Tobacco Cessation Treatment Preferences among Veteran Smokers

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Research Protocol: Tobacco Cessation Treatment Preferences among Veteran Smokers
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PURPOSE

The overall goal of this study is to understand and improve tobacco abstinence rates among Veteran smokers receiving specialty medical care. The specific aims of the study are to:

AIM 1a: To qualitatively explore smoking cessation treatment preferences among Veteran smokers living with HIV, and to quantitatively evaluate perspectives on relapse-prevention messages among Veterans and smokers living with HIV.

AIM 1b: To quantitatively evaluate satisfaction with relapse-prevention messages among a de-identified online sample of Veterans and smokers living with HIV, and general-population smokers.

AIM 1c: To qualitatively explore smoking cessation treatment perspectives among ID health care staff who serve Veterans living with HIV.

AIM 2: To quantitatively examine trends and determine health disparities by HIV status and demographic characteristics in use of smoking cessation aids among patients receiving VHA clinical care.

AIM 3: To use a successive cohort design to develop a technology-assisted health (eHealth) smoking cessation intervention tailored for Veterans living with HIV.

AIM 4: To conduct a randomized clinical trial of an eHealth smoking cessation intervention in medical specialty care clinics.

BACKGROUND AND SIGNIFICANCE

There are significant barriers to tobacco cessation treatment for patients and providers in specialty care clinical settings (Rojewski et al., 2019). Specialty providers in general cite several prominent barriers to delivering evidence-based tobacco cessation care, including insufficient time, lack of training in tobacco cessation, a perception of low motivation in their patients, and concerns about tobacco cessation discussions being a sensitive topic to discuss (Meijer et al., 2019). There is also great variability in the extent to which specialty providers believe that tobacco cessation care is consistent with their specific medical role (Meijer et al., 2019). Beyond difficulties accessing cessation services, a large proportion of patients who are prescribed NRT or initiate behavioral treatment do not achieve initial abstinence (Piper, Vasilenk, Cook, & Lanza, 2016). Given the reality of treatment non-response, it could be immensely effective to offer smoking cessation treatment plans that can be personalized to patients as they progress through treatment. Use of healthcare technology (i.e., telehealth, electronic health record, and computerized treatment algorithms based on patient data) to personalize treatment has the potential to increase patient engagement and proactively address treatment non-response.

There is a lack of research on strategies to bring patient-centered care to tobacco cessation in specialty clinics. Given that tobacco cessation is most efficacious using an intensive, combined pharmacological-counseling approach, this new care model has the potential to increase long-term tobacco abstinence rates within specialty care clinical populations. This study will design and pilot test a novel model of care

for tobacco cessation in two specialty care VA clinics, the Infectious Disease Clinic and the Cardiology Section.

Rationale for Infectious Disease Clinic
Among the over 1 million people living with HIV in the U.S., the smoking rate is two to three times higher than in the general U.S. population (Kariuki et al., 2016; Moscou-Jackson, Commodore-Mensah, Farley, & DiGiacomo, 2014). Similarly, people living with Hepatitis C smoke at three times the rate of those without Hepatitis C (Kim et al., 2018). Estimates from studies of VHA patients indicate that 63% of HIV-positive Veterans currently smoke cigarettes (Crothers et al., 2005) and 58% of Veterans living with Hepatitis C currently smoke cigarettes (Lynch et al., 2018). Tobacco use disproportionately increases health risks for people living with HIV and/or hepatitis C (Mallat et al., 2008; Pacek & Cioe, 2015). Given the health risks of smoking for individuals with chronic infectious diseases, it is imperative to address tobacco use for this population.

Few smoking cessation interventions have been rigorously tested in people living with HIV or in people living with hepatitis C, and to date there have been no randomized controlled (RCT) trials of eHealth smoking cessation interventions for Veterans living with HIV and/or hepatitis C. One RCT tested the effectiveness of an NP-led counseling/NRT intervention, but tobacco abstinence at follow up was not biochemically verified (Reid et al., 2020). According to two recent systematic reviews, there are only five known large randomized smoking cessation trials among smokers with HIV (Moscou-Jackson et al., 2014; Cooperman, 2016). One of the most promising smoking cessation interventions for people living with HIV to date consisted of telehealth CBT (Vidrine, Marks et al., 2012), but did not show long-term efficacy. Despite a nearly 80% session completion rate (Vidrine, Marks et al., 2012), at 6-month follow-up, the smoking abstinence rate was only 5% (Gritz et al., 2013). This high treatment adherence and low quit rate indicate that this population would likely benefit from an approach that is more accessible and more intensive. Thus, there is a need for novel, intensive eHealth approaches to smoking cessation in this population.

Veterans living with HIV and/or Hepatitis C face numerous barriers to both treatment access and smoking abstinence. In groups who experience marginalization, common barriers to abstinence include lack of support for quitting from health care providers, high prevalence of smoking in the community, difficulties with stress management, and chronic pain (Twyman, Bonevski, Paul, & Bryant, 2014). For smokers with HIV specifically, barriers to abstinence include poor access to smoking cessation treatment, social networks that support smoking, alcohol and drug use, poor health, and mental health comorbidity (Karuiuki et al., 2016). Additionally, Veterans living with HIV have reported in qualitative interviews that referral to substance use treatment outside of the ID or primary care setting is burdensome (Minick et al., 2016). These patients further note that receiving HIV-specific care for addictions would help overcome this barrier (Minick et al., 2016). Individually tailored and HIV-targeted approaches to follow-up messaging have been recommended in the literature (Moscou-Jackson et al., 2014; Pacek & Cioe, 2015), but are yet to be tested as part of a multi-component approach for smokers with chronic infectious disease.

Rationale for Cardiology Section
The causal link between tobacco use and cardiovascular disease is well-established (Burns, 2003). Nationally representative data indicates that while a recent myocardial infarction increases motivation to quit tobacco, it has *no effect* on likelihood of tobacco cessation (Gaalema et al., 2018). Although many cardiac patients are motivated to quit tobacco, meta-analytic data suggests that low-intensity counseling for hospitalized patients does not significantly increase the odds of tobacco cessation (Rigotti

et al., 2012). Rather, intensive counseling in addition to adaptive pharmacotherapy are indicated to be most effective for tobacco cessation among cardiac patients (Benowitz & Prochaska, 2013). There is also evidence that intensive counseling for tobacco cessation among cardiac patients is both effective and cost-effective (Lapado et al., 2011).

In the VA-BEST Trial, an implementation package designed to increase delivery of the 5 A's tobacco cessation intervention for hospitalized Veterans (Katz et al., 2014). Although adherence to the 5 A's increased, and more Veterans in the implementation arm received tobacco cessation care, there was *no significant difference* in likelihood of tobacco cessation. In this study, the authors concluded that "more intensive interventions are needed to promote long-term cessation" (Katz et al., 2014).

Despite these calls for personalized, intensive counseling, there is a lack of intensive care models designed to optimize integration into existing clinical care models while promoting highly effective, intensive tobacco cessation interventions.

AIM 1 METHODS – QUALITATIVE FORMATIVE ANALYSIS

A qualitative patient sample (*N* = 20 or until saturation is reached) will include VHA patients with HIV who currently smoke or recently quit smoking. These patients will complete in-person qualitative interviews. A separate qualitative sample of ID health care staff who serve Veterans living with HIV will be collected (*N* = 15).

