Pragmatic Implementation Science Approaches to Assess and Enhance Value of Cancer Prevention and Control in Rural Primary Care

NCT04897568

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P50 Pragmatic Implementation Science Approaches to Assess and Enhance Value of Cancer Prevention and Control in Rural Primary Care

Protocol Number: 19-1706

National Clinical Trial (NCT) Number: NCT04897568

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Coordinating Center and Lead Principal Investigator:

Funded by: The National Cancer Institute

PROTOCOL AMENDMENT HISTORY

Version	Date	Description of Change	Brief Rationale
07.09.2019	11.25.2019	Original Phase 1 only	For JIT submission, one day turn around.
03.09.2020	03.09.2020	All years 1 & 2 activities added	Needed to add years 1 & 2 additional activities to original submission.
02.0210.2021	02.0210.2021	Alzheimer's disease and related diseases (ADRD) and Care Partners supplemental grant activities added Please see page 38-40 for more details.Small details added to Project 1, Phase 2 protocol. Dates adjusted to reflect delayed start due to COVID-19.	The purpose of this amendment is to include a supplemental project, led by Hillary Lum, MD, PhD. To avoid confusion, we will refer to and highlight the proposed amendments as "ADRD Supplement" throughout the document where appropriate. Please note, the activities listed in this supplement are closely related to Project #3.Dates needed to be adjusted due to COVID-19 delays. Details are just process items that

Version	Date	Description of Change	Brief Rationale
		This work will now continue into year 3.	have been worked out in the meantime.
03.18.2021	03.18.2021	Requested a change of IRB protocol from EXEMPT to EXPEDITED	In order to be able to register in clinicaltrials.gov our IRB protocol cannot be EXEMPT.
04.28.2021	04.28.2021	Added screening phase to the pilot trial Change of eligibility criteria	In order to invite patients to participate, we need to screen for eligible patients. Based on the new USPSTF recommendation, we are adjusting eligibility criteria to follow their new recommendation for LCS
05.27.2021	05.27.2021	Revised screening variables Revised recruitment details	Added all collected screening variables Specified planned minimum and maximum of recruited patients per practice
10.08.2021	10.08.2021	New flyer Revised recruitment materials Revised eligibility	Specific to the ADRD Supplement
10.08.2021	10.08.2021	Social Determinants of Health (SDOH) supplemental grant activities added.	The purpose of this amendment is to include a supplemental project, led by Andrea Nederveld, MD, MPH. To avoid confusion, we will refer to and highlight the proposed amendments as "SDOH Supplement" throughout the document where appropriate.

Version	Date	Description of Change	Brief Rationale
10.08.2021	10.08.2021	Project 1 change from stepped wedge trial design to pre-post.	Slow uptake in recruitment due to Covid and limited eligible patients for trial.
11.10.2021	11.10.2021	Adding "fax" to recruitment methods	If preferred clinics will fax participant lists instead of saving via Egnyte as planned originally
01.24.2022	01.17.2022	Revised eligibility	Specific to ADRD Supplement

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STATEMENT OF COMPLIANCE

This is an investigator-initiated study. The principal investigator (PI), Russell Glasgow, is conducting the study and acting as the sponsor. As the sponsor-investigator, both the legal/ethical obligations of a PI and those of a sponsor will be followed.

The trial will be carried out in accordance with Good Clinical Practice (GCP) as required by applicable United States (US) laws and applications, including but not limited to United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46).

The PI will assure that no changes to the protocol will take place without documented approval from the Institutional Review Board (IRB). All personnel involved in the conduct of this study have completed Human Subjects Protection Training.

I agree to ensure that all staff members involved in the conduct of this study are informed about their obligations in meeting the above commitments.

Sponsor-Principal Investigator: Russell Glasgow
Print/Type Name

Signature: _____ **Date:** _____

NOTE FOR REVIEWERS:

Being a Center, our program of research involves multiple smaller studies which fall into differing review categories. This submission is all encompassing for Years' 1 & 2 & now year 3 Center activities that involve human subjects. We have delineated each activity below and noted throughout as to which activity is being presented. Some activities do not share certain components (i.e. one activity does not involve an intervention and therefore is not represented in the intervention information section).

PARTICIPATING SITES

Rural primary care practices associated with our SNOCAP practice based research network. Specific practices not yet identified.

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Protocol Title: **Pragmatic Implementation Science Approaches to Assess and Enhance Value of Cancer Prevention and Control in Rural Primary Care**

Initial center projects recalled by the numbers below:

Project #1. Shared decision making in rural primary care lung cancer screening and smoking cessation

- Expedited: Category 62

Project #2. Cost collection template in order to objectively capture cost in implementation activities of project #1

- Exempt: Category 2

Project #3. Qualitative assessment of value and benefits of shared decision making for lung cancer screening and smoking cessation in rural primary care as defined by the RE-AIM framework, across multiple stakeholder groups.

- Exempt: Category 2

Project #4 ADRD Supplement: Stakeholder experiences of shared decision making for cancer screening and prevention activities in rural primary care: Impact of Cognitive Impairment

Project # 5 SDOH Supplement: Colorado ISC3 Environmental Scan for Health Equity - Administrative Supplement

Objectives:

- ***Primary Objective:***
  1. We will use qualitative and quantitative methods to assess the availability and existing infrastructure related to lung cancer screening (LCS) in rural areas. Using this information, we will develop a patient decision aid (PtDA) for lung cancer screening (LCS) and implement in Colorado rural primary care (State Networks of Ambulatory Practices and Partners, SNOCAP) after rapid-cycle design prototyping. In later years, results will be replicated in a national primary care network, National Research Network.
  2. We will refine our published cost capture template to categorize costs associated with the various RE-AIM outcomes and pilot test the revised templates in three local primary care practices varying on size, geographic location, and history of involvement in PBRN research that are delivering LCS and smoking cessation services.
  3. A. Through qualitative interviews and surveys, we will strive to understand the perspectives and values rural stakeholders

hold about LCS. We will establish the perceived costs and benefits of using shared decision making in LCS and LCS itself.

3. B. *Develop and pilot a brief survey of preferences related to the relative importance of RE-AIM outcomes (e.g., reach, implementation, maintenance) to assess benefits of various RE-AIM outcomes across stakeholders (patients, providers, and staff). Assess relationships between RE-AIM outcome preferences and selection of different CPC programs. Use rapid human-centered design procedures to develop and pilot a graphical value feedback display*

4. A. Identify experiences related to shared decision making for cancer prevention and control activities in rural primary care settings from the perspective of patients with mild cognitive impairment or early dementia, care partners of persons with dementia, and primary care stakeholders (health care provider or staff member).

4.B. Identify how primary care clinics adapt shared decision making or communication approaches to cancer screening and smoking cessation to meet the specific needs of patients and care partners affected by dementia.

5 A. Conduct an environmental scan of SDOH within site-specific geographic areas and supplement the cross-ISC3 standard data extraction.

5 B. Survey clinician-patient dyads during wellness-focused visits to evaluate the influence of SDOH on cancer prevention and screening decision processes among primary care clinicians and patients.

Endpoint:

- ***Primary Endpoint:***
  1. Determine the best processes for implementation and the feasibility of a future trial of implementation of a PtDA for LCS program in a national, rural practice based research network-based study.
  2. Evaluate and compare the feasibility and results of applying the cost templates via interview, observation, and staff tracking methods.
  3. Compare and contrast perspectives of stakeholder groups related to values, perspectives, costs and benefits around 1) LCS, shared decision making and smoking cessation, and 2)

different decision aids for shared decision making for LCS. Findings will be replicated across national rural primary care practices and data will be analyzed in the same way in years 3-5 of Center programming.

