., Gollub, E., Kuhn, R., & Shpaner, M. (2001). The co-occurrence of AIDS and homelessness: results from the integration of administrative databases for AIDS surveillance and public shelter utilisation in Philadelphia. *Journal of Epidemiology and Community Health, 55*, 515-520.

Erbes, C.R., Stinson, R., Kuhn, E., Polusny, M., Urban, J., Hoffman, J., Ruzek, J.I., Stepnowsky, C., & Thorp, S.R. (2014). Access, utilization, and interest in mHealth applications among veterans receiving outpatient care for PTSD. *Military Medicine, 179*, 1218-22.

Fiore, M.C., Bailey, W.C., Cohen, S.J., et al. (2000). *Treating Tobacco Use and Dependence. Clinical Practice Guideline.* Rockville, MD: U.S. Department of Health and Human Services.

First, M.B., Spitzer, R.L., Gibbon, M. & Williams, J.B.W. (1997). *Structured Clinical Interview for DSM-IV Axis I Disorders*. Washington, DC: American Psychiatric Press, Inc.

Fiscella, K. & Franks, P. (1996). Cost-effectiveness of the transdermal nicotine patch as an adjunct to physicians' smoking cessation counseling. *JAMA*, 275, 1247-51.

Gilpen, E.A., Pierce, J.P. & Farkas, A.J. (1997). Duration of smoking abstinence and success in quitting. *J Natl Cancer Inst*, 89, 572-76.

Gold, M.R., Siegel, J.E., Russel, L.B. & Weinstein, M.C. (1996). *Cost-effectiveness in Health and Medicine*. New York: Oxford University Press.

Goodman, S.H., Sewell, D.R., Cooley, E.L., & Leavitt, N. (1993). Assessing levels of adaptive functioning: The Role Functioning Scale. *Community Mental Health Journal, 29*, 119-131.

Heatherton, T.F., Kozlowski, L.T., Frecker, R.C. & Fagerström, K.O. (1991). The Fagerström Test for Nicotine Dependence: A revision of the Fagerström Tolerance Questionnaire. *Br J Addict*, 86, 1119-27.

Heckathorn, D.D. (1997). Respondent-Driven Sampling: A New Approach to the Study of Hidden Populations. *Social Problems, 44*, 174-199.

Heil, S.H., Higgins, S.T., Berstein, I.M., et al. (2008). Effects of voucher-based incentives on abstinence from cigarette smoking and fetal growth among pregnant women. *Addiction*, 103, 1009-18. PMCID: PMC2731575.

Hendricks, P.S., Wood, S.B., Baker, M.R., Delucchi, K.L., & Hall, S.M. (2011). The Smoking Abstinence Questionnaire: Measurement of smokers' abstinence-related expectancies. *Addiction,* 106, 716–728.

Hertzberg, J.S., Carpenter, V.L., Kirby, A.C., Calhoun, P.S., Moore, S.D., Dennis, M.F., Dennis, P.A., Dedert, E.A., & Beckham, J.C. (2013). Mobile contingency management as an adjunctive smoking cessation treatment for smokers with posttraumatic stress disorder. *Nicotine and Tobacco Research,* 15, 1934-1938.

Horvath, A.O., & Luborsky, L. (1993) Role of therapeutic alliance in psychotherapy. *Journal of Consulting and Clinical Psychology, 61*, 561-573.

Hughes, J., Keely, J., Niaura, R., et al. (2003). Measures of abstinence in clinical trials: Issues and recommendations. *Nicotine Tob Res*, 5, 13-25.

Hughes, J.R., Benowitz, N., Hatsukami, D., Mermelstein, R.J. & Shiffman, S. (2004). Clarification of SRNT workgroup guidelines for measures in clinical trials of smoking cessation therapies. *Nicotine Tob Res*, 6, 863-4.

Hughes, J.R. & Brandon, T.H. (2003). A softer view of hardening. *Nicotine Tob Res*, 5, 961-62.

Krull, J.L. & MacKinnon, D.P. (1999). Multilevel mediation modeling in group-based intervention studies. *Eval Rev*, 23, 418-44.

Lewis-Esquerre, J.M., Colby, S.M., Tevyaw, T.O., et al. (2005). Validation of the timeline follow-back in the assessment of adolescent smoking. *Drug Alcohol Depend*, 79, 33-43.

McBride, C.M., Bastian, L.A., Halabi, S., Fish, L., Lipkus, I.M., Bosworth, H.B., Rimer, B.K., & Siegler, I.C. (2002). A tailored intervention to aid decisionmaking about hormone replacement therapy. *American Journal of Public Health*, 92, 1112-1114.

McBride, C.M., Curry, S.J., Grothaus, L.C., et al. (1998). Partner smoking status and pregnant smoker's perceptions of support for and likelihood of smoking cessation. *Health Psychol*, 17, 63-69.

McBride, C.M., Curry, S.J., Lando, H.A., et al. (1999). Prevention of relapse in women who quit smoking during pregnancy. *Am J Public Health*, 89, 706-11.

McFall, M., Saxon, A., Malte, C., et al. (2010). Integrating tobacco cessation into mental health care for posttraumatic stress disorder: A randomized controlled trial. *JAMA*, 304, 2485-93.

Mokdad, A.H., Marks, J.S., Stroup, D.F. & Gerberding, J.L. (2004). Actual causes of death in the United States. *JAMA*, 291, 1238-45.

Murray, D.M., McBride, C., Lindquist, R. & Belcher, J.D. (1991). Sensitivity and specificity of saliva thiocyanate and cotinine for cigarette smoking: A comparison of two collection methods. *Addict Behav*, 16, 161-66.

