OHSU Knight Cancer Institute

Cancer Prevention, Control and Epidemiology Protocol

Screening More patients for CRC through Adapting and Refining Targeted Evidence-based Interventions in Rural settings (SMARTER CRC)

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1.0 ABSTRACT

This two-phase project is designed to achieve the Cancer Moonshot objectives by reducing the burden of CRC on the US population. Specifically, we aim to improve CRC screening rates, follow-up colonoscopy, and referral to care in rural Medicaid patients by implementing a direct mail fecal testing program with targeted outreach and patient navigation for follow-up colonoscopy. We leverage partnerships with the Oregon Rural Practice-based Research Network (ORPRN), Kaiser Northwest Center for Health Research, and Medicaid Health Plans and deliver training and implementation support to participating rural primary care clinics using practice facilitation. For the pragmatic trial, we anticipate working with 3 CCOs and 30 clinics reaching approximately 4,500 Medicaid patients. For the scale up trial, we anticipate partnering with 20 organizations to facilitate program implementation with 130 primary care clinics (reaching 17,000+ rural Medicaid patients). The mailed FIT and patient navigation interventions will be implemented as part of standard care by health system or clinic staff.

In Phase I (Year 01), we will conduct a milestone driven pilot to build the necessary infrastructure for a large-scale trial, including adapting the clinic-health plan-vendor supported direct mail program for rural Medicaid patients that have not established care and/or never been screened; conducting a pilot study testing the feasibility and acceptability of patient navigation to support follow-up colonoscopy following an abnormal fecal test; engaging Medicaid Health Plans and recruiting 30 primary care clinics located in rural and frontier counties in Oregon; and developing the training and support materials needed to implement a large-scale trial in these settings.

In Phase II (Years 02-05), we will test our intervention using a two-arm cluster randomized control trial in 30 rural primary care clinics using program training and practice facilitation to support implementation. Participating clinics will be randomized into two groups: Intervention and Usual Care. Randomization will be stratified on health system. As in the pilot, the intervention combines: (1) a clinic-health plan-vendor supported direct-mail fecal testing program with targeted outreach for patients who have never been screened or who have yet to establish care and (2) patient navigation for those who are referred for colonoscopy as either the primary screening or for follow-up from an abnormal fecal test. We will evaluate effectiveness, implementation, and maintenance of the intervention through quantitative and qualitative measures. Results from the trial will inform scale-up of the program through partnerships with 20 regional and national organizations that serve rural/frontier primary care clinics using webinars, train-the-trainer workshops and collaborative learning activities.

2.0 BACKGROUND / RATIONALE

Colorectal cancer (CRC) is the third-leading cause of cancer deaths in the United States[2] and the second leading cause among Oregonians.[3] CRC is 90% curable with timely detection and appropriate treatment of precancerous growths.[1] If not found until a patient is symptomatic, however, survival rates drop to 50%.[4] However, 1 in 3 age-eligible adults is not up-to-date for CRC screening.[5] Projections indicate that increasing CRC screening to 80% from current levels could prevent 277,000 cases and 203,000 deaths from the disease over the next 12 years.[6] Achieving this goal will require concerted efforts as approximately 25 million US adults aged 50–75 (33%) are not currently up-to-date.[7]

CRC screening rates are particularly low among adults in rural communities and sub-populations within these settings (e.g., Medicaid enrollees, Hispanic patients, Native Americans).[1,8-10] Rural areas cover 97% of the US land area and are home to approximately 60 million people. Within rural areas, frontier counties are the most remote and sparsely populated (having fewer than 7 people per square mile).[11] CRC incidence and mortality are disproportionately high among residents of rural regions;[9,12] disparities driven in part by differences in adherence to screening guidelines.[9,13] Medicaid enrollees are a key underserved group in rural areas. In 2016, Medicaid provided health insurance and access to preventive health services to 82 million people, including 1 million in Oregon.[14] Medicaid covers nearly 1 in 4 rural resident under age 65 (24%).[15] This is important as Medicaid members aged 50-64 years have relatively low rates of CRC screening, as demonstrated in national data (47% for Medicaid vs. 60% for private/Medicare aged 50-64)[16] and Oregon data for CRC screening in newly age eligible patients (34.9% for Medicaid vs. 42.8% for private).[17] Medicaid members also display less favorable CRC outcomes compared to commercially insured adults.[18,19]