In qualitative coding and analysis, two complementary methodologies will be used: conventional content analysis (Hsieh & Shannon, 2005) and inductive thematic analysis (Braun & Clarke, 2006). Using these two sequential, complementary approaches will maximize the validity of findings and minimize researcher bias (Miles, Huberman, & Saldaña, 2014).

QUALITATIVE SAMPLE RECRUITMENT. Purposive sampling will be used to identify participants for the qualitative patient sample (*N* = 20). We anticipate that we will have to screen 30 participants to reach 20 completers. The sample will include 20 HIV-positive VHA patients who either currently smoke ≥ seven cigarettes per week or are lifetime smokers (smoked ≥ 100 lifetime cigarettes) who quit within the past 2 years. Veteran patients with an HIV diagnosis and documented tobacco use within the past 2 years will be identified from patient records of the Durham VAHCS via a data pull from VA's Regional Data Warehouse. We will sample VHA patients with diverse backgrounds with respect to gender identity, sexual orientation, race/ethnicity, age, and medical/psychiatric comorbidities. Potential participants will be sent an introductory letter signed by the PI that describes the study and invites participation. Veterans who do not decline will be called to determine interest in the study and basic study eligibility. We will also recruit by presenting information about the study to clinicians throughout the medical center, who can then provide a referral to Dr. Wilson by adding her as a co-signer to CPRS notes. The third recruitment method will involve pre-screening potential participants who have clinic appointments in the Infectious Diseases clinic (8A). Study staff will monitor whether pre-screened patients have arrived in the clinic via VetLink. Study staff will indicate potential participants to 8A clinic staff, and clinic staff will inquire whether patients interested in hearing about an observational, single-visit research study about smoking. If a patient affirmatively indicates to their provider that they would like to hear about the study, they will be approached by a study staff member for screening and informed consent. The sample size has a high likelihood of reaching data saturation, which we define as the point in data collection when additional interviews do not result in new themes (Guest, Bunce, & Johnson, 2006).

Guest et al. have experimentally demonstrated that after 12 interviews, there are diminishing returns on new themes; furthermore, at 18 interviews, 96% of themes are coded (Guest, Bunce, & Johnson, 2006).

A convenience sample of 15 local ID health care staff will be recruited from the Durham VA Health Care System. A wide variety of staff will be contacted in order to gather diverse opinions and perspectives regarding smoking cessation care, including physicians, nurse practitioners, physician assistants, social workers, psychologists, nurses, and pharmacists. A number of recruitment methods will be used: 1) recruitment email sent to clinic staff, 2) recruitment brochures and flyers displayed in the staff room in the 8A clinic, 3) announcements made during the ID clinic staff meeting, and 4) clinic staff will be approached during the 8A ID clinic (after receiving an email) to ascertain whether they would be willing to participate.

QUALITATIVE PROCEDURES. All interviews will be completed by either Dr. Wilson or trained study staff. For patients following informed consent, the interviewer will complete a 60-minute semi-structured interview with the participant. The format of the interview is funnel-shaped (Brinkman & Kvale, 2015), such that interview questions are initially broad and gradually narrow. An example of initial broad questions includes "For you personally, what would [be/have been] the best treatment to get to help you quit smoking?" Later interview questions will elicit feedback on specific examples of treatment options and relapse-prevention messages. For example, participants will be asked, "I'd like for you to tell me about the pros and cons of some different types of messages (I'll give examples of each type)." The qualitative interviewers will take notes during each interview, and all interviews will be audio recorded and transcribed by members of the study team at Durham. Veteran participants will be compensated $30 for completing the interview. Based on the first interview transcript, a codebook will be developed under the following categories: areas for expansion/tailoring for Veteran smokers with HIV; new themes for relapse-prevention messages; and reactions to messages. Following creation of the codebook, the coding scheme will be updated as necessary following each of the first three participant interviews. Once the final codebook is established, interview transcripts will be dually coded by the PI and another study staff member, with coding discrepancies resolved by consensus.

The medical records of participants will be reviewed to determine HIV disease status, use of smoking cessation medications and/or specialty clinic visits, comorbid diagnoses, and healthcare utilization patterns.

For clinic staff, documentation of informed consent will be waived. No HIPAA authorization will be collected, as no protected health information is being collected by clinicians. At the beginning of each interview, the interviewer will capture consent on the audio record. Interviews will last approximately 30 minutes, and will consist of questions derived from the Consolidated Framework for Implementation Research (CFIR; Damschroder et al., 2009). Questions will center on the following CFIR constructs: intervention characteristics, outer setting, and inner setting. Based on the first interview transcript, a codebook will be developed under the following categories: evidence strength and quality, relative advantage, adaptability, complexity, patient needs and resources, structural characteristics, tension for change, and compatibility. Once the final codebook is established, interview transcripts will be dually coded by the PI and another study staff member, with coding discrepancies resolved by consensus.

QUANTITATIVE PROCEDURES. The study team will receive a dataset from Duke University Health System, where Dr. Wilson will collect data from Amazon Mechanical Turk (MTURK; https://www.mturk.com). Data from MTurk will be collected by the Duke team via an anonymous survey hosted by Duke Qualtrics. Data will be moved to VA from Duke in accordance via a VA-owned

thumbdrive. All data will be de-identified, such that the study team will neither collect nor retain any PII or PHI. Data will include: HIV, smoking, and veteran status; demographic information (age; race; ethnicity; relationship status; sexual orientation; gender identity; U.S. state/territory; education; income; VHA patient status); and for HIV-positive participants only, age at HIV diagnosis, last CD4 count, and last viral load). Data will also include participants' ratings of satisfaction with 148 relapse prevention text messages used in the SmokefreeVET library, as well as additional messages developed by the Duke research team.

AIM 2 METHODS – QUANTITATIVE GAP IN VHA CARE ANALYSIS

To identify potential treatment moderators and further understand current health services for smoking cessation among Veterans, it is essential to determine existing health disparities in cessation treatment among VHA patients with a variety of chronic care conditions.

For this study aim, the data source will be a data request from Corporate Data Warehouse (CDW). We will create two complimentary datasets. First, we will investigate predictors of tobacco cessation pharmacotherapy fills among a cohort of Veteran tobacco users (FY 2018). Second, we will investigate overall rates of tobacco cessation pharmacotherapy fills over time (2011 to present).

Pharmacotherapy Disparities among a Cohort of Tobacco Users

Veteran health data, which may include PHI (e.g., dates of care and patient address), will be gathered starting from FY18 (pre-pandemic). After requesting data access via the Data Access Request Tracker (DART), Veterans who have positive tobacco use health factors will be identified from VA's Regional and/or Corporate Data Warehouse. During the retrospective observation period, tobacco use will be determined based on a validated algorithm for identifying smoking status from the EMR (Calhoun et al., 2017; McGinnis et al., 2011). Data will be extracted on tobacco use health factors, pharmacy records of medications dispensed, primary care/ID clinic outpatient healthcare encounters, pain intensity vital sign data, history of positive homelessness screening, history of positive food insecurity screening, patient demographics (race, ethnicity, service-connected disability, birth sex, gender identity, county, address), and diagnosis codes for comorbid disorders of interest (including but not limited to HIV, Hepatitis C coinfection, cardiovascular disease, cancer, and psychiatric disorders). Number of clinic visits attended in the 12-month period prior to the positive health factor will be collected as a control variable. Patient county and address will be used to extract data on neighborhood deprivation (Bhavsar et al., 2018) and economic inequality (GINI; Bee, 2012).

