Promoting Smoking Cessation in Lung Cancer Screening through Proactive Treatment (PROACT)

Funding Agency: HSR&D

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9/29/21

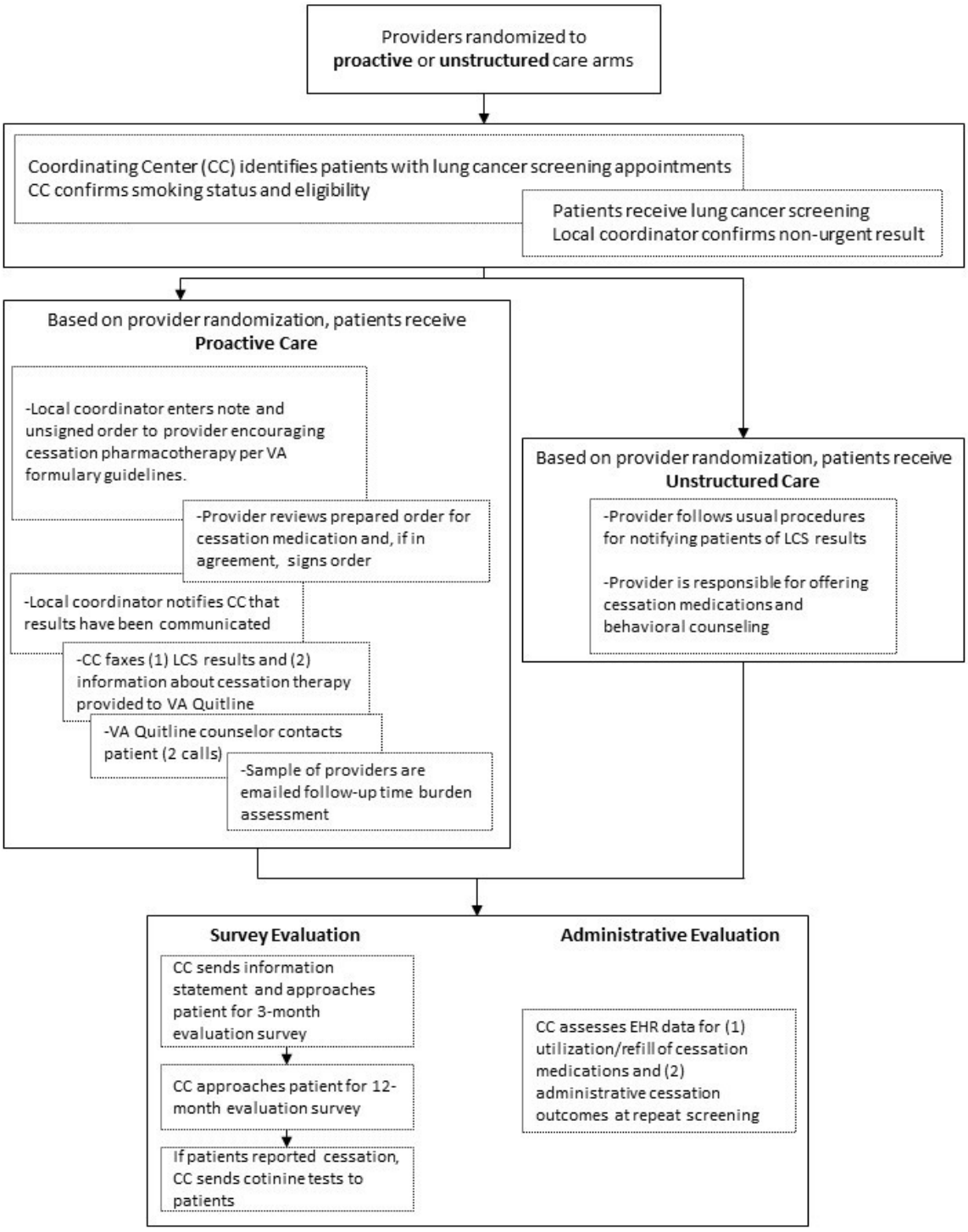
Abstract

VA Medical Centers are beginning to offer eligible Veterans lung cancer screening following national recommendations including the US Preventive Services Task Force's "B" recommendation for annual screening.[1] Preliminary evidence from the VA Lung Cancer Screening Demonstration Project suggests that 900,000 Veterans will be eligible for screening and over half will be current smokers with a long history of smoking.[2,3] It is critical that offering screening to current smokers reinforces the importance of cessation and does not reduce motivation to quit.[4,5] Providing cessation support as part of lung cancer screening is mandated for reimbursement by Centers of Medicare and Medicaid Services, and is recognized by VA as a critical component of delivering high quality care. Integrating cessation counseling challenging, in part because of limited time and clinic resources, but also because of many current smokers' misperception that screening provides a "protective" effect.[6] In the National Lung Screening Trial, primary care providers offering screening adequately addressed smoking cessation with only 10% of current smokers.[7]

The PROACT trial will evaluate the value of providing proactive support to current smokers as part of participating in lung cancer screening including behavioral and pharmacotherapy support. Cessation support guidelines have emphasized the importance of providing both behavioral and pharmacotherapy support at every opportunity. Cessation support will be integrated with the reporting of screening results. In our pilot study of the proactive telephone counseling component of the proposed intervention, we increased participation in behavioral cessation treatment to 44% among participants who received proactive counseling from 11% among control patients who did not receive proactive counseling, and quit rates more than doubled to 19% in the proactive group from 7% in the control group.[8] Screening patients often report being motivated to participate in screening to find out how much smoking has harmed them.[6] The proactive care activities are designed to convert this level of patient engagement into an opportunity to encourage cessation. Integrating the proactive cessation treatment approach into the screening process ensures that all screening patients are offered cessation support by default, and removes the precondition of providing pharmacotherapy support only to patients who agree to set a specific quit date. Over 14 trials[9] have shown that providing pharmacotherapy support to all current smokers using an opt-out approach (rather than requiring patients to request treatment) significantly increases quit rates, and providers have begun adopting opt-out approaches to offering tobacco treatment.

The PROACT trial is a pragmatic randomized trial targeting the care of current smokers who are participating in lung cancer screening at VA Providence (Rhode Island) and VA NY Harbor. Primary care providers at VA Providence and VA NY Harbor will be randomized to provide their patients either *proactive* cessation support or *unstructured* cessation support (as usually provided during lung cancer screening). The proactive cessation support will ensure that patients receive more elements of care that are currently available in VA but are not always systematically provided, specifically including telephone counseling from VA Quitline counselors and pharmacotherapy support recommended by VA's national formulary. The primary endpoint is biochemically confirmed 7-day abstinence 12 months after screening. Based on prior trials and our pilot data, the trial is powered to detect an improvement in quit rates from 9% with 5A's counseling and unstructured treatment to at least 18% with proactive treatment.

Figure 1: Study Overview



List of Abbreviations

Provide a list of all abbreviations used in the protocol and their associated meanings.

