Identifying Effective Treatment for Veterans Unwilling to Quit Smoking

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Project Summary

Aims and Rationale: Tobacco use is the leading preventable cause of premature death in the United States. Veterans smoke at a higher rate than the U.S. population (21.6% vs. 15%), and therefore suffer disproportionately from smoking–related illness. To reduce the enormous health and economic harms of smoking amongst Veterans, we need a comprehensive approach to engage all Veterans who smoke in treatment that effectively helps them stop smoking. Unfortunately, most smokers are unwilling to make a quit attempt at any given time (70%-90%), and we know little about how to effectively engage such smokers in treatment and help them quit. The standard recommended intervention for such smokers, brief advice to quit, is far too minimal to mobilize most smokers to make an aided quit attempt. Thus, a critical public health challenge is to identify successful interventions that motivate smokers to make quit attempts and improve their likelihood of success when they try. The proposed research will address gaps in smoking treatment by evaluating Enhanced Chronic Care, an intervention designed to increase treatment engagement and abstinence amongst Veterans initially unwilling to quit smoking. Enhanced Chronic Care provides ongoing motivational interventions and interpersonal support designed to promote readiness to change, with facilitated access to both smoking reduction and cessation treatments that are appropriate for all smokers (both those *willing* and *unwilling* to make quit attempts). Enhanced Chronic Care will be compared with Standard Care (brief advice to quit once per year) on criteria that are of great clinical and public health importance: long-term abstinence (primary outcome), treatment reach, cost-effectiveness, and implementation. Such comprehensive data will permit identification of an optimal smoking treatment strategy for VA clinical practice.

Methods: We will evaluate these interventions using a rigorous 2-arm randomized controlled trial (RCT). Veterans who smoke daily, but who are *not willing to enter smoking cessation treatment* (the vast majority of smokers), will be eligible to participate, with no obligation to quit or reduce their smoking. Participants (N=500) will be randomized to one of the following treatments: 1) Enhanced Chronic Care (n=250) or 2) Standard Care (n=250). These intervention conditions will last 2 years to permit analysis of their cumulative impact on abstinence (primary outcome) and treatment use, and to gather information on factors, including cost-effectiveness, that could affect the implementation and effectiveness of Enhanced Chronic Care.

Significance: This research will provide the most comprehensive evaluation of a chronic care smoking treatment to date, one that rigorously tests the effectiveness of a chronic care intervention involving an ongoing motivational intervention with ready access to evidence-based reduction and cessation treatment, while simultaneously gathering implementation data to inform subsequent implementation efforts and research. This research has important clinical and public health significance because smoking is especially common amongst Veterans and is the leading preventable cause of disease and disability. Success in treating smoking in healthcare has been limited because smokers use smoking treatments far too infrequently and the treatments that they do receive are typically of modest intensity and effectiveness. The proposed research builds on our expertise and prior research findings to address these critical knowledge gaps by identifying an intervention that, over time, should greatly increase both Veterans' use of effective treatments and their quitting success, thereby leading to significant declines in tobacco-related morbidity and mortality.

Background and Significance

The health, economic, and human costs of tobacco use are profound. Smoking is the leading preventable cause of death and disease, and causes about 30% of all cancer deaths in the

US[18]. Smoking cessation reduces the risk of cancer, cardiovascular disease, and stroke[19]. US Veterans smoke at a higher rate than the US population (21.6% vs. 15%[10]), and therefore suffer disproportionately from smoking–related illness. During 2010, VHA spent 2.7 billion on smoking-related ambulatory care, prescription drugs, hospitalization, and home healthcare. Helping more Veterans quit could result in millions of dollars in savings from averted medical costs and result in substantial reductions in morbidity and mortality[10]. This starkly illuminates the importance of improving the tobacco treatment provided in the VA healthcare system.

The VA offers evidence-based treatment comprising counseling and medication that can increase cessation rates 2-3 fold[11,12], but Veterans who smoke rarely use such treatments[13]. *A recent study of over 5,000,000 Veterans over a 1-year period found that only 3.8% of Veterans with tobacco use disorder received appropriate evidence-based treatment that included both counseling and medication*[20]. This means that 96% of Veterans who smoke did not receive recommended, effective tobacco treatment – a core element of healthcare. Thus, at present, the smoking treatment resources of the VA are underused.

Gaps in Smoking Treatment

Several factors contribute to the limited reach and effectiveness of smoking treatments. One is that the vast majority of smokers in the VA healthcare system receive only brief provider advice to quit as a smoking treatment. This results in a huge gap between this very brief, relatively ineffective intervention[11] and the dire needs of the Veterans who smoke. Many such smokers have risk factors that thwart success in quitting: severe tobacco dependence, poverty, psychiatric comorbidities,[21-23] motivational deficits, and an unwillingness to use quitting aids. Their unwillingness to quit and their many risk factors mean that few will succeed if they receive only brief provider advice. This underscores the need to provide chronic care that increases smoker involvement in more intense and effective treatment over time.

One factor limiting smoking treatment reach is that most healthcare systems (including the VA) offer and provide effective treatment only to smokers who are already motivated to make aided quit attempts. Healthcare systems offer little to those who are *not* ready to make a quit attempt immediately— *a group comprising the majority of smokers at any given time (70%-90%*)[14,24]. This means that at any point in time few Veterans leave healthcare visits with effective treatment for tobacco dependence[13]. *Thus, a critical public health challenge is to identify interventions that effectively engage more Veterans in evidence-based treatment to help them quit, including smokers who are not initially willing to quit.*

This study will address gaps in smoking treatment by comparing Standard Care (**SC**) with Enhanced Chronic Care (**ECC**), a treatment designed to increase cessation treatment engagement and abstinence amongst Veterans who smoke. ECC provides ongoing motivational interventions and interpersonal support designed to promote readiness to change, with facilitated access to smoking treatments that are appropriate for all smokers (both those willing and unwilling to make quit attempts). We have enhanced chronic care by providing ongoing, easy access to both smoking cessation and reduction treatment. Reduction treatment is an evidence-based approach that provides smokers unwilling to quit with a non-cessation treatment alternative, one that increases quit attempts and the success of those attempts. This research will compare SC (brief advice to quit once per year) and ECC on criteria that are of great clinical and public health importance: long-term abstinence (primary outcome), treatment reach, cost, cost-effectiveness, reach and representativeness, treatment acceptability, implementation, and maintenance. Such comprehensive data will permit identification of an optimal smoking treatment strategy for VA clinical practice.

Rationale for Interventions

Chronic Care. The US Public Health Service (PHS) Clinical Practice Guideline, *Treating Tobacco Use and Dependence* [11], recommends advising patients to quit at every clinic visit; however, this intervention is too rarely executed and too minimal to mobilize most smokers to make an aided quit attempt[11]. In addition, when the small percentage of smokers who choose to use smoking treatment do so, the great majority typically use it once, relapse, and then essentially disengage from the treatment process for months or often, years. We need a chronic care strategy that over time efficiently involves many more smokers in treatment, including

those unwilling to quit. Such a treatment should comprise elements that are supported by prior research, establish an ongoing supportive relationship with the smoker, and adjust treatment in response to the smoker's evolving needs. The ECC strategy proposed here has three major elements: 1) Motivational components; 2) Enhanced Treatment Access, and 3); Availability of Effective treatments for smokers who are either willing or unwilling to quit. Thus, ECC is intended to *motivate* the smoker to make change attempts, reduce barriers to treatment, and provide effective treatments when the smoker is ready to change. Importantly, these three resources are coordinated so that intervention is adjusted to meet the Veteran's needs and goals as they evolve over time. The Motivational components are intended to activate three major motivational dimensions consistent with Self-Determination Theory (SDT[25]); i.e., it will activate intrinsic motives for change, provide interpersonal support, and affirm the patient's sense of agency and control over his/her change efforts[25,26]. The Treatment Access component will offer treatment over time, provide treatment choice, and facilitate access via mechanisms such as warm hand-offs. The Effective treatments will comprise both cessation and reduction treatments (treatments for smokers willing or unwilling to quit) that each include counseling and medication interventions that have been shown to work well together to achieve clinically meaningful change.

The proposed ECC intervention involves manualized, continuing (i.e., longitudinal) care with proactive, phone-based outreach, patient education and support, and coordination of care[27] delivered by a trained research Health Counselor (HC)[28]. Tobacco dependence chronic care models have been tested in two RCTs[2,3], both of which suggest that chronic care improves treatment use and abstinence over at least 18 months. ECC adds important elements to treatments used in those prior successful RCTs[11,29]; our approach will involve phone-based delivery of proactive treatment invitations, motivational interventions designed to promote readiness to change and offer of cessation treatment, promotion of lifestyle changes supportive of change attempts, support for current treatment use, and so forth[30]. Such a chronic care approach answers repeated recommendations to treat smoking as a chronic condition[11,31,32]. Its feasibility is also consistent with the increasing use of chronic care approaches to improve the clinical management of costly chronic conditions such as diabetes and depression[27,33,34]. However, tobacco use, the most costly and lethal preventable chronic condition, remains undertreated relative to other chronic conditions[29].