Interventions are needed to address disparities is CRC screening, follow-up, and treatment in rural Medicaid patients. While mailed FIT and patient navigation are effective methods of improving screening and follow-up, no existing program incorporates these strategies into a resource-efficient, sustainable program that can be broadly implemented in rural geographic regions. Our study, Screening More patients for CRC through Adapting and Refining Targeted Evidence-based Interventions in Rural settings (SMARTER CRC), supports implementation of a targeted, multilevel program that incorporates tailored outreach, direct mail and patient navigation to address CRC disparities in rural Medicaid patients. A primary component of these interventions will be supporting collaborations between clinics, Medicaid health plans operating as ACOs, and commercial vendors to optimize and sustain program components. Through the course of a pilot test, large-scale pragmatic trial, and scale-up study, we anticipate working with 30 regional and national organizations to facilitate the program's implementation with an estimated 130 rural primary care clinics (17,000+ rural Medicaid patients). We will assess drivers of program success at the patient-, clinic-, and community-levels. SMARTER CRC will produce an implementation guide and resources to support program spread across rural settings serving Medicaid enrollees and other underserved populations.

SMARTER CRC is a partnership between faculty and staff at the Oregon Rural Practice-based Research Network (ORPRN) at Oregon Health & Science University (OHSU) and at the Kaiser Permanente Northwest Center for Health Research. This study fills key evidence and implementation gaps and supports Biden's Cancer Moonshot objectives by providing a model for how to rapidly adapt and scale-up multilevel interventions through clinic-health plan partnerships to reduce the burden of CRC on the US population.

3.0 OBJECTIVES

Primary Objective:

Adapt, pilot, then test the implementation and scale-up of targeted direct mail and patient navigation programs.

4.0 STUDY POPULATION

The study team will recruit eligible CCOs and rural clinics, and we will work in turn with clinics to engage providers, staff, and patients. Our eligibility criteria for CCOs, clinics, clinics staff, patients and organizational partners are below.

CCOs/CCO staff: 1) serving a majority of counties that are predominantly rural based on 2010 RUCA Codes (Codes 4-10); 2) willing to participate in data collection activities (e.g., producing claims data, interviews).

Clinics: 1) Clinics will be eligible for the cluster randomization if there are 30 or more patients eligible for screening, 2) are classified as rural according to RUCA (Codes 4-10) or Oregon Office of Rural Health designations, 3) are served by CCOs agreeing to participate in the project; and 4) willing to implement the intervention into their clinic for the study.

Clinic Staff/Providers: 1) employed as a clinician or ancillary staff member in a participating clinic; 2) willing to participate in data collection activities (e.g., interviews, observation, surveys).

Patients: 1) attributed to participating clinic; and 2) are enrolled in Medicaid or Dual eligible; 3) eligible for CRC screening;

a. For the subset of patients that will be invited to participate in key informant interviews, a 5th eligibility criteria is consent to participate.

Exclusion criteria: Clinics are excluded if they have current or ongoing participating in other mailed fecal testing research projects in the Medicaid population. Patients are excluded if they are current for screening, have comorbid conditions that make patients poor candidates for screening based on clinical judgment (e.g., end-stage renal disease, enrollment in hospice), are not an established patient or for other reasons documented by the clinics.

Community or regional/organizational partners (includes endoscopy providers, community-based outreach workers, or leaders from regional or national organizations who participate in the pilot, pragmatic trial, or scale-up study) 1) involved in study activities (training, care delivery); 2) willing to participate in data collection activities (e.g., trainings, interviews, surveys).

For this project, we expect to recruit at least three CCOs and 33 Oregon clinics, which allows up to a 10% attrition rate to achieve our target of 30 rural primary care clinics. Based on Census Bureau data (https://www.census.gov/quickfacts/or), as of 2017, Oregon residents are 50.4% female and 13.1% Hispanic or Latino. Also based on Census data, Oregon resident diversity consists of 2.2% African American, 1.8% American Indian or Alaskan Native, 0.4% Native Hawaiian and other Pacific Islander, 4.7% Asian, 87.1% white, and 3.8% two or more races. Based on the Census Bureau's data, we expect the participating individuals to make up a representative sample of Medicaid individuals across the state.