5As – Guidelines for recommended approach to providing counseling about tobacco use: Ask about tobacco use at every visit, Advise all tobacco users to quit, Assess readiness to quit, Assist tobacco users with a quit plan, Arrange follow-up visits

BAA - Business Associate Agreement

CDW - Corporate Data Warehouse

CIS - Cancer Information Services

COIN - Center of Innovation

CT- Computerized tomography

FDA - Federal Drug Administration

FHCRC - Fred Hutchinson Cancer Research Center

HSR&D - Health Services Research and Development

ISO - Information Security Officer

JAMA - Journal of the American Medical Association

JLV – Joint Legacy Viewer

LCS – Lung cancer screening

LSI - Local Site Investigator

Lung-RADS - Lung Imaging Reporting and Data System

MI - Motivational Interviewing

NIH - National Institute of Health

NRT - Nicotine Replacement Therapy

PCP – Primary care provider

SAE - Severe Adverse Events

VAPSHCS - VA Puget Sound Health Care System

VHA - Veteran Health Administration

VINCI - VA Informatics and Computing Infrastructure

VistAWeb – Portal accessible through CPRS, user interface for VA electronic health record

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Protocol Title: Promoting Smoking Cessation in Lung Cancer Screening through Proactive Treatment (PROACT)

1.0 Study Personnel

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2.0 Introduction

Smoking remains the leading preventable cause of death and morbidity among Veterans. Cigarette smoking is responsible for over 440,000 deaths annually and adds $193 billion in direct health care expenditures and productivity losses each year in the U.S. Over 50% of ever-smokers in the U.S. population have been able to successfully stop smoking.[10] Quit rates among Veterans are lower than the general population, which has been attributed to demographic and socio-economic factors including lower social support, higher levels of addiction to nicotine, co-occurring addictions such as alcohol addiction, military trauma and post-traumatic stress disorder.[11,12]

Tobacco treatment is effective but underutilized. Connecting smokers to pharmacotherapy and behavioral support has been shown to increase quit rates.[13] Although VA has pioneered a wide range of cessation services, they are not fully utilized.[14,15] While VA has very high rates (>80%) of primary care providers following Public Health Service guidelines for addressing smoking cessation during clinic visits, including the 5A's, fewer than 10% of smokers utilize pharmacotherapy or other smoking cessation aids.[16,17] This is similar to a recent review of Medicaid and Medicare data, which found that only 7.6% of current smokers received a prescription or order for a nicotine dependence medication.[18] Cessation medications have been firmly established as a critical component of successfully quitting.[19, 20] The value of pharmacotherapy support may be especially important for Veterans who currently smoke because of their high levels of nicotine dependence.[11,23]

No model exists for integrating cessation counseling into lung cancer screening. The National Lung Screening Trial (NLST) struggled with providing smoking cessation support to its trial enrollees during the screening process. Primary care providers in the NLST were instructed to follow the 5As in addressing smoking cessation when offering screening. However, only 10% of current smokers received adequate support.[7] Two recent reviews have highlighted the lack of knowledge about how best to offer smoking cessation support in the context of lung cancer screening, one noting that a proactive approach may be preferred in which all smokers seeking lung cancer screening receive access to cessation support regardless of their reported motivation to set a quit date.[21] To our knowledge, no studies have investigated proactive cessation support or proactive telephone counseling as part of delivery of lung cancer screening services. The pragmatic PROACT trial will fill this knowledge gap, and the findings from the trial, which utilizes the national VA Quitline, will provide important guidance for how VHA can implement proactive smoking cessation support in the context of lung cancer screening across all VHAs.

Rationale for including or excluding certain populations. The study targets providers who have ordered LCS CT scans for Veterans. No provider subjects will be excluded from the pragmatic trial on the basis of gender, race, age, or ethnicity. Vulnerable subject populations will not be targeted for inclusion, but pregnant providers will not be excluded from participating.

Patients of these providers who are current smokers participating in lung cancer screening will be approached for participating in survey evaluation activities. No patient subjects will be excluded on the basis of gender, race or ethnicity. Vulnerable subject populations including minorities, prisoners, or institutionalized individuals will not be targeted for inclusion. The age criteria for lung cancer screening of 55-80 and the smoking history criteria of 30+ pack-year history of smoking will limit eligibility of pregnant women, and if pregnant women meet the eligibility criteria for screening they will not be eligible to participate in the study. No children (anyone under the age of 18) will be eligible to be included in the subject population. Patient

subjects with severe behavioral disorders (identified by ICD-10 codes as specified in IRQ) will be excluded.

3.0 Objectives

Objectives. We will test the value of systematically providing evidence-based tobacco treatment using a pragmatic trial of providers whose patients receive lung cancer screening in two VA Medical Centers – New York Harbor and Providence. Currently providers are encouraged to ask patients about their readiness to quit and use their judgement to arrange treatment (5As framework: Ask, Advise, Asses, Assist, Arrange). Providers have many resources to support cessation, including the VA Quitline (1-855-QUIT-VET) for behavioral counseling support and VA formulary guidelines for smoking cessation pharmacotherapy. Providers will be randomized to two study arms. In one arm, Providers will not receive any additional guidance from the study team about how to effectively utilize available VA resource. This arm is labeled as the unstructured care arm.

The study team will develop a proactive, automated structure in which all VA resources are combined into a template that is proactively activated by a patient's screening results letter. This template will reflect pharmacy ordering instructions and other pathways activities in place at the study site. This will be considered proactive care. Primary care providers offering proactive smoking cessation care will be provided guidance to offer cessation pharmacotherapy to all current smokers when notifying the patient of the results of their screening test. Patients of providers in the proactive care arm will also uniformly receive proactive telephone outreach from VA Quitline counselors, which will review the screening results letter and any provided pharmacotherapy. Each local screening program will send a standardized letter notifying the patient that they will be proactively contacted by a telephone counselor. This letter will be in addition to any individualized letters/telephone reporting of results of their screening test by the patient's provider.

The primary aim of this trial is to:

1. Conduct a pragmatic randomized trial among smokers participating in lung cancer screening comparing proactive smoking cessation care with unstructured care. We will assess the differences between the two care approaches on 7-day smoking abstinence 12 months after receipt of screening. Assignment of providers to the two care arms will continue until the study is on track to have 540 patients responding (270 responders per arm) to the 12-month survey. Based on our preliminary findings in a pilot study of proactive care, and related trials in other populations of smokers, we hypothesize that smoking abstinence 12 months after screening will be twice as high (18%) in the proactive group compared to expected abstinence rates in the unstructured group (9%).[9]

The secondary aims are to:

2a. Assess whether proactive smoking cessation care impacts three psychological and two behavioral change processes derived from health behavior change theory, including: (a) motivation, (b) perceived susceptibility to the harmful effects of smoking, (c) self-efficacy for quitting, (d) likelihood of making a quit attempt, and (e) likelihood of utilizing pharmacotherapy.

2b. Assess acceptance of and satisfaction with the proactive care approach among providers referring Veterans for lung cancer screening.

2c. Monitor the costs of implementing the proactive care approach including intervention staff effort, provider time, costs of telephone counseling and pharmacotherapy costs.

4.0 Resources and Personnel

Coordinating Center. The majority of research activities, which include primarily survey evaluation activities and medical record review, will be conducted at the Seattle/Denver HSR&D Center of Innovation (COIN) in Seattle, which will serve as the study Coordinating Center. The Coordinating Center will identify eligible provider participants by querying the Corporate Data Warehouse and identifying patients who have lung cancer screening tests ordered. After identifying providers historically performing lung cancer screening at the two study sites, the Coordinating Center will send them an information sheet describing the study, including the randomization process and procedures for declining participation in the study, via mail, email, and Lync instant message.