4. Evaluate SDOH needs across the 7 ISC3 network sites.
5. See endpoint 3.

- ***Secondary Endpoints:***
  1. Improved LCS practice in rural primary care with the use of a formal PtDA that we provide.
  2. After rapid modification as needed, we will compare the perspectives of providers, staff and patients on the cost of delivering smoking cessation and lung cancer screening activities in up to 10 different SNOCAP practices.
  3. Standardized assessment approaches and interview guides that can be shared with other research groups

Population:

❖ ***Population information below encompasses <u>all</u> Center activities over years 1 & 2 & part of 3:***

- ***Sample size***
  - *Maximum number of participants that can be enrolled in all projects within our program is 500 (allow for screen failures and drop out)*
  - *Minimum number of participants to be enrolled 100 (number of participants needed to answer scientific question/aims)*
- ***Gender*** *Male and Female*
- ***Age Range*** *18-100 (generally for UCCC studies this will be 18-100)*

Demographic group

English or Spanish speaking;
Patients: eligible for lung CA screening – Age 50-80, English or Spanish speaking, asymptomatic, tobacco smoking history of 20+ pack-years; current smoker or quit within 15 years, .
Clinicians: Physicians and advanced practice providers;
Staff: Nurses, administrators, medical assistants, social workers, and other clinic personnel;
Leaders of rural clinics, hospitals, and radiology sites serving patients from the rural clinics.

- Family and/or caregivers: People living with or caring for patients as detailed above. ***General health status*** asymptomatic; tobacco smoking history of 20+ pack-years; current smoker or quit within last 15 years

- ***Geographic location*** 30-40 rural clinics and approximately 10 urban clinics from our State Networks of Colorado Ambulatory Practices & Partners (SNOCAP) practice-based research network (PBRN)

ADRD Supplement:
As above, with slight modifications:

- Patients: Age 55+; Diagnosis of mild cognitive impairment or dementia in the medical record [e.g. Alzheimer's disease, vascular dementia, dementia, dementia associated with Parkinson disease, dementia not otherwise specified (NOS), etc.; Seen in one of the clinic practices in the past year
- Family and/or care partners: Care partner of a patient with ADRD who has ability to provide informed consent; or, care partner of a person with dementia who lacks decision making capacity to provide informed consent to participate in the study
  Clinicians: Physicians and advanced practice providers;
  Staff: Nurses, administrators, medical assistants, social workers, and other clinic personnel;

Geographic location: 2-4 rural clinics from SNOCAP (same as above) and 2-4 rural clinics from the National Research Network; community members responding to study flyer, regardless of location

SDOH Supplement:
As above with slight modifications:

- Patients: Age 45+; Seen in one of the clinic practices in the supplemental funding period.
- Clinicians: Physicians and advanced practice providers;

Geographic location: 4-6 rural clinics from SNOCAP (same as above)

Phase:	Various across projects as listed.
Participating Sites:	To be defined: State Networks of Ambulatory Practices and Partners & National Research Network
Description of Study Intervention:	***The intervention is within Projects #1 & 2 only. Project #3, #4 & #5 do not have an intervention component.*** *Aim1b.*

Our implementation package includes three interrelated interventions being implemented simultaneously. We aim to improve adherence to the LCS guidelines and CMS coverage criteria to conduct SDM and provide smoking cessation services in rural primary care practices.

- *Lung CA Screening Guideline*: The USPSTF recommends annual LCS with low-dose CT in adults aged 50 to 80 (CMS coverage up to 77) years who have a 20 pack-year smoking history and currently smoke or have quit in the past 15 years.
- *Lung CA PtDA*: CMS mandates use of shared decision making and our intervention will help clinicians meet this mandate using our adaptation of an effective lung cancer PtDA and strategies tailored to sites.
- *Locally appropriate smoking cessation counseling and/or referral*. The evidence-based smoking cessation strategies in our implementation package will be developed with input from project investigators and advisors with many years of combined experience studying tobacco cessation.

Aim2a.

Implementation of a cost collection tool to better assess cost data with respect to SDM in LCS and smoking cessation.

- Revise/Adapt cost collection template for 4 stakeholder groups.
- Compare observation vs. interview cost collection methods

Project #5 SDOH Supplement:

Cross-ISC3 Aim 1: to conduct an environmental scan of social determinants of health within site-specific geographic areas of all 7 ISC3 sites.

Brief Approach to Cross-ISC3 Aim 1: Final measures will be selected and collected by the end of the first quarter of the award period and will be updated each quarter over the funding period. The final quarter of the project will be spent on data cleaning, development of the cross-center data repository, and publications, presentations, and pilot project planning.

COISC3 Supplement Aim 1: To supplement the cross-ISC3 standard data extraction on SDOH measures with enriched metrics of food insecurity, transportation access, and social isolation from the rural Western Colorado regions served by the n=4-6 PEACHnet practices that are part of our ISC3 Implementation Laboratory.

COISC3 Supplement Aim 2: Informed by the 5 As framework, we will survey clinician-patient dyads in our Colorado COISC3 rural primary care clinics during a wellness-focused visit to evaluate the influence of SDOH on cancer prevention and screening decision processes among:

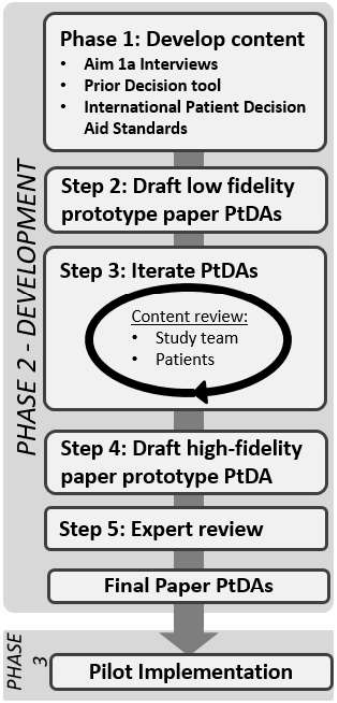
- Aim 2a: primary care clinicians
- Aim 2b: patients

Brief COISC3 Supplemental Aim 1 Approach: We will access additional population-level data for the rural regions served by our 6 purposively selected PEACHnet clinics in rural Western Colorado. Our COISC3 analyst will add these to the database containing the other social needs data for these regions that were captured by the cross-ISC3 aim.
Brief COISC3 Supplemental Aim 2 Approach: Using the procedures and processes that our Implementation Laboratory have found to be feasible, we will survey clinicians and patients in 4-6 rural Colorado ISC3 sites. We will work with practices that are geographically diverse and have established screening processes for unmet social needs.

Study Duration: 5 year

Participant Duration: No more than 3 years (Patients ~2 yrs; Staff ~3 yrs; over all activities – any one person should only be involved for a maximum of one year.)

1.3 STUDY SCHEMA



Aims 2a-2e Schema (Project #2 & 3 & 4)

Activity	**Description**
Refine stakeholder based cost capture procedures (Aim 2a)	Revise/adapt cost collection templates for 4 stakeholder types to assess costs by RE-AIM dimension
Cost assessment methods study (Aim 2a)	Compare observation vs. interview cost data collection methods
Benefits – Qualitative assessment (Aim 2b and Project 4: ADRD supplement)	Interviews and focus groups to understand stakeholder perspectives on benefit of each of RE-AIM outcomes
Benefits – Quantitative assessments – Phase I (SNOCAP) (Aim 2b)	a. Qualitative interviews of different stakeholders perceptions of benefits of LCS by RE-AIM dimension survey b. Pilot test of survey with n=4 SNOCAP practices
Benefits – Quantitative assessments – Phase II (NRN) (Aim 2b)	National survey of approximately n = 80 NRN and SNOCAP practices – compare involvement in and perceived benefit of providers vs. delivery staff vs. patients; comparing LCS, colorectal cancer screening and smoking cessation activities; and across RE-AIM dimensions
Study relationship of benefit priorities to choice of cancer interventions. (Aim 2c) ADRD Supplement: As above with condition "as well as relationship with dementia severity to choice or adaptation"	Mixed methods study to identify relationships between stakeholder perspectives on value to selection of different RTIPS programs varying on RE-AIM outcomes

	ADRD Supplement: As above with condition "including impact of level of dementia on choice of CPC approaches and/or potential adaptations"
Develop Value feedback procedures and displays (Aim 2d)	Rapid human-centered design procedures to develop and pilot graphical value feedback methods (based on RE-AIM dimensions) to aid in CPC decision making

2 INTRODUCTION

2.1 STUDY RATIONALE

We developed an administrative and leadership structure that ensures our Developing Implementation Science Cancer Control Center (ISC3) integrates our Implementation Studies and Methods Units to enhance the inclusion of value from multiple perspectives in implementation science models, measures, and methods. This structure also integrates our Implementation Laboratory to both advance the study of value in dissemination and implementation science (D&I) and enhance our knowledge of cancer prevention and control (CPC) implementation in rural settings. This, along with our original submission, covers all Center activities. Further amendments will be written to address later phases, but they are included in figures below to provide context.