Evidence Base for Enhanced Chronic Care

Substantial research evidence supports the proposed elements of ECC. For instance, evidence shows that the Motivation components can enhance both treatment entry/use and treatment success[35-38]. Thus, we will use the decisional balance exercise[39] to encourage smokers to weigh intrinsic reasons for quitting vs. motives for smoking (e.g., smoking is rewarding or enjoyable)[40]. And, the assignment of feasible specific steps, including lifestyle modifications such as home smoking bans and eliminating smoking in a few key contexts, are intended to serve two purposes. First, they should foster later cessation likelihood[41], because decreasing smoking cues and increasing smoking restrictions both support quit attempts and quitting success[2,3,42]. Second, success with these feasible goals should build self-efficacy, which is highly associated with cessation success[43], which the HC will reinforce with social support. The social support from the HC will form a strong working alliance with the participant, a construct associated with making increased quit attempts via phone counseling[43,44]. There is also considerable support for the Treatment Access element of the proposed ECC intervention. Studies show that the following all increase treatment engagement: 1) proactive calls offering treatment[45,46], 2) choice between reduction and cessation treatment[1], and 3) warm hand-offs to reduce barriers to treatment access[30,47]. These resources will be made especially effective as they will be sustained over time; research shows that ongoing delivery of similar resources significantly increases smokers' treatment engagement and abstinence[2,3,37,45]. Such research shows that relapsed smokers are often willing to make an additional quit attempt if treatment access is easy and treatment offers are sustained over time[1].

Reduction Treatment. Although chronic care shows great promise for engaging smokers and promoting abstinence, its effects would likely be enhanced by providing a non-cessation treatment alternative for smokers initially unwilling to quit. Such a treatment would ideally

increase treatment reach and provide alternative pathways to abstinence, either by directly encouraging quit attempts (without use of formal cessation treatment[1,5]), or indirectly by encouraging subsequent uptake of cessation treatment[1]. Fortunately, smoking reduction treatments have been developed that are expressly designed to increase treatment use and abstinence rates in smokers not yet ready to quit. Smoking reduction treatment comprises use of nicotine replacement therapy (NRT) and brief reduction counseling, consistent with PHS clinical practice guidelines, that are intended to help smokers reduce their smoking and motivate quitting. Reduction counseling is offered at the VA Tobacco Treatment Clinic. The goal of this research is to greatly increase the *use* of reduction treatment and benefits amongst Veterans.

Cessation Treatment*.* There is also strong support for the cessation treatment that will be made available to participants in this study; it includes combination NRT (nicotine patch + nicotine gum or lozenge) and counseling that is consistent with the PHS Clinical Practice Guideline. Both treatment elements are supported by numerous studies[11]. Moreover, the use of this cessation treatment enhances the dissemination potential of this research since this form of cessation treatment is widely available in VA healthcare. However, this treatment resource is currently underutilized in VAHC; an ultimate goal of this research is to greatly increase its *use* and benefits across the whole population of VA smokers.

Rationale for the Combined Elements of Enhanced Chronic Care. There are sound reasons for combining the elements of ECC. The *Motivation* components are intended, over time, to induce a high proportion of Veterans to enter reduction and/or cessation treatment and to increase the success of those treatments when the Veteran decides to use them. For instance, proximal goals of the Motivation intervention such as increased motivation for change, reductions in smoking contexts, and increased self-efficacy, are all significantly related to cessation success[43,49]. The *Treatment Access* components are made to "strike while the iron is hot." There is copious evidence that smokers are much more likely to engage in treatment if offered immediate connection to it (e.g., warm hand-offs). Further, access to evidence-based treatments will be offered repeatedly over time because smokers often make multiple change attempts before quitting smoking permanently. In addition, evidence shows that willingness to enter treatment is fairly labile; the smoker who is disinterested on one day is often willing to enter treatment a short time later[50]. Finally, the availability of both reduction and cessation treatments should increase the number of smokers entering evidence-based treatment. Moreover, easy transfer from reduction to cessation treatment will leverage the head start that reduction treatment provides for the quit attempt; i.e., earlier exposure to reduction appears to increase the success of cessation treatment[1]. *Thus, we believe that all of these elements will work together in a complementary manner so that ECC, relative to SC, will significantly: 1) enhance smoking abstinence rates (primary aim); 2) Enhance quit attempts; and, 3) Enhance entry into evidence-based cessation treatment.*

Suitability of Interventions among Vulnerable VA Populations. ECC should be well suited to two VA subpopulations especially likely to suffer from smoking related harms: those with mental health and/or substance use disorders. These subpopulations, relative to others, are more likely to: smoke, have greater difficulty quitting, and die from smoking[51]. The Practice Guidelines for the Treatment of Patients with Substance Use Disorders[52] recommends smokers with mental health and substance use disorders receive long-term smoking treatment that addresses motivational deficits and provides combined behavioral support and pharmacotherapy. Consistent with these recommendations, the features of ECC (ongoing motivational interventions and interpersonal support designed to promote readiness to change, with facilitated access to smoking treatments) address such needs. In addition, offering a reduction treatment goal (versus cessation) may be especially attractive to smokers with a history of failed quit attempts (though abstinence is the ultimate goal of reduction treatment). Consistent with this notion, patients who endorse heavier alcohol consumption and those with history of treatment for anxiety are more likely to enter reduction than cessation treatment[4]. In the proposed research, we will determine the proportion of smokers with mental health and/or substance use disorders who enter reduction versus cessation treatment, and whether initial use of reduction treatment increases the likelihood of eventual abstinence amongst these smokers.

Evaluation of Implementation Factors

The overarching aim of this research is to develop an effective treatment for smokers who are unwilling to quit: one that is suitable for dissemination in VA healthcare. Since implementation challenges are major impediments to adoption and use of smoking treatments in healthcare (e.g., [53,54]), we will collect data on factors that might affect ECC adoption, implementation, and effectiveness in VA settings. This Hybrid Type 1 design, in which implementation assessment is integrated with a comparative effectiveness design[6,7], should significantly enhance the translation potential of this work. Cost-effectiveness is one such factor that could affect ECC implementation. While smoking cessation treatment is the gold standard for cost-effective preventive interventions[8], a recent review found wide variation in the cost-effectiveness of 10 counseling and 27 pharmacotherapy treatments[55]. Thus, relative cost-effectiveness could be a key element in decisions about treatment adoption. As recommended by the US Panel on Cost-Effectiveness in Health and Medicine, we will compute cost per quit and incremental cost-effectiveness ratios (ICERs) for ECC relative to SC.

This project will also gather information on other key factors that influence treatment adoption, implementation, and effectiveness as suggested by the RE-AIM (Reach, Effectiveness-Adoption, Implementation, and Maintenance[56]) model and by research on tobacco treatment implementation[57,58]. RE-AIM factors, adapted to be appropriate for this Hybrid Type 1 research, will be assessed for both SC and ECC as appropriate, generating important comparative data. The RE-AIM Effectiveness component will be measured via abstinence (primary aim) as described elsewhere in this proposal. Measures of reach and representativeness, treatment acceptability by Veterans, implementation, and patient-level maintenance will be gathered via multiple methods (surveys, semi-structured interviews, electronic medical records (EMR), and quantification of study processes/outcomes). We will not assess system-level maintenance or staff or setting adoption, as these factors are not appropriate for this research (e.g., research personnel will serve as Health Counselors, only one site is involved[56]). VA leaders, administrators, and VA clinical personnel will be consulted during the development of the implementation assessments to ensure that information gathered addresses information needs of vital stakeholders within VA healthcare. Finally, we will carefully evaluate how the research methods per se might affect the clinical relevance of the implementation findings.

Rationale for the Research Approach

Use of Standard Care (SC) as the Comparison Group. The aim of this research is to evaluate whether ECC improves abstinence and treatment engagement when compared with SC, a *clinically meaningful* treatment used by the VA (i.e., a treatment of representative length, intensity, and content). This research is ***not*** intended to tease apart the effects of intervention content or intensity; e.g., we will not compare ECC with a less meaningful control treatment of the same length/intensity. As such, the proposed design reflects effectiveness research principles that enhance the rapid translation of research findings into clinical practice; i.e., establishing that ECC performs better than a representative standard of care[9]. However, in order to increase internal validity of this research, both ECC and SC will be administered by research staff. Thus, we balance internal and external validity by delivering treatments with good dissemination potential in a manner that decreases some sources of variability (e.g., provider variability).

Use of Proactive Care. Although primary care is an important venue for treating smoking[11], we opted to use proactive care (i.e., treatment invitation mailings to all tobacco users with low-barrier phone-based interventions) for several reasons. In primary care, smoking treatment is limited by whether 1) the Veteran makes a healthcare visit; 2) the Veteran is willing to engage in treatment at the time of the visit; and 3) the clinician has the time, motivation, and knowledge to provide smoking treatment. All these factors make it unlikely that patients in primary care will receive effective smoking treatment[59]. Also, treating smokers in primary care disadvantages those who do not live near VA medical centers (e.g., Veterans living in rural areas), whereas proactive care increases treatment access[60]. Fu et al.[60] found that a proactive smoking intervention decreased smoking prevalence in Veterans. However, that study involved only one proactive call offering cessation treatment. We believe that the benefits of proactive care can be

enhanced greatly by offering it repeatedly (via chronic care) and by offering treatment that appeals to smokers who are both ready and not ready to quit (reduction and cessation treatment)[46].