In collaboration with providers and lung cancer screening care providers, the Coordinating Center will work with local coordinators at the two study sites to structure care for the proactive care arm. The local coordinator will be notified by the Coordinating Center of each provider's randomization assignment. Following randomization, providers assigned to the proactive arm will be sent an email notifying them of which arm they are assigned to and what intervention activities to expect going forward. They will receive a similar notification email after ordering their first lung cancer screening test, following the start of the study. No notifications will be sent to providers in the unstructured arm. Providers will remain randomized to a single study arm for the duration of the trial. If a new provider orders a lung cancer screening test for the first time, he or she will be approached similarly recognizing that the care of the patient that alerted the Coordinating Center to the provider's identity may not be influenced by the study if the opt-out consent and randomization process cannot occur before the screening test is performed.

Once providers have been randomized, we will monitor for prospective patients referred for screening. The Coordinating Center will review all prospective patients for study eligibility, confirming the patient is documented in the EHR as a current smoker.

For providers assigned to the proactive arm, local coordinators will review prior cessation medication history in each patient's chart and enter a note to the provider recommending providing cessation medication as patients are receiving their screening results. Local coordinators will follow national and local VA treatment guidelines in recommending a cessation medication to the provider (https://www.publichealth.va.gov/docs/smoking/cessationguidelinepart2_508.pdf#). Study clinicians (Au, Feemster, Becker) will be available to local coordinators to answer any questions with interpreting VA treatment guidelines. Local coordinators will be trained by the study team to follow local protocols for ordering medications, such as ordering templates created by local pharmacists. The proactive note to the provider will provide a summary of clinical logic and confirm that the coordinator assessed any potential contraindications, such as unstable angina or serious arrhythmia. Local coordinators will also be available to providers to help facilitate all proactive care activities, including refill monitoring for prescribed cessation medications.

Once a screening result letter has been mailed, the Coordinating Center will send contact information for each participant in the proactive care group to the VA Quitline counselors for proactive telephone counseling. The study will contract with the VA Quitline, operated out of the Fred Hutchinson Cancer Research Center, to perform the proactive telephone counseling services and collect information about participation in telephone counseling sessions, including the number of sessions completed.

The Coordinating Center will extract baseline demographic and clinical characteristics of participants from the Corporate Data Warehouse at the time of screening, including documenting screening results and confirming that the screening test did not identify findings suspicious for malignancy requiring immediate biopsy/attention. Approximately 2-4% of patients have such findings, and will be withdrawn from the study and will not receive any further study activities.

At 3 months and 12 months following screening, the Coordinating Center will conduct an evaluation survey to collect outcome data. Telephone follow-up will be conducted by the Coordinating Center to increase response rate for the surveys. Additional clinical and outcome data will be extracted at 12 months from the Corporate Data Warehouse.

All data analyses will be performed by the Coordinating Center.

Study Staff Table

Name	Location	Role	PHI	Recruiting	Consent	Survey Admin	Data Analysis
Steven Zeliadt, PhD MPH	Seattle	PI	Yes	No	No	No	Yes
David Au, MD MS	Seattle	Co-I Clinician	Yes	No	No	No	Yes
Laura Feemster, MD MS	Seattle	Co-I Clinician	Yes	No	No	No	Yes
Spencer Hildie	Seattle	Project Coordinator	Yes	Yes	Yes	Yes	Yes
Peter Rise, MS	Seattle	Data Analyst	Yes	No	No	No	Yes
Lawrence Swanson, BA	Seattle	Database Administrator	Yes	Yes	Yes	Yes	Yes

Data Use Agreements (DUAs). DUAs will be executed with the VA National Corporate Data Warehouse (CDW) repository and CAPRI/JLV for access and use of data and subject records. Data will be obtained electronically from the VA National Corporate Data Warehouse (CDW) repository, which the study team will access via the VA Informatics and Computing Infrastructure (VINCI) platform. Variables from the CDW will be used to identify referral for lung cancer screening and current smoking status at the time of screening. Patient contact information, including phone number, will be accessed for proactive telephone counseling, and mailing address information will be used for inviting participants to complete the 3- and 12-month study surveys. Social security numbers will be used for research staff to look up patient medical records in CAPRI/JLV as well as to enter notes into CPRS. SSNs are also required by the VA R&D Purchasing and Fiscal Office to process checks for payments.

The Coordinating Center staff will obtain CAPRI/JLV access following VHA procedures that serve as an agreement to adhere to conditions of electronic health records access and use stipulated by VA Health Information Access (HIA). The purpose of accessing patient records is to confirm information identified in CDW notes about comorbidities and exclusion criteria to

ensure patients are appropriate to contact (i.e., no reported difficulty communicating by telephone. If verified, that patient would not be approached).

Contracted Services. We will enter into a contract with the Seattle-based Fred Hutchinson Cancer Research Center's Cancer Information Service (CIS) to provide individualized smoking cessation counseling to the patients in the proactive care arm of the study. This will facilitate careful tracking of services provided and cost estimates. The CIS is an NCI-funded national telephone clearinghouse of cancer information serving individuals who have questions about cancer prevention and treatment. They are knowledgeable, caring, and experienced at explaining medical information. Their services are confidential. The CIS operates both the general information line (1-800-4-CANCER) which helps counsel patients about diagnosis and treatment options, and the NCI's Smoking Quitline (1-877-44U-QUIT), which provides free cessation information and support to smokers who wish to quit free of charge.

The CIS also contracts nationally with VHA to provide the VA Quitline (1-855-QUIT-VET) which is free to all Veterans. We will contract with CIS to develop a database to track utilization and conduct counseling calls. They will use the database to provide information about completed telephone sessions, treatment fidelity, and cost of service provision. Veterans' contact information will be sent by secure fax to the CIS team once they are identified as patients of providers randomized to the proactive care arm. The telephone counselors will make 3 attempts to reach each Veteran, leaving voicemails with a specific telephone number that will reach a VA Quitline counselor who is trained in the study counseling activities. (See *National telephone counselor introductory script*).

The VA Quitline counselor will attempt to provide 2 sessions of individualized smoking cessation therapy, and will repeat the 3-attempt protocol to conduct the 2nd session. A Veteran can decline participation in the counseling activity. (See *National telephone counselor introductory script).*

The VA Puget Sound Healthcare System is purchasing services from Cancer Information Service at the Fred Hutchinson Cancer Research Center, and will enter into a Data Use Agreement to facilitate and allow the exchange of PHI between these two entities. The DUA will follow ORD policies regarding data exchange with Non-Federal Entities and will require approval by the Privacy Officer and ISO at VA Puget Sound, and authorities at the Fred Hutchinson Cancer Research Center (see https://ww.research.va.gov/resources/policies/default.cfm).

The VA Quitline routinely records counseling calls for quality assurance purposes. We have applied for a waiver of informed consent to obtain patient data from these quality assurance recordings, in order to conduct a fidelity evaluation of a sample of the calls.

