Pennsylvania State University, College of Medicine, Department of Family and Community Medicine Research Division	
Document	Protocol
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HRP-591 - Protocol for
Human Subject Research

Protocol Title:
Increasing cancer screening among women in rural and segregated areas: A multilevel intervention based on self-screening and adapted educational materials

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1.0 Objectives

1.1 Study Objectives

In this study, we will deliver self-sampling HPV tests and FIT kits, as well as adapted cancer screening educational materials, by mail to 110 women who are out-of-date for both cervical and colorectal cancer screenings, recruited through federally qualified health centers (FQHCs) in rural, segregated counties of Pennsylvania. A control group of 110 women, also recruited through FQHCs in rural, segregated counties of Pennsylvania, will be used for comparison; these women will receive standard-of-care reminders for cancer screening and complete the baseline and follow-up surveys.

The hypothesis is that delivering self-sampling HPV tests and FIT, as well as adapted educational materials, to women in rural, segregated areas could help overcome environment- and person-level barriers and thereby increase cancer screening, reduce geographic cancer disparities, and improve public health.

1.2 Primary Study Endpoints

Differences in overall cervical cancer screening rate and the overall colorectal cancer screening rate at the end of the study between the two arms.

2.0 Background

2.1 Scientific Background and Gaps

In 2018, an estimated 4,100 women in the United States died from cervical cancer, and 23,240 women died from colorectal cancer.[1] It is possible to prevent many of these deaths through screening (e.g., with the human papillomavirus [HPV] test for cervical cancer or fecal immunochemical test [FIT] for colorectal cancer).[2,3] Women ages 50-65 are eligible for routine screening for both cancers, yet screening for both cancers falls below national goals. Mortality and screening patterns for these cancers vary by geographic factors. For example, colorectal cancer mortality is 16% higher,[4] and screening is 9% lower,[5] in rural than in urban areas. Furthermore, urban/rural differences in screening may be greatest in areas that are also racially segregated,[6] i.e., areas with high spatial concentrations of a given racial group.

Women in areas that are both rural and segregated face unique barriers to screening for cervical and colorectal cancers. Social Cognitive Theory[7] posits that environment-, person-, and behavior-level factors influence health. Interventions that target determinants at only one level fail to adequately address screening barriers and to account for geographic differences in behaviors.

2.2 Previous Data

The principal investigator (PI) has conducted several studies on geographic disparities in cancer prevention and control relevant to this proposal. Most broadly, the PI published a research study demonstrating that, while cancer incidence is only 3% higher in rural compared to metropolitan areas, cancer mortality is 10% higher[4]; this mortality disparity increases to 13% for cervical cancer and 16% for colorectal cancer. Another study focused on cervical cancer described a clustering of risks for women in rural areas, including lower density of primary care providers, lower participation in Pap screening, and higher cervical cancer incidence.[8] Further, the authors demonstrated that eliminating urban/rural differences in access to and utilization of screening would completely eliminate the disparity in incidence.

The PI has also led research studies that incorporate other dimensions of the social environment into the analysis of rural cancer control (e.g., socioeconomic status, racial residential segregation). The PI has

a forthcoming study describing urban/rural differences in cervical and colorectal cancer screening, which were greatest in counties that were highly racially segregated (Moss & Landrine, *in prep*). In addition, an upcoming study describes geographic patterns in "complete" participation in cancer screening, i.e., receiving all of the recommended screenings for a given gender and age group (Moss & Cronin, *in prep*). The finding most relevant to this proposal is that more than 50% of women ages 45-65 living in rural and highly-segregated counties were out-of-date with both cervical and colorectal cancer screenings. Extending these findings, the PI and collaborators have demonstrated that cancer risk perceptions, healthcare access, and participation in cervical cancer screening were lowest in areas that were both rural and segregated (although colorectal cancer screening was lower in rural areas, the interaction between rurality and segregation did not reach statistical significance)[9].

Most recently, the PI has conducted several formative research studies of the target population, including surveys, in-depth interviews, and focus groups. These studies aimed to identify factors that affect cancer screening within rural, segregated counties of Pennsylvania. These studies are in the final phases of data collection and analysis. Preliminary results show that the target study population is receptive to using home cancer screening kits for both cervical and colorectal cancer (>90% willing to use a self-sampling test). Person- and environment-level barriers to care have been identified. Finally, data collected during the focus groups were used to tailor the educational materials that will be utilized in the proposed study.

Taken together, these preliminary studies emphasize the urgent need for interventions to improve cervical and colorectal cancer screening behaviors in these communities. Individual-level barriers (e.g., attitudes) and environment-level barriers (e.g., access to care) both play an important role in explaining the associations of screening with rurality and racial residential segregation.