5.0 INCLUSION/EXCLUSION CRITERIA

Inclusion criteria:

	Included	*Excluded*
Children		All patients we recruit will be at least 45 years of age or older, and clinic/CCO staff will be at least 18 years of age or older.

Elderly	Yes – we anticipate that a limited number of clinic and CCO staff, or community organization representatives may be elderly; we limit our patient recruitment to those aged 45-75.	
Rural	Yes	
Inner City	No	
Low Income	Yes	
Disabled	Yes	
Chronic Care	Yes	
End of Life	Yes - This is possible, but we predict limited numbers because of the types of individuals we are recruiting: clinic and CCO staff, and patients who are not currently in hospice care.	
Minorities	Yes	
Both Genders	Yes	

This study will not include any vulnerable populations. We will not collect any information about subjects' status as prisoners, pregnant women, children, neonates, and/or adults lacking capacity.

6.0 METHODOLOGY

Throughout this trial we will collect data from multiple sources to assess process and outcomes data and drivers of program success at the patient-, clinic-, and community-levels aligned with a social ecological model for the quality of cancer care. These sources of data include:

- CCO interview, readiness assessment, and survey
- Clinic survey, readiness assessment, observation and interviews
- Patient interviews
- Interviews and surveys with regional and organizational partners
- Patient outcomes data (e.g., claims, vendor reports and electronic health record) and patient navigation registry data

7.0 STUDY PROCEDURES AND SCHEDULE OF EVENTS

CCO interview, readiness assessment, and survey: CCOs that express interest in participating in the trial will be invited to participate in a semi-structured interview (in-person or via phone) and complete a baseline survey to confirm CCO characteristics (e.g., size, number of primary care clinics in rural/frontier counties) as well as information about CCO data infrastructure, relationships with clinics, and quality improvement capacity. Readiness questions will be drawn from the literature and explore the CCO's prior experience with payment and quality improvement initiatives related to CRC screening and follow-up care.

Clinic survey, readiness assessment, observation and interviews: For clinics expressing interest in the trial, we will conduct semi-structured interviews (in-person or via phone) with clinic leadership to assess clinic characteristics, capacity and readiness to adopt the program and participate in the trial. Clinic characteristics will include descriptive data (e.g., ownership, primary care clinician number and FTE, EHR vendor and version), baseline CRC screening rates and if the clinic currently utilizes audit and

feedback, and details on current workflows related to CRC screening and follow-up (including provider CRC screening modality preferences). Capacity questions will explore general capacity as well as specific capacity related to CRC screening. Readiness questions will draw on prior work by Weiner, Hannon, and others,[20] and utilize a clinic-level readiness survey piloted by our team during Dr. Davis' K07.

We will conduct clinic surveys, interviews, and observations with clinic staff in various roles related to the program (e.g., outreach workers, patient navigators, quality improvement leads) to assess clinic/health system level factors that may influence outcomes. These assessments will happen at baseline and after implementation of the pilot as well as for each arm of the trial (post-implementation at 6-9 months as well as implementation context, maintenance, and sustainability approximately 12 months later [i.e., clinic exit interviews]).

Patient interviews: We will conduct one-on-one interviews with patients who receive the direct mail and patient navigation programs. Interviews will explore patient experiences with the program, including reaction, acceptability, satisfaction, and perceptions of usefulness; facilitators of, and barriers to, participating in the program and obtaining a follow-up colonoscopy; unintended consequences; and suggestions for improvement

Interviews and surveys with regional and organizational partners: To assess perceptions of the intervention and its impact on the broader community, we will interview CCO leaders, endoscopy providers (e.g., GI specialists, general surgeons, primary care clinicians) who treated study participants, and community organizations, including transportation service providers. Up to three interviews will occur throughout the duration of the study, including at baseline (pre-implementation), at the mid-point (approximately 12 months after the first-year implementation start), and post-implementation (approximately 12 months after the second-year implementation start). To evaluate the impact of scale-up activities we will conduct interviews and brief evaluation surveys with organizational leaders who participate in the trainings.