Innovation

To date, little research has been done to engage smokers unwilling to quit in treatment. Therefore, the great majority of smokers seen in clinical settings receive no smoking intervention, other than brief advice to quit. It is critical that we identify interventions that motivate smokers to make quit attempts and that also improve the success of those attempts. While smoking is a chronic, relapsing condition and there have been repeated calls for the development of effective chronic care interventions for it[11,63], little research exists on the chronic care of smoking[2,3], including amongst Veterans. The proposed research is innovative in multiple ways: 1) It will be the first study to experimentally evaluate chronic care for smokers who are initially *unwilling* to make a quit attempt. 2) It will evaluate the most comprehensive chronic care treatment to date, involving an ongoing motivational intervention, heightened treatment access, with access to evidence-based reduction and cessation treatment. 3) It will be the first study to examine the effects of such a comprehensive chronic care program on a wide range of outcomes of great relevance to its potential for adoption, implementation and dissemination: long-term abstinence, quit attempts, use of cessation treatment (expanding cessation treatment reach), representativeness of reach, maintenance of participants in treatment over time, treatment acceptability, cost-effectiveness, and so on. *Rigorously evaluating the effectiveness of ECC while simultaneously gathering implementation data is highly innovative and will support rapid translation of findings into implementation research, thereby accelerating ultimate dissemination into the VA healthcare setting[7].*

Relevance for Veterans

Smoking is a common and treatable addictive disorder that remains the leading preventable cause of death[65]. US Veterans smoke at a higher rate than the US population (21.6% vs. 15%[10]), and therefore suffer disproportionately from smoking–related illness. About 50% of Veterans who smoke will die prematurely from a smoking-related illness unless they quit[66]. Thus, of the estimated 4,117,200 Veterans who currently smoke, ***over 2 million will die prematurely from smoking-related causes***[10]. Those Veterans who continue to smoke, despite the decreasing prevalence of smoking in the general population, represent smokers for whom current motivational efforts and contemporary cessation therapies have failed. This starkly illuminates the importance of utilizing innovative treatment and methodologies to increase the effectiveness of tobacco treatment provided in the VA healthcare system. The VA has enormous potential to promote abstinence from tobacco through connecting all smokers with evidence-based care. Results from this project will offer the VA a blueprint for optimized ways to connect more Veterans with evidence-based smoking cessation treatment and decrease smoking prevalence, thereby decreasing smoking-related death and disease.

PRELIMINARY STUDIES

Relevant Experience and Expertise

The research team has a long history of successful collaboration, including: 1) collaborating with the VA for Dr. Cook's (PI) currently funded VA Merit grant; 2) recruiting over 1700 primary care patients interested in smoking treatment[14,70,71]; 3) engaging over 1000 patients who are unwilling to quit in reduction treatment[1]; 4) evaluating implementation of tobacco use assessment and treatment, including inclusion of smoking status in vital signs assessment in primary care, which is now the standard of care (marker of quality on which healthcare systems are measured) (e.g., [67]), 5) conducting cost-effectiveness analyses of smoking interventions (e.g., [68,69]) ; 6) providing phone-based behavioral interventions (e.g., motivational interventions; smoking reduction counseling) including among Veterans [1,70-73], 7) administering behavioral interventions to Veterans[72,73], and, 8) using qualitative and mixed methods to inform intervention refinement and implementation (e.g., [74,75]).

Evidence for Use of Smoking Reduction in Smokers Unwilling to Quit

Dr. Cook (PI) completed a randomized 4-factor (2X2X2X2) factorial experiment to identify especially promising intervention components that increase quit attempts and cessation success among smokers unwilling to quit (*N*=517, *not Veterans*[1]). Results of this research showed that offering reduction treatment increased participation in evidence-based treatment by about 1/3 and showed that a standard 6-week treatment comprising reduction counseling and nicotine *gum* yielded especially promising effects with respect to quit attempts, smoking reduction, and abstinence (the nicotine patch showed no benefit[1]). In addition, participants had excellent rates of treatment engagement: attendance rates ranged from 70% - 87% for all treatment contacts (phone/in-person). Moreover, over half of participants chose to continue receiving additional treatment after completion of the initial 6-week intervention (i.e., repeat the motivation treatment or enroll in cessation treatment). Finally, among those assigned to Nicotine Gum, 257/264 (97.3%) reported using the gum; they used an average of 3.61 (*SD*=2.10) pieces per day. Strong adherence rates for nicotine gum suggest that smokers who are not yet ready to quit are willing to use ad lib NRT. Finally, nicotine gum was well tolerated by smokers not ready to quit. Thus, the reduction treatments used in our previous work were acceptable and effective for smokers unwilling to quit. Based on the results of this factorial experiment, we have identified an abstinence-optimized treatment that is both effective and well-tolerated by smokers unwilling to quit: 6 weeks of reduction counseling plus nicotine gum or lozenge (with the option to repeat the 6-week treatment).

Evidence for Use of Chronic Care Treatment

Our P01 Longitudinal Treatment Project is a study of the feasibility of chronic care, involving repeated offers of treatment over time. Patients (not Veterans) participating in an initial cessation treatment are offered retreatment repeatedly thereafter (chronic care) if they have relapsed. As of July 2018, among 593 participants who relapsed after the initial cessation treatment, 485 (82%) have transitioned to continued treatment. There is virtually no attrition from those making this transition; 97% (472 of 485) remain in chronic care. The chronic care strategy, similar to that proposed in this research, has produced a 65% cessation re-engagement rate, with many of the participants receiving only a small number of retreatment offers. Thus, as suggested by other research[2,3] our findings suggest that smokers stay involved in chronic care and that it can lead to a high rate of treatment engagement and re-engagement.

Recruitment

Our research group has recruited very successfully for multiple studies over the past decade. Some have used a proactive outreach recruitment strategy similar to that proposed in this experiment. For instance, in a recent study funded by CMS[76] we offered Wisconsin State quitline users $40 to contact the research program, *which required an in-person visit*. Of the 2418 smokers who were notified of the study opportunity via the quitline and who were eligible (e.g., smokers and Medicaid recipients), 980 (41% of the 2418) entered cessation treatment. We believe we will be even more successful in the proposed research in recruiting since an in-person assessment visit is not required and because recruits do not have to initially commit to trying to make a quit attempt and use treatment.

Summary of Preliminary Studies

In sum, our prior research demonstrates our success in: engaging smokers unwilling to quit in treatment, meeting enrollment goals, evaluating implementation and using mixed and qualitative methods to inform intervention implementation, maintaining engagement in long-term treatment, and delivering behavioral and pharmacologic treatments. Moreover, our research provides evidence for the feasibility and effectiveness of chronic care treatment for smoking. Our experience uniquely positions this research group to address key knowledge gaps and enable us to successfully complete the proposed research and produce a smoking treatment that promotes abstinence in Veterans who are initially unwilling to quit smoking.

Research Design and Methods

Study Objective

The primary goal of the proposed research is to examine whether Enhanced Chronic Care (ECC), relative to Standard Care (SC), improves abstinence at 2 years post study entry in Veterans who are not initially willing to enter smoking cessation treatment.

Specific Aims/Study Objectives

Primary Aim:

Aim 1: To compare ECC with SC on biochemically confirmed abstinence at 2 years post study entry. It is hypothesized that ECC will significantly increase 2-year abstinence compared with SC.

Secondary Aim:

Aim 2: To compare ECC with SC on treatment use (reach): i.e., use of cessation treatment over 2 years of treatment access.

Tertiary Aim:

Aim 3: Gather information on factors with the potential to affect the implementation and effectiveness of ECC relative to SC, including: a) cost and cost-effectiveness, b) treatment acceptability (e.g., overall satisfaction with the program, satisfaction with transitions across care), c) representativeness of reach/treatment use (e.g., with regard to race, gender, psychiatric comorbidities entering and using treatments), d) implementation (e.g., percent treatment calls taken, perceived burden of treatment elements), and e) patient-level maintenance (patient attrition/loss of contact rates for treatment elements, persistence of behavior change).

Design Overview

The proposed research is a 2-arm RCT designed to evaluate whether ECC, relative to SC, increases abstinence amongst smokers initially unwilling to quit. Participants (*N*=550) will be randomized to one of two treatments: 1) Enhanced Chronic Care; ECC (*n*=275); 2) Standard Care; SC (*n*=275). ECC involves four calls per year to provide ongoing motivational interventions, interpersonal support, and facilitation of smoking cessation and reduction treatment access. SC involves one intervention call per year involving brief advice to quit and information on cessation treatment access (viewed as a minimal acceptable level of treatment offer[11]). Participants can elect to engage in treatment (or not) at any time up to Month 22 of the 24 Month study period (to allow completion of treatment prior to 2-year follow up). They may engage in the same treatment multiple times as this is a goal of chronic care (e.g., to re-engage smokers in cessation treatment after a relapse), and because we do not believe over-use will be a problem. All participants will complete phone assessments at Baseline and Months 6, 12, 18, and 24 post-study enrollment. The primary outcome is biochemically confirmed point-prevalence abstinence at 2 years; the secondary outcome is: use of cessation treatment.

Recruitment

The proposed research will be conducted at the Madison VA Medical Center (VAMC). The Health Factors Database identified 10,269 Veterans as tobacco users at the Madison VAMC (of 42,671 Veterans). Tobacco users identified via this database will receive mailed study invitations offering Veterans an opportunity to call to learn about resources for smokers. A website with the consent form will be included in the mailed study invitations. Veterans will be told that *they do not need to try to quit smoking* to participate in the program and that they will earn $40 for making the call regardless of whether they decide to participate. We believe that far more than 10% of these Veterans will call to learn more about the program based on our prior research: as per Fraser et al.[86]. Research Health Counselors (HC) will first obtain oral consent to record the caller's identity and demographics, and to send the $40 payment. (We must record who receives payment to reduce multiple claims; data on participant demographics will allow us to characterize those who do not join the research program). Then, the HC will assess interest in quitting within the next 30 days (an approach consistent with real-world practice[21]), and refer

all smokers interested in quitting to the VA Tobacco Treatment Clinic (approximately 20%[6,7]). Next, the HC will describe available VA resources including the study, screen for interest and eligibility, and obtain oral consent for study procedures for interested and eligible patients. A printed informed consent form will follow by mail. Consent will also be documented in VA medical records. Our prior research suggests that at least 50% of Veterans unwilling to quit will be eligible and willing to participate[21]. The estimated 5% who are interested in treatment but ineligible for the study will be referred to the VA Tobacco Treatment Clinic (our exclusion criteria are minimal). We will send multiple mailings each year, as treatment motivation is fluid and it may take multiple offers for a smoker to engage in the program. Additionally, flyers will be posted at physical and online locations with high Veteran traffic.