2.3 Study Rationale

The impact of the proposed project is to improve cancer screening in vulnerable communities, specifically women living in rural, segregated areas of Pennsylvania through the use of home cancer screening kits for cervical and colorectal cancer. This will be achieved through the use of adapted educational materials while addressing environment- and person-level barriers to screening.

For the purposes of this study, target areas are those designated as "rural" by the United States Department of Agriculture and with a dissimilarity index of racial residential segregation greater than the national mean. These counties in Pennsylvania include Clarion, Clearfield, Crawford, Forest, Greene, Huntingdon, Indiana, Lawrence, McKean, Northumberland, Schuylkill, Somerset, Union, and Wayne.

3.0 Inclusion and Exclusion Criteria

3.1 Inclusion Criteria

1. Female
2. 50-65 years of age at time of study enrollment
3. Lives in rural, segregated county of Pennsylvania
4. Able to speak, read, and communicate well in English
5. Out of date for both cervical and colorectal cancer screening
6. Active patient at selected Primary Health Network clinics

3.2 Exclusion Criteria

1. Has had a partial or complete hysterectomy
2. Has a family history of colorectal cancer (family member diagnosed 40 years of age or younger)
3. Has a personal history of cervical or colorectal cancer
4. Males

5. Persons who are cognitively impaired
6. Persons who are incarcerated

3.3 Early Withdrawal of Subjects

3.3.1 Criteria for removal from study

There are no foreseeable reasons why a study participant might be removed by the investigators from the study. Participants can voluntarily withdraw from the study at any time and for any reason.

3.3.2 Follow-up for withdrawn subjects

The withdrawal will be documented and the subject will be replaced if the timeline allows.

4.0 Recruitment Methods

4.1 Identification of subjects

Potentially-eligible women will be identified from the electronic health record (EHR) of partner FQHC clinics by an employee of the FQHC.

4.2 Recruitment process

4.2.1 How potential subjects will be recruited.

Once identified via the means listed under section 4.1, an employee of the FQHC will send all potentially-eligible women an initial invitation letter and email to participate in the study. This initial invitation letter will include information from both the FQHC and the study team, and will be signed by both the PI and a representative of the FQHC. Included in this mailing will be directions about how to contact the study team if interested in study participation, and a copy of the summary explanation of research. The email will contain the same information as the letter, but without the summary explanation of research as this cannot be sent as an attached file. The email message will indicate that the summary explanation of research document has been included in the mailed invitation they have received. If the response rate is low, as assessed 6 weeks after mailing the initial invitation letter, an employee of the FQHC will do follow-up calls to women who were initially contacted but did not respond to the initial invitation letter or email.

4.2.2 Where potential subjects will be recruited.

Potential participants will be recruited from participating FQHC patient populations using EHR data.

4.2.3 When potential subjects will be recruited.

An employee of the FQHC will contact potentially-eligible women by mail and email using the initial invitation letter within one month of identification from the EHR data. Interested women will contact a member of the study team to express their desire to participate in the study via phone, email, the study website, or by completing and returning an included post card. A member of the study team will follow-up with the potentially-eligible women by phone to screen for eligibility and complete the baseline survey.

4.2.4 Describe the eligibility screening process and indicate whether the screening process will occur before or after obtaining informed consent. Screening begins when the investigator obtains information about or from a prospective participant in order to determine their eligibility. In some studies, these procedures may not take place unless HIPAA Authorization is obtained OR a waiver of HIPAA Authorization when applicable for the screening procedures

is approved by the IRB. [*For FDA regulated studies, consent for any screening activities would need to be obtained prior to screening unless specifically waived by the IRB.]*

A member of the study team will contact potentially-eligible women by phone to discuss the study, screen for eligibility, and obtain verbal consent from interested individuals.

5.0 Consent Process and Documentation

5.1 Consent Process:

Check all applicable boxes below:

☐ **Informed consent will be sought and documented with a written consent form *[Complete Sections 5.2 and 5.6]***

☒ **Implied or verbal consent will be obtained – subjects will not sign a consent form (waiver of written documentation of consent) *[Complete Sections 5.2, 5.3 and 5.6]***

☐ **Informed consent will be sought but some of the elements of informed consent will be omitted or altered (e.g., deception). *[Complete section 5.2, 5.4 and 5.6]***

☐ **Informed consent will not be obtained – request to completely waive the informed consent requirement. *[Complete Section 5.5]***

The following checkbox is for all locations EXCEPT Penn State Health and College of Medicine:

☐ **<u>Exempt Research at all Locations Except Penn State Health and the College of Medicine</u>: If you believe that the research activities outlined meet one or more of the criteria outlined in "HRP-312- Worksheet- Exemption Determination." Please verify by checking this box that if conducting an exempt research study, the consent process will disclose the following (all of which are included in "HRP-590- Consent Guidance for Exempt Research"):**

Penn State affiliation; name and contact information for the researcher and advisor (if the researcher is a student); the activities involve research; the procedures to be performed; participation is voluntary; that there are adequate provisions to maintain the privacy interests of subjects and the confidentiality of the data; and subjects may choose not to answer specific questions.