National Institute of Health. (2006). National Institutes of Health state-of-the-science conference statement: Tobacco use: Prevention, cessation, and control. *Ann Intern Med*, 145, 839-44.
Nicholson, L.M., Schwirian, P.M., Kleing, E.G., Skybo, T., Murray-Johnson, L., Eneli, I., Boettner, B., French, G.M., & Groner, J.A., (2011). Recruitment and retention strategies in longitudinal clinical studies with low-income populations. *Contemporary Clinical Trials, 32*, 353-362.
Perl, L. (2012). Veterans and Homelessness. *Congressional Research Service*, 1-45.
Raudenbush, S.W. & Bryk, A.S. (2002). *Hierarchial linear models*. Thousand Oaks, CA: Sage.
Reynolds, N.R. (2009). Cigarette smoking and HIV: More evidence for action. *AIDS Education and Prevention, 21*, 106-121.
Robertson, M.J., Clark, R.A., Charlebois, E.D., Tulsky, J., Long, H.L., Bangsberg, D.R., & Moss, A.R. (2004). HIV seroprevalence among homeless and marginally housed adults in San Francisco. *American Journal of Public Health, 94*, 1207-1217.
Rogers, R.G. & Powell-Griner, E. (1991). Life expectancies of cigarette smokers and nonsmokers in the United States. *Soc Sci Med*, 32, 1151-59.
Roll, J.M., Higgins, S.T. & Badger, G.J. (1996). An experimental comparison of three different schedules of reinforcement of drug abstinence using cigarette smoking as an exemplar. *JABA*, 29, 495-505
Sherman, S.E., Joseph, A.M., Yano, E.M., et al. (2006). Assessing the institutional approach to implementing smoking cessation practice guidelines in Veterans Health Administration facilities. *Mil Med*, 171, 80-7.
Sherman, S.E., Yano, E.M., Lanto, A.B., Simon, B.F. & Rubenstein, L.V. (2005). Smokers' interest in quitting and services received: Using practice information to plan quality improvement and policy for smoking cessation. *American Journal of Medical Quality*, 20, 33-39.
Shiffman, S., Balabanis, M.H., Paty, J.A., et al. (2000). Dynamic effects of self-efficacy on smoking lapse and relapse. *Health Psychol*, 19, 315-23.
Shipley, R.H., Steffen, P. & Riley, K. (1999). Effectiveness of a stop smoking program for veterans with and without psychiatric diagnoses. *Vet Health Sys J*, 4, 65-67.
Simons, J., Correia, C. J., Carey, K. B., & Borsari, B. E. (1998). Validating a five-factor motives measure:Relations with use, problems and alcohol motives. *Journal of Counseling Psychology, 45*, 265–273.
Song, F., Raftery, J., Aveyard, P., et al. (2002). Cost-effectiveness of pharmacological interventions for smoking cessation: A literature review and a decision analytic analysis. *Med Decision Making*, 22, S26-37.
Spitzer, R.L., Kroenke, K. & Williams, J.B. (1999). Validation and utility of a self-report version of PRIME-MD: The PHQ primary care study. Primary care evaluation of mental disorders. Patient health questionnaire. *JAMA*, 282, 1737-44.
Stead, L.F. & Lancaster, T. Group behavior therapy programmes for smoking cessation. The Cochran Collaboration: JohnWiley & Sons, Ltd; 2002.
Stoops, W.W., Dallery, J., Fields, N.M., et al. (2009). An internet-based abstinence reinforcement smoking cessation intervention in rural smokers. *Drug Alcohol Depend*, 105, 56-62. PMCID: PMC2743786.
The EuroQol Group (1990). EuroQol-a new facility for the measurement of health-related quality of life. *Health Policy, 16*(3), 199-208.
Tsai, J., Edens, E.L. & Rosenheck, R.A. (2011). Nicotine dependence and its risk factors among users of veterans health services, 2008-2009. *Prev Chron Dis*, 8, A127. PMCID: PMC3221569.
Tsai, J. & Rosenheck, R.A. (2012). Smoking among chronically homeless adults: Prevalance and correlates. *Psychiatr Serv*, 63, 569-76.
Wang, V., Smith, V.A., Bosworth, H.B., et al. (2012). Economic evaluation of telephone self-management interventions for blood pressure control. *Am Heart J*, 163, 980-86.
Weathers, F.W., Litz, B.T., Keane, T.M., et al. (2013). The PTSD Checklist for DSM-5 (PCL-5). Scale available from the National Center for PTSD at www<dot>ptsd.va.gov.

West, R., Hajek, P., Stead, L. & Stapelton, J. (2005). Outcome criteria in smoking cessation trials: Proposed for a common standard. *Addiction*, 100, 299-303.

Willan, A. & Briggs, A.H. (2006). *Statistical Analysis of Cost-Effectiveness Data*. West Sussex, England: John Wiley & Sons Ltd.

Wisniewski, S.R., Leon, A.C., Otto, M.W., & Trivedi, M.H. (2006). Prevention of missing data in clinical research studies. *Biological Psychiatry, 59*, 997-1000.

Yano, E.M., Rubenstein, L.V., Farmer, M.M., et al. (2008). Targeting primary care referrals to smoking cessation clinics does not improve quit rates: Implementing evidence-based interventions into practice. *Health Serv Res*, 43, 1637-60. PMCID: PMC2653889.

Zhou, X., Nonnemaker, J., Sherrill, B., et al. (2009). Attempts to quit smoking and relapse: Factors associated with success or failure from the ATTEMPT cohort study. *Addict Behav*, 34, 365-73.