Patient outcomes data and patient navigation registry (Evaluation): Direct mail outreach and patient navigation activities will be tracked using reports from direct mail vendors, claims data from participating Medicaid health plans, clinic data from the electronic health record, chart abstraction data conducted by ORPRN or clinic staff, and data on navigation from a REDCap database. The mailed FIT and patient navigation interventions will be delivered by clinic and health plan staff as part of standard care. Clinics will be randomized to implement the interventions in different years to provide comparison groups. Claims data will be sent to the research team at OHSU from the participating payers based on their data pull of patients eligible for CRC screening in the clinics randomized to implement the intervention. Vendor reports will be sent to the CCO and research team based at OHSU. A clinic-level chart audit will be used to evaluate CRC screening and follow-up colonoscopy for patients with an abnormal FIT in intervention and control clinics.

Data for this project (i.e., process and survey data elements and patient navigation outcomes (such as number of patients who received patient navigation, number of patients with missed / canceled appointments or inadequate bowel preparation), will be stored in OCTRI's installation of REDCap, a highly secure and robust web-based research data collection and management system.

Features of REDCap that protect participants' privacy and data security include:

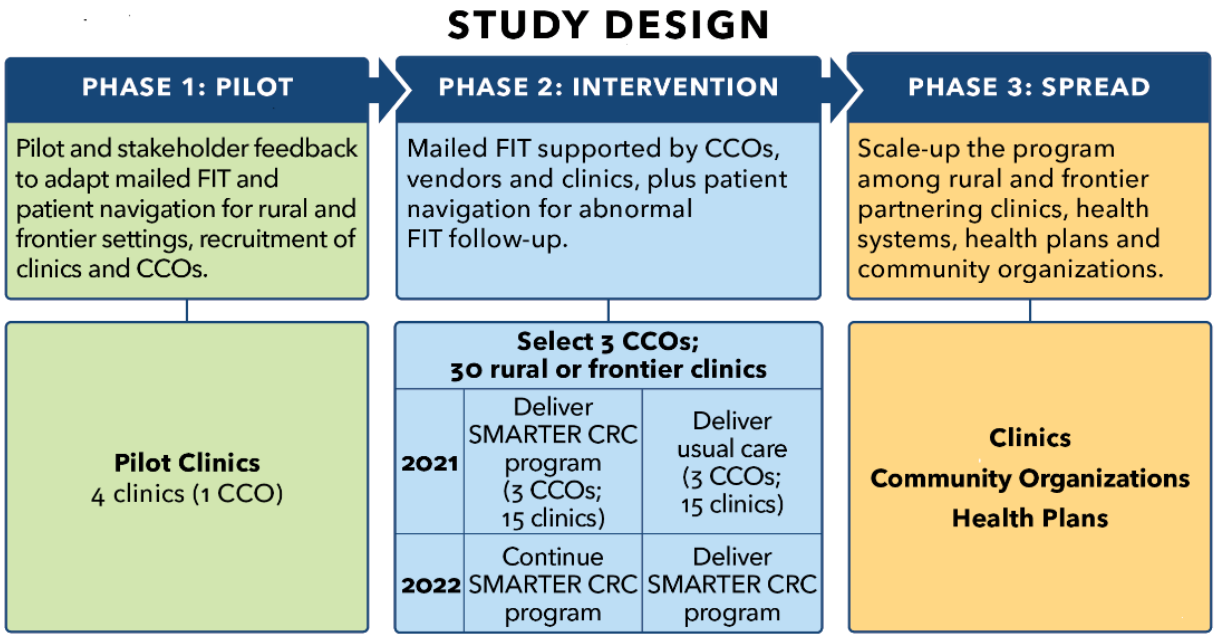
- Physical Security: OCTRI's REDCap software is housed on servers located in ITG's Advanced Computing Center providing locked physical security

- Electronic Security: The REDCap servers are housed behind both the OHSU firewall and a second ACC firewall. All transmissions of data from the application are encrypted over HTTPS with the industry standard TLS 1.1 protocol (AES 256-bit encryption).
- Controlled User Access: REDCap employs a robust multi-level security system that enables researchers to easily implement "minimum necessary" data access for their research staff, including specification of data fields that are identifiers. This feature includes “single click” ability to provide completely deidentified (removing all identified data fields and shifting dates) for analysis or other purposes. User activities are logged to enable auditing of all data access. Access is integrated with OHSU's network such that users who are also OHSU employees are authenticated against their OHSU network credentials.
- Data Integrity: REDCap is jointly managed in accordance with OHSU Information Security Directives by ACC staff and members of OCTRI's Biomedical Informatics Program, ensuring fidelity of database configuration and back-ups. User activities are logged to enable auditing of all data changes.