If the research includes the use of student educational records include the following language in this section (otherwise delete): The parent or eligible student will provide a signed and dated written consent that discloses: the records that may be disclosed; the purpose of the disclosure; the party or class of parties to whom the disclosure may be made; if a parent or adult student requests, the school will provide him or her with a copy of the records disclosed; if the parent of a student who is not an adult so requests, the school will provide the student with a copy of the records disclosed.

Note: If this box has been checked, skip the remainder of section 5 and proceed to section 6 of this protocol. If the investigator's assessment is inaccurate, an IRB Analyst will request revision to the protocol and that an informed consent form be submitted for review and approval. Except for exemptions where Limited IRB Review (see "HRP-312- Worksheet- Exemption Determination") is required or where otherwise requested by the IRB, informed consent forms for research activities determined to be exempt without Limited IRB Review are generally not required to be submitted for review and approval by the University Park IRB.

5.2 Obtaining Informed Consent

5.2.1 Timing and Location of Consent

Participants will be consented by a member of the research team over the phone, after eligibility is confirmed, using the Summary Explanation of Research. Participants will have previously received a copy of the Summary Explanation of Research in the mail with recruitment materials.

5.2.2 Coercion or Undue Influence during Consent

After a review of the research study via the Summary Explanation of Research, participants will be asked if they would like to continue to participate in the baseline survey. They will be reminded that participation in the study will not alter or impact their care in any way. Participants will be reminded that they may refuse to answer any question, and may end their participation at any time.

5.3 Waiver of Written Documentation of Consent

5.3.1 Indicate which of the following conditions applies to this research:

☒ The research presents no more that minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

OR

☐ The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern. (*Note: This condition is not applicable for FDA-regulated research. If this category is chosen, include copies of a consent form and /or parental permission form for participants who want written documentation linking them to the research.)*

OR

☐ If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained. (*Note: This condition is not applicable for FDA-regulated research.)*

Describe the alternative mechanism for documenting that informed consent was obtained:

5.3.2 Indicate what materials, if any, will be used to inform potential subjects about the research (e.g., a letter accompanying a questionnaire, verbal script, implied consent form, or summary explanation of the research)

Potential participants identified via the means outlined in section 4.1 will receive the initial invitation letter, initial invitation email, and the initial invitation post card inviting them to participate in the research. These documents will direct them to the study team website (research.med.psu.edu/casper). The FQHC recruitment script will be used to as a secondary means of recruitment, if necessary. The summary explanation of research will be sent to participants with the mailed recruitment materials.

5.4 Informed consent will be sought but some of the elements of informed consent will be omitted or altered (e.g., deception).

5.4.1 Indicate the elements of informed consent to be omitted or altered

Not applicable.

5.4.2 Indicate why the research could not practicably be carried out without the omission or alteration of consent elements

Not applicable.

5.4.3 Describe why the research involves no more than minimal risk to subjects.

Not applicable.

5.4.4 Describe why the alteration/omission will not adversely affect the rights and welfare of subjects.

Not applicable.

5.4.5 If the research involves using identifiable private information or identifiable biospecimens, describe why the research could not be practicably be carried out without using such information or biospecimens in an identifiable format.

Not applicable.

5.4.6 Debriefing

Not applicable.

5.5 Informed consent will not be obtained – request to completely waive the informed consent requirement

5.5.1 Indicate why the research could not practicably be carried out without the waiver of consent

Not applicable.

5.5.2 Describe why the research involves no more than minimal risk to subjects.

Not applicable.

5.5.3 Describe why the alteration/omission will not adversely affect the rights and welfare of subjects.

Not applicable.

5.5.4 If the research involves using identifiable private information or identifiable biospecimens, describe why the research could not be practicably be carried out without using such information or biospecimens in an identifiable format.

Not applicable.

5.5.5 Additional pertinent information after participation

Not applicable.

5.6 Consent – Other Considerations

5.6.1 Non-English-Speaking Subjects

Not applicable.

5.6.2 Cognitively Impaired Adults

5.6.2.1 Capability of Providing Consent

Not applicable.