For each the year12-month period following each patient's positive tobacco use health factor, in which patients are determined to be smoking, three outcomes will be assessed: pharmacotherapy orders for any tobacco cessation pharmacotherapy (NRT, bupropion, or varenicline), pharmacotherapy orders for best-practice tobacco cessation pharmacotherapy (dual pharmacy dispensation of NRT [patch plus lozenge/gum/inhaler] or varenicline), and pharmacotherapy fills for any tobacco cessation pharmacotherapy, bupropion, or any smoking cessation pharmacotherapy (NRT, bupropion, or varenicline). Specifically, pharmacotherapy dispensation prescriptions will be coded dichotomously (yes/no) based on presence/absence of a pharmacy record within each 12-month observation period. Among those who received any pharmacotherapy prescriptions, pharmacotherapy fills will also be coded dichotomously.

We will examine a range of variables to detect disparities in pharmacotherapy utilization prescriptions and fills. Demographic information will include age, race, and ethnicity, and service-connected disability. Social determinants of health will include food insecurity, homelessness, neighborhood deprivation, and

neighborhood economic inequality. HIV, Hepatitis C, and psychiatric disorder will be based upon the ICD-9 and ICD-10 codes. Given previous work in the area of treatment access disparities, we will include the following psychiatric disorders as variables: psychotic disorder, bipolar disorder, PTSD, other anxiety/mood disorder, and any substance use disorder (all time-invariant, coded in year 1). Pain is coded 0-10 at each VHA healthcare visit as the fifth vital sign, and will be averaged over each 12-month monitoring period and dichotomized as severe (≥ 7) vs. mild/moderate (0-6) (Volkman et al., 2015).

Pharmacotherapy Prescriptions Over Time

Veteran health data, which may include PHI (e.g., dates of care), will be gathered starting from FY15 through present. After requesting data access via the Data Access Request Tracker (DART), Veterans who have positive tobacco use health factors will be identified from VA's Regional and/or Corporate Data Warehouse.

The population of tobacco users will be determined by fiscal year using health factors. For each fiscal year, the pharmacotherapy prescription rate will be calculated for each type of pharmacotherapy by dividing the total number of Veterans receiving a prescription for tobacco cessation pharmacotherapy by the total number of Veterans who meet criteria for current tobacco use.

We will examine trends over time, as well as systems-level determinants, including geographical region, facility-level proportion of Veteran patients who live rurally (extracted by year and by facility from the Rural Veterans Health Care Atlas), and state-level tobacco use prevalence.

AIM 3 METHODS – SUCCESSIVE COHORT DESIGN FOR TREATMENT REFINEMENT

We will use a successive cohort design to integrate and user-test the proposed intervention. The successive cohort design is an iterative process that is designed to refine behavioral treatments in the initial development stage (Epstein et al., 2007). This design involves multiple steps of development: 1) identifying theoretically-supported treatment models; 2) identifying key intervention elements; 3) developing preliminary intervention materials; and 4) revising the intervention iteratively based upon qualitative and quantitative data collected during successive patient cohorts. See below for proposed preliminary intervention methodology, as well as methodology for iteratively revising the intervention based upon patient qualitative feedback.

SAMPLE RECRUITMENT

A total of 3 cohorts of 5 patients each (*N* = 15) will complete the intervention and provide feedback after the treatment phase is complete. Participants will be recruited from the Durham VAHCS. Inclusion criteria are: VHA patient, HIV positive serostatus, currently smoking ≥ 7 cigarettes per week, and willing to complete study procedures. Exclusion criteria are: current hospitalization, acute risk for suicide documented in the medical record, or inability to complete study procedures.

We will primarily recruit by presenting information about the study to clinicians in the Infectious Disease (ID) Clinic, who can then provide a referral to Dr. Wilson by adding her as a co-signer to CPRS notes. In order to facilitate provider referral, Veteran patients with an HIV diagnosis and documented tobacco use within the past 2 years who have clinic appointments in the Infectious Diseases clinic (8A) will be identified from patient records of the Durham VAHCS via chart review in the Computerized Patient Reporting System (CPRS). Study staff will indicate potential participants to 8A clinic staff, and clinic staff will inquire whether patients interested in hearing about the study. If a patient affirmatively indicates to their provider that they would like to hear about the study, they will be approached by a study staff member for screening and informed consent. If an insufficient number of patients are recruited in this

manner, potential participants with an HIV diagnosis and documented tobacco use within the past 2 years will be sent an introductory letter signed by the PI that describes the study and invites participation. Veterans who do not decline will be called to determine interest in the study and basic study eligibility.

PROCEDURES

Immediately following screening and informed consent (Session 0), patients will complete baseline measures and will begin the active treatment, Mesh (see below for details). Table 2 describes the measures that will be used in Aim 3 as well as their administration schedule. Whenever possible, we have selected Common Data Elements from the PhenX Toolkit (Hamilton et al., 2011; Version 13.3) in order to maximize the impact of the proposed study. Participants will be scheduled for counseling session 1 with a stop smoking interventionist within 7 days of study enrollment.

Participants enrolled in the first cohort will be invited to utilize SmokefreeVET, a mobile text messaging service for military Veterans trying to quit smoking. SmokefreeVET was developed by a joint effort of the National Cancer Institute and the U.S. Department of Veterans Affairs. The program was created to provide 24/7 encouragement, advice, and tips to help smokers quit smoking and stay quit. It is a 6 to 8 week program, depending on when you set your quit date. Users will receive 1-5 messages per day and can receive additional quit support at critical points in the quit process by using one of SmokefreeVET's keywords (URGE, STRESS, or SMOKED). Participants can opt out of supportive text messaging at any time by sending the keyword STOP. Consistent with the structure of SmokefreeVET, participants interested in utilizing it will be assisted in signing up for the program within two weeks before their planned quit date. Participants will not be required to use the texting program. Participants of cohort 2 and 3 and in the RCT (Aim 4) will be invited to sign up for personalized text messaging support (see details of this treatment component below) using the VA Annie app. Annie is an automated, short message service (SMS) text message system designed to promote Veteran self-care. At the baseline session, Veterans will be asked to complete an agreement to use Annie, and will be walked through the process of registering a personal phone number and setting message preferences. The SMS feature of Annie will function on either a basic cell phone or a smartphone. During this time, Veterans will be informed that Annie is not designed for direct communication with a provider, and should a medical emergency arise to contact their provider or emergency services through traditional means.

Treatment sessions with the interventionist and the qualitative interview will be audio recorded. These recordings will be used to develop a fidelity system as a secondary goal of the cohort design.

Following completion of all intervention components (through end of treatment), each participant will complete a structured interview. Post-treatment interviews will include questions regarding strengths and weaknesses of the intervention as well as suggestions for ways to improve the overall treatment approach. See Data Analysis section for details on qualitative coding and analysis.