5.0 Study Procedures

5.1 Study Design

Study design. We are proposing a pragmatic cluster-randomized trial comparing usual lung cancer screening care to a proactive approach, which will integrate smoking cessation support into lung cancer screening. Providers will be randomized to one of two care groups. The

randomization protocol will ensure that providers with large panel sizes, and therefore high lung cancer screening volume, will be distributed between the two groups. The two provider care groups will be called **proactive** and **unstructured**. The **proactive** group will receive guidance about providing proactive cessation support that utilizes supplemental counseling from national counselors at the VA Quitline. The **unstructured** care group will not receive any additional support. All current primary care providers who may have patients eligible for lung cancer screening will be block randomized at the beginning of the study by panel size, as this is a surrogate for prior LCS screening volume. New primary care providers will be randomized when they are first hired and become eligible to order LCS at one of the study sites. Although national lung cancer screening recommendations highlight integrating cessation support for current smokers (and reimbursement of lung cancer screening by Medicare is contingent on documentation that cessation support was provided), there are currently no established methods for how cessation support should be integrated into the delivery of screening care. The proactive care activities are designed to reflect guidelines from the broader primary care setting based on decades of evidence that both behavioral and pharmacotherapy support should be routinely provided to patients. Additionally, the study focuses on testing a proactive care approach that has potential for broad dissemination nationally across VA, including centralized proactive telephone counseling using VA Quitline counselors and providing cessation pharmacotherapy in accordance with VA formulary guidelines. We will standardize study activities as much as possible to ensure they are provided uniformly, however, as this is a pragmatic trial of care as it is delivered in actual practice, providers may vary how they deliver the intended proactive and unstructured care components.

At the beginning of the study, the Coordinating Center, located in Seattle, will access retrospective Corporate Data Warehouse (CDW) patient data to identify providers who have ordered lung cancer screening CTs in the past. These data will be from CDW accessed through VINCI and will be used to review provider lung cancer screening volume and provider's historical use of cessation medications ordered at the time of lung cancer screening. Throughout the study, the Coordinating Center will also prospectively identify patients scheduled for lung cancer screening by scanning CDW twice weekly. The Coordinating Center will confirm the scheduled patient's eligibility criteria, including current smoking status through CAPRI/JLV. A local clinical coordinator based at either of the intervention sites (NY Harbor or Providence, RI) will be notified when patient eligibility is confirmed and the ordering provider is identified. The local coordinator will work with the provider subjects at the intervention sites to adapt study guidance to the lung cancer screening clinical pathways in use at each of the intervention sites. Once a patient's screening results are available, the study team will confirm continued eligibility (e.g. no indication of a highly suspicious finding requiring biopsy).

For patients of providers assigned to the proactive study group, the local coordinator will review the patient's cessation medication history in CAPRI/JLV. If the patient is not currently being provided cessation support medication, the coordinator will enter a note for the provider about the recommended medication indicated by VA formulary guidelines.

For those patients receiving proactive care, once the screening results are available and patients are confirmed to meet eligibility criteria, including not having findings requiring immediate follow-up (e.g. LungRADS 4 or 5), each local screening program will send a standardized letter notifying the patient that they will be proactively contacted by a telephone counselor. This letter will be in addition to any individualized letters/telephone reporting of results of their screening test by the patient's provider.

For those patients receiving proactive care, the Coordinating Center will forward information about the non-suspicious screening result, s to the VA Quitline via secured fax. A VA Quitline counselor will attempt to provide two sessions of proactive telephone support.

Three months after the date of the screening procedure, the Coordinating Center will invite patient participants to participate in an evaluation survey. A second evaluation survey will be sent to the patient at 12 months. Participants will be compensated $25 for each returned evaluation survey.

Demographic, clinical and administrative smoking cessation information available in from the Corporate Data Warehouse will be extracted for all invited patients, including those who do not complete the evaluation surveys.

Provider participants in the proactive arm will be sent a short evaluation survey via email. The survey will assess providers' evaluation of the value of proactive care. If providers offer lung cancer screening to multiple patient, the survey will only be sent once per quarter.

As a pragmatic trial, provider participants in the proactive arm will be sent periodic study status updates via email. These emails will include study level feedback on cessation medication prescription rates and reminders to continue proactively prescribing the recommended medications. It will also include general study updates as well as feedback by patients provided to the local coordinators, coordinating center and Quitline counselors that will be of interest to providers and help them understand how patients are responding to participating in the study.

Cost and resource assessment. Cost and resource data will be collected as part of the study, including the cost of provided pharmacotherapy, additional medication fills, and cost of telephone counselor contact. A waiver of informed consent to collect this information on all study participants is requested.

Risks associated with provider assignment to intervention. The risks associated with the study activities are minimal. All patient participants are current smokers, and VA and US Public Health Services guideline recommend clinicians provide cessation support at all clinic visits and as part of lung cancer screening.

The difference in risks associated with behavioral counseling between the unstructured and proactive arms are minor. In the unstructured arm, patients receive about cessation counseling by their provider and are provided with the VA Quitline's telephone number (1-855-QUIT-VET) as a free resource for telephone counseling. In the proactive arm, subjects are proactively contacted by telephone counselors to receive this same support. The proactive counseling calls may be associated with the following risks: 1) annoyance from proactive counseling outreach, or 2) increased anxiety or worry related to discussions around lung cancer screening results and smoking cessation with VA Quitline telephone counselors. We will mitigate this risk by having the VA Quitline caller remind subjects that participation in the proactive calls is voluntary. Notably, in the pilot study 89% of Veterans indicated they were completely or somewhat satisfied with the proactive telephone counseling calls, with 1 individual reporting they were neither satisfied or dissatisfied, and 2 participants declining to respond.

The difference in risks associated with pharmacotherapy support between the unstructured and proactive arms is also minimal. Although guidelines indicate all smokers should be offered pharmacotherapy support at every visit, this happens infrequently. A recent review found that only 7.6% of current smokers received a cessation pharmacotherapy order

following a primary care visit, [18] and fewer than 10% of smokers participating in screening in the NLST received such an order.[17] Patients who are current smokers should be appropriately provided with smoking cessation support as they participate in lung cancer screening, although this doesn't consistently happen. A potential risk of this study is that current smokers receiving care from providers in the unstructured care group who are eligible for behavioral counseling or pharmacologic cessation support will not receive it. Another potential risk is that providers in the proactive care group will perceive that the study is assuming responsibility for providing cessation support and the quality of support offered by providers will decrease. The primary difference between the study arms is encouraging providers assigned to proactive care to remove the precondition to providing pharmacotherapy that the patient set a quit date and offer pharmacotherapy to all screening participants who are current smokers. This is intended to result in more patients in the proactive care arm receiving pharmacotherapy and may be associated with 1) inappropriate use of cessation medications, or 2) risks associated with use of cessation medications. We will encourage providers to follow VHA formulary guidelines for recommending pharmacotherapy including assessment of contraindications, and all orders are required to be signed by a primary care provider associated with the patient. The local coordinator will review patients' medication history as well as any potential medication risk factors and provide a note in CPRS with a summary for the provider to assist in assessing potential contraindications and facilitating adherence to VHA formulary guidelines.

We also note that following publication of a large double-blind, placebo controlled trial specifically designed to assess risks of cessation pharmacotherapies including the nicotine patch, varenicline and bupropion, [22] the U.S. Food and Drug Administration (FDA) has determined the risk of serious side effects on mood, behavior, or thinking with the stop-smoking medicines varenicline and bupropion is lower than previously suspected and removed a black box warning previously placed on varenicline. The risk of these mental health side effects was equivalent among all forms of medications in the trial. The results of the trial confirm that the benefits of stopping smoking outweigh the risks of these medicines, so the main risk in this study is that cessation rates will be lower among one of the study arms.

Risks associated with survey and administrative data collection. The main potential research risk to patient subjects is loss of confidentiality of personal information, including CDW data, information present in their electronic patient medical records, information collected by the VA Quitline counselors, or information shared via the study survey. We will take multiple precautions to protect confidentiality while working with primary and secondary data, as well as extra precautions with the collection and exchange of subject data with CIS.