Data from the vendor and REDCap database will be merged with claims data to generate evaluation reports. To avoid bias in colonoscopy capture across baseline and follow-up time-points, ORPRN practice facilitators will perform a chart audit on all patients who were eligible for the direct mail program. The chart audit will confirm FIT completion and monitor for colonoscopy referral and receipt, pathology results, and referral to care (i.e. surveillance or cancer treatment), as indicated.

Researchers are requesting a waiver of authorization to access medical record data. ORPRN study staff plan to conduct the chart audit at each clinic over the course of 1-3 days. Data will be stored on the OHSU instance of REDCap or stored securely on OneDrive and ORPRN staff and select Kaiser Permanente research team members will have access to the data by utilizing a password-protected file on OneDrive or a REDCap user login. OneDrive and REDCap user permissions will be matched to roles as described in the established Data Use Agreement between Kaiser Permanente and OHSU and to the IRB. PHI will never be disclosed outside of the study team and all PHI will be destroyed upon completion of the study. Through data use agreements, a limited dataset will be shared with the sponsor, the National Cancer Institute. The following data elements will be included in the limited data set: patient identifier, age group, sex, Hispanic or Latino origin, race, state of residence, county of residence and primary health insurance. When possible, the data set will also include primary language, ZIP code of residence, individual history of CRC, most recently performed screening test date and result, and diagnostic colonoscopy date and result.

SCHEDULE OF EVENTS



8.0 TIMELINE AND MILESTONES

Phase I practice and CCO participants will be recruited Fall 2019, with the pilot intervention complete by the end of year 1. Phase II practice and CCO participants will be recruited in Fall/Winter 2020-2021 and first year of implementation will occur in 2021, with second-year implementation occurring in Spring 2022.

Phase I Milestones and Timeline				
Aim	**Milestones**	**Information sources**	**Measurement / Validation**	**Timeline**
1. Adapt direct mail materials and outreach to hard-to engage rural patients	**a.** Identify and recruit rural Medicaid patients to participate in Boot Camp Translation.	ORPRN, CHARA, CCOs, primary care clinics	Number approached and engaged. Demographic and geographic characteristics	Oct 2019 – Dec 2019
	b. Host Boot Camp Translation sessions; adapt program and identify outreach for patients at risk (unestablished, never screened).	Boot Camp Translation, relevant literature	Session attendance, evaluations, modifications of program messaging, timing, materials	Jan – May 2020
2. Conduct pilot to test the feasibility, effectiveness and acceptance of patient navigation program.	**a.** Update registry tools (tools will track total FIT kit mailings, test results, receipt of follow-up care, and display patient's previous CRC screening history). Implement patient navigation pilot.	Claims, vendor/lab data, EHR data Navigation registry	Registry; vendor to identify patients needing follow-up; tools for tracking navigated patients and CRC-related outcomes in EHR or registry.	Oct 2019 – Apr 2020
	b. Obtain data on patients participating in direct mail program and FIT results; Assess the pilot intervention's preliminary reach and effectiveness based on receipt of direct mail, FIT or colonoscopy completion, and proportion of patients receiving navigation.	Claims, vendor/lab data, EHR data	N FITs completed / FITs mailed; across stratification variables. N patients with abnormal FITs; documented receipt of navigation and outcome.	Apr – Jul 2020
	c. Assess the interventions feasibility and acceptance, based on one-on-one interviews with patients and debrief interviews with clinic/CCO staff.	Relevant literature	Feedback from patients and providers.	Apr – Jul 2020

Phase I Milestones and Timeline				
Aim	**Milestones**	**Information sources**	**Measurement / Validation**	**Timeline**
3. Engage CCOs and recruit clinics; conduct baseline assessment; use results from pilot to prepare to conduct a large-scale, pragmatic implementation-effectiveness trial and scale-up (see Phase II).	**a.** Creation of a list of inclusion and exclusion criteria for CCOs and clinic participation in Phase II.	Relevant literature, statistical power requirements	Feedback from local advisory board on inclusion and exclusion criteria	Jan – Mar 2020
	b. Develop CCO and clinic recruitment materials	Relevant literature	Feedback from local advisory board	Jan – Mar 2020
	b. Successfully engage 3 CCOs and 30 rural/frontier clinics for the main trial	Feasibility data from pilot study	List of participating CCOs and selected clinic characteristics	Mar – Sep 2020
	d. Develop manual outlining trial protocols (including quality assurance protocols), scopes of work, and associated budgets.	Feasibility data from pilot study	Feedback from advisory board on recruitment materials; study protocol; scope of work	Apr – Sep 2020