2.2 BACKGROUND

Lung cancer is the leading cause of cancer death, with over 155,000 deaths annually in the US. In December 2013, the United States Preventive Services Task Force recommended annual screening for lung cancer with low-dose computed tomography (LDCT) with a grade B recommendation following the positive results of the National Lung Screening Trial. However, LDCT is associated with a high rate of false positives and a large number of patients who screen positive will receive unnecessary and invasive procedures. As such, the Center for Medicare & Medicaid Services (CMS) mandated both shared decision making and smoking cessation counseling as part of their coverage criteria for LDCT.

According to the National Health Interview Survey, of the 6.8 million smokers eligible for LDCT screening in 2015, less than 4% received it. This raises two questions: 1) What factors contribute to the low LDCT screening rates? and 2) How can we facilitate the implementation of

SDM and smoking cessation to improve the perceived value of LCS among patients and practices? This pilot project will address these two questions in our Implementation Laboratory of rural primary care practices, as well as advance the field by leveraging our initial methods projects.

ADRD Supplement: With the increasing prevalence of dementia of different etiologies, especially Alzheimer's disease, shared decision making related to CPC activities must appropriately meet and adapt to the needs of these older adults who already or will eventually lack decision making capacity. There is limited guidance available to primary care settings for selecting, adapting, and implementing evidence-based CPC programs for individuals with ADRD and their care partners, who often serve as surrogate decision makers. The potential burden and challenges of unwanted or over-screening for cancer may be quite substantial, affecting the individual, family care partners, and healthcare systems. Importantly, under-screening for individuals with ADRD is also possible in the context of prognostic uncertainty related to dementia trajectory and potential clinician or care partner biases that limit shared decision making. Evidence-based cancer prevention approaches like smoking cessation interventions are critically important given that smoking is a modifiable risk factor for cancers and dementia.

SDOH Supplement: A recent statement from the National Academies of Science, Engineering, and Medicine calls for health care system activities at both the individual and community level to facilitate the integration of social care into health care delivery. A 5 As framework is proposed, which includes awareness, assistance, adjustment, alignment and advocacy. At the individual patient level, and in a primary care context, the most crucial are awareness, assistance, and adjustment. In the rural medical practices in our Colorado ISC3 (COISC) implementation laboratory, and in many other states, there are increasing efforts to screen patients for social needs such as food, transportation, and social isolation (awareness); connect those with needs to resources (assistance). This supplement from the COISC3 will meet this challenge by partnering with the six other ISC3 centers to create a set of outer context common data elements (OC-CDE) that will be collected for all centers.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

We believe this research study presents no more than minimal risk to all participants. We will collect basic demographics (age, gender, educational level, health insurance status, employment), and other pertinent medical history, as well as health literacy and subjective numeracy. We will also have data on practice characteristics to provide qualitative contextual information. These data will allow us to report the representativeness of patients who receive this intervention. Participants in key informants interviews or focus groups will be audio recorded with their consent though no identifying information will be collected. Their participation would not affect their employability or adversely impact their health or safety.

2.3.2 KNOWN POTENTIAL BENEFITS

Using a mixed methods design to engage multiple stakeholders (patients, care partners, providers, staff, LCS related leaders) our initial pilot projects will generate high-quality preliminary data to inform our national dissemination study (years 3-5) and advance the field by testing pragmatic methods and tools developed by our Methods Unit. Successful implementation of PtDA could streamline work flows in rural primary care and provide higher levels of care to patients. There will be no immediate benefit to participants.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

We believe this research study presents no more than minimal risk to all participants. The pilot test of our qualitative assessment of stakeholder perspectives on costs, benefits and preferences across RE-AIM outcomes provides a novel application of mixed methods to advance the measurement and understanding of significant contextual and system factors that continue to be a challenge in implementation science.

REQUIRED TEXT:

The risks to participants are reasonable in relation to the anticipated benefits to participants and/or society, and in relation to the importance of the knowledge that may reasonably be expected to result, thereby falling in favor of performing the study:

- To Participant: There are no more than minimal risks to all participants. This study only intends to collect opinions and considerations from participants.
- To Society: Engaging multiple stakeholders will generate high quality preliminary data to inform our national dissemination study and advance the field by testing pragmatic methods and tools developed by our Methods Unit.
- Justify the importance of the knowledge gained: The pilot test of our qualitative assessment of stakeholder preferences across RE-AIM outcomes provides a novel application of mixed methods to advance the measurement and understanding of significant contextual and system factors related to perceptions of cost, benefit and value that continue to be a challenge in implementation science and health care in general.

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Primary		

We will use quantitative and qualitative methods to assess the availability and existing infrastructure related to LCS in rural areas.	• Establish the availability of infrastructure related to LCS in rural areas. • Elicit and understand values and perspectives around LCS, shared decision making and smoking cessation in these rural settings.	Engaging multiple stakeholders will generate high quality preliminary data to inform our national dissemination study and advance the field by developing and testing pragmatic methods and tools developed by our Methods Unit.

4 STUDY DESIGN

4.1 OVERALL DESIGN

Our pilot test of shared decision-making and smoking cessation guidelines for LCS will provide a practical test of our initial methods project to refine, develop and validate methods to measure both cost and benefit components of value from multiple stakeholder perspectives. First, though, in this initial pilot, we will refine the pragmatic implementation and replication cost measurement tools our team has already developed, and use these tools in the LCS pilot. *A necessary first step is understanding what costs and outcomes are important to different stakeholders and we will develop and test methods to assess preferences of patients, providers and staff across multiple RE-AIM outcomes in the LCS pilot*. A cost capture template will be piloted and refined during the local implementation of the PtDA. Each project, PtDA for LCS, cost capture template and quantitative/qualitative assessment of value and perspective, will inform our nation dissemination of the PtDA in years 3-5. This will also inform generalizability of the methods and measures developed with respect to other modes of cancer screening.

Our pilot intervention will engage no more than 216 patients using a pragmatic, pre-post design guided by our enhanced RE-AIM/PRISM framework. The primary goal of this intervention is to improve LCS practice by offering a formal SDM process and smoking cessation support aligned with the CMS coverage criteria. We will conduct a type II effectiveness implementation hybrid trial using a pre-post design to evaluate the effectiveness (co-primary outcomes of LCS and decision quality) and implementation at four rural clinics. Space precludes discussion of pragmatic design features, but we have designed this study to be pragmatic using the PRECIS-2 criteria and it scores highly on almost all PRECIS-2 dimensions.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

Lung cancer is the leading cause of cancer death, with over 155,000 deaths annually in the US. In December 2013, the United States Preventive Services Task Force recommended annual screening for lung cancer with low-dose computed tomography (LDCT) with a grade B recommendation following the positive results of the National Lung Screening Trial. However, LDCT is associated with a high rate of false positives and a large number of patients who screen positive will receive unnecessary and invasive procedures. As such, the Center for Medicare & Medicaid Services (CMS) mandated both shared decision-making and smoking cessation counseling as part of their coverage criteria for LDCT.

According to the National Health Interview Survey, of the 6.8 million smokers eligible for LDCT screening in 2015, less than 4% received it. This raises two questions: 1) What factors contribute to the low LDCT screening rates? and 2) How can we facilitate the implementation of SDM and smoking cessation to improve the perceived value of LCS among patients and practices? This pilot project will address these two questions in our Implementation Laboratory of rural primary care practices, as well as advance the field by leveraging our initial methods projects.