Inclusion and Exclusion Criteria

Five hundred fifty participants will be enrolled. For inclusion in the study, participants must: 1) be uninterested in setting a quit date in the next 30 days; 2) report smoking an average of 4 or more cigarettes daily for at least six months; 3) read, write, and speak English; 4) be medically eligible to use NRT; 5) if female, use an approved method of birth control if they use nicotine replacement therapy; 6) agree to participate in the study. Exclusion criteria related to NRT use will be re-assessed prior to initiating treatment as these may change over the course of the study.

To enhance generalizability, prior treatment use or participation in prior smoking cessation research, use of other forms of tobacco or e-cigarettes, and psychiatric status are not exclusionary, but will be tracked and analyzed. Veterans who express imminent intent for harm to self or others at any point in the study will be referred for VA emergency care.

Assessments

Participants in this project will complete four types of assessments: 1) Universal, 2) Treatment Initiated (if they initiate cessation or reduction treatment), and 3) Biochemically Confirmed Abstinence. 4) A subset of 40 randomly selected Veterans from the Enhanced Chronic Care arm (20 who are abstinent and 20 who are smoking at 2-years post study enrollment) will receive a semi-structured phone interview regarding treatment acceptability and burden. Assessments may be mailed to the participant if they are not able to be completed via phone.

Universal Assessments. All participants will complete a baseline telephone assessment with the HC upon entering this research (see Table 1). The 15-minute assessment will include: the Fagerstrom Test for Cigarette Dependence[77]; self-efficacy/motivation items; demographics, mental health and substance use disorders[78]; a brief Smoking History Questionnaire; decisional balance items; mood questionnaires; treatment knowledge items; smoking context items; quit plans items; healthcare use and VA treatment use items.; and COVID-19 items. Participants will also complete the Universal Assessment calls at months 6, 12, 18, and 24 post-study entry. These 15-minute calls will assess smoking frequency and heaviness, use of alternative nicotine products, use of any smoking treatment, withdrawal, craving, self-efficacy/ motivation, quit attempts and quit plans, and healthcare-related items. Universal Assessments that occur within 1 month of a Treatment Initiated Assessment call will be combined into a single assessment call to reduce burden. At the 24-Month call, 40 randomly selected participants from the Enhanced Chronic Care arm will complete surveys evaluating their treatment in terms of burden and acceptability, and satisfaction with program features[80].

Table 1. Universal Assessment Schedule

Assessments	Baseline	6 Mo	12 Mo	18 Mo	24 Mo
Demographics	X				
Mental health and alcohol use	X				
Smoking history	X				
Self-efficacy, Motivation	X	X	X	X	X
Decisional Balance	X	X	X	X	X
Mood (POMS, PHQ, Stress)	X	X	X	X	X
Treatment knowledge	X	X	X	X	X
Smoking contexts	X	X	X	X	X
Smoking 7-day follow-back		X	X	X	X
Quit attempts		X	X	X	X
Quit plans	X	X	X	X	X
Universal Medication Use		X	X	X	X
Alcohol, Other Tobacco Products	X	X	X	X	X
Healthcare Use	X	X	X	X	X
Quality of Life	X		X		X
Salivary cotinine/anabasine & CO					X*
Study Treatment and HC Satisfaction					X
VA Treatment Satisfaction, VA Use	X				X
COVID-19 Impact	X		X		X

*Participants who report 7-day point prevalence abstinence will be invited to biochemically confirm abstinence.

Treatment Initiated Assessments. All participants initiating a cessation or reduction treatment will receive phone assessments from research personnel. For cessation treatment, assessments will occur at 1-week pre-Target Quit Day (TQD), TQD, and at 2 and 12 Weeks following the TQD. For reduction treatment, assessments will occur weeks 1, 3, 6, 12 weeks. following treatment initiation. These 10-minute assessment calls, for both treatment types, will collect information on smoking status over the past week including abstinence days and smoking heaviness on days of smoking, alcoholic drinks per day over the past week, use of all tobacco products, use of study medication, as well as withdrawal, mood, self-efficacy, and adverse events.

Assessment Description

Demographic Information Questionnaire. Standard demographic information will be gathered via self-report at baseline to describe the study sample and to allow examination of any systematic differences between the two treatment groups.

Mental Health and Alcohol. While not exclusionary, psychiatric status and history will be tracked and analyzed. Participants will be asked whether they have been diagnosed with or treated for a list a mental health disorders (i.e., depression, anxiety disorder, PTSD, panic disorder, etc.). Participants will also be asked about their drinking habits for the past 12 months.

Smoking History Questionnaire and Nicotine Dependence Assessment. Standard smoking history information such as number of previous quit attempts and years smoked will be collected. The Fagerstrom Test for Nicotine Dependence (FTND)[93] will be used as a continuous measure of nicotine dependence.

Self-efficacy/motivation. HC will assess participant's motivation to quit smoking and confidence that they have the skills to quit, and mood. These single-item constructs, all which have been successfully used in our prior research, will be assessed via 7-point rating scales.

Decisional Balance. We will assess participant's opinions on factors related to their decision to smoke on a 5-point scale.

Mood. We will assess positive and negative mood states using items from the Profile of Mood States (POMS) and Patient Health Questionnaire (PHQ).

Treatment Knowledge. HC will assess participant's knowledge of smoking resources at

the VA using a 7-point scale.

Smoking Contexts. We will assess the contexts of the participant's environment where smoking is allowed.

Smoking Status. Number of cigarettes smoked each day will be assessed at baseline and at every call. We will assess long-term outcomes in a manner consistent with the recommendations of the Society for Research on Nicotine and Tobacco (SRNT) Workgroup on Biochemical Confirmation[1]. The main outcome analyses are based on 7-day point prevalence abstinence (i.e., reported abstinence for at least the 7 days prior to the assessment).

Quit Attempts and Plans. Participant's plans to quit will be assessed at baseline and at every assessment call. We will also assess any quit attempts made by the participant and days abstinent.

Alcohol Consumption. Number of alcoholic drinks consumed each day for the past seven days will be assessed during all follow-up assessment visits.

Withdrawal. We will monitor withdrawal severity at baseline, throughout treatment, and follow-up using the Minnesota Withdrawal Scale. This will allow for the assessment of the severity of withdrawal symptoms.

Medication use and adverse events. Adherence to the nicotine patch, gum, and lozenge will be queried at each treatment call following initiation of NRT. NRT side effects will also be assessed at each call. Potential differences in NRT use between treatment groups will be examined and incorporated into statistical models if a meaningful relation with outcomes is detected but medication use itself is not being tested for efficacy. Participants will also be assessed for use of stop smoking medications not provided by study staff.

Use of other tobacco/nicotine products, alcohol, and CBD. Use of other products containing nicotine (smokeless tobacco, cigars, e-cigarettes, etc.) will be assessed. We will also assess use of alcohol and CBD oil.

Healthcare Use, VA Treatment, and Quality of Life. Use of healthcare such as visits to see a provider or the Emergency Department will be assessed. We will also assess participant's satisfaction with their healthcare and how good they feel their health is.

COVID-19. Impact of COVID-19 on participant's life and smoking.

Cotinine and CO. Bioverification will be determined for abstinence self-reports made during the 24-Month Universal Assessment. Those who report 7-day point-prevalence abstinence at these 24-month assessment calls will be invited to the VA clinic to provide a saliva sample that will be tested for cotinine and anabasine to verify nicotine abstinence and a CO test to verify nonsmoking. Participants who are invited but unable or unwilling to drive to the Madison VA will be offered to have the salivary cotinine testing kit mailed to them. The cotinine test reflects smoking over a longer time span, but might reflect vaping or NRT use. If NRT or vaping is reported, CO will then be the determinant abstinence criterion. Anabasine (a biomarker of combustible nicotine) will be used to enhance the specificity of biochemically verified measure of abstinence from combustible tobacco. Participants will also report their 7-day tobacco use at the biochemical confirmation visit.

System Outcomes. All participants will receive an assessment at the end of the study regarding how effective they think the program was for them, how easy it was obtain treatment for their tobacco use, and whether they would recommend the treatment program to other Veterans. Items will be assessed on 7-point scales. Treatment-specific questions will also be asked to assess satisfaction, motivation for choosing treatment, and ways to improve treatment delivery in the future.

Therapist Competence and Adherence to Treatment. Treatment sessions in both conditions will be audio recorded, and a random selection of one session for each condition of the audio recordings will be rated shortly thereafter by trained coders to assess therapist adherence to and competence with the treatment protocol. Audio recordings will be on a secure VA server and accessible only by the study staff and will be stored at the VA indefinitely, per VA policy. Separate rating checklists developed for the Enhanced Chronic Care and Standard Care protocols will be used.