Participants will also be followed up at 3-months and at 6-months to assess clinical outcomes and treatment acceptability. Study measures are shown in Table 1. Secondary smoking outcomes will include 7- and 30-day point prevalence abstinence at each assessment. Abstinence will be verified by salivary cotinine assay (≤ 10 ng/ml), which improves self-report validity. When in-person visits are allowed post-COVID-19 pandemic, participants will also be asked to provide expired carbon monoxide (CO) breath readings at baseline, post-treatment, and 3- and 6-month follow-up.

Following treatment completion for each cohort of *n* = 5 participants, qualitative data will be analyzed and based upon results, the intervention structure and content will be revised. Intervention content that may be subject to revision includes the computerized algorithms, CBT module content, and content and timing of SMS text messages.

Table 1. *Aim 3 Measures*

Measure	No. Items	Completed by	Month				Sessions
			0	Quit Date	3	6	
BACKGROUND AND PROCESS VARIABLES							
1. Demographics	32	Self-report	X	-	-	-	-
2. Smoking history/current smoking	6	Self-report	X	-	-	-	-
3. HIV Disease Progression – CD4, Viral Load (EMR)	-	Self-report	X	-	-	-	-
4. Fagerstrom Test for Nicotine Dependence	7	Self-report	X	-	-	-	-
5. The Everyday Discrimination Scale	10	Self-report	X	-	-	-	-
6. Pain, Enjoyment of Life, and General Activity (PEG) Scale	3	Self-report	X	-	X	X	-
7. Smoking and Nicotine Knowledge	14	Self-report	X	-	X	-	-
8. Non-VA Treatment Utilization	9	Self-report	X	-	X	X	-
TREATMENT PERSONALIZATION MEASURES							
9. Smoking Cessation Motivation	1	Self-report	X	X	X	X	-
10. Smoking Cessation Self-Efficacy	1	Self-report	X	X	X	X	-
11. Stages of Change	2	Self-report	X	-	X	X	-
12. PTSD Checklist of *DSM-5* (PCL-5)	20	Self-report	X	-	X	X	-
13. Patient Health Questionnaire (PHQ-9)	9	Self-report	X	-	X	X	-
14. Alcohol Use Disorders Identification Test (AUDIT-C)	3	Self-report	X	-	X	X	-
15. Non-Cigarette Smoking Behavior	6	Self-report	X	-	X	X	-
16. Smoking Cessation Weight-Grain Concerns	2	Self-report	X	-	-	-	-
17. Smoking to Cope with Pain	1	Self-report	X	-	-	-	-
18. Exposure to Smoking Cues	1	Self-report	X	-	-	-	-
19. Pharmacotherapy Adherence – Visual Analog Scale (personalized to pharmacotherapy use)	1-3	Self-report	-	X	X	X	-
20. Tobacco Exposure Questionnaire	6	Self-report	X	-	X	X	-

CLINICAL MEASURES							
21. 7-day, 30-day Point Prevalence Abstinence	2	Research Interventionist	X	-	X	X	-
22. Prolonged Abstinence	2	Research Interventionist	-	-	X	X	-
23. Timeline Follow-back (cigarettes per day)	1	Research Interventionist	-	-	X	X	-
OUTCOME MEASURES							
24. Patient Recruitment	-	Research Interventionist	X	-	-	-	-
25. Treatment Retention	-	Research Interventionist	-	X	X	X	-
26. Withdrawals	-	Research Interventionist	X	X	X	X	-
27. Patient Satisfaction – Treatment Acceptability	8	Self-report	-	X			X
28. Therapist Satisfaction – Treatment Feasibility	7	Research Interventionist's Self-report	-	X			X
29. Clinician Time	4	Research Interventionist	X	X	-	-	-

Mesh Treatment Components

Treatment Personalization Algorithm. During session 1, the interventionist will complete a treatment personalization algorithm with the participant. This algorithm requires participant self-report data in addition to data from the electronic health record. Data inputs are shown in Table 2.

Table 2. *Treatment Personalization Algorithm Components*

ALGORITHM	CONSTRUCT	MEASURE
Baseline CBT Algorithm	Motivation; Self-efficacy, Social influences; Substances and Alcohol; Mental Health; Pain; Pharmacotherapy	Smoking Cessation Motivation; Smoking Cessation Self-Efficacy; Stages of Change; PTSD Checklist of DSM-5 (PCL-5); Patient Health Questionnaire (PHQ-9); Alcohol Use Disorders Identification Test (AUDIT); Non-Cigarette Smoking Behavior; Smoking to Cope with Pain; Exposure to Smoking Cues
Quit Week CBT Algorithm	Relapse prevention; Weight gain; Self-efficacy; Motivation; Pharmacotherapy adherence;	Relapse Situation Efficacy Questionnaire (RSEQ); Smoking Cessation Weight-Grain Concerns; Pharmacotherapy Adherence – Visual Analog Scale (personalized to pharmacotherapy use); If necessary: Smoking Cessation Motivation; Smoking Cessation Self-Efficacy; Stages of Change

Post-Quit Relapse-Prevention Messaging Algorithm	Preferences regarding message type: Inspirational; Medication reminders; Help with lapses; Trigger information; Behavioral skills	Preference ratings
Baseline Pharmacotherapy	Willingness; Preference; Contraindications	Self-report
Quit Week Pharmacotherapy	Status; Adherence; Willingness	Self-report
Quit Week Algorithm for Revising Pharmacotherapy Regimen (Initially Prescribed Dual-NRT)	Willingness; Contraindications	Self-report
Quit Week Algorithm for Revising Pharmacotherapy Regimen (Initially Prescribed Varenicline)	Willingness; Preference	Self-report
Quit Week Algorithm for Revising Pharmacotherapy Regimen (Initially Prescribed Bupropion)	Willingness; Preference	Self-report
Quit Week Algorithm for Revising Pharmacotherapy Regimen (Initially Prescribed Single-Formulation NRT)	Willingness; Preference; Contraindications	Self-report

Personalized Smoking Cessation Facilitation Meetings. Mesh facilitators will meet with participants between 5 to 7 sessions. For completion of stop smoking facilitation sessions, participants will be offered the choice of whether to complete sessions using a personal telephone, a personal digital device (i.e., tablet, laptop, or desktop computer with webcam), or a VA-issued digital device (i.e., 4G-enabled tablet with webcam). For those who request a VA-issued personal digital device, a consult will be placed to Prosthetics Service to issue the Veteran a 4G-enabled tablet in order to complete subsequent counseling sessions via VA Video Connect.

Core CBT modules include: identifying reasons for quitting, setting a quit date, breathing relaxation technique, identifying smoking triggers, identifying social support, and education about relapse prevention. We will also use the Session 1 treatment personalization algorithm to individually tailor counseling to provide an adaptable selection of discrete counseling modules in addition to core modules that all participants will receive. CBT treatment personalization algorithms are based upon the following assessments: self-efficacy, motivation for quitting, depression, PTSD, alcohol use, comorbid non-cigarette smoking, tobacco exposure, smoking to cope with pain, adherence to pharmacotherapy, and concerns about weight gain. Two to three of these 5- to 15-minute modules will be included in each session, and modules will focus on building each participant's skills that are needed to achieve cessation and long-term abstinence. Optional modules will address low motivation to quit, low self-efficacy for quitting and relapse prevention, comorbid psychiatric concerns, alcohol/drug use, tobacco exposure and poly-tobacco use, pain management, pharmacotherapy adherence, and healthy eating/exercise. Each session will last 30-60 minutes.