ADRD Supplement: As above with condition "including impact of level of dementia on choice of CPC approaches and/or potential adaptations"

4.3 END OF STUDY DEFINITION

The end of this phase of our Center's activities is defined by a saturation of major themes collected and organized, applied to the design of a successful PtDA and cost capture template. Readiness for national dissemination will be the endpoint and compilation of these first 3 projects in the program.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

REQUIRED TEXT:
In order to be eligible to participate in this study, an individual must meet all of the following criteria 1-4 and at least one of the criteria 5-9:

1. Provision to sign and date the consent form.
2. Stated willingness to comply with all study procedures and be available for the duration of the study.
3. All participants: Be a Male or Female aged 18 – 100 (50-80 for patients)
4. All participants: English or Spanish speaking

5. Patient participants: Asymptomatic; tobacco smoking history of 20+ pack-years; current smoker or quit within last 15 years
6. Clinicians: Physicians or advanced practice providers
7. Staff: Nurses, administrators, medical assistants, social workers, or other clinic personnel.
8. Leaders of rural clinics, hospitals, or radiology sites serving patients from the rural clinics.Care partner participants: patient family member, non-paid companion, or a designated health care proxy

ADRD Supplement:
All of the above, with the following conditions:

- Patients: Age 55+; Diagnosis of mild cognitive impairment or dementia in the medical record [e.g. Alzheimer's disease, vascular dementia, dementia, dementia associated with Parkinson disease, dementia not otherwise specified (NOS), etc.;
- Seen in one of the clinic practices in the past year or community member responding to study flyer
- Family and/or care partners: Care partner of a patient with ADRD who has ability to provide informed consent; care partner of a person with dementia who lacks decision making capacity to provide informed consent to participate in the study

SDOH Supplement:
As above with slight modifications:

- Patients: Age 45+; Seen in one of the participating practices for a wellness focused visit during the supplemental funding period.
- Clinicians: Physicians and advanced practice providers;

5.2 EXCLUSION CRITERIA

REQUIRED TEXT:
An individual who does NOT meet the criteria listed in 5.1 will be excluded from participation in this study.

5.3 LIFESTYLE CONSIDERATIONS

N/A

5.4 SCREEN FAILURES

Those who appear to meet inclusion criteria but fail to screen for our Project #1, Phase 1 pilot will be excluded then.

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

Phase 1. Practices within the SNOCAP practice based research network have agreed to partner in University of Colorado programs of research by their involvement in the PBRN.

Practice personnel and patients will be approached in person, via phone, or email to enroll them in the program.

We will conduct key informant interviews until we reach saturation for each group and anticipate completing up to 180 interviews (7-8 per group) or until we reach saturation. (Up to 60 interviews per project)

Phase 2. Practice staff and care managers will be asked to assist in recruitment by identifying eligible patients under their care that meet the requirements for LCS. This will be done using screening for eligibility criteria from their EHR. We will recruit a minimum of **9** patients and maximum of 12 patients per practice during each of the four 2-month time blocks for survey completion for a total to not exceed 216 patients across 4 practices. Potential participants will be informed and consented by network/research staff.

Practices will be asked to assist in recruitment by identifying eligible patients through review of the EHR, and follow-up with PBRN research staff.

- Option 1: PBRN research staff works with clinic scheduler to strategically identify eligible patients who have upcoming appointments. A list of appointment dates of eligible patients is provided to PBRN research staff including gender, age, smoking status and smoking history (as described in patient eligibility criteria) and contact information.
- Option 2: PBRN research staff mail out letters to eligible patients offering them an opportunity to reach out to us if interested to learn more about the study during their next visit, or a phone call.
- Option 3: When conducting reminder calls, clinic staff offer patients the opportunity to participate. Nurses will then share a list of patients who showed interest for PBRN research staff to reach out.
- Option 4: PBRN research staff traditionally recruit in the waiting room using a flyer or other tool. In past experience, however, this has not been the most efficient strategy given current pandemic restrictions.

A maximum of three (3) attempts will be made to contact participants if non-responsive after recruitment (i.e. phone, email).

ADRD Supplement

- Post flyer in community-based setting where allowed by the organization.
- Accept self-referrals from care partners and patients who respond to flyers. These people do not have to be patients of our participating practices.

SDOH Supplement

- Execute a data use agreement with HealthLandscape to provide SDOH data
- Use same process as outline in options above for Phase 2 trial to survey clinicians and patients.

6 STUDY INTERVENTION

6.1 STUDY INTERVENTION(S) ADMINISTRATION

(The intervention component is only within Projects #1 & 2)
The study intervention will begin toward the end of our year one activities and after its formative development in phases 1 and 2.

We will follow a multi-faceted implementation strategy that our team has used on similar studies, including:

- *Basic clinician education*: All clinics will receive education on: 1) lung CA screening; 2) SDM, and 3) innovative smoking cessation strategies that integrate with busy primary care workflows.
- *Fidelity to core intervention elements and adaptation to local context*: Our study will achieve an appropriate balance between fidelity and local adaptation. We will emphasize fidelity to core components of the interventions (e.g., PtDA delivered before or during an encounter; delivered by staff or providers at the clinic) and produce both a study protocol made available through clinicaltrials.gov and an implementation and adaptation guide. We will consult on and document adaptation to local settings as necessary for successful implementation using procedures validated by Rabin et al.
- *Centralized patient identification:* Eligible patients will be identified through a central procedure at each site, utilizing site-based EHR system reports, and eliminating reliance on the clinician. As noted above, we will use the approaches of the Moonshot-funded cessation smoking C3I to obtain accurate smoking history data, as well as the extensive experience of Drs. Nease and Ritzwoller with EHRs and patient registries.
- *Audit and feedback:* Sites, clinics, and individual clinicians will receive audits and feedback on their LCS services, including SDM and smoking cessation efforts. Information on use of the PtDA, delivery of smoking cessation advice and counseling/referral (most likely to be to the state Quit line) will come from either EHR or chart review of eligible patients as appropriate to each setting. Reports will be produced and disseminated monthly during the

intervention phases. Audits may be conducted in the form of pre/post surveys, direct observation, and/or brief interview about progress (if in-person observation is not allowed).

6.1.1 STUDY INTERVENTION DESCRIPTION

Project #1 & 2 within our program of research include an intervention: the PtDA for shared decision making in LCS and cost collection tool.

PtDA: Modification of the LCS PtDA and smoking cessation procedures for rural primary care will occur simultaneously with the phase one key informant interviews. We will review existing PtDAs with stakeholders and develop a modified version for use in rural primary care in collaboration with Tanner Caverly and colleagues at the University of Michigan[28,29] who developed an existing LCS tool for use during a primary care encounter using "designing for dissemination" principles[30,31,32]. We will follow the stepwise method (see Study Schema) in modifying the SDM content for our LCS pilot.[12]

- *Step 1*: The initial content will be based on a review of existing PtDAs using the International Patient Decision Aid Standards (IPDAS).[33] Testing of Dr. Caverly's LCS PtDA showed significant improvements in knowledge, decision conflict, and improved concordance between patients' preferences and screening recommendations.[28]
- *Step 2*: Based on existing lung cancer PtDAs, we will draft a low-fidelity paper or digital version allowing for rapid iteration. We will incorporate a host of innovations that we have found facilitate implementation. Our iterative development process follows a user-centered design perspective for the purpose of improving acceptability among end-users, facilitating future implementation.[39] The PtDAs are intended to be used by different end-users, and should be meaningful, helpful and accepted by all. Not only does this provide additional feedback, it creates investment among end users. Additionally, we provide "gist" language to supplement statistics to improve understanding among patients with lower literacy.[40]
- *Step 3*: We will iteratively review a paper-based or digital PtDA with the *multiple stakeholders* engaged in phase one. This review will occur immediately after the qualitative interview.
- *Step 4*: Once modifications are complete, we will draft a high-fidelity, encounter-based version using graphic design resources available at ACCORDS in the Colorado Program for Patient-Centered Decisions.
- *Step 5*: The tool will undergo a final review with leaders of the rural Colorado PBRNs, front line staff, patients, and the cancer center to assure that the resultant PtDA meets the needs of these stakeholders.
- *Step 6*: Participating site staff will determine the best work flow strategy after our implementation process detailed above. We will follow the progress of implementation of the intervention.
- *Step 7*: Pre-Implementation Survey – practice staff will complete a pre-implementation survey capturing items related to decision aid use and practice culture. Patients will complete a survey directly following their first appointment assessing the use of decision support during their visit and their view on the decisions made.

- *Step 8*: Audit & Feedback – Center staff will audit intervention progress by either in-person observation or short call with practice staff, compile responses, and deliver feedback in the form requested by the practice.
- *Step 9:* Post-Implementation Survey - practice staff will complete a post-implementation survey capturing items related to decision aid use and practice culture. Patients will complete a survey directly following a last appointment in the study period assessing the use of decision support during their visit and their view on the decisions made.