Study Procedures

Study Consent and Baseline

Screening Telephone Call. Research Health Counselors (HC) will first obtain oral consent to record the callers' identity and demographics and to send the $40 payment. (We must record who receives payment to reduce multiple claims; data on participants' demographics will allow us to characterize those who do not join the research program). Then, the HC will assess interest in quitting in the next 30 days (an approach consistent with real-world practice[1]), and refer smokers interested in quitting to the VA Tobacco Treatment Clinic (TTC) (approximately 20%[15,24]). Next, the HC will describe VA resources including the study, screen for interest and eligibility, and obtain oral consent for study procedures. A printed informed consent form and HIPAA authorization will follow by mail.

Randomization Process. Randomization (via the research database) to either ECC or SC will occur at the patient-level and will be stratified by race (White vs. Non-white), and sex (*biological variable*) to ensure adequate representation across the two treatment conditions. Consistent with VA TTC procedures, 3 attempted phone calls will be made for every scheduled treatment contact.

Treatment Interventions

Enhanced Chronic Care (ECC). ECC involves four 10-minute chronic care calls/year from the Health Counselor. During these calls, the HC will follow motivational interventions based on the 2008 Clinical Practice Guideline[11]. The motivational interventions are designed to increase intrinsic and autonomous motives for quitting, provide intra-treatment support, and tip the balance of pros and cons in favor of quitting. During these counseling calls, the HC will help the patient explore his/her goals and concerns with regard to smoking, engage in a nondirective, supportive motivational intervention, and then adapt counseling and actions to support the participant's current goal(s): e.g., lifestyle changes that support reducing or quitting, support for the participant's current treatment use, and reinforcement for progress. Treatment options (reduction or cessation) and ways to initiate treatment will be discussed during each of the calls (warm hand-off[30] via the HC). Consistent with a chronic care model, participants who elect to engage in reduction or cessation will begin treatment with the same HC immediately. Patients will work with the same HC for 2 years to foster rapport and trust.

Cessation Treatment. The full experimental sample of *N*=500 will have access to cessation treatment. Cessation treatment involves evidence-based cessation counseling and combination nicotine replacement therapy (nicotine patch plus nicotine gum or lozenge). The cessation treatment is based on recommendations in the 2008 PHS Guideline[11] and includes all elements of cessation treatment offered in VA facilities[13]. The efficacy of cessation treatment is not being tested.

Cessation Counseling. Cessation counseling will comprise a 20-min telephone preparation counseling session with the HC at 1-week prequit, and 15-min phone counseling sessions on the target-quit-day (TQD) and at Weeks 1 and 2 postquit. Consistent with VA standard care practice, additional counseling calls may be added during the 12-week treatment period to support participants as clinically indicated. Prior to quitting, HCs will reinforce reasons for quitting, discuss Veterans' past quit experiences, and develop a plan. Postquit sessions will involve anticipating high-risk situations, coping with craving, providing intra-treatment support, and dealing with a lapse/relapse[11]. The efficacy of cessation counseling is not being tested.

Combination Nicotine Replacement. Participants will be screened for NRT contraindications during the initial screening call and then further screened by the HC at the patient's first cessation call (the few participants who cannot safely use NRT will be retained in the study but not included in the final analysis sample). NRT will be prescribed consistent with VA standard of

care, cessation treatment will involve combination NRT (patch + participant choice of nicotine gum or lozenge). All participants will be given complete instructions on proper NRT use[11]. Medication use and side effects will be assessed at all calls. Any concerns regarding nicotine patch, gum or lozenge use will be reviewed by Dr. Gruber in the Tobacco Treatment Clinic, who may interview participants should further information be required. Dosage/use alterations as per good clinical practice will be recommended if the participant experiences symptoms of nicotine toxicity or side effects. The efficacy of NRT for smoking cessation is not being tested.

Reduction Treatment. Those randomized to ECC will also have access to reduction treatment. Consistent with VA standard of care, reduction treatment involves a 12-week regimen of nicotine gum or lozenge accompanied by phone counseling. The efficacy of reduction treatment is not being tested.

Reduction Counseling. Reduction counseling involves 7, 10 to 20-minute phone counseling sessions over a 12-week period. During the initial meeting and subsequent counseling calls, the HC will work with participants to develop strategies for changing smoking patterns such as reducing cigarettes, increasing time between cigarettes, delaying smoking, or eliminating smoking in specific situations. The counseling will emphasize the development of smoking control skills via feasible, specific, and graded assignments involving the modification of smoking patterns. The HC will explicitly address pragmatic issues such as work contexts, smoking policies, smokers at home, and habits that interfere with the development of new smoking control skills[1]. Exercises will emphasize competence and self-efficacy, both which will be directly linked to the practice of smoking reduction skills and success in changing smoking patterns. The HC will suggest the strategic use of nicotine gum/lozenge to help achieve goals, and will ask if the participant wishes to enter cessation treatment, but will not pressure the smoker to quit[1]. The efficacy of reduction counseling is not being tested.

Nicotine gum or lozenge. The HC will instruct participants to use nicotine gum or lozenge in place of smoking and in a scheduled manner, consistent with the 2008 PHS Guideline[11] and VA clinical care. All participants will be given an information sheet that conveys all medication instructions as well as a phone number to call if they have concerning side effects or other questions about their medication. Any concerns regarding nicotine gum or lozenge use will be reviewed by Dr. Gruber in the Tobacco Treatment Clinic, who may interview participants should further information be required. Dosage/use alterations as per good clinical practice will be recommended if the participant experiences symptoms of nicotine toxicity or side effects. The efficacy of NRT for smoking reduction is not being tested.

Standard Care (SC). Standard Care involves one call per year, ensuring that treatment is offered yearly to every smoker[11]. During the SC calls, the smoker will be encouraged to quit smoking, reminded of the cessation treatment available to him/her, and provided with a number to call should they become interested in treatment. This will *not* involve a formal motivational intervention or facilitated treatment entry (i.e., a warm hand-off). Cessation treatment provided in both ECC and SC will involve treatment delivery by the same research HCs to increase consistency of treatment delivery across the ECC and SC treatments. However, in order to approximate current VA clinical practice involving clinician referral for cessation treatment, SC participants opting to try to quit will be informed that they will receive a subsequent call to schedule the first counseling session (i.e., no warm hand offs or long-term contact with the same HC as in ECC).

Retention of Participants

Our prior research indicates that we can recruit 550 smokers unwilling to quit, engage them in long-term research participation and achieve anticipated participant flow. Participants will be compensated up to $140 for completing Universal Assessment Calls ($30/assessment calls at Months 6, 12, and 18, and $50 for the primary outcome assessment call at Month 24). Participants who miss their 6, 12, or 18-month Universal Assessment calls may complete the assessment by mail and receive $15 for their time. Participants who miss their 24-month Primary Outcome Assessment call may complete the assessment by mail and receive $20 for their time. Moreover, they will be paid $75 for completing assessments that biochemically

confirm abstinence at 2 years post-study enrollment (saliva cotinine/anabasine when assessed via mail kit; saliva cotinine/anabasine and CO test when assessed in person). Participants will not be informed of the contingency between self-reported abstinence at the 24 Month Universal Assessment call and the invitation to make a bioverification visit in an effort to discourage invalid reports of abstinence. Thus, if participants complete the abstinence bioverification visit, they can earn up to $215. If a participant decides to engage in treatment, they will be paid $10 for completing each Treatment Initiated Assessment, or $40 total for completing all assessments within a round of treatment. In addition, the subset of 40 Veterans from the Enhanced Chronic Care arm (20 who are abstinent and 20 who are still smoking 2-years post study enrollment) randomly selected to receive a semi-structured phone interview about their experiences with the study will receive $30 for their participation. Finally, retention during follow-up will be promoted by making multiple attempts to reach participants at their preferred number, following up with letters, or My HealtheVet messages, and reminding participants what they can earn for follow-up interviews.

Retrospective Chart Review

A CPRS chart review will collect data from all Veterans who contacted the study team in response to a recruitment mailing and consented to screening during the active recruitment period (November 2019 – August 2023). This includes Veterans who consented to the full study and those who consented to the screening but did not consent to the study, either due to ineligibility or choice. Medical records and CPRS problem lists will be reviewed for key markers associated with tobacco use, including: physical health conditions, mental health diagnoses, substance use diagnoses, service era, religion, race, ethnicity, birth sex, combat veteran status, service connection rating, MST (military sexual trauma) status, marital status, suicidality screening, tobacco treatment medication use, consults to the Tobacco Treatment Clinic. Data will be collected from the Veteran's medical record cover sheet, problem list, medication history, and Tobacco Treatment Clinic notes. Data collected from participants who enrolled in the full study will provide additional information that was not collected during study assessments. Data will be collected only from the potential participation period (November 2019 – August 2025, two-years after enrollment) and will not collect data after potential study participation has ended. Chart review data will inform future outreach efforts and determine differences in groups who choose tobacco treatment versus research. Waiver of consent requested for retrospective chart review as data collected go back to November 2019 and it would not be possible to contact previous participants and obtain informed consent. The medical record is the best source of PHI and only the minimum necessary PHI needed will be collected. Data will be collected both from Veterans who enrolled in the study as well as those who consented to screening but did not enroll in the study, either due to ineligibility or choice. Retrospective chart review adds no additional risk to the study procedures as the chart review will not impact participants in any way. Activities are limited to the use of data from medical records and there are sufficient measures in place to protect the data. **Data and Safety Monitoring Plan**

To identify unanticipated problems or complications, study participants will be provided at enrollment with contact information for the studyteam, principal investigator, and the VA hospital patient relations representative. Any unanticipated problems or complications will be reported to the IRB per UW-Madison campus policy and the VA R&D per VA regulations. Corrective actions, such as changes to the research protocol or informed consent process, will be taken in order to protect the safety, welfare or rights of study subjects or others. The study pharmacist, Dr. Stephanie Gruber, and PI, Dr. Jessica Cook, will determine whether corrective actions need to be taken as a result of the SAE and unanticipated event review process. Clinical Science Research and Development (CSRD) has decided that due to the low risk nature of this study, a CSRD Data Monitoring Committee is not necessary.