At Session 3 (1 week post-quit), the participant will be asked several treatment personalization questions (see Table 1). These responses will be entered into the treatment personalization algorithm to determine additional post-quit modules depending on the following: self-reported quit status at Session 3 (defined as complete abstinence since most recent quit date), self-efficacy, motivation, pharmacotherapy adherence, and barriers to abstinence. Additional modules to be added to counseling include: relapse prevention, motivational interviewing, decisional balance, pharmacotherapy adherence (or pharmacotherapy motivational interviewing), and review of barriers and protective factors.

Personalized Smoking Cessation Pharmacotherapy. Participant pharmacotherapy recommendations will be based upon the study treatment personalization algorithm and will be sent to the participant's clinic team. All pharmacotherapy prescriptions will be managed as part of routine clinical care by the participant's VA healthcare providers, who may choose to follow study pharmacotherapy recommendations at their discretion.

At the baseline session, a study staff member will ask questions regarding tobacco cessation pharmacotherapy preferences and contraindications directly to the study participant. The interventionist will also review the participant's electronic medical record to note any additional potential contraindications to pharmacotherapy. Pharmacologic recommendations will be based upon a recent meta-analysis of smoking cessation pharmacotherapy as well as VA Pharmacy Benefits Management Services guidelines (Cahill et al., 2013). Similar to Cropsey et al.'s (2015) algorithm methodology, participants will be followed 1 week post-quit to assess abstinence and pharmacotherapy adherence. If they are using tobacco and have poor adherence (<70% adherence) and are willing to increase pharmacotherapy use, then adherence will be more heavily targeted in CBT. If, however, they are using tobacco in the context of adherent use, the algorithm will suggest an alternative medication regimen if possible (e.g., switching from single-formulation NRT to dual-NRT).

Personalized Annie Messaging Support. If the participant has a working cell phone and is willing to receive SMS text messages, supportive SMS text messages will be sent to the participant starting after Session 1 and extending through 6 months post-quit. Individual tailoring of follow-up messages will be based upon the post-quit patient mHealth survey, which will measure the following: desired frequency of messages (1-3 per day); specific abstinence-related concerns (i.e., weight gain, difficulty coping with stress); preferred types of messages (skills-focused, health informational, encouragement); and personalized reasons for staying quit. Participants can opt out of follow-up messaging at any point. All messages will be sent via the VA Annie texting capability. As stated above, Annie is a standard VA SMS text message capability designed to promote Veteran self-care.

AIM 4 – PILOT FEASIBILITY RANDOMIZED CONTROL TRIAL (RCT)

The proposed RCT is a two-arm experimental design to demonstrate the feasibility of a larger trial and the acceptability of the intervention design. Participants (*N* = 30) will be stratified by clinic and randomized to either the active treatment or to standard of care VA Quitline (telehealth intervention including 5 sessions of CBT) plus SmokefreeVET (text-messaging intervention). The comparison group was selected in order to assess the feasibility of recruitment, retention, and randomization procedures. We will assess acceptability of the active treatment among patients, providers, and key VA stakeholders.

SAMPLE RECRUITMENT

A total of *N* = 30 will be enrolled in the study. Participants will be recruited from the Durham VAHCS. Inclusion criteria are: Durham VA patient, willing to complete study procedures, appointment in Durham

VA Infectious Disease (ID) Clinic or Durham VA Cardiology Section within the past 12 months, and currently smoking ≥ 7 times per week (cigarettes, cigars, cigarillos, hookah, etc.) and/or using ≥ 1 can of smokeless tobacco per week. Exclusion criteria are: participation in Aim 3 (already received the intervention), current hospitalization (recent hospitalization is acceptable), currently not using combustible or smokeless tobacco (vaping only), acute risk for suicide documented in the medical record, or inability to complete study procedures.

We will recruit in several different ways. First, clinicians in the ID Clinic and Cardiology Section can provide a direct study referral by adding the PI and/or Project Coordinator as a co-signer to a CPRS notes. Second, study information sheets will be made available in ID Clinic and Cardiology Service clinical spaces for potential participants to peruse and self-refer to the study. Third, potential participants with documented tobacco use within the past 2 years who have been seen within the past 2 years in the ID Clinic or Cardiology Service will be sent an introductory letter signed by the PI that describes the study and invites participation. Veterans who do not decline will be called to determine interest in the study and basic study eligibility.

PROCEDURES

Screening

Veterans who are interested in study participation will be screened via telephone or in clinic for study inclusion criteria. Potential participants will be asked questions regarding current weekly tobacco use and current hospitalization at any location, and CPRS documentation will be screened to ensure the Veteran is a patient in one or both of the identified clinics, is not currently hospitalized at Durham VA, and does not have a high-risk suicide flag in their chart. Potential participants will then complete informed consent with a trained study staff member. Where possible, we will utilize DocuSign to obtain informed consent and HIPAA authorization. Immediately following screening and informed consent (Session 0), patients will complete baseline measures and randomization.

Communication with Enrolled Participants

Communication with enrolled participants will take place via mail, telephone, VA Video Connect, another approved telehealth platform (http://vaww.telehealth.va.gov/technology/covid19-tech.asp), or Azure RMS (in accordance with guidance issued in VA document “Use of Protected Health Information in Microsoft Office Applications”).

Measures

Table 3 describes the measures that will be used in Aim 4 as well as their administration schedule. Whenever possible, we have selected Common Data Elements from the PhenX Toolkit (Hamilton et al., 2011; Version 13.3) in order to maximize the impact of the proposed study.

Table 3. *Aim 4 RCT Measures*

Measure	Completed by	Time Point		
		Baseline	3-Month Follow Up	6-Month Follow Up
BACKGROUND AND PROCESS VARIABLES				
1. Demographics	Self-report	X	-	-
2. Tobacco use history/current tobacco use	Self-report	X	-	-