Cost Collection Template:

- *Step 1:* We will conduct a scoping literature review to identify published approaches to stakeholder-based cost, benefit and value assessment methods.
- *Step 2:* We will conduct a scoping review of LCS procedures and develop a flow diagram to represent specific activities within shared decision making for LCS and smoking cessation.
- *Step 3:* We will refine our published cost capture templates (which assess costs from provider/clinic; staff; and patient/family perspectives) to categorize costs associated with the various RE-AIM outcomes, and pilot test the revised templates in three SNOCAP practices varying on size, geographic location, and history of involvement in PBRN research that are delivering LCS and smoking cessation services. This step will evaluate and compare the feasibility and results of applying the cost templates as described in Rhodes et al[62] via interview, observation, and staff tracking methods. After rapid modification as needed, we will compare the perspectives of providers, staff and patients on the cost of delivering smoking cessation and lung cancer screening activities in 10 different SNOCAP practices.
- *Step 4:* We will use the cost capture template during the implementation project described above to summarize and feedback cost information to participating clinics.

6.2 STUDY INTERVENTION COMPLIANCE

Study intervention compliance will be assessed by diary review completed by experienced interviewers.

7 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION (STUDY STOPPING RULES)

We do not anticipate the need to discontinue the intervention. However, the Sponsor-Investigator has the right to discontinue the intervention at any time. Reasons for discontinuation may include, but are not limited to, the following:

- Intervention not feasible, after multiple iterations, to incorporate into work flows

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM STUDY

REQUIRED TEXT:
Participants are free to withdraw from participation in the study at any time upon request.

In addition, the investigator has the right to withdraw a patient from the study at any time. Reasons for withdrawal from the study may include, but are not limited to, the following:

- Patient withdrawal of consent at any time
- Patient non-compliance
- Lack of resource (patients or practices) to carry out intervention
- Patient's unwillingness to participate in shared decision making
- Any medical condition that the Sponsor-Investigator determines may jeopardize the patient's safety if he or she continues in the study.
- Sponsor-Investigator determines it is in the best interest of the patient

Patients must discontinue study intervention if they experience any of the following:

- Discomfort in answering the questions

Every effort should be made to obtain information on patients who withdraw from the study. The primary reason for withdrawal from the study should be documented on the appropriate eCRF.

7.3 LOST TO FOLLOW-UP

There will be 3 attempts to contact participants, after which time they will be excluded from the study.

8 STUDY PROCEDURES

8.1 STUDY PROCEDURES/EVALUATIONS

Through the course of our year 1 pilot projects, primary care practice personnel and patients will be enrolled to participant in interviews. We will continue to interview participants throughout this period until we reach 180 total interviews or saturation is reached among major themes surrounding the availability and cost/benefits of existing LCS infrastructure. (up to 60 interviews per project). In years 2 and 3 an additional 216 total patients will be surveyed 2 times within our Phase 2 pilot trial. A minimum of 6 and maximum of 18 practice staff will be surveyed 2 times throughout the Phase 2 pilot trial.

ADRD Supplement: At least four rural primary care clinics that have the capacity to identify patients with ADRD, care partners, and primary stakeholders. We plan to engage two SNOCAP

clinics that have a high prevalence of older patients and two National Research Network (NRN) practices, which have more lung cancer screening experience.

SDOH Supplement: The study team will receive a de-identified dataset from an external contractor with affiliation to AAFP to accomplish the environmental scan of SDOH. Each center in the ISC3 will receive similar data under this agreement. We will also perform a paired clinician-patient survey in a convenience sample during routine clinical visits. We plan to engage up to 6 clinics in the SNOCAP network.

8.2 STUDY SCHEDULE

8.2.1 Screening Within participating rural sites, we will identify and approach a convenience sample of clinicians, staff, and decision makers and invite patients meeting the above criteria to participate in an interview- within 18 months of program start. Patient ID will differ depending on resources available at practice sites. We will work with our rural PBRN partners to use EHR abstraction when available or other means if not.

8.2.2 Enrollment/Baseline Participants screened for the study will be approached and offered up to $100 compensation for their participation in key informant interviews or focus groups, including brief surveys. This will establish a baseline for the participant population highlighting preferences and perceptions of costs, benefit, and value with respect to shared decision making in lung cancer screening and smoking cessation and cost capture methodology. This will take place within 18 months of program start.

ADRD Supplement: Patient and care partners will each receive a $50 gift card for participating in a 1-hour interview. Primary care stakeholders will receive a $100 gift card. Each clinic will receive $2,000 for their assistance.

SDOH Supplement: Participating clinics will be provided a $500 stipend for collecting paired clinician-patient surveys over a two-week period. Patients will receive a $5 gift card for completing the survey.

8.2.3 INTERVENTION VISITS

The study team will schedule an initial visit for educational purposes and how to appropriately implement our PtDA and cost capture tool.

8.2.4 FOLLOW-UP VISITS

The study team will schedule up to 4 follow-up visits with participating sites to deliver audit and feedback, and ensure fidelity to the key elements of the study.

8.2.5 EARLY TERMINATION VISIT

NOT APPLICABLE

8.2.6 SCHEDULE OF EVENTS TABLE

Table 2: Timeline and pre-post design for Phases 1-2												
	Year 1				Year 2				Year 3			
Aim 1a – Decision Needs												
Aim 1b Adaptation phase– PtDA modification												
Aim 1b Implementation phase – Data collection												
SNOCAP clinic #1						C	C	C	I	I	I	
SNOCAP clinic #2							C	C	C /I	I	I	
PEACHnet clinic #3 & 4*							C	C	C /I	I	I	
C=Comparison (pre-implementation); I=Intervention (post-implementation)												

*Rationale for practice combination: only one provider participating from each and within the same health system.

Table 4. Methods Unit Study Initial Project Activities by Time Period		
Activity	**Months**	**Description**
Refine stakeholder based cost capture procedures (Aim 2a)	1-3	Revise/adapt cost collection templates for 3 stakeholder types to assess costs by RE-AIM dimension
Cost assessment methods study (Aim 2a)	4-9	Compare observation vs. interview cost data collection methods
Benefits – Qualitative assessment (Aim 2b and Project 4: ADRD)	10-12	Interviews and focus groups to understand stakeholder perspectives on benefit of each of RE-AIM outcomes
Benefits – Quantitative assessments – Phase I (SNOCAP) (Aim 2b)	13-18	a) Human-centered design rapid development of quantitative benefits by RE-AIM dimension survey b) Pilot test of survey with n=6 SNOCAP practices
Benefits – Quantitative assessments – Phase II (NRN) (Aim 2b)	16-27	National survey of approximately n = 80 NRN and SNOCAP practices – compare perceived benefit ratings of providers vs. delivery staff vs. patients; and across RE-AIM dimensions. Surveys administered based on participant's preference (online, paper or phone) with up to 3 reminders.
Study relationship of benefit priorities to choice of cancer interventions. (Aim 2c)	25-32	Mixed methods study to identify relationships between stakeholder perspectives on value to selection of different RTIPS programs varying on RE-AIM outcomes

Develop Value feedback procedures and displays (Aim 2d)	31-36	Rapid human-centered design procedures to develop and pilot graphical value feedback methods (based on RE-AIM dimensions) to aid in CPC decision making

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS (AE)

REQUIRED TEXT: Being key informant interviews or focus groups, shared decision making and cost capture practices, we do not anticipate any adverse events.

ADRD & SDOH Supplements: n/a

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS (SAE)

REQUIRED TEXT: Being key informant interviews or focus groups, shared decision making and cost capture practices, we do not anticipate any serious medical, adverse events.
ADRD & SDOH Supplements: n/a

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

N/A

8.3.3.1 SEVERITY OF EVENT

REQUIRED TEXT

N/A

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION

REQUIRED TEXT: Being key informant interviews or focus groups, shared decision making and cost capture practices, we do not anticipate any serious medical, adverse events.

The clinician's assessment of an AE's relationship to study procedure is part of the documentation process, but it is not a factor in determining what is or is not reported in the study. If there is any doubt as to whether a clinical observation is an AE, the event should be reported. All AEs must have their relationship to the study procedure assessed. To help assess, the following guidelines are used.

- **Related** – The AE is known to occur with the study procedure, there is a reasonable possibility that the study procedure caused the AE, or there is a temporal relationship

between the study procedure and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study procedure and the AE.

- **Not Related** – There is not a reasonable possibility that the study procedure caused the event, there is no temporal relationship between the study procedure and event onset, or an alternate etiology has been established.