Safety and Protection of Human Subjects

Subject privacy will be protected during the course of this study and HIPAA regulation will be followed. Only relevant, applicable study data will be collected, and will be entered in a secure web-based system with restricted access. Any required paper data will be kept in a confidential locked area, with no personal identifying information in our data set. This will be available only to primary study staff directly responsible for this data, and to representatives of the VA Research and Development Committee or University of Wisconsin IRB. Access to data will be removed if study staff are no longer part of the study team. Informed consent will be obtained by study staff. The PI and staff pharmacist, Drs. Cook and Gruber, will review all serious adverse events. Medical emergency and safety plans will be established, and serious adverse events will be reported in a timely manner to appropriate committees.

In accordance with VA policy, in the case of reporting incidents, i.e. theft or loss of data or storage media, unauthorized access of sensitive data or storage devices or non-compliance with security controls, the Information Security Officer, Privacy Officer, and ACOS for Research will be notified within one hour to determine an appropriate course of action.

VA research data and information will be maintained per VA Records Control Schedule (RCS) 10-1 regulations for a period not to exceed 7 years after the close of the study.

Statistical Considerations

Sample size was based on the power needed to detect significant differences in 2-year abstinence, our primary aim. We increased the number of our initial sample size by 50 to account for expected dropouts and non-completers. We used SAS PROC POWER to identify the necessary sample size to ensure that comparisons of ECC versus SC would have sufficient power to detect an 8% increment in abstinence (≥ .80, 2-tailed test, $\alpha < .05$), the minimum effect size we believe would be cost-effective and of clinical and public health significance for an intervention of the ECC intensity. We assume that the rate of 2-year biochemically confirmed abstinence for those in SC will range from 4-7%. This is consistent with meta-analyses that show abstinence rates of 2-5% in follow-up over 1-2 years in studies involving smokers unwilling to quit *and who are assigned to control conditions*[5,17]. Not only would an 8 percentage point increment be meaningful, but there is considerable evidence that it is feasible. Meta-analytic evidence shows that pharmacotherapy + counseling *reduction* interventions alone produce an increment of about 6% over control conditions amongst smokers initially unwilling to quit[17]. For instance, studies amongst smokers unwilling to quit involving nicotine gum produce an abstinence rate of 11% in the gum condition vs. 4% in the control condition[17]. While those studies involved participants committed to reducing their smoking, such studies did not use chronic care intervention to enhance use of both reduction and cessation treatments. We believe that the seamless availability of both cessation and reduction treatments will meaningfully enhance abstinence rates when offered via chronic care on an ongoing basis. This will occur for several reasons. First, the use of reduction treatment appears to boost use of cessation treatment when both are available; within a 4-month period,19% of participants receiving reduction treatment entered cessation treatment[1] (we expect closer to 50% of reduction participants when offers are made over a 2-year period). Second, use of reduction treatment may increase cessation treatment effectiveness. We found an abstinence rate of 38% amongst primary care patients using both reduction and cessation versus 18% of primary care patients using a comparably intense cessation treatment alone[1,70]. Third, both reduction and cessation treatments will be offered with chronic care outreach; similar programs have yielded high rates of treatment engagement over time[2,3,46]. For instance, four, 6-month cycles of chronic care outreach led to impressive uptake of pharmacotherapy (with 67%, 41%, 24%, 25% of smokers participating/cycle[2] and counseling engagement (91%. 68%, 57%, 54%/cycle). Therefore, we are confident that the basic 6-percentage point increment produced by NRT based reduction treatments will be significantly boosted, at least by 4%, by ready availability of

cessation treatment along with ongoing chronic care contacts containing motivational and supportive elements. Although we expect to detect at least a 10% increment in ECC over SC, there is good power to detect an 8 percentage point increase relative to ST abstinence rates ranging from 4-7% (power would be even greater for SC rates < 4%).

Data and Record Keeping

Data elements will be collected and stored during the screening assessment, all phone contacts, and the final visit. Data elements and study questionnaires will be collected via a web-based computer program called REDCap. The VA Informatics and Computing Infrastructure (VINCI) will be used as a central location for data processing and management. Vanderbilt University, with funding from the National Institutes of Health (NIH) and collaboration from a consortium of institutional partners, has developed a software toolset and workflow methodology for electronic collection and management of research and clinical trial data. REDCap (Research Electronic Data Capture) data collection projects rely on a thorough study-specific data dictionary defined in an iterative self-documenting process. REDCap was developed specifically around HIPAA-Security guidelines. VA REDCap servers are housed at the VA Informatics and Computing Infrastructure (VINCI), physically located at the VA Austin Information Technology Center (AITC) in Austin, Texas. VA REDCap is accessible through the VA intranet only. Only validated members of the study team will have access to the study's REDCap database. No study data will be stored on a PC hard drive

The study will utilize a unique study ID for storing all data related to individual participants. Information linking that study ID to participant identifying information will be maintained by the PI. Subject identifying information will only be available to those study staff with whom subjects have direct contact. Data being used for analysis will be identified with the study ID only. The study will not routinely utilize any paper or non-electronic records; if paper records are used as a back-up during a period when a functioning computer is not available, they will be maintained in a locked area after their entry has been properly verified. Paper data will likely be kept in room G22 (VHAMADBrubaE) or G13 (VHAMADWebstK) of the VA hospital. Electronic records may be obtained on a mobile device that is protected with VA approved encryption technology that is FIPS 140-2 validated. Mobile devices will not contain the only copy of research information.

The name, contact information, and study schedule for interested and enrolled participants will be kept in a separate database. The automated list of potential participants to whom informational letters will be sent will be maintained in a separate database as well. This identifiable information is maintained in order to contact and follow-up with interested potential participants or enrolled participants. No study data will be stored in these databases. All identifiable data will be stored on secure, password-protected servers located at the Madison VA and only study personnel will be granted access. All data that is not identifiable (forms collected after enrollment that are identified only by study number) is stored on the secure VA REDCap server with a copy of this data retained on a VA server.

Data will be maintained by the Madison, WI VAMC following the completion of the study.

Safety and Protection of Data Collected in REDCap

The research team will manage study data through REDCap. REDCap is an electronic data management system that will be used to capture, edit, manage, and export study data for analysis. REDCap is a HIPAA-secure survey tool obtained through licensing agreement with the University of Wisconsin Department of Medicine and promoted for research by DoIt

The VA Informatics and Computing Infrastructure (VINCI) will be used as a central location for data processing and management. REDCap was developed specifically around HIPAA-Security guidelines. VA REDCap servers are housed at the VA Informatics and

Computing Infrastructure (VINCI), physically located at the VA Austin Information Technology Center (AITC) in Austin, Texas. VA REDCap is accessible through the VA intranet only. Subject identifiable information is restricted at multiple levels:

1. Access to the REDCap system is restricted to those that have been granted access by the software administrators. User access requires supervisor approval, completion of HIPAA and Human Subjects Protection training, and completion of role-based training in the REDCap system.
2. In addition, users' access is limited to protocols for which they have some responsibility of protocol, subject, or data management.
3. Within those protocols, the ability to view and modify data is restricted based on their role in the conduct of the research project (e.g. regulatory staff do not have the privilege to view subject identifiable information).

In addition, the technical components of this software are managed by the UW-Madison's Bioinformatics Computing Group (for server maintenance, software upgrades, etc.), and security and software support is provided by CTRI staff. CTRI staff are able to access subject information in order to help end users of the software program when questions arise.

All communication between the clients and the REDCap application takes place via Hypertext Transfer Protocol over Secure Socket Layer or HTTPS. HTTPS provide the ability for normal web based communication over an encrypted Secure Socket Layer (SSL) connection. This ensures that data passing between the client and REDCap is protected from unauthorized attempts to access the data.

The REDCap system is web-based software, with data stored on secure servers. Data exported from the REDCap system is exported with indirect identifiers (i.e. with study ID number per subject) for statistical and data monitoring purposes in an MS Excel or SAS format. Upon exportation, the clinical research management system has no control over how it is manipulated or managed. REDCap data is backed up regularly.