3. Fagerstrom Test for Nicotine Dependence (Cigarette and ST Versions)	Self-report	X	-	-
4. The Everyday Discrimination Scale	Self-report	X	-	-
5. Pain, Enjoyment of Life, and General Activity (PEG) Scale	Self-report	X	X	X
6. Smoking and Nicotine Knowledge	Self-report	X	X	-
7. Non-VA Treatment Utilization	Self-report	X	X	X
8. Stages of Change	Self-report	X	X	X
9. Smoking Cessation Motivation*	Self-report	X	X	X
10. Smoking Cessation Self-Efficacy*	Self-report	X	X	X
11. PTSD Checklist of *DSM-5* (PCL-5)*	Self-report	X	-	-
12. Patient Health Questionnaire (PHQ-9)*	Self-report	X	-	-
13. Alcohol Use Disorders Identification Test (AUDIT-C)*	Self-report	X	X	X
14. Non-Tobacco Smoking Behavior*	Self-report	X	X	X
15. Smoking Cessation Weight-Grain Concerns*	Self-report	X	-	-
16. Smoking to Cope with Pain*	Self-report	X	-	-
17. Exposure to Smoking Cues*	Self-report	X	-	-
18. Pharmacotherapy Adherence – Visual Analog Scale*	Self-report	-	X	X
CLINICAL MEASURES				
19. Tobacco Exposure Questionnaire	Self-report	X	X	X
20. Timeline Follow-back (TLFB; tobacco used per day, tobacco cessation medication used per day, quit attempts, control group treatment sessions)	Study Staff Member	-	X	X
21. Abstinence Outcomes (7-day, 30-day, Prolonged)	Study Staff Member, based on TLFB	-	X	X
22. Exhaled Carbon Monoxide (CO)	Biochemical Measure	-	X	X
23. Salivary Cotinine	Biochemical Measure	-	X	X
OUTCOME MEASURES				
24. Patient Recruitment	Study Staff Member	X	-	-
25. Treatment Retention	Study Staff Member	-	X	X
26. Withdrawals	Study Staff Member	X	X	X
27. Patient Satisfaction – Treatment Acceptability	Self-report	-	X	X
28. Therapist Satisfaction – Treatment Feasibility	Research Interventionist	Immediate Post-Treatment		
29. Clinician Time	Research Interventionist	During Treatment Period		
CPRS DATA EXTRACTION				
30. HIV Disease Progression – CD4, Viral Load	Study Staff Member	X	-	-
31. Tobacco Cessation Medication Prescriptions and Fills	Study Staff Member	-	X	X

* Measure also used for treatment personalization in Mesh intervention

Randomization

Immediately following completion of baseline measures, participants will be randomized 1:1 to either the active treatment (Mesh) or to a best practice comparison condition (described below). Randomization will be concealed, stratified, and blocked. Given the two separate recruitment settings, randomization will be stratified by clinical setting (ID clinic and cardiology). For participants who are involved in both clinical settings, stratification arm will be decided by a virtual coin toss (https://cgi.cs.duke.edu/~des/vct/vct.cgi). In order to ensure consistent referrals for sessions with intervention facilitators, randomization will be blocked for every five participants recruited. Allocation to study condition will be computer-generated in random blocks of four and six, with the allocation block sizes and sequence only accessible by a non-investigator study staff member who is not involved in study recruitment or treatment delivery.

Intervention Arms

Participants randomized to the Mesh treatment arm will be scheduled for a first session with a quit facilitator within 10 business days of randomization. See section above "Mesh Treatment Components" for a description of the intervention arm, which includes personalized recommendations for tobacco cessation pharmacotherapy, 5 to 7 sessions, and Annie messaging. Participants will be asked to select their preferred frequency of Annie messaging: standard (about 3 times per day) or low (about 1 time per day). Study therapists will be asked to audio record a selection of sessions. A random sample of sessions will be selected for fidelity rating by a PhD-level study staff member.

Participants randomized to the best practice comparison condition arm will receive best-practice VA telehealth. This includes information on medications, referral to VA quitline, and referral for tobacco cessation text messaging. Study staff will provide the participant with a VA information sheet on tobacco cessation medications (copied directly from https://www.mentalhealth.va.gov/quit-tobacco/how-to-quit.asp). Participants will also be offered a warm handoff to Quit Vet, VA's Quitline 1-855-QUIT-VET (1-855-784-8838). If they are not interested in a warm handoff during the baseline session, they will be provided with an information sheet about Quit Vet and encouraged to call as soon as possible to initiate counseling. Participants will be asked to sign up for SmokefreeVET. Participants will be informed that standard text messaging rates apply for this texting program. Veterans will not be required to participate in SmokefreeVET. Participants can also opt out of text messaging at any time by sending the keyword STOP. Participants will be signed up for SmokefreeVET during the initial visit either by visiting https://veterans.smokefree.gov/tools-tips-vet/smokefreevet or by texting VET to 47848 on the participant's mobile phone. If the Veteran declines at the baseline session to be signed up for SmokefreeVET, they will be provided with an information sheet on how to sign up.

Participant Compensation

Participants will receive $50 for the baseline visit. For the 3- and 6-month follow-up visits, participants will receive $100 for coming in for CO and cotinine sample. If a participant is not able to attend the follow-up in person, they will receive $50 for a telephone-only follow-up and mailed saliva sample (with payment contingent upon receiving saliva sample via mail).

COVID-19 Temporary Study Procedures

Participants in the study will be asked to follow medical center procedures for mitigation of COVID-19 risk (e.g., mask-wearing, physical distancing). When possible, participants will be asked to complete study procedures via phone, VA Video Connect, another approved telehealth platform (http://vaww.telehealth.va.gov/technology/covid19-tech.asp), or via Azure RMS (in accordance with

guidance issued in VA document "Use of Protected Health Information in Microsoft Office Applications").

PRIVACY, CONFIDENTIALITY, AND INFORMATION SECURITY

1. Lists of Data Reviewed and/or Collected for Screening/Recruitment and Conduction of Study:
The Personal Health Information that will be obtained, used, and/or shared for this study includes:

Identifier(s)	Source(s) of Health Information
☒ Names	☒ Medical history & physical exam information
☒ All geographic subdivisions smaller than a State, including street address, city, county, precinct, and zip code. Describe: Participants' addresses will be collected during the study in order to pay them for participation.	☒ Photographs, videotapes, audiotapes, or digital or other images
☒ All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, visit or treatment dates, etc.; and all ages over 89, Describe: Date of participation will be collected. In addition, treatment records, laboratory results, etc. will be collected.	☒ Biologic specimens (e.g., blood, tissue, urine, saliva). Describe: Collection of saliva samples for salivary assay.
☒ Telephone numbers	☒ Progress notes
☐ Fax numbers	☒ Diagnostic / Laboratory test results
☒ Electronic mail addresses	☐ Operative reports
☒ Social Security Numbers	☐ Imaging (x-ray, CT, MRI, etc.)
☒ Medical record numbers	☐ Discharge summaries
☐ Health plan beneficiary numbers	☒ Survey / Questionnaire responses
☒ Account numbers	☐ Billing records
☐ Certificate and/or license numbers	☒ HIV testing or infection records
☐ Vehicle identifiers and serial numbers, including license plate numbers	☐ Sickle cell anemia information
☐ Device identifiers and serial numbers	☒ Alcoholism or alcohol use information
☐ Web Universal Resource Locators (URLs)	☒ Drug abuse information
☐ Internet Protocol (IP) address numbers	☐ Mental health (not psychotherapy) notes
☐ Biometric identifiers, including finger & voice prints	☐ Psychological test results
☐ Full-face photographic images and any comparable images	☐ Genetic testing
☒ Any other unique identifying number, linked study ID, characteristic, or code, describe: study ID number	☐ Other, describe:

2. Data and/or Specimen Acquisition:
Data for this study will be collected through (*check all that apply*):

☒ Prospective data and/or specimen collection obtained from participants. Aim 1 patient data will be obtained through a 60-minute, semi-structured interview. Aim 1 VA staff data will be obtained through a 30-minute, structured interview. No data collection is involved in Aim 2.
☒ Retrospective data collection and/or specimens obtained from medical chart review/data access. Describe how data will be obtained (e.g., fileman, CDW, etc.):
Aim 1: In accordance with a Waiver or Alteration of HIPAA Authorization, names, addresses, telephone numbers, social security numbers, and diagnostic information of potential participants will be obtained from the VA's Regional Data Warehouse. For study Aim 2, health data will be obtained from VA's Corporate Data Warehouse.
☐ Retrospective data collection and/or specimens obtained from an IRB-approved data and/or specimen repository. Indicate the repository source including name, VA location, and IRB number: Aim 1b: Survey data from Duke University Health System will be shared with the VA team via a VA-owned thumbdrive.
Note: for data and/or specimens obtained from a VA approved data repository, a Data Use Agreement (DUA) must be executed prior to obtaining data and/or specimens. See VHA Handbook 1200.12 for further information.