OR

For all collected AEs, the clinician who examines and evaluates the participant will determine the AE's causality based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

- **Definitely Related** – There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out.
- **Probably Related** – There is evidence to suggest a causal relationship, and the influence of other factors is unlikely.
- **Possibly Related** – There is some evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after study procedure). However, other factors may have contributed to the event (e.g., the participant's clinical condition, other concomitant events). Although an AE may rate only as "possibly related" soon after discovery, it can be flagged as requiring more information and later be upgraded to "probably related" or "definitely related", as appropriate.
- **Unlikely to be Related** – A clinical event, whose temporal relationship to study procedure makes a causal relationship improbable (e.g., the event did not occur within a reasonable time after study procedure) and in which other factors provide plausible explanations (e.g., the participant's clinical condition, other concomitant treatments).
- **Not Related** – The AE is completely independent of study procedure, and/ or evidence exists that the event is definitely related to another etiology. There must be an alternative, definitive etiology documented by the clinician.

8.3.3.3 EXPECTEDNESS

REQUIRED TEXT: Being key informant interviews or focus groups, shared decision making and cost capture practices, we do not anticipate any serious medical, adverse events.

The principal investigator will be responsible for determining whether an AE is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study intervention.

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

REQUIRED TEXT: Being key informant interviews or focus groups, shared decision making and cost capture practices, we do not anticipate any serious medical, adverse events.

The occurrence of an AE or SAE may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care, or upon review by a study monitor. All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate CRF. Information to be collected includes event description, time of onset, clinician's assessment of severity, (if applicable) relationship to study intervention (assessed only by those with the training and authority to make a diagnosis), and time of resolution/ stabilization of the event. All AEs occurring while on study must be documented appropriately. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE. UAPs will be recorded in the data collection system throughout the study.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

The PI will record all reportable events with start dates occurring any time after informed consent is obtained until 30 (for non-serious AEs) or until resolution or stabilization (for SAEs) after the last day of study participation. At each study visit, the investigator will inquire about the occurrence of AE/ SAEs since the last visit.

8.3.5 ADVERSE EVENT REPORTING

REQUIRED TEXT: The investigator must record non-serious adverse events and report to DSMC and IRB according to timetable for reporting specified in section 10.1.6.

8.3.6 SERIOUS ADVERSE EVENT REPORTING

REQUIRED TEXT: The investigator must record all serious adverse events and report to DSMC and IRB according to timetable for reporting specified in section 10.1.6.

- Other SAEs will be submitted to the National Cancer Institute within 72 hours of site awareness.

8.3.7 EVENTS OF SPECIAL INTEREST

N/A

8.3.8 REPORTING OF PREGNANCY

N/A

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS (UAP)

REQUIRED TEXT FOR SINGLE-SITE STUDIES:

This study will use the COMIRB definition of UAP. An unanticipated problem is any event or information that was unforeseen and indicates that the research procedures caused harm (including physical, psychological, economic, or social harm) to participants or others or indicates that participants or others are at increased risk of harm than was previously known or recognized.

8.4.2 REPORTING OF UNANTICIPATED PROBLEMS

REQUIRED TEXT FOR SINGLE-SITE STUDIES:
This study will follow COMIRB's guidance for UAP reporting and the DSMC's requirements (discussed below). AEs, noncompliance and protocol violations will be recorded and reported as required either promptly (within 5 days of Sponsor-Investigator's knowledge) or at the time of the study's continuing review.

It is the responsibility of the PI to report incidents or events that meet the criteria for UAPs reporting to their IRB using the IRB's standard UAP form. The PI is responsible for reporting the UAP to the UCCC DSMC.

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

Reach: We will assess the percentage of eligible patients that receive one or more elements of the intervention. Representativeness will be assessed by comparing participants to those who opt out on available demographic and clinical indicators (e.g., age, gender, comorbidities) from chart review.

Effectiveness: We will assess the measures at the time points indicated in Table 3. Patients will be consented and provided a small incentive to answer surveys about their experiences. The primary outcomes will be:

- *SDM rates:* We will use single item measures of decision predisposition, choice, and enactment. We will also perform EHR/chart review as appropriate to each setting to document receipt of SDM.
- *Decision quality*: Decision quality is defined as "the extent to which the implemented decision reflects the considered preferences of a well-informed patient."[56] It consists of two domains: knowledge and values. Knowledge will be measured using a measure validated by Dr. Caverly and team.[28] Value-treatment concordance will be measured using the values-clarity sub-scale of decision conflict.[57] Across all projects and for all measures, we will use versions validated in Spanish, and when not available, the scales will be translated into Spanish, back translated and tested for cultural appropriateness by our Cancer Center Outreach staff.
- *Receipt of smoking cessation advice/counseling/referral*: We will obtain information from both EHR extracts or chart reviews and patient surveys.

Additionally, we will collect the following secondary outcomes:

- *IPDAS process measures*: We will use six questions based on key domains of decision process as outlined in the IPDAS background document. Dr. Matlock used these questions and found they had high internal consistency (Cronbach's alpha of 0.78).[58]
- *The Decision Conflict Scale (DCS)*: DCS assesses decisional uncertainty.[57] DCS reliability measures include test-retest correlation and Cronbach's alpha coefficients exceeding 0.78-0.90. It discriminates between groups who make and delay decisions.
- *Understandability and acceptability*: will be measured using the Ottawa Acceptability Scale (OAS). The OAS consists of 8 questions on a 5-point Likert scale.[59]

Patient characteristics data we collect will include basic demographics (age, gender, educational level, health insurance status, employment), and other pertinent medical history, as well as health literacy [60] and subjective numeracy.[61] We will also have data on practice characteristics to provide qualitative contextual information. These data will allow us to report the representativeness of patients who receive this intervention.

Adoption: RE-AIM defines adoption as the absolute number, proportion, and representativeness of a) settings and b) staff who are willing to initiate a program. We will measure adoption by the

number of clinics participating (3) divided by the number we invite, and similarly the number of staff who participate vs. those invited. We will also describe the representativeness of participating clinics, compared to other SNOCAP rural primary care clinics, and complete the Expanded CONSORT figure to transparently report on generalizability.[19]

Implementation: RE-AIM defines implementation as the extent to which the intervention is implemented as intended. Consistency of PtDA delivery will be assessed across SNOCAP clinics, patient subgroups, and time via surveys, EHR data and chart reviews. Additionally, we assess organizational factors associated with variation in implementation. Key informant interviews will be conducted at baseline and after implementation of the intervention with the clinic director and other staff involved. The goals of these interviews are to identify issues related to implementation/adaptation using procedures of Hall et al (2017) and Rabin et al (2018) and to explore strategies that may be useful in the refinement of subsequent roll-outs and future dissemination. Patients will complete a survey evaluating if and how the patients used the PtDAs with their clinicians. Finally, we will evaluate costs of the intervention and the implementation strategies using the time driven activity-based costing methods used by Drs. Ritzwoller and colleagues[4],[62] adapted as described in the Methods Unit below.

Maintenance: This will be assessed primarily by exploring whether each of the 3 clinics decides to continue; drop, or adapt/modify using the PtDAs and smoking cessation actions at the end of the study.

SDOH Supplement:

We anticipate generating descriptive data characterizing the outer contextual environment of the ISC3 network across the seven identified domains. Our overall analytic approach for this will consist of summarizing SDOH measures using descriptive statistics and data visualization methods to characterize the outer context across CHCs in our laboratories. We will examine the relationship between outer context and cancer prevalence, cancer-related behaviors, and policies across the ISC3 network, likely at the zip code and state level, since this would reflect the local and state-level policy context. We will examine the relationship between the seven contextual domains and cancer prevention behaviors (e.g. are cancer preventive behaviors better in jurisdictions that have lower levels of food and housing insecurity and other social needs?), and cancer-relevant policies (e.g. are cancer-relevant policies more prevalent in jurisdictions with more or fewer social needs?). We also anticipate comparing SDOH and health outcomes across several Centers at the relationship between outer context and cancer prevention outcomes, with analyses conducted at the practice-level. For example, we will assess the association between outer context measures and practice variation in rates of cervical and colorectal cancer screenings and smoking cessation intervention in practices located in specific states, including within and across state variation using multi-level modeling.