References

1. Cook JW, Baker, TB., Collins LM, Fiore MC, et al. Comparative effectiveness of motivation phase intervention components for use with smokers unwilling to quit: a factorial screening experiment. *Addiction.* 2016;111(1):117-128.
2. Ellerbeck EF, Mahnken JD, Cupertino AP, et al. Effect of varying levels of disease management on smoking cessation: a randomized trial. *Ann Intern Med.* 2009;150(7):437-446.
3. Joseph AM, Fu SS, Lindgren B, et al. Chronic disease management for tobacco dependence: a randomized, controlled trial. *Arch Intern Med.* 2011;171(21):1894-1900.
4. Petersen A, Mermelstein R, Berg KM, et al. Offering smoking treatment to primary care patients in two Wisconsin healthcare systems: Who chooses smoking reduction versus cessation? *Prev Med.* 2017;105:332-336.
5. Moore D, Aveyard P, Connock M, Wang D, et al. Effectiveness and safety of nicotine replacement therapy assisted reduction to stop smoking: systematic review and meta-analysis. *BMJ.* 2009;338:b1024.
6. Bernet AC, Willens DE, Bauer MS. Effectiveness-implementation hybrid designs; implications for quality improvement science. *Implement Sci.* 2013;8(Suppl 1):52.
7. Curran GM, Bauer M, et al. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. *Med Care.* 2012;50(3):217-226.
8. Eddy DM. David Eddy ranks the tests. *Harv Health Lett.* 1992;(special suppl):10-11.
9. Glasgow RE. What does it mean to be pragmatic? Pragmatic methods, measures, and models to facilitate research translation. *Health Educ Behav.* 2013;40(3):257-265.
10. Odani S, Agaku IT, Graffunder CM, Tynan MA, Armour BS. Tobacco product use among military veterans - United States, 2010-2015. *MMWR* 2018;67(1):7-12.
11. Fiore MC, Jaen CR, Baker TB, et al. *Treating tobacco use and dependence: 2008 update.* Rockville, MD: U.S. Department of Health and Human Services, U.S. Public Health Service; 2008.
12. Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. *Cochrane Database Syst Rev.* 2013(5):CD009329.
13. Jonk YC, Sherman SE, Fu SS, Hamlett-Berry KW, Geraci MC, Joseph AM. National trends in the provision of smoking cessation aids within the Veterans Health Administration. *Am J Manag Care.* 2005;11(2):77-85.
14. Piper ME, Baker TB, Mermelstein R, et al. Recruiting and engaging smokers in treatment in a primary care setting: developing a chronic care model implemented through a modified electronic health record. *Transl Behav Med.* 2013;3(3):253-263.
15. Etter JF, Perneger TV, Ronchi A. Distributions of smokers by stage: international comparison and association with smoking prevalence. *Prev Med.* 1997;26(4):580-585.
16. Hollis JF, Bills R, Whitlock E, Stevens VJ, Mullooly J, Lichtenstein E. Implementing tobacco interventions in the real world of managed care. *Tob Control.* 2000;9(Suppl 1):I18-124.
17. Ali A, Kaplan CM, Derefinko KJ, Klesges RC. Smoking cessation for smokers not ready to quit: meta-analysis and cost-effectiveness analysis. *Am J Prev Med.* 2018;55(2):253-262.
18. Lortet-Tieulent J, Goding Sauer A, Siegel RL, et al. State-level cancer mortality attributable to cigarette smoking in the United States. *JAMA Intern Med.* 2016;176(12):1792-1798.
19. Centers for Disease Control and Prevention. Health effects of cigarette smoking. 2017. https://www.cdc.gov/tobacco/data_statistics/fact_sheets/health_effects/effects_cig_smoking/index.htm. Accessed 6 Sep 2017.

20. Kelly MM, Sido H, Rosenheck R. Rates and correlates of tobacco cessation service use nationally in the Veterans Health Administration. *Psychol Serv.* 2016;13(2):183-192.
21. Twyman L, Bonevski B, Paul C, Bryant J. Perceived barriers to smoking cessation in selected vulnerable groups: a systematic review of the qualitative and quantitative literature. *BMJ Open.* 2014;4(12):e006414.
22. Cosci F, Pistelli F, Lazzarini N, Carrozzi L. Nicotine dependence and psychological distress: outcomes and clinical implications in smoking cessation. *Psychol Res Behav Manag.* 2011;4:119-128.
23. Christiansen B, Reeder K, Hill M, Baker TB, Fiore MC. Barriers to effective tobacco-dependence treatment for the very poor. *J Stud Alcohol Drugs.* 2012;73(6):874-884.
24. Wewers ME, Stillman FA, Hartman AM, Shopland DR. Distribution of daily smokers by stage of change: Current Population Survey results. *Prev Med.* 2003;36(6):710-720.
25. Williams GC, McGregor HA, Sharp D, et al. Testing a self-determination theory intervention for motivating tobacco cessation: supporting autonomy and competence in a clinical trial. *Health Psychol.* 2006;25(1):91-101.
26. Deci EL, Ryan RM. *Intrinsic motivation and self-determination in human behavior.* New York: Plenum; 1985.
27. Bodenheimer T, Wagner EH, Grumbach K. Improving primary care for patients with chronic illness: the chronic care model, Part 2. *JAMA.* 2002;288(15):1909-1914.
28. Burke MV, Ebbert JO, Schroeder DR, McFadden DD, Hays JT. Treatment outcomes from a specialist model for treating tobacco use disorder in a medical center. *Medicine (Baltimore).* 2015;94(44):e1903.
29. Bernstein SL, Yu S, Post LA, Dziura J, Rigotti NA. Undertreatment of tobacco use relative to other chronic conditions. *Am J Public Health.* 2013;103(8):e59-65.
30. Richter KP, Faseru B, Shireman TI, et al. Warm handoff versus fax referral for lnking hospitalized smokers to quitlines. *Am J Prev Med.* 2016;51(4):587-596.
31. Batra V, Patkar AA, Weibel S, Leone FT. Tobacco smoking as a chronic disease: notes on prevention and treatment. *Prim Care.* 2002;29(3):629-648.
32. Steinberg MB, Schmelzer AC, Lin PN, Garcia G. Smoking as a chronic disease. *Curr Cardiovasc Risk Rep.* 2010;4(6):413-420.
33. Unutzer J, Katon W, Callahan CM, et al. Collaborative care management of late-life depression in the primary care setting: a randomized controlled trial. *JAMA.* 2002;288(22):2836-2845.
34. Renders CM, Valk GD, Griffin S, Wagner EH, et al. Interventions to improve the management of diabetes mellitus in primary care, outpatient and community settings. *Cochrane Database Syst Rev.* 2001(1):CD001481.
35. Klemperer EM, Hughes JR, Solomon LJ, et al. Motivational, reduction and usual care interventions for smokers who are not ready to quit: a randomized controlled trial. *Addiction.* 2017;112(1):146-155.
36. Christiansen BA, Reeder KM, TerBeek EG, Fiore MC, Baker TB. Motivating low socioeconomic status smokers to accept evidence-based smoking cessation treatment. *Nicotine Tob Res.* 2015;17(8):1002-1011.
37. Carpenter MJ, Hughes JR, et al. Both smoking reduction with nicotine replacement therapy and motivational advice increase future cessation among smokers unmotivated to quit. *J Consult Clin Psychol.* 2004;72(3):371-381.
38. Bernstein SL, Bijur P, Cooperman N, et al. A randomized trial of a multicomponent cessation strategy for emergency department smokers. *Acad Emerg Med.* 2011;18(6):575-583.
39. Dijkstra A, Conijn B, De Vries H. A match-mismatch test of a stage model of behaviour change in tobacco smoking. *Addiction.* 2006;101(7):1035-1043.
40. Vangeli E, Stapleton J, Smit ES, Borland R, West R. Predictors of attempts to stop smoking and their success in adult general population samples: a systematic review. *Addiction.* 2011;106(12):2110-2121.

41. McCarthy DE, Piasecki TM, Jorenby DE, Lawrence DL, Shiffman S, Baker TB. A multi-level analysis of non-significant counseling effects in a randomized smoking cessation trial. *Addiction.* 2010;105(12):2195-2208.
42. Pizacani BA, Martin DP, Stark MJ, Koepsell TD, Thompson B, Diehr P. A prospective study of household smoking bans and subsequent cessation related behaviour: the role of stage of change. *Tob Control.* 2004;13(1):23-28.
43. Gwaltney CJ, Metrik J, Kahler CW, Shiffman S. Self-efficacy and smoking cessation: a meta-analysis. *Psychol Addict Behav.* 2009;23(1):56-66.
44. Klemperer EM, Hughes JR, Callas PW, Solomon LJ. Working alliance and empathy as mediators of brief telephone counseling for cigarette smokers who are not ready to quit. *Psychol Addict Behav.* 2017;31(1):130-135.
45. Vickerman KA, Keller PA, Deprey M, Lachter RB, Jenssen J, Dreher M. Never quit trying: reengaging tobacco users in statewide cessation services. *J Public Health Manag Pract.* 2018;24(3):e25-e33.
46. Sherman SE, Takahashi N, Kalra P, et al. Care coordination to increase referrals to smoking cessation telephone counseling: a demonstration project. *Am J Manag Care.* 2008;14(3):141-148.
47. Mussulman LM, Faseru B, et al. A randomized, controlled pilot study of warm handoff versus fax referral for hospital-initiated smoking cessation among people living with HIV/AIDS. *Addict Behav.* 2018;78:205-208.
48. Ebbert JO, Hughes JR, West RJ, et al. Effect of varenicline on smoking cessation through smoking reduction: a randomized clinical trial. *JAMA.* 2015;313(7):687-694.
49. Bolt DM, Piper ME, McCarthy DE, et al. The Wisconsin Predicting Patients' Relapse questionnaire. *Nicotine Tob Res.* 2009;11(5):481-492.
50. Hughes JR, Solomon LJ, Naud S, Fingar JR, Helzer JE, Callas PW. Natural history of attempts to stop smoking. *Nicotine Tob Res.* 2014;16(9):1190-1198.
51. Hall SM, Prochaska JJ. Treatment of smokers with co-occurring disorders: emphasis on integration in mental health and addiction treatment settings. *Annu Rev Clin Psychol.* 2009;5:409-431.
52. American Psychiatric Association. *Practice guidelines for the treatment of patients with substance use disorders, 2nd edition.* Washington, D.C.: American Psychiatric Association; 2006.
53. Blumenthal DS. Barriers to the provision of smoking cessation services reported by clinicians in underserved communities. *J Am Board Fam Med* 2007;20(3):272-279.
54. Thorndike AN, Rigotti NA, Stafford RS, Singer DE. National patterns in the treatment of smokers by physicians. *JAMA.* 1998;279(8):604-608.
55. Ruger JP, Lazar CM. Economic evaluation of pharmaco- and behavioral therapies for smoking cessation: a critical and systematic review of empirical research. *Annu Rev Public Health.* 2012;33:279-305.
56. Gaglio B, Shoup JA, Glasgow RE. The RE-AIM framework: a systematic review of use over time. *Am J Public Health.* 2013;103(6):e38-46.
57. Feldstein AC, Glasgow RE. A practical, robust implementation and sustainability model (PRISM) for integrating research findings into practice. *Jt Comm J Qual Patient Saf.* 2008;34(4):228-243.
58. Glasgow RE, Klesges LM, et al. Evaluating the impact of health promotion programs: using the RE-AIM framework to form summary measures for decision making involving complex issues. *Health Educ Res.* 2006;21(5):688-694.
59. Papadakis S, McDonald P, Mullen KA, et al. Strategies to increase the delivery of smoking cessation treatments in primary care settings: a systematic review and meta-analysis. *Prev Med.* 2010;51(3-4):199-213.
60. Fu SS, van Ryn M, Sherman SE, et al. Proactive tobacco treatment and population-level cessation: a pragmatic randomized clinical trial. *JAMA Intern Med.* 2014;174(5):671-677.