3. Level of Data:
The following level(s) of data will be acquired/maintained for this study (*check all that apply*):
☒ Identified (e.g., names, addresses or other identifiers included)
☒ Coded (direct and/or all identifiers removed, but study code/ID included)
☒ De-Identified (all HIPAA 18 and study ID/code removed):
- ☐ Verified Statistically

OR

- ☒ Verified by Absence or Removal of HIPAA 18 and study ID

☐ Limited Data Set
☐ Other: Describe:

4. Location of Data and/or Specimens, and Data Retention Plan:
A. Data and/or Specimen Location:
Aims 1, 3, and 4:
Data will be stored electronically in \\vhadurhsmcifs01.v06.med.va.gov\Mesh. For Aim 1, data that will be stored electronically include name, address, phone number, social security number, amount of study payment earned, and date of visits (in Study Logbooks location). The study logbook will contain the key connecting PHI and the study identification number. Paper records of data include study consent form and HIPAA authorization (identified) and interview notes (coded); these will be stored in a locked filing cabinet in a locked office suite in Bldg. 1, Room C10006; Building 8, Room 206 of the main Durham VA Health Care System campus; or in Legacy Tower Suite 600 (HSR&D). Audio recordings of qualitative interviews and to establish interrater reliability will be captured using VA's WebEx. Recordings will be moved from WebEx to the "Study Logbooks" location listed above. For long term storage, audio recordings may be moved to an encrypted DVD that is password-protected. Any encrypted DVDs will be stored in a locked filing cabinet in a locked office. Transcriptions from the study interviews will be stored electronically at the Study Logbooks location listed above. Data received from Duke University Health System will be moved to \\vhadurhsmcifs01.v06.med.va.gov\Mesh for storage and analysis.

Aim 2:
Data collected via a DART pull will be stored locally at \\v06.med.va.gov\DUR\Mesh.

☐ Data will be also be placed at the VA Informatics and Computing Interface (VINCI; http://vaww.vinci.med.va.gov/vincicentral/VINCIWorkspace.aspx). The VA Informatics and Computing Infrastructure is a partnership between the VA Office of Information Technology and the Veterans' Health Administration Office of Research and Development. Researchers and operations staff can use VINCI to access data and statistical analysis tools in a virtual working environment through a certified VHA network computer using the VA Intranet or Virtual Private Network (VPN).

B. Data Retention Plan

☒ Research records will be maintained and destroyed according to the National Archives and Records Administration, Records Schedule Number: DAA-0015-2015-0004. Records destruction, when authorized, will be accomplished using the then current requirements for the secure disposal of paper and electronic records. Currently, destruction of research records (see DAA-0015-2015-0004, section 7.6 "Research Investigator Files" for materials included in research records) is scheduled for 6 years after the cut-off (the cut-off is the completion of the research project) and may be retained longer if required by other federal agencies. Records will not be destroyed without pre-notification to the facility records manager.

☐ Other data retention plan, describe:

5. Data Access and Data Recipients:

Aims 1, 3, and 4:

Only members of our DVAMC research team will have access to identifiers and coded data. All VA research personnel who have access to VHA records are instructed, in accordance with VA policy, on the requirements of Federal privacy and information laws and regulations, VA regulations and policies, and VHA policy. All study personnel who are VA employees working within the VA system have fulfilled all required HIPAA and other VA security and privacy policy training requirements and have agreed to follow guidelines pertaining to the protection of patient data. All research staff sign VA Rules of Behavior, and all study staff are up-to-date with VHA Privacy Policy Training and the VA Office of Cyber and Information Security Awareness Training Course. The data security and privacy procedures summarized in that course include logging off or locking the computer when walking away from it; no sharing of access codes, verify codes or passwords; not allowing anyone else to use the computer under one's password; and disposing of sensitive information using VA-approved methods (e.g., shredder bins). Access to study data will be removed for all study personnel when they are no longer part of the research team.

Aim 2:

Only Dr. Wilson (PI) and study statistician will have access to identifiers and coded data. All VA research personnel who have access to VHA records are instructed, in accordance with VA policy, on the requirements of Federal privacy and information laws and regulations, VA regulations and policies, and VHA policy. All study personnel who are VA employees working within the VA system have fulfilled all required HIPAA and other VA security and privacy policy training requirements and have agreed to follow guidelines pertaining to the protection of patient data. All research staff sign VA Rules of Behavior, and all study staff are up-to-date with VHA Privacy Policy Training and the VA Office of Cyber and Information Security Awareness Training Course. The data security and privacy procedures summarized in that course include logging off or locking the computer when walking away from it; no sharing of access codes, verify codes or passwords; not allowing anyone else to use the computer under one's password; and disposing of sensitive information using VA-approved methods (e.g., shredder bins). Access to study data will be removed for all study personnel when they are no longer part of the research team.

6. Data and/or Specimen Transportation and/or Transmission for all data and/or specimens involved in the study:

I. ☒ Data and/or specimens will not be transported or transmitted outside of Durham VAMC environment. Please note: Data will not be transported outside the Durham VA environment. Specimens will, see item IIIb below.

II. ☒ Data and/or specimens will be transported BETWEEN sites that are under the auspices of the Durham VA Medical Center. Please describe what is being transported, who will be responsible for transporting (study titles rather than names) how it will be secured during transport, and whether additional stops will be made while transporting the data/specimens. Study mail and correspondence will either be stored in Legacy Tower, Suite 600 (HSR&D space) or will be moved from HSR&D space at Legacy Tower to DVAMC, Building 1, C10006. The study coordinator will be responsible for moving these documents. Data will be secured in a briefcase or lock bag with the notice below attached. No stops will be made while transporting the documents.

a. ☒ Local DVAMC memorandum "Authorization to Use, Process, Store, or Transmit VA Sensitive Information Outside VA Owned or Managed Facilities" has been pre-filled out for each study team member who may transport the data and/or specimens off-site. This (these) forms are included with the IRB materials.

b. ☒ Containers (e.g., briefcase, bin) are labeled with the following notice (label placed on the outside of container):

NOTICE!!!
Access to these records is limited to: AUTHORIZED PERSONS ONLY.
Information may not be disclosed from this file unless permitted by all applicable legal authorities, which may include the Privacy Act; 38 U.S.C. §§ 5701, 5705, 7332; the Health Insurance Portability and Accountability Act; and regulations implementing those provisions, at 38 C.F.R. §§ 1.460 – 1.599 and 45 C.F.R. Parts 160 and 164. Anyone who discloses information in violation of the above provisions may subject to civil and criminal penalties.