Potential risks to patient subjects may also include emotional distress from responding to survey questions, which might cause confusion or make them uncomfortable. Patients may also feel pressure to participate in the survey unwillingly because they mistakenly fear their access to services might be affected if they do not complete the survey. We will reiterate what will also be provided in writing in the information sheet: that their decision not to participate in the survey will be kept confidential, and will in no way affect their access to services or the quality of care they receive at the VA.

Minimization of risk. We will obtain IRB approval prior to initiating any study activities. Prior to study commencement, all members of the research team will complete trainings in human subject protection and ethical research practices, as required by IRB. Approvals from the VA Information Security Officer (ISO), VA Privacy Officer (PO), and Research and Development Committee at all sites will also be obtained prior to commencing research.

Protection against emotional distress. All patients will have discussed lung cancer screening with their provider and have been determined by their provider to be eligible and appropriate for screening. To avoid the possibility of the patient mistakenly thinking they are being contacted by the national telephone counselor because they might have lung cancer, the counselor will remind the individual of the reason for the call and include a clarifying statement to assure patients this is not the reason they are being contacted. We will emphasize their participation in the proactive call from the VA Quitline is being offered by the VA as an option and their participation in the call is voluntary. We will reassure them their refusal to participate will in no way affect their medical care or access to services at the VA. All national counselors are trained in assessing risks to subjects and will be reminded to be sensitive to expression of significant distress around topics of cancer and smoking. Similarly, when we contact patients with 3- and 12-month surveys, we will remind them in the accompanying letter that receipt of surveys does not in any way indicate that they have lung cancer, and that their participation in the survey is voluntary.

Protection against risks of missing contraindications to cessation medications. All study personnel will be trained in VHA formulary guidelines for recommended cessation medications including potential contraindications. A primary care provider associated with the patient will confirm the appropriateness of all medications suggested by the study. The provider will be required to review and sign the order for the suggested medication before it is dispensed. Additionally, the study team will work closely with pharmacy providers at each of the study sites who are aware of the study activities and will also provide additional review of medications prior to dispensing. A study clinician (Drs. Feemster or Au) will be available to the all study personnel for additional guidance if necessary. Although the local coordinator will enter a recommendation in the note, the provider may opt for an alternate treatment type within the VA formulary (or none at all).

Detailed VA educational materials will accompany all cessation medications and are provided by the clinical pharmacy when the medications are sent. These materials will remind patients of any potential contraindications. Additionally, VA Quitline counselors will have copies of all instructions and will review these medication instructions and potential contraindications with each subject based on the type of medication provided. Quitline counselors will help patients formulate questions to ask their provider about any medication use, and if necessary contact the study team directly and notify a study clinician (Drs. Feemster or Au) with any potential concerns about medications. The study clinician will contact the patient's provider as appropriate.

Protection of data. Study staff will execute Data Use Agreements with CDW and CAPRI/JLV prior to use of any repository data, and comply with the stipulations outlined in the agreement contracts. Strict data protection protocols at the Coordinating Center will be implemented to protect the confidentiality of the data, in accordance with the Center of Innovation for Veteran-Centered and Value-Driven Care (COIN) data security policy. Only IRB-approved project staff will have access to study data. All data at the Coordinating Center will be maintained on a COIN secure-access drive in permission-restricted folders only accessible to project staff. At no time will copies of data will be placed on laptops, computer desktops, hard drives, portable media, or any other form of media or hardware. Please see the Data and Safety Monitoring Plan for more details about how data will be protected and subject confidentiality will be maintained. Any data included in manuscripts or publications stemming from this study will be presented as aggregate data only, and in a way that no individual could be identified. At the end of the study, after all manuscripts are published, all identifiable files and crosswalks will be destroyed in accordance

with VA policy - Records Control Schedule 10-1. Electronic media used to store all data will be cleaned or destroyed so the data is not retrievable. As a result of these measures, we do not expect any invasion of privacy or breach of confidentiality.

Protection against risk: Data and Safety Monitoring Plan. VA Informatics and Computing Infrastructure (VINCI), in conjunction with our COIN Database Administrator, will facilitate the secure, electronic data transfer from the VA data repertories, including CDW, and Vital Status data to COIN servers. Study staff will execute Data Use Agreements with CDW and CAPRI/JLV prior to use of any repository data, and comply with the stipulations outlined in the agreement contracts.

We will protect the confidentiality of VA patient data through a number of procedures. We will limit our acquisition of identifiable information to the minimum amount of information necessary to link subject data, obtain contact information for recruitment of subjects, and collect pertinent data necessary to complete the study aims. To ensure confidentiality and protection of subject data, data will only be analyzed and stored electronically on secure servers at the COIN. The study team will be trained and reminded to not save copies of data on laptops or portable media. Only secure VA remote access will be used to access the data. Anti-virus protection is maintained on all servers and workstations at the COIN office. All workstations and servers are physically secured in locked offices, reside behind the VA firewall, and fully participate in Windows NT security. We will store the identifier crosswalk in a separate data file location, accessible only by the COIN Database Administrator and study PIs. Access to the study data folder will be restricted to those VA study project staff approved by our local VA IRB. The data study folder will be further safe-guarded against unauthorized access by network user login authentication controls. In no case will patient identifiers or data be provided to any person or entity outside the IRB-approved project team, and we will ensure that all study results are presented in a way that no individual can be identified.

In order to ensure Veteran contact data is protected as it is provided to the VA Quitline, we will utilize a secure fax line to send instructions to VA Quitline for contacting patients of providers in the proactive care group. This will be reviewed by the VA Puget Sound Privacy Officer and described in the Data Use Agreement between VA Puget Sound and the VA Quitline.

The VA Quitline will follow current procedures for protecting data with two exceptions. The VA Quitline currently conducts quality assurance by having senior staff listen to a sample of calls. The study team will develop a fidelity tool for the VA Quitline/Fred Hutchinson Cancer Research Center staff to use as part of this quality assurance process and report the summary results of the fidelity tool. No audio recordings will be removed from VA Quitline facility. The VA Quitline will provide a CD of participation records (number of completed calls/length of calls). Instructions for providing this data will be included in the Data Use Agreement between VA Puget Sound and the VA Quitline/Fred Hutchinson Cancer Research Center. This CD will include only a coded study ID provided by the Coordinating Center and no other identifying information. The CD will be sent by certified US mail.

Upon completion of the research project, the PI in conjunction with the VA Information Security Officer (ISO), and in accordance with VA policy, will ensure that study data containing sensitive, confidential information will be sanitized and removed from all servers, desktops, removable storage devices, etc. We will follow Records Control Schedule 10-1 and destroy study materials 6 years after completion of the study. When any study personnel are no longer a part of the research team, the PI will remove that person’s access to all study data and notify the VA Information Security Officer of such action. COIN Information Technology personnel will be

responsible for maintaining COIN servers where study data will be kept, and will move, backup and remove study data from servers and control access to data stored on COIN servers. The PI will request termination of data access rights for study personnel who are no longer part of the study team. All study team personnel with access to sensitive patient data will stay current on their VA approved information security training and VA approved privacy policy training.

Any data included in manuscripts or publications stemming from this study will be presented as aggregate data only, and in a way that no individual could be identified. Current and future use of the data will require approval of a written protocol by both the investigator's controlling IRB as well as their local R&D committee. In no case will patient identifiers or data be provided to any person or entity outside the IRB-approved project team, and we will ensure that all study results are presented in a way that no individual can be identified.