61. Hernandez-Lopez M, Luciano MC, Bricker JB, Roales-Nieto JG, Montesinos F. Acceptance and commitment therapy for smoking cessation: a preliminary study of its effectiveness in comparison with cognitive behavioral therapy. *Psychol Addict Behav.* 2009;23(4):723-730.
62. Klesges LM, Estabrooks PA, Dzewaltowski DA, et al. Beginning with the application in mind: designing and planning health behavior change interventions to enhance dissemination. *Ann Behav Med.* 2005;29 Suppl:66-75.
63. Steinberg MB, Schmelzer AC, Richardson DL, Foulds J. The case for treating tobacco dependence as a chronic disease. *Ann Intern Med.* 2008;148(7):554-556.
64. Collins LM, Baker TB, Mermelstein RJ, et al. The Multiphase Optimization Strategy for engineering effective tobacco use interventions. *Ann Behav Med.* 2011;41(2):208-226.
65. Mokdad AH, Marks JS, Stroup DF, Gerberding JL. Actual causes of death in the United States, 2000. *JAMA.* 2004;291(10):1238-1245.
66. Centers for Disease Control and Prevention. Quitting smoking among adults - United States 2001-2010. *MMWR.* 2011;60(44):1513-1519.
67. Fiore MC, Jorenby DE, Schensky AE, Smith SS, Bauer RR, Baker TB. Smoking status as the new vital sign: effect on assessment and intervention in patients who smoke. *Mayo Clin Proc.* 1995;70(3):209-213.
68. Mundt MP, Fiore MC, Baker TB, Fraser DL, Smith SS, L. Z. Cost-effectiveness analysis of the Wisconsin CMS Medicaid Quitline Incentive Program. Paper presented at: North American Primary Care Research Group (NAPCRG)2017; Montreal, Canada.
69. Mundt MP, Fiore MC, Baker TB, Fraser DL, Smith SS, Zakletskaia L. Cost-effectiveness of financial incentives to Medicaid patients to quit smoking. Paper presented at: Addiction Health Services Research (AHSR)2017; Madison, WI.
70. Piper ME, Fiore MC, Smith SS,... Cook, JW, Baker, TB. Identifying effective intervention components for smoking cessation: a factorial screening experiment. *Addiction.* 2016;111(1):129-141.
71. Schlam TR, Fiore MC, Smith SS,…Cook, JW, Baker, TB. Comparative effectiveness of intervention components for producing long-term abstinence from smoking: a factorial screening experiment. *Addiction.* 2016;111(1):142-155.
72. Voils CI, Coffman CJ, Yancy WS, Jr., et al. A randomized controlled trial to evaluate the effectiveness of CouPLES: a spouse-assisted lifestyle change intervention to improve low-density lipoprotein cholesterol. *Prev Med.* 2013;56(1):46-52.
73. Voils CI, Olsen MK, Gierisch JM, et al. Maintenance of weight loss after initiation of nutrition training: a randomized trial. *Ann Intern Med.* 2017;166(7):463-471.
74. Voils CI, Gierisch JM, Yancy WS, Jr., et al. Differentiating behavior initiation and maintenance: theoretical framework and proof of concept. *Health Educ Behav.* 2014;41(3):325-336.
75. Oguss M, McCarthy DE, Fraser DL, ...Baker, TB. Primary care clinic staff attitudes towards addressing tobacco use before and after implementing a smoking treatment referral program (Poster accepted for presentation). 24th Annual Meeting of the Society for Research on Nicotine and Tobacco; 2018; Baltimore, MD.
76. Fraser DL, Fiore MC, Kobinsky K,... Baker, TB. A randomized trial of incentives for smoking treatment in Medicaid members. *Am J Prev Med.* 2017;53(6):754-763.
77. Fagerstrom K. Determinants of tobacco use and renaming the FTND to the Fagerstrom Test for Cigarette Dependence. *Nicotine Tob Res.* 2012;14(1):75-78.
78. Tedeschi GJ, Cummins SE, Anderson CM, Anthenelli RM, Zhuang YL, Zhu SH. Smokers with self-reported mental health conditions: a case for screening in the context of tobacco cessation services. *PLoS One.* 2016;11(7):e0159127.
79. Welsch SK, Smith SS, Wetter DW, Jorenby DE, Fiore MC, Baker TB. Development and validation of the Wisconsin Smoking Withdrawal Scale. *Exp Clin Psychopharmacol.* 1999;7(4):354-361.

80. Ross CK, Steward CA, Sinacore JM. A comparative study of seven measures of patient satisfaction. *Med Care.* 1995;33(4):392-406.
81. Rose JE, Behm FM, Westman EC, Kukovich P. Precessation treatment with nicotine skin patch facilitates smoking cessation. *Nicotine Tob Res.* 2006;8(1):89-101.
82. Baker TB, Collins LM, Mermelstein R, et al. Enhancing the effectiveness of smoking treatment research: conceptual bases and progress. *Addiction.* 2016;111(1):107-116.
83. Kraemer HC. A source of false findings in published research studies: adjusting for covariates. *JAMA Psychiatry.* 2015;72(10):961-962.
84. Glick HA, Doshi JA, Sonnad SS, et al. *Economic evaluation in clinical trials.* Oxford: Oxford University Press; 2007.
85. Cromwell J, Bartosch WJ, Fiore MC, Hasselblad V, Baker T. Cost-effectiveness of the clinical practice recommendations in the AHCPR guideline for smoking cessation. Agency for Health Care Policy and Research. *JAMA* 1997;278(21):1759-1766.
86. Hockenberry JM, Curry SJ, Fishman PA, et al. Healthcare costs around the time of smoking cessation. *Am J Prev Med.* 2012;42(6):596-601.
87. Centers for Medicare and Medicaid Services. Physician fee schedule. 2012. http://www.cms.gov/apps/physician-fee-schedule/overview.aspx.
88. O'Hagan A, Stevenson M, Madan J. Monte Carlo probabilistic sensitivity analysis for patient level simulation models: efficient estimation of mean and variance using ANOVA. *Health Econ.* 2007;16(10):1009-1023.
89. Fraser D, Christiansen BA, Adsit R, Baker, TB, Fiore, MC. Electronic health records as a tool for recruitment of participants' clinical effectiveness research: lessons learned from tobacco cessation. *Transl Behav Med.* 2013;3(3):244-252.
90. Sandelowski M. Combining qualitative and quantitative sampling, data collection, and analysis techniques in mixed-method studies. *Res Nurs Health.* 2000;23(3):246-255.
91. Piper ME, Loh WY, Smith SS, Japuntich SJ, Baker TB. Using decision tree analysis to identify risk factors for relapse to smoking. *Subst Use Misuse.* 2011;46(4):492-510.
92. Bolt DM, Piper ME, Theobald WE, Baker TB. Why two smoking cessation agents work better than one: role of craving suppression. *J Consult Clin Psychol.* 2012;80(1):54-65.
93. Trail JB, Collins LM, Rivera DE, Li R, Piper ME, Baker TB. Functional data analysis for dynamical system identification of behavioral processes. *Psychol Methods.* 2014;19(2):175-187.
94. Glasgow RE, Bull SS, Gillette C, Klesges LM, et al. Behavior change intervention research in healthcare settings: a review of recent reports with emphasis on external validity. *Am J Prev Med.* 2002;23(1):62-69.
95. Glasgow RE, Lichtenstein E, Marcus AC. Why don't we see more translation of health promotion research to practice? Rethinking the efficacy-to-effectiveness transition. *Am J Public Health.* 2003;93(8):1261-1267.
96. Glasgow RE, Klesges LM, Dzewaltowski DA, et al. The future of health behavior change research: what is needed to improve translation of research into health promotion practice? *Ann Behav Med.* 2004;27(1):3-12.