We will also collect survey responses from clinicians and patients to investigate the relationships between cancer screening tests and being referred for, accepting or declining these tests.

9.2 SAMPLE SIZE DETERMINATION

Using the approach described by Hussey, et. al,[63] we find that our proposed sample size (n=108) will provide >80% power to detect a .91 effect size difference between controls and intervention patients on continuous outcomes. While this study is not powered to detect smaller differences, it will be useful to obtain estimates of means, variability, and intraclass correlation for key outcomes to aid in planning the future study.

We have since added calculation for the Phase 2 trial and our proposed sample size of 216 participants will provide >80% power to detect a .58 effect size. Being a pilot, this feasibility data will be sufficient to lead to a larger trial aimed to produce a greater effect.

9.3 POPULATION FOR ANALYSES

1. Patients: Age 50 - 80; English or Spanish speaking, asymptomatic; tobacco smoking history of 20+ pack-years; current smoker or quit within last 15 years.
2. Clinicians: Age 18-100; English or Spanish speaking; Physicians and advanced practice providers
3. Staff: Age 18-100; English or Spanish speaking; Nurses, administrators, medical assistants, social workers, and other clinic personnel.
4. Leaders of rural clinics, hospitals, and radiology sites serving patients from the rural clinics; Age 18-100; English or Spanish speaking.

ADRD Supplement:

1. Patients: Age 55+; English or Spanish speaking, Diagnosis of dementia in the medical record [e.g., Alzheimer's disease, vascular dementia, dementia associated with Parkinson disease, dementia NOS (not otherwise specified), etc.].
2. Care Partners: Age 45+; English or Spanish speaking, care partner of a person with ADRD defined as family member, non-paid companion, or a designated health care proxy

SDOH Supplement:
As above with slight modifications:

1. Patients: Age 45+; Seen in one of the clinic practices in the supplemental funding period.
2. Clinicians: Physicians and advanced practice providers

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

Analysis of qualitative data will be a continuous process beginning with initial interviews and continuing throughout and beyond the data generation period.

9.4.2 ANALYSIS OF THE PRIMARY EFFICACY ENDPOINT(S)

A multidisciplinary team led by Drs. Matlock and Huebschmann, and guided by Dr. Holtrop will begin the analysis process with repeated readings of the transcripts to achieve immersion. The team will then develop and apply a list of codes using an emergent rather than a priori approach, to emphasize interviewee perspectives and de-emphasize team member speculations. All coded data will be entered into ATLAS.ti v 8.0 (GmbH, Berlin) for data management. Coded transcripts will be analyzed by the qualitative analyst within and across sites and settings to develop the major themes or concepts reported. The trustworthiness of study results will be enhanced through triangulation of the data and an "audit trail" throughout the data collection and analysis process. Analysis results will inform both the design of the implementation for the second study phase, and the initial methods projects.

RedCap or similar software will be used to conduct surveys and store survey data. The same team (above) with the addition of Dr. Dickinson will lead the quantitative analysis. Multiple outcomes from each individual on the five RE-AIM outcomes will produce repeated measures as we wish to compare ratings across outcomes; general linear mixed models can accommodate both levels of clustering. Since primary effects of interest are between individuals within clinics (or within individuals), the intraclass correlation coefficient will have less impact than in the case of between-clinic comparisons and is not considered here. Adjusted for multiple comparisons (providers vs. staff vs. patients), a sample size of 6 to 10 individuals per clinic (2 - 3 providers, 2 - 3 staff, 2 - 3 patients) from 80 clinics (160 to 240 per stakeholder type, 480 to 720 total) will provide a power of >80% to detect an effect size of 0.3 SD to .37 SD. For differences across respondent types on a single RE-AIM dimension. For the RE-AIM dimensions within individuals, adjusted for multiple comparisons, this sample size will provide .80 power to detect a .24 to .30 effect size difference between any two RE-AIM outcome dimensions.

In Phase 2, no less than 9 patients per clinic per step and 2-3 practice staff from up to 6 clinics will provide a power of >80% to detect a effect size of 0.58. SD will vary depending on final number of clinics enrolled. Being a small feasibility trial, we will enroll clinics up to 6, to achieve our goal of understanding feasibility of the use of our PtDA in a larger, national trial.

SDOH Supplement:

We will conduct separate models for different cancer preventive care outcomes as the outer context may have differential impact. We will consider random effects for state to account for clustering, and will utilize several statistical criteria to determine relative contributions of multi-level factors, including but not limited to: interpretations of measures of relative risk (e.g., odds ratios, rate ratios) and effect sizes, statistical significance, explained variation for GLMMs, and model diagnostics. Paired survey data will be analyzed primarily using descriptive statistics.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

N/A

9.4.4 SAFETY ANALYSES

N/A

9.4.5 BASELINE DESCRIPTIVE STATISTICS

N/A

9.4.6 PLANNED INTERIM ANALYSES

N/A

9.4.7 SUB-GROUP ANALYSES

N/A

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

N/A

9.4.9 EXPLORATORY ANALYSES

N/A

9.5 ENROLLMENT/RANDOMIZATION/MASKING PROCEDURES

Project #1 - Shared Decision Making in Lung Cancer Screening and Smoking Cessation Intervention: We considered three potential designs for this trial. A classic patient-level randomization is not ideal since practices (rather than patients) are the primary targets. A traditional cluster randomized trial would be disadvantaged by the small number of sites. Therefore, we propose a multicenter trial with a pre-post design where all the groups will receive the intervention. This design has been effectively used with rural Colorado PBRN practices. We propose a pilot study using a pre-post design with two time blocks of approximately 3 months each (Table 2) and will enroll approximately 36-48 patients per practice over a 12-month period for a total of 144-192 patients across all four practices. We will not exceed 6 practices and 216 patients.

SDOH Supplement: No randomization planned.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

Participants will be consented using an IRB approved post card consent form with verbal consent before enrolling.

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

REQUIRED TEXT:

Consent forms describing in detail the study procedures, and risks will be offered to the participant and written documentation of informed consent is required prior to starting intervention/ administering study.

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

REQUIRED TEXT:

Informed consent process will be initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Extensive discussion of risks, though minimal and possible benefits of participation will be provided to the participants and their families.

Consent forms will be IRB-approved and the study team with read and review the document with the participant. The investigator will explain the research study to the participant and answer any questions that may arise. All participants will receive a verbal explanation in terms suited to their comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the consent form and ask questions prior to consenting. The participants will have the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document or give verbal consent via audio recording prior to any procedures being done specifically for the study.

ADRD Supplement:
For individuals with diagnosis of ADRD, the informed consent process will use a functional demonstration of decision making capacity through a teach-back method. The "teach-back" method maximizes the ability of older adults with early dementia to participate and protects those individuals who cannot "teach-back" consent information in their own words.

The participants may withdraw consent at any time throughout the course of the trial. A copy of the informed consent document will be offered to the participants for their records. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

The study allows the inclusion of Spanish speaking and non-reading participants. Witnesses to these consent processes will be individuals not associated with the trial and will not have a conflict of interest.

SDOH Supplement: Same as center above.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

We do not anticipate discontinuation of these pilots.

10.1.3 CONFIDENTIALITY AND PRIVACY

REQUIRED TEXT:

Participant confidentiality is strictly held in trust by the participating investigators, their staff, and the sponsor-investigator(s) and their agents. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

The study monitor, other authorized representatives of the sponsor-investigator, or representatives of the IRB may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by local IRB and Institutional regulations.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored on the secured server at the University of Colorado's Adult and Child Consortium for Health Outcomes Research and Delivery Science. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. At the end of the study, all study databases will be de-identified and archived at the University of Colorado Cancer Center.

10.1.4 FUTURE USE OF STORED SPECIMENS OR DATA

REQUIRED TEXT *:*
Data collected for this study will be analyzed and stored on the secured server at ACCORDS, under the supervision of the Program Manager, for use by other researchers including those outside of the study. Some data may be shared or collaborated upon using the University's Egnyte server, a HIPAA compliant, cloud based server service provided by the university.

10.1.5 KEY ROLES AND GOVERNANCE

Data collected for this study will be analyzed and stored on the secured server at ACCORDS, under the supervision of the Program Manager, for use by other researchers including those outside of the study. Some data may be shared or collaborated upon using the University's Egnyte server, a HIPAA compliant, cloud based server service provided by the university. Egnyte automatically compiles a log of changes to data detailing who made changes and when they were made.