Analysis of risk vs. potential benefit. The benefits outweigh the risks involved, especially given that this is a study assessing the effectiveness of an implementation strategy (using proactive notes to providers and a centralized telephone counseling resource) in promoting the adoption of what is considered high quality care but often is not routinely provided to patients due to limited clinical time.

Subjects receiving proactive care will receive support related to screening and help understanding their screening result, counseling about smoking cessation services and support for use of cessation medications. The counseling sessions provided by the VA Quitline counselors may help patients crystallize their thoughts and feelings about lung cancer screening and the health benefits of smoking cessation. The study also encourages providers to provide cessation medication, and participants could benefit by receiving and using these medications. The intervention could have a positive influence on subjects' health behaviors, such as connecting them to additional smoking cessation services such as group counseling or additional telephone counseling. Potential benefits could also come from the overall contribution of the study findings to care for future Veterans and help improving the healthcare field in general. Possible study findings could lead to implementation of improved care practices and/or services, which may include expansion of smoking cessation services through increased understanding and funding allocation for smoking cessation resources and heightened public awareness of the health benefits of smoking cessation.

5.2 Recruitment Methods

Number of Subjects Needed.

Patients. We will assess CDW and CAPRI/JLV records for up to 15,000 patients (~10,000 to identify retrospective LCS orders, and ~5,000 to identify prospective LCS orders) who were offered lung cancer screening at NY Harbor and Providence to identify potential provider participants. Of these subjects, only current smokers will be approached. We anticipate approaching up to 1,350 eligible potential subjects (mailing them a study invitation packet) to invite them to participate in the survey. In order to ensure non-missing data are available on a sufficiently powered study sample, recruitment will continue until 270 subjects have completed the 12-month assessment survey in each of the care arms (total target n = 540).

Providers. We expect to recruit approximately 300 providers, 180 from Providence, RI and 120 from NY Harbor, in order to reach 540 patients (completed surveys).

Identification and Recruitment of Subjects.

Providers. We will obtain a Waiver of Informed Consent for recruitment to facilitate the identification of primary care providers ordering LCS CT scans at the NY Harbor and Providence VAs. At the beginning of the study, the study team will examine historical CDW data to identify providers who have previously ordered LCS tests. Providers who meet eligibility will then be contacted via mail, then email, and finally by Lync/Skype for Business instant message and given the recruitment materials. Any new providers who are hired at VA NY Harbor or Providence and are eligible to order a LCS CT scan, who were not identified by the historical review, will be similarly recruited when they are first identified.

Patients. We will obtain a HIPAA Waiver and Waiver of Informed Consent for recruitment to facilitate the identification of providers' eligible patients. The study team will query the CDW twice weekly over 5 quarters (15 months) to identify study providers' recently ordered LCS CT scans at the NY Harbor and Providence, RI VAs. Upon discovery that a screening CT has been ordered, the study team will review the patient's chart to assess for eligibility/ineligibility criteria and, if patient is eligible, enter patient information into a tracking system. At 2.5 months following their LCS, we will confirm subject eligibility criteria, including non-urgent LCS result, and obtain mailing address information in the electronic medical record. Current smokers receiving unstructured or proactive care who meet general eligibility criteria according to the National Center for Health Promotion and Disease Prevention Guidelines for lung cancer screening (including age, comorbidity, and other health history eligibility criteria, as detailed below in Inclusion and Exclusion Criteria) will be contacted by mail at 3 months following their LCS. The study packet will include an Information Sheet (included in Appendix) and the printed survey (included in Appendix). If the mailed survey has not been received by the study team within 10 days, telephone follow-up will be initiated. We will conduct five attempts to complete the telephone version of the survey (one call per day; see appendix containing follow-up telephone script for unreturned surveys). If no telephone contact can be made, we will mail a 2nd attempt of the full survey. We will conduct a 3rd mailing of a shorter survey focusing on the primary outcomes to subjects who do not complete the full survey within 14 days of the 2nd mailing. This 3rd mailing will be followed by three additional phone attempts, with the goal of completing the abbreviated survey over the phone if the subject is willing. Please refer to the telephone script for patient callers requesting additional information or to opt-out of calls (included in Appendix) for language to answer potential questions from patients regarding privacy and legal concerns. We will offer to mail the patient a copy of the Notice of Privacy Practices upon request. We will use an "Address Service Requested" envelope, for automatic forwarding to new mailing addresses. The same schedule of mailing and phone calls will be followed for the 12-month survey. Subjects who do not respond to the 3-month survey will be mailed a 12-month survey, altered to include some of the questions from the missing 3-month survey (included in attachments).

Payments to Subjects. Subjects will be informed as part of the initial information sheet when the surveys are mailed that they will receive a $25 check for completion of each survey (at 3 and 12 months after lung cancer screening).

The information sheet also clarifies that the study team and VA Pharmacy are working together to ensure that any co-payments for medications received as part of the study will be paid by study funds and not by the participant.

5.3 Informed Consent Procedures

Providers

Waiver of written documentation of informed consent for provider participation. Providers who order lung cancer screening tests are the target for this pragmatic study. Based on recent estimates of lung cancer screening participation at VA NY Harbor and VA Providence, approximately 300 providers have ordered lung cancer screening procedures for 2000-4000 Veterans. The purpose of the pragmatic trial is to test a structured approach to supporting providers to better integrate smoking cessation as part of reporting screening results to patients. A high level of participation of all VA providers who order lung cancer screening tests is critical to this pragmatic trial as the goal is to answer if this structured support is both feasible to implement and effective at improving patient outcomes. We have designed an opt-out approach to help lead to a wide range of provider participation, as requiring providers to opt-in to study participation would potentially bias the results or make them generalizable only to a small subset of providers and not VA overall.

We will send all primary care providers who are ordering lung cancer screening tests a letter and Information Sheet in the postal mail to their office mailing address. We will then send a copy of the letter and Information Sheet via email, and finally follow up via Lync/Skype for Business (instant message, with link to Information Sheet and invitation letter in PDF format attached). In each communication, we will make clear that if we do not hear back from them, they will be enrolled in the study.

Patients

A Waiver of Informed Consent is requested for administrative medical record review of historical provider screening volumes. In order to ensure balance in randomization by provider volume (as some providers order hundreds of screening CTs per year and other providers order only one or two), we are requesting access to patient screening data between 1/1/2013 and 12/31/2017. We will need to access thousands of records in the Corporate Data Warehouse as NY Harbor and Providence have screened an estimated 2000-4000 Veterans. It is impracticable to obtain consent for all patients in the database, and the risk for loss of confidentiality is minimal.

A Waiver of Informed Consent is requested to review administrative medical record data in the CDW for all prospective patients offered lung cancer screening after provider randomization. Patients who participate in lung cancer screening after their provider is randomized to one of the two study arms who meet eligible criteria will be considered study participants. This record review will be used to identify these patients and invite them to participate in survey activities to evaluate outcomes of the care they received. This waiver also includes reviewing medical record data for all participants who do (and do not) respond to the 3- or 12-month survey in order to document potential differences between patients who complete the survey and those who do not (e.g. age/comorbidity), and to conduct an administrative assessment of administrative cessation outcomes such as subsequent documentation by the provider in the medical record of continued smoking or cessation.

Alteration of Informed Consent Process. We are requesting a waiver of documentation of informed consent for survey participation. We will mail participants an evaluation survey at 3 months and 12 months after the screening CT scan; we are requesting that returning the survey serve as a substitute for documentation of informed consent. Requiring participants to complete a written informed consent document in addition to the survey would be unnecessarily burdensome.