Aims	**Assessment/ Measurement**	**Data Sources**	**Description**	**Timeline**
Aim 1. Conduct a large-scale pragmatic study, cluster randomized control trial, to assess the implementation, effectiveness, and maintenance of the program piloted in Phase I in 30 rural primary care clinics (n ~ 3,960 patients aged 45 – 75) using practice facilitation to support implementation. Using a mixed methods approach, identify patient-, clinic/health system-, and payer/policy/community-level factors that are associated with reach, effectiveness, implementation and maintenance and to assess program adaptations.	Assessment of effectiveness (patient and clinic level).	Administrative data, claims data, EHR data from clinics, vendor data, laboratory data, survey data.	Patient Level Outcome (Primary): Completion of any CRC screening Clinic Level Outcome: Proportion of Medicaid patients screened for CRC We will compare the intervention vs. control clinics after adjusting for baseline at 6 and 12 months. The primary endpoint is 6 months. Secondary outcomes: completion of testing types (fecal testing, FIT-DNA, CT Colonography, Colonoscopy, Flex Sigmoidoscopy; patient level) and % completion (clinic level); time to screening from study-eligible patient list pull (patient level); FIT results (patient level); follow-up colonoscopy completion (patient level); time to colonoscopy from abnormal FIT result (patient level); and adenomas or cancers detected (patient level).	2021-Sep 2024
	Assessment of implementation (compliance rate with program components at clinic level).	Administrative data, claims data, vendor data, laboratory data, survey data including debriefs.	Proportion of core activities performed (e.g., mailed FITs, patient navigation calls) by clinics/CCOs	2021-2024
	Assessment of maintenance (compliance rate with program over time at clinic level).	Administrative data, claims data, vendor data, laboratory data, survey data.	Proportion of intervention clinics sustaining program in second year (N core activities sustained in second year/ N core activities, in intervention clinics/CCOs). Effectiveness of the program in intervention clinics in Year 2.	2021-2024
	Assessment of maintenance (compliance rate with program at patient level)		Proportion of patients who completed FIT in Year 1 who complete in Year 2, in intervention clinics.	

	Assessment of program second year implementation and adaptations.	Clinic/CCO surveys and interviews.	Types of and reasons for program adaptations, based on Wiltsey-Stirman FRAME framework.	May 2023-Sep 2024
Aim 2. Partner with regional and national organizations (n~20) to scale-up the program to additional clinics serving rural and underserved patients in high priority geographic regions of the US (n ~ 130 clinics; 17,000+ patients) using webinars, train-the-trainer workshops and collaborative learning approaches. Assess trainings delivered, program adoption and adaptations and determinants of dissemination success.				
	a. Assessment of adoption by clinics and community organizations.	Participation in workshops, training, and collaborative learning activities; survey data; use of program tools and implementation materials.	N clinics, community organizations, and staff that participate in training workshops, train-the-trainer sessions, and collaborative learning activities. Adoption as reported on 6-month survey data of workshop participants. Use of program tools; downloads of training and implementation materials.	2021-2024
	b. Assessment of program adaptations.	Clinic and community organization surveys and interviews.	Types of and reasons for program adaptations.	Oct 2023-Sep 2024

9.0 BIOSTATISTICAL CONSIDERATIONS

Phase I: Because this is the pilot phase, in which the primary purpose is to examine the feasibility and acceptability of the intervention and not to test a hypothesis, we have not performed a power analysis to determine the required sample size for this phase. Instead our primary goal was to evaluate the feasibility and acceptability of the program.[21-23]

Phase II, Aim 1 (Implementation-Effectiveness Trial): We will test our hypotheses using a two-arm cluster randomized control trial. Participating clinics will be randomized into two groups: Intervention and Usual Care. Randomization will be stratified on health system. Our study design aligns with the core principles of the PRECIS-2 framework.[24-26] Our **eligibility criteria** are broad and consistent with the realities of rural primary care (e.g., small sample sizes, limited quality improvement capacity). Our patient recruitment approach for the direct mail and navigation programs is aligned with routine care and standard quality improvement approaches and requires no individual consent. Participating clinics will serve populations that display CRC screening disparities, and be diverse in terms of EHR, rural geographic locations, and populations served. Our intervention is flexible and is designed to be adapted according to payer and clinics' resources and preferences. Our primary outcome, completion of any CRC screening, is pragmatic and relevant to patients, clinics, and payers (CCOs), and our primary analysis follows the intention-to-treat concept.[27] We will collect data 6 times from the CCOs. Data will be transferred every 6 months from the Spring of 2021 to the Fall of 2023 to be able to capture up to 18 months of follow-up following each mailing.