5.6.2.2 Adults Unable to Consent

Not applicable.

5.6.2.3 Assent of Adults Unable to Consent

Not applicable.

5.6.3 Subjects who are not yet adults (infants, children, teenagers)

5.6.3.1 Parental Permission

Not applicable.

5.6.3.2 Assent of subjects who are not yet adults

Not applicable.

6.0 HIPAA Research Authorization and/or Waiver or Alteration of Authorization

6.1 Authorization and/or Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

Check all that apply:

☐ **Not applicable, no identifiable protected health information (PHI) is accessed, used or disclosed in this study.** *[Mark all parts of sections 6.2 and 6.3 as not applicable]*

☐ **Authorization will be obtained and documented as part of the consent process.** *[If this is the only box checked, mark sections 6.2 and 6.3 as not applicable]*

☐ **Partial waiver is requested for recruitment purposes only (Check this box if patients' medical records will be accessed to determine eligibility before consent/authorization has been obtained).** *[Complete all parts of sections 6.2 and 6.3]*

☐ **Full waiver is requested for entire research study (e.g., medical record review studies).** *[Complete all parts of sections 6.2 and 6.3]*

☒ **Alteration is requested to waive requirement for written documentation of authorization (verbal authorization will be obtained).** *[Complete all parts of sections 6.2 and 6.3]*

6.2 Waiver or Alteration of Authorization for the Uses and Disclosures of PHI

6.2.1 Access, use or disclosure of PHI representing no more than a minimal risk to the privacy of the individual

6.2.1.1 Plan to protect PHI from improper use or disclosure

Information is included in the "Confidentiality, Privacy and Data Management" section of this protocol.

6.2.1.2 Plan to destroy identifiers or a justification for retaining identifiers

Identifying information will be destroyed after the completion of data analysis.

6.2.2 Explanation for why the research could not practicably be conducted without access to and use of PHI

PHI is necessary for processing the self-sampling tests. Participant date of birth is required when completing the Pathology Services Special Account Requisition form. Thus, the research question regarding completion of self-sampling tests cannot be answered without use of PHI. Additionally, participant address and email address is necessary for mailing study materials and compensation.

6.2.3 Explanation for why the research could not practicably be conducted without the waiver or alteration of authorization

Alteration of authorization is necessary since participants will be giving hipaa authorization via verbal consent, over the phone prior to data collection. All data collection for the proposed study will be conducted over the phone; written consent is not feasible since none of the study activities will not be in person.

6.3 Waiver or alteration of authorization statements of agreement

Protected health information obtained as part of this research will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other permitted uses and disclosures according to federal regulations.

The research team will collect only information essential to the study and in accord with the 'Minimum Necessary' standard (information reasonably necessary to accomplish the objectives of the research) per federal regulations.

Access to the information will be limited, to the greatest extent possible, within the research team. All disclosures or releases of identifiable information granted under this waiver will be accounted for and documented.

7.0 Study Design and Procedures

7.1 Study Design

The study is a prospective, two-arm, randomized intervention. Participants will be randomized to receive either (1) a standardized letter informing them that they are out-of-date for both cervical and colorectal cancer screenings and should schedule an appointment with their provider to receive these screenings, i.e., standard of care (control arm), or (2) cervical and colorectal cancer self-sampling kits, instructions for completing the self-sampling kits, and educational materials about cervical and colorectal cancer (intervention arm). Participants in the intervention arm will mail their completed self-sampling kits to the Penn State Health Clinical Labs for processing; FIT kits will then be sent to and processed by Quest diagnostics. All participants will complete a baseline and follow-up survey.

7.2 Study Procedures

7.2.1 Baseline survey- Week 0

Once a participant has been identified, recruited, and consented as described above, she will complete the baseline survey with a member of the study team via phone. After completion of the baseline survey, the participant will receive a thank you letter from the study team.

7.2.2 Randomization- Week 0

Once a participant has completed the baseline survey, she will be randomly assigned to either the control arm or the intervention arm by a member of the study team. A simple randomization scheme, with 1:1 randomization, will be used to ensure equal sample sizes in the intervention and control arms.

7.2.3 Control arm- Week 1

Participants randomized into the control arm will be mailed a standardized letter informing them that they are out-of-date for both cervical and colorectal cancer screenings and should schedule an appointment with their provider to receive these screenings.