Study personnel training. All study staff have been trained and will remain current with the VA requirements for Human Subjects Protections and Good Clinical Practices.

5.4 Inclusion/Exclusion Criteria

Inclusion Criteria

Providers

- All providers who schedule patients for an LCS at NY Harbor and Providence, RI VA systems will be eligible

Patients (assessed via patient information in CAPRI/JLV)

- Offered LCS by a primary care provider at NY Harbor and Providence VA systems and scheduled for a LCS visit.
- Meets eligibility criteria according to the National Center for Health Promotion and Disease Prevention guidelines (age ≤ 80; history of smoking ≥ 30 pack-years)
- Current smoker and eligible for at least one cessation medication on VA Formulary.
- There are at least 3 business days between the date the lung cancer screening test order is identified by the Coordinating Center and when it is scheduled. This is necessary to allow the study team time to confirm that there are no exclusionary criteria and enter proactive study notes prior to the result of the screening test being available to the ordering provider.
- Ability to speak and understand English (no language disability noted in VHA medical record) and communicate by telephone (no deafness or difficulty hearing on telephone is noted in VHA medical record)
- Phone number and mailing address present in VHA medical record

Exclusion Criteria

Providers

- Provider currently systematically provides cessation medication to all current smokers.

Patients (assessed via patient information in CAPRI/JLV)

- Patients with urgent findings requiring biopsy/immediate attention on the screening CT will be excluded. These patients will not be sent any study surveys, and no information will not be provided to the VA Quitline for patients of proactive arm providers. (LCS results are anticipated to identify highly suspicious findings requiring immediate attention for suspected malignancy among <4% of participants).
- Patients receiving active therapy for cancer, except skin cancer
- Diagnosis of pancreatic, esophageal, or liver cancer – or life expectancy < 6 months
- Prior diagnosis of lung cancer
- Indication in chart review of difficulty communicating or participating in telephone counseling sessions, per patient and PCP notes entered in electronic medical record.
- Patients with evidence in CDW of ICD10 codes for severe behavioral disorders will be excluded. These include: Manic/bipolar disorder severe – F30.2, F31.1-6;

Dissociative/conversion disorders – F44; Paranoid/Unstable personality disorder – F60; Mental retardation – F70-F79; Pervasive speech/language development disorders – F84.

- Patients with cognitive impairment and/or dementia (including ICD10 codes G31.84; F01-F03)
- Pregnant or subjects reporting they may be pregnant
- Temporary beginning 12/12/2019: Patients assigned to primary care providers at New York Harbor in the proactive arm who have a “Non-exempt” co-pay status and are not already currently being prescribed smoking cessation medications, will be excluded until mechanisms with clinical pharmacy have been established to ensure these patients do not receive a co-pay.

5.5 Study Evaluations

Patient evaluations. The study team will query CDW twice weekly to identify scheduled LCS tests at the NY Harbor and Providence VAs. Eligibility for lung cancer screening requires the patient’s provider conduct a thorough assessment of a patient’s smoking history to ensure they have smoked at least 30 pack-years over their lifetime. Current smokers who meet general eligibility criteria for lung cancer screening including age, comorbidity, and other health history eligibility criteria, will be approached.

Upon identifying LCS screening patients, study staff at the Coordinating Center will enter them into a tracking database, recording information such as the date they were screened or are scheduled to be screened. We will extract information about their screening results, including withdrawing those few individuals (<4%) who are identified with highly suspicious findings who are no longer eligible for participation in the study evaluation. For subjects receiving proactive care, we will extract information about medications provided by the provider, and date their contact information was provided to the VA Quitline.

The tracking system will prompt Coordinating Center staff at 2.5 months following the date of the patient’s LCS test. We will re-confirm their eligibility, reviewing any changes to their screening results associated with repeat tests in CDW, and will mail a 3-month assessment survey using the mailing address information in the EMR. If the mailed survey has not been received by the study team within 10 work days, telephone follow-up will be initiated. We will conduct five attempts to complete the telephone version of the survey (one call per day). If no telephone contact can be made, we will mail a 2nd attempt of the full survey. We will conduct a 3rd mailing of a shorter survey focusing on the primary outcomes to subjects who do not complete the full survey within 14 days of the 2nd mailing. This 3rd mailing will be followed by three additional phone attempts, with the goal of completing the abbreviated survey over the phone if the subject is willing. Please refer to the Telephone Script (included in Appendix) for language to answer potential questions from patients regarding privacy and legal concerns. We will offer to mail the patient a copy of the Notice of Privacy Practices upon request. We will use an “Address Service Requested” envelope, for automatic forwarding to new mailing addresses.

The sameschedule of mailing and phone calls will be followed for the 12-month survey. Subjects who do not respond to the 3-month survey will be mailed a 12-month survey, altered to include some of the questions from the missing 3-month survey (included in attachments), unless they have contacted the study team requesting to opt out from further contact.

Provider Evaluations. A brief email survey will be sent to providers participating in the study. The main purpose of this brief survey (see Appendices) is to capture any perceptions by providers that the study is adding to their workload or saving them time, and to give providers an opportunity to share their experiences about the study with the study team. If providers have offered LCS to more than one patient, they will only receive this survey once per quarter.

5.6 Data Analysis

Sample size determination. Our target sample size of 270 respondents per arm with complete 12-month outcome information was selected to have sufficient (80%) power to detect a doubling of abstinence rates (Relative Risk = 2) using a multilevel random effects model with patients clustered by randomized provider. The assumed intraclass correlation coefficient for the provider clustering effect is assumed to be 0.01. Power is based on a two-sided test with type-1 alpha error rate of 0.05%. Due to randomization, we do not anticipate needing to adjust for patient covariates.

Intent-to-treat (ITT) analysis We will utilize an intent-to-treat approach and include all participants who meet study eligibility criteria and are assigned to a study arm, regardless of whether they participated in all of the care components of that arm (e.g. declined proactive telephone counseling). Our primary analysis will focus on participants for whom we have complete 12-month abstinence (target n=270 per arm).

Missing outcome data. For secondary analyses, we will examine outcomes for all eligible screening patients who are current smokers offered screening by a participating randomized provider during the study period. This analysis will include patients who do not participate in the survey assessment of cessation outcomes. We will perform two secondary analyses. The first will assume that patients who do not participate in the survey assessment (e.g. missing abstinence outcomes) will be considered continued smokers, which is a typical intent-to-treat approach for cessation trials. We do not anticipate differential missing data across study arms. Second, we will address potential missing cessation data by requesting a HIPAA waiver and waiver of informed consent to review EMR data for all eligible patients to estimate an administrative assessment of cessation, based on HealthFactors data and whether patients report quitting at a subsequent visit or when they return for annual lung cancer screening. The methods developed by McGinnis et al, will be used to construct this administrative cessation variable.

(Note, due to COVID pandemic changes in lung cancer screening utilization and study enrollment timelines, the missing data protocol using EMR data was adapted for the primary outcome. See the Statistical Analysis Plan.)

All data will be maintained and analyzed at the Seattle offices of the Seattle/Denver Center of Innovation for Veteran-Centered and Value-Driven Care. Dr. Zeliadt will oversee all project staff conducting data analysis activities. See below for description of data and privacy protections at our Center of Innovation.

5.7 Withdrawal of Subjects

Patient participants may be withdrawn without their consent if they no longer meet the study eligibility criteria (e.g. their LCS test or a short-term follow-up test identifies lung cancer or a highly suspicious finding, or if the subject becomes pregnant which is unlikely given the age eligibility for LCS). A participant may also be withdrawn if either of the responsible VA clinicians, Drs. Au or Feemster, deems it appropriate to ensure that no harm occurs to the subject.