The primary effectiveness outcome of this study at the patient level is the completion of any colorectal cancer (CRC) screening (for study-eligible patients). Consistent with the pragmatic nature of the trial, we will use claims, vendor data, and EHR data for calculating CRC screening outcomes. Comparing the likelihood of receiving CRC screening between intervention and usual care groups at 6-month post participant list-pull date, we hypothesize that CRC screening will be more likely in patients allocated to the intervention group versus the usual care group. To examine the effectiveness of the program CRC screening completion at 6 months, we will use the generalized form of the hierarchical linear model (HLM; using a logit link and binomial distribution, aka multilevel logistic regression) to account for the clustering of patients within clinics and the assignment to arm at the clinic level. The variables that will be included in the model are the clinic baseline screening rate (if available) and a binary indicator of arm (1=tailored, 0=standard) as fixed effects and clinic is a random effect. A positive and significant coefficient for arm would provide support for the effectiveness of the intervention. We will do a moderator analysis at all levels to explore the impact of patient and clinics characteristics (see outcomes table above), and implementation components affecting outreach on completion likelihood in groups of patients determined at analysis (e.g. never screened, Hispanic, etc.).

10.0 ETHICAL AND REGULATORY REQUIREMENTS

10.1 Protocol Review

The protocol and informed consent form for this study must be reviewed and approved in writing by the OHSU Knight Cancer Institute (Knight) Clinical Research Review Committee (CRRC) and appropriate Institutional Review Board (IRB) prior to any patient being registered on this study.

10.2 Informed Consent

We are requesting a waiver of documentation of written consent for participation in the main trial. The waiver of informed consent is requested because CRC screening is standard care and all activities proposed to be undertaken with the research project are minimal risk. There are no interventions or other procedures for participants for which written documentation of consent is normally required for research activities.

We intend to collect verbal consent from participants who participate in qualitative interviews. Researchers will disseminate an information sheet for the surveys and interviews and will obtain verbal consent from participants before continuing with the study interview. Completion of the survey will serve as consent to participate. We will obtain verbal consent prior to the interview.

The research team will conduct chart review for all participants who are eligible for CRC screening. The high number of charts to be reviewed renders contact of each individual to obtain written authorization impractical as contact information may not be available and the time and resources it will require to obtain written consent is not commensurate with a low-risk chart audit review. A Waiver of Authorization for the chart review components of this study is included with the application. All data collected via chart audit will be handled per section 10.4.

10.3 Changes to Protocol

Any modification of this protocol must be documented in the form of a protocol revision or amendment signed by the principal investigator and approved by the CRRC and IRB, before the revision or amendment may be implemented. The only circumstance in which the amendment may be initiated without regulatory approval is for a change necessary to eliminate an apparent and immediate hazard to the patient. In that event, the investigator must notify the CRRC and IRB in writing within 5 working days after the implementation. Investigators holding the IND must notify FDA of substantive changes to the protocol.

10.4 Privacy, Confidentiality, and Data Security

This research study involves minimal risk to human subjects. The magnitude of harm or discomfort anticipated in the proposed research is not greater in and of itself than that ordinarily encountered in everyday life. The information sheet will describe the project purpose, study activities, participant's rights, benefits, and who to contact with questions and will be used to obtain consent.

Data entered or sent to the study offices will be handled in a highly confidential manner consistent with the high standards established at OHSU and ORPRN. Data presented in all presentations and publications will not be associated with the name of any participating person or practice. All computer systems at OHSU and ORPRN are protected from possible external access using network security systems. Only study researchers and staff at ORPRN and Kaiser Permanente will have access to the data. We will use industry standard Secure Sockets Layer (SSL) technology with server and client certificates to insure the confidentiality of data use and any data transfer.