If preferred, practices can fax their patient lists versus sharing via Egnyte. Faxes can be sent to the Department of Family Medicine (DFM) fax line. In accordance with HIPAA regulations, practices will use a cover sheet. The fax will be addressed to a member of the study team that is part of the High Plains Research Network (HPRN), which is housed in DFM. The HPRN study team will coordinate with practices choosing to fax information to ensure a member of the team is present to receive the fax and to confirm receipt. The fax will be scanned, and the electronic version will be saved on Egnyte. Hard copies will be locked in a cabinet in the study team member's office, which is also locked. Hard copies will be shredded upon completion of recruitment.

10.1.6 SAFETY OVERSIGHT

NCT04897568

REQUIRED TEXT FOR SINGLE-SITE STUDIES:

Non-Interventional IIT (No Additional Risk)

The principal investigator will be responsible for the conduct of this study, overseeing participant safety, executing the data and safety monitoring (DSM) plan, and complying with all reporting requirements to local and federal authorities. This oversight will be accomplished through additional oversight from the Data and Safety Monitoring Committee (DSMC) at the University of Colorado Cancer Center (CU Cancer Center). The DSMC is responsible for ensuring data quality and study participant safety for all trials at the CU Cancer Center. A summary of the DSMC's relevant activities is as follows:

- Conduct of internal audits
- May submit recommendations for corrective actions to the CU Cancer Center's Executive Committee

Study audits conducted by the DSMC will consist of a review of the regulatory documents, consent forms, and source data verification. Documentation of the audit conducted by the DSMC will then need to be submitted to the IRB of record at the time of the IRB's continuing review of this trial (if applicable).

10.1.7 CLINICAL MONITORING

REQUIRED TEXT:

Clinical site monitoring will be conducted to ensure that the rights and well-being of human participants are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/ amendment(s), with GCP, and with applicable regulatory requirement(s). Monitoring for this study will be performed by ACCORDS staff in accordance with the clinical monitoring plan (CMP).

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

REQUIRED TEXT:

Quality Control (QC) procedures will be implemented beginning with the data entry system and data QC checks that will be run on the database will be generated. Any missing data or data anomalies will be communicated to the site(s) for clarification/ resolution.

Following written SOPs, the study monitor will verify that the clinical trial is conducted and data are generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirements.

The investigational site will provide direct access to all trial-related sites, source data/ documents, and reports for the purpose of monitoring and auditing by the DSMC audit team, and inspection by local and regulatory authorities.

10.1.9 DATA HANDLING AND RECORD KEEPING

Data handling and record keeping will be done within a secured Egnyte file-sharing platform. This storage is IRB/HIPAA compliant and encrypted.

Any faxed data will be locked in a secure location within Academic Office 1 and will be shredded upon the culmination of the pilot work.

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

REQUIRED TEXT:
Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site PI. The PI is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

10.1.9.2 STUDY RECORDS RETENTION

REQUIRED TEXT:
Study documents will be retained for a minimum of 7 years per HIPAA regulations. These documents will be retained for a longer period, however, if required by local regulations or institutional policies. No records will be destroyed without the written consent of the sponsor-investigator.

10.1.10 PROTOCOL DEVIATIONS

REQUIRED TEXT:
A protocol deviation is any noncompliance with the clinical trial protocol, GCP, or SOP requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly. These practices are consistent with ICH E6, sections:

- 4.5 Compliance with Protocol, sections 4.5.1, 4.5.2, and 4.5.3.
- 5.1 Quality Assurance and Quality Control, section 5.1.1.

- 5.20 Noncompliance, sections 5.20.1 and 5.20.2.

It is the responsibility of the study team to use continuous vigilance to identify and report deviations within 7 working days of identification of the protocol deviation, or within 30 working days of the scheduled protocol-required activity. All deviations must be addressed in study source documents, reported to the DSMC and COMIRB. Protocol deviations must be sent to the local IRB per their guidelines. The site PI/ study staff is responsible for knowing and adhering to their IRB requirements. Further details about the handling of protocol deviations will be included in the -SOP and/or study procedures manual.

10.1.11 PUBLICATION AND DATA SHARING POLICY

REQUIRED TEXT:
This study will ensure that the public has access to the published results of this research, and also meet obligations of the NCI funder.

10.1.12 CONFLICT OF INTEREST POLICY

REQUIRED TEXT:
Independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed.by the University of Colorado Denver's (UCD) Office of Regulatory Compliance Conflict of Interest and Commitment Management (COIC) program. Persons with a perceived conflict of interest will have such conflicts managed in a way that is appropriate to their participation in the trial. Conflict of Interest management plans are project-specific and are reviewed at least annually. UCD has integrated the institutional conflict of interest management program with its existing program.

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Project Plan - Alzheimer's disease supplement

Lay Summary: What are the experiences of persons with mild cognitive impairment/early dementia, family care partners, and primary care team members in rural areas related to:

a) risks, benefits, burdens of cancer prevention and screening (such as lung cancer screening, colon cancer screening, and smoking cessation) (all stakeholders);

b) communication and shared decision making, especially in the context of cognitive impairment and involvement of care partners (all);

c) barriers to screening and dementia care services in rural areas (care partner, primary care perspectives)

d) if/how primary care processes for colon/lung cancer screening are adapted to meet the needs of patients/ families living with dementia (primary care stakeholder perspectives)?

Settings

At least four rural primary care clinics that have the capacity to identify patients with Alzheimer's disease and related dementias (ADRD), care partners, and primary care stakeholders. We plan to engage two HPRN clinics that have a high prevalence of older patients (which may have more colon cancer screening experience) and two NRN practices (which have more lung cancer screening experience)

Participants

- **Patients** with mild cognitive impairment (MCI)/early dementia (3-4 per clinic)
- **Care partners** of those with MCI/early dementia (3-4 per clinic; recruited as dyads; interview sequentially)
- **Care partners** of patients with advanced dementia (2-3 per clinic)
- **Primary care clinicians** (MD, NP, PA) (2-3 per clinic); **primary care team members** (care managers, RN, SW) (2-3 per clinic)

Eligibility

Patients with mild cognitive impairment/early dementia AND decision making capacity, defined as the ability to provide informed consent to study participation (n=12-16 patients in total, or 3-4 per clinic) with the following inclusion criteria:

- Age 55+; English or Spanish speaking,
- Seen in one of the clinic practices in the past year, and
- Diagnosis of dementia in the medical record [e.g., Alzheimer's disease, vascular dementia, dementia associated with Parkinson's disease, dementia NOS (not otherwise specified), etc.].

Care partners, defined as someone the patient agrees to as their study partner, such as a family member, non-paid companion, or a designated health care proxy. (**n=20-26** care partners in total)

- Care partner of a patient with early dementia who has the ability to provide informed consent (12-16 care partners, as part of patient-care partner dyads). These care partners will be recruited with the patient.

  OR

- Care partner of a person with dementia who lacks decision making capacity to provide informed consent to participate in the study (n=8-10 care partners, or 2-3 per clinic). These care partners will be directly recruited, and then the person with ADRD (if available) can participate by providing assent.

Primary care stakeholders (n=25, or approximately 4-6 clinicians or staff based on clinic size):

- Clinicians (n=8-12): Physicians and advanced practice providers
- Staff (n=8-12): Social workers, case managers, nurses, clinic administrators, or others.

Recruitment

- HPRN team and/or PRAs will identify and work with clinic champions to purposively sample for participants with diverse racial/ethnic, and social determinants of health backgrounds.
- Identified patients and/or care partners will be contacted by phone or text (if appropriate) using approved scripts.
- Patient and care partner reasons for declining to participate will be monitored.

Informed consent – patients and care partners

Patients will be contacted by phone, screened for eligibility, and invited to participate using a modified informed consent process (postcard consent) to promote understanding. The informed consent process uses a functional demonstration of decision making capacity through a teach-back method. The "teach-back" method maximizes the ability of older adults with early dementia to participate and protects those individuals who cannot "teach-back" consent information in their own words.

Patients who are able to provide consent will be asked to provide a name of a "care partner" who could be a family member, friend, companion, or designated health care proxy who will also be contacted for consent to participate in the study.

Care partners and practice members will be consented in accordance with good clinical practice guidelines as well.