Both patient and provider participants may withdraw from the study at any time without incurring any consequences. Participants may notify the study team or Principal Investigator at any time to withdraw from the study. Contact information will be provided in all communications, including on the Information Sheet and survey mailings provided to all participants. Language emphasizing the freedom to withdraw at any point during the study will be included on communications with study participants.

6.0 Reporting

Collection of Safety Information. The study activities do not involve any invasive procedure, and it is not anticipated that serious adverse events or unanticipated problems will occur, including events that would trigger suspension of research. However, in the rare chance such an incident does occur, all serious adverse events and unanticipated problems will be reported according to regulatory and reporting requirements outlined in the VHA Handbook 1058.01 within 5 business days of the incident. The Coordinating Center will complete and submit an Unanticipated, Serious Adverse Event (SAE) Report form or Problem Report for each incident to the VA Human Subjects Boards as per the regulatory requirements at each site and the study protocol.

The project coordinator will be responsible for reporting relevant information to the PI on a weekly basis. Any clinical or data safety concerns will be reported to the PI and responsible VA clinician within 24 hours. If the PI is unavailable, the project coordinator will contact an available Co-Investigator (Dr. Becker, Dr. Au, Dr. Feemster). The PI will determine whether the event is a) serious or non-serious and b) anticipated or unanticipated. The PI will ensure that any necessary actions are taken immediately to address the current patient situation, and then will decide if the team needs to make any changes in the protocol and/or consent forms to prevent future occurrences or better inform future participants. Any deviation to protocol or safety concerns resulting from the study will be communicated by the project coordinator via the submission of an Unanticipated, Serious Adverse Event (SAE) Report form or Problem Report to the VA IRB as per the VHA regulatory requirements and protocol, within 5 business days of an incident.

Method of Collection of Safety Information. If the study is made aware of any Adverse Events through notification by a study participant, VA Quitline Counselor, or email/contact from a study provider, the project coordinator will be responsible for completing the above safety & regulatory report forms (i.e., SAE forms), which the PI will sign prior to submission. Adverse Events will be reported to the VA Human Subject Review Board using the appropriate Central IRB forms.

Frequency of Safety Data Collection. Oversight of project activities and data by the PI will begin immediately. Collection of CDW data will begin as soon as IRB approval is obtained. Twice-weekly lists of potential subjects will be continued until target recruitment goals are met.

Any event that adversely affects participant safety will be recorded as soon as possible after it occurs and be reported within 24 hours to the PI.

Notification of Subjects of Findings Affecting Health and Welfare. This study does not involve any invasive procedure, and it is not anticipated that any findings identified by the study (e.g. survey results) will require notification.

7.0 Privacy and Confidentiality

PHI. Protected Health Information and personal identifying information will be obtained from existing sources (Corporate Data Warehouse, CAPRI/JLV) and from patient subjects. Names, social security numbers, birthdates, ages, appointment dates, treatment dates, date of CT screenings, telephone numbers, and patient addresses will be obtained. Limited screening data will be entered into an electronic subject tracking database that will be maintained on secure servers at the COIN at VA Puget Sound. The tracking database will be used to log subject recruitment and completion of surveys. The tracking database will include subject name, SSN, address, phone number, date they were offered lung cancer screening by their VA provider, and date of receipt of lung cancer screening. The tracking database will also serve as the crosswalk between the subject name and the study ID sequentially assigned by project staff. Data collected as part of this study (subject responses to surveys) will include a study ID with no other patient identifiers, and will be stored separately from the tracking/ crosswalk data.

Data security. Data collection, storage and management for this research project will adhere to all applicable VA policies, the VA Puget Sound Health Care System's Automated Information Systems Security Policy, and the established Data Security Policy of the Seattle/Denver COIN. All electronic study data – including protected health information and de-identified analysis files – will be stored in secure, password protected folders and/or SQL databases on the Seattle HSR&D network. Access will be restricted to the study team. Protected health information will not be disclosed, copied, transmitted by email, or transmitted in total or in part to anyone not connected with the approved protocol and not approved by the VA (via a Data Use Agreement, if necessary) to access the identifiers.

All electronic study data will be in secured and stored in electronic files on the COIN's secure servers at VA Puget Sound. Files will be secured behind the VA firewall with strong password protection restrictions in accordance with VA policy. Access to study files will be restricted to study staff only. The data collected in this study will be used solely for the purpose described in the study protocol.

At no time will copies of data will be placed on laptops, computer desktops, hard drives, portable media, or any other form of media or hardware. Screening data for potential subjects identified in Corporate Data Warehouse data repository will be transferred and stored in electronic format to the VA Informatics and Computing Infrastructure (VINCI) server using secure server-to-server, password-protected media/ technology. Data Use Agreements between project staff and repositories will be executed prior to all data access. The historical and screening CDW data will remain within our designated VINCI workspace environment, which will be restricted to approved project staff only. The VINCI workspace will be accessed remotely from workstations located within COIN offices at VA Puget Sound.

Hardcopies of all study data (such as survey responses) will be kept in locked file cabinets in COIN offices. CDs containing participation records obtained from VA Quitline will also be stored in locked file cabinets in COIN offices, and will be labeled only with a coded study ID (no patient identifiers).

The PIs, co-investigators, and project coordinator will be responsible for monitoring data and study activities. Any deviation from the data security or privacy rules will be immediately reported to the Database Administrator, Privacy Officer and Information Security Officer. Study investigators will access data to identify prospective patients offered lung cancer screening on an ongoing (approximately weekly) basis. The project team will hold regular, biweekly meetings to provide updates and review analyses. Additional, ad hoc meetings will be scheduled to discuss specific findings or challenges.

Upon completion of the research project, the PI in conjunction with the VA Information Security Officer (ISO), and in accordance with VA policy, will ensure that, study data containing sensitive, confidential information will be sanitized and removed from all servers, desktops, removable storage devices, etc. in accordance with Records Control Schedule 10-1. When any study personnel are no longer a part of the research team, the PI will remove that person's access to all study data and notify the VA Information Security Officer of such action. COIN Information Technology personnel will be responsible for maintaining COIN servers where study data will be kept, and will move, backup and remove study data from servers and control access to data stored on COIN servers. All study team personnel with access to sensitive patient data will stay current on their VA approved information security training and VA approved privacy policy training.

8.0 Communication Plan

Each site (NY Harbor and Providence) will submit and obtain R&D approvals. We anticipate NY Harbor and Providence R&D committees will provide guidance about requirements for annual review and/or submitting presentations/manuscripts prior to publication.

The project manager at the Coordinating Center in Seattle will be the point of contact for ensuring that any changes to the protocol or any Serious Adverse Events or Unanticipated Problems will be promptly will be responsible for managing local R&D paperwork and assisting with IRB paperwork.

Dr. Zeliadt assumes primary responsibility for oversight of study logistics; formative evaluation, fielding and analyzing survey data; conduct of qualitative interviews; synthesis of formative evaluation findings into feedback reports. Dr. Zeliadt will provide oversight of the Project Manager. Dr. Zeliadt will assume responsibility for ensuring the study meets overall project deadlines and adheres to the proposed timeline; communication with study team members and participants about study events and results; and timely reporting of study findings internally to operational stakeholders, VA researchers and the scientific community.

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