III. ☐ Data and/or specimens will be transmitted to other VA sites using the following method(s):

A. Data

☐ Data are de-identified and thus will be sent via unencrypted e-mail or unencrypted disk (encryption is optional).

☐ Data are coded or contain identifiers and thus will be sent

☐ Other, describe:

B. Specimens

☐ Specimens are de-identified and thus will be sent via standard carrier (tracking is optional).

☒ Specimens are coded or contain identifiers and thus will be sent via VA-authorized carrier with tracking.

☐ Other, describe:

IV. ☐ Data and/or specimens will be transported to non-VA/VHA sites (e.g., academic affiliates, laboratories, etc.) using the following method(s):

A. Data

☐ Data are de-identified and thus will be sent via unencrypted e-mail or unencrypted CD.

☐ Data are coded or contain identifiers and thus will be sent via <chose method of transfer such as FIPS 140-2 encrypted CD or FIPS 140-2 encrypted hard drive/flash drive> using VA—approved carrier with tracking.

☐ Data are coded or identified and will be uploaded to sponsor website using electronic case report form (eCRF) <insert information including sponsor name and URL and the encryption the site uses.>

☐ Other, describe:

B. Specimens

☐ Specimens are de-identified and thus will be sent via standard carrier (tracking is optional) or will be hand-delivered by research study personnel. Specify method of delivery:

☐ Specimens are coded and thus will be sent via VA-approved carrier with tracking or will be hand-delivered by research study personnel. Specify method of delivery:

In accordance with the HIPAA and the Privacy Act, for any coded or identifiable data or specimens released from the Durham VAMC (with the exception of Limited Data Sets), an Accounting of Disclosure (AOD) will be maintained (e.g., in a database or spreadsheet) that includes the participant's name, date of the disclosure, description of the nature of the Individually Identifiable Information (III) disclosed, purpose of each disclosure, and the name and address of the person/agency to whom the disclosure was made.

7. Risk Mitigation Strategies:

☐ Data are fully de-identified (stripped of HIPAA 18 and study ID/code) before being shared outside of Durham VAMC.

☐ Specimens are fully de-identified (stripped of HIPAA 18 and study ID/code before being shared outside of Durham VAMC.

☒ Direct identifiers will be maintained separately from data and or specimens by using a code to "identify" subjects. In a separate database (i.e., a "linking" or "cross-walk" database) this code will be linked to identifying subject information.

☐ Other, specify:

8. Suspected Loss of VA Information:

Should any incident such as theft or loss of data, unauthorized access of sensitive data or non-compliance with security controls occur it will be immediately reported according to VA policy. All incidents regarding information security/privacy incidents will be reported to the ISO and PO within 1 hour of acknowledgement of issue and done so using the VHADUR Research Events Report e-mail group (VHADURResearchEventReport@va.gov).

9. Reporting of Results:

☒ Reporting of results, such as in scientific papers and presentations, will never identify individual subjects. Data will be presented in aggregate and individual-level data will not be published.

☐ Other results reporting plan, describe:

10. Future Use of Data:

☐ Data will be retained for future use. This is described elsewhere in the protocol and is noted in the HIPAA authorization.

☒ Future Use of data is optional (i.e., not required by the research subject).

☐ Future Use of data is required for participation in the study.

☐ No future use of data is currently planned.

11. Use of Mail Merge Technology

☒ Mail merge programs will be used to generate letters and/or address labels for mailings to potential or already enrolled research subjects. The study team is aware that to reduce risk of mail merge related privacy incidents, use of mail merge programs requires a 25% accuracy check to verify that (potential) research subject name and mailing address are properly "matched". If discrepancies are found, a 100% accuracy check is required before letters may be mailed.

DATA ANALYSES

Aim 1:

Sequential Exploratory Mixed Analysis. Qualitative data collection will constitute the initial idea-generation step in treatment development, and thus findings will be used to do the following: 1) conceptualize ways to adapt intervention content to increase its specificity and appropriateness for a population of Veteran smokers living with HIV; 2) identify additional CBT content needed to increase relevance to the population; and 3) generate relapse-prevention message content specifically needed for this population. After qualitative data collection and analysis are completed, appropriate updates will be made to the CBT treatment manual and relapse-prevention message library.

Qualitative Analysis. Data will be analyzed in two phases – an initial phase of conventional content analysis followed by an inductive, thematic approach to identify patterns in the data. Coded data will be analyzed for emergent patterns and themes that may adhere to or contradict the investigators' expectations. Data management and coding will use NVivo8 software on VA VINCI website, or ATLAS.ti on a VA secured computer.

Quantitative Analysis. Regarding quantitative data received from Duke, data from veterans who smoke, people living with HIV who smoke, and members of the general public who smoke will be analyzed separately. First, data will be cleaned. Participants will be excluded from analysis if they meet any of the following criteria: greater than 2 endorsed bogus items, self-reported "very little" or "no" effort or attention, or a "no" response to the question "In your honest opinion, should we use your data in our analyses in this study?" After data cleaning, the following descriptive statistics will be calculated for satisfaction ratings on each SmokefreeVET message: range, mean, and standard deviation. Items falling below an 8 on mean satisfaction will be reviewed by the study staff in the context of qualitative findings to make final decisions regarding their inclusion in the final relapse-prevention message library.

Aim 2:

In order to examine disparities in healthcare delivery of smoking cessation prescriptions, we will use a longitudinal retrospective design. Generalized linear mixed modeling (GLMM) with a logit link and binomial variance will be used to determine differences by variables of interest in likelihood of pharmacotherapy dispensation following positive tobacco health factors screening. GLMMs appropriately accommodate multi-level data structures with unbalanced design for analyzing repeated observations across multiple individuals nested within clinics. Clinic- and person-level random effects will be included in statistical models to account for correlation among patients within the same clinic and repeated measurements on the same individual over time, respectively. Covariates will be assessed for collinearity before entering them simultaneously into the GLMM.

Aim 3:

We will use rapid qualitative analytic methods to analyze participant feedback from post-treatment qualitative interviews (Watkins, 2017). For each study cohort of 5 participants, study staff will complete written summaries of interview audio recordings, and will enter these summaries into a study database. Interview summaries across participants will be displayed by their structural content (i.e., intervention strength, intervention weaknesses, and areas for improvement). Then, thematic analysis will be used to code emergent themes and patterns within each content area. Given the sample size for this successive cohort study (*N* = 15), it is estimated that we will identify and be able to address 97% of usability problems in the treatment personalization program (Faulkner, 2003).

Aim 4:
Analysis and interpretation will focus on describing the acceptability of the intervention and the feasibility of the trial approach. Given power limitations of using a small sample in a two-group study, it is not appropriate to perform any efficacy analyses. Regarding feasibility, we will describe patient recruitment, treatment retention, the proportion of patients who withdraw after randomization, and the proportion of patients who withdraw from treatment. In order to ascertain acceptability of the intervention, we will describe patient satisfaction, therapist satisfaction, and app utilization metrics. We will describe the proportion of patients that quit in each arm (but will not test group differences in abstinence).

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