Surveys and interview transcripts will be de-identified; unique numerical identifiers will be assigned for clinic and practice participants. The audio recordings from interviews will be destroyed after analysis. Text files will be stored in a password protected, encrypted computer file on a secure workstation at OHSU.

10.4a. Risks and Benefits

- Risks to Subjects

There is minimal foreseeable risk, discomfort, hazard, or inconvenience to the subjects relating to this chart review. There is a minimal risk of breach of confidentiality. The unlikely event of a loss of confidentiality could occur through a data transfer oversite.

- Potential Benefits to Subjects

There are no direct benefits to subjects.

10.5 Maintenance of Records

Study data will be stored on OHSU's secure Box.com.

If the investigator relocates or for any reason withdraws from the study, the study records will be transferred to OHSU Knight Cancer Institute Clinical Research Management. Records will be maintained according to sponsor requirements.

OHSU is one of multiple study sites funded by the National Cancer Institute (NCI) through this funding opportunity called the Accelerating Colorectal Cancer Screening and Follow-up through Implementation Science (ACCSIS). NCI is establishing a data use agreement with each ACCSIS grantee for submission of a limited consolidated data set in order for NCI to establish a repository for further evaluation of funded activities.

10.6 OHSU IRB Reporting of Unanticipated Problems and Adverse Events

Unanticipated Problems (UP) and Adverse Events (AE) will be reported to IRB according to the policies, procedures and guidelines posted on the OHSU IRB web site:

- Fatal and life-threatening UP will be reported to OHSU IRB within 5 days of notification of the event. All other UP reports will also be submitted to OHSU IRB no later than 5 days of occurrence or notification of the event. Copies of the report documents will be kept in the study regulatory binder.
- UP and AE reports are submitted through OHSU eIRB and will be reviewed by OHSU Knight Cancer Institute and IRB. Monthly accumulative reports will be reviewed by a DSMC Oncologist and forwarded to the CRRC.

10.7 MedWatch Reporting

Not applicable.

10.8 OHSU Knight Cancer Institute Data and Safety Monitoring Plan

Not applicable. Patients will not be treated under this protocol.

10.9 Inclusion of Women, Minorities and Children

The projected gender, racial, and ethnic composition of the study will represent that of the state of Oregon.

Table 1: Population Demographics - Oregon (%)

Ethnic Category	**Sex/Gender**		
	Females	Males	Total
Hispanic or Latino	5.85	5.85	11.7
Not Hispanic or Latino	44.15	44.15	88.3
Ethnic Category: Total of all subjects*	50	50	100*
Racial Category			
American Indian or Alaskan Native	0-1	0-1	1.4
Asian	1.85	1.85	3.7
Black or African American	0-1	0-1	1.8
Native Hawaiian or other Pacific Islander	0-1	0-1	0.3
White	41.8	41.8	83.6
More than one race	1.9	1.9	3.8
Unknown/Other	2.65	2.65	5.3
Racial Category: Total of all subjects*	50	50	100*
TOTALS	50.4	49.6	100*

Source: U.S. Census Bureau, 2010 *Totals may not equal 100 due to rounding.

Table 2: Projected Accrual for the Present Study

Ethnic Category	**Sex/Gender**			
	Females	Males	Unknown	Total
Hispanic or Latino	1,159	1,141	-	2,299
Not Hispanic or Latino	7,756	7,633	-	15,389
Unknown	-	-	-	-
Ethnic Category: Total of all subjects*	8,915	8,774	-	17,688
Racial Category				
American Indian or Alaskan Native	178	176	-	354

Ethnic Category	Sex/Gender			
	Females	Males	Unknown	Total
Asian	356	351	-	708
Black or African American	178	176	-	354
Native Hawaiian or other Pacific Islander	90	87	-	177
White	7,756	7,632	-	15,389
More than one race	356	351	-	708
Unknown	-	-	-	-
Racial Category: Total of all subjects*	8,915	8,774	-	17,688*

Source: Adapted from U.S. Census Bureau, 2010 *Totals may not equal 100 due to rounding.

10.10 Inclusion of Children

This protocol does not include children for the following reason: We are surveying and interviewing adult staff working in primary care practices and CCOs. Patients who are interviewed are in the CRC screening-eligible population (50-75 years old).

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12.0 APPENDIX I - TOXICITY CRITERIA

Not applicable.