7.2.4 Intervention arm- Week 1

Participants randomized into the intervention arm will be mailed cervical and colorectal cancer self-sampling kits, instructions for completing the self-sampling kits, a lab requisition form, and educational materials about cervical and colorectal cancer. Participants will also receive an intervention cover letter that describes the contents of the package and what they are being asked to do. Participants will be asked to complete both cervical and colorectal cancer self-sampling kits within 3 days of each other via the intervention cover letter. Once complete, participants will mail the kits within 3 days of completing both tests to the Penn State Hershey Clinical Labs in a prepaid mailer provided by the study team. Notably, deviations from the timing of sampling and returning the test kits is quite flexible, since studies show that these samples are stable for up to 28 days.

7.2.4.1 Reminder postcard- Week 6

Participants who have not completed and returned both their cervical and colorectal cancer self-sampling kits within 6 weeks of receipt of kits will be mailed a reminder letter from the study team.

7.2.5 Follow-up survey- Week 10

Participants will complete the follow-up survey with a member of the study team via phone. This will occur regardless of whether the participant was in the intervention or the control arm, and regardless of whether the participant completed and returned the self-sampling kits if in the intervention arm.

7.3 Duration of Participation

Participants will be considered enrolled in the study from the time of consent until the completion of the follow-up survey. We anticipate a total participation of approximately 1 hour and 35 minutes for those in the intervention arm over the course of 10 weeks; this includes ~45 minutes to complete the baseline survey, ~20 minutes for the follow-up survey and up to ~15 minutes to complete each cervical

and colorectal cancer screening test kits. We anticipate a total participation of approximately 1 hour and 5 minutes for those in the control arm, over the course of 10 weeks; this includes ~45 minutes to complete the baseline survey and ~20 minutes for the follow-up survey.

7.4 Test Article(s) (Study Drug(s) and/or Study Device(s))

7.4.1 Description

The Evalyn® Brush is a self-sampling kit that screens for HPV, a leading cause of cancer death among women. This tool has recently been FDA approved, but has not been incorporated into national clinical guidelines. This product is a small pink capped brush that can be used to take a sample of cervical cells.

The InSure® test (Fecal Globin by Immunochemistry) is a fecal occult blood test that detects human hemoglobin from blood in fecal samples. The test is recommended for use by healthcare professionals to screen for colorectal cancer.

7.4.2 Treatment Regimen

Participants will take a sample of their cervix cells that amounts to a few millimeters of bio specimen.

Participants will collect a fecal sample from toilet water using the provided tools and brush the sample on the InSure® FOBT test card.

7.4.3 Method for Assigning Subject to Treatment Groups

Once a participant has completed the baseline survey, she will be randomly assigned to either the control arm or the intervention arm by a member of the study team. A simple randomization scheme, with 1:1 randomization, will be used to ensure equal sample sizes in the intervention and control arms.

7.4.4 Subject Compliance Monitoring

Subject compliance will be confirmed once their lab results are received from the Penn State Heath Clinical lab.

7.4.5 Blinding of the Test Articles

Not applicable.

7.4.6 Receiving, Storage, Dispensing and Return

7.4.6.1 Receipt of Test Article

HPV self-sampling kits (Evalyn Brush, Rovers Medical Devices) are purchased from the manufacturer and shipped to the PI's office at Penn State Health. The study test article will be mailed to each participant in the intervention arm in original, unopened packaging, including 1 brush, 1 protective cap, 1 container/package for the brush, and 1 plastic bag for return mailing. The mailing will also include a lab requisition form (including a unique participant ID) to link each participant with their returned test kit.

FIT kits (InSure test, Fecal Globin by Immunochemistry) are purchased through Quest Diagnostics and shipped to the PI's office at Penn State Health. The study test article will be mailed to each participant in the intervention arm in original, unopened packaging, including 1 sample card, 1

collection brush, 1 self-adhesive label, and 1 reply form. The mailing will also include a lab requisition form (including a unique participant ID) to link each participant with their returned test kit.

The mailing will also include a pre-stamped and pre-addressed return shipping container for the participant to use to mail both kits to the PSH Clinical Lab. The unique participant ID will also be printed on this envelope and other participant materials.

7.4.6.2 Storage

Before HPV self-sampling kits are sent to study participants, they will be stored in a locked cabinet in the Department of Family and Community Medicine offices at 134 Sipe Ave. Kits mailed to the lab will be disposed of after analysis.

Before colorectal self-sampling kits are sent to study participants, they will be stored in a locked cabinet in the Department of Family and Community Medicine offices at 134 Sipe Ave. Kits mailed to the lab will be disposed of after analysis.

7.4.6.3 Preparation and Dispensing

Before it is sent to the participant, the Penn State Heath Clinical lab Pathology Services Special Account Requisition documents will be labeled with the participant's study ID #, date of birth, and sex (as required by the Requisition form). The mailing will include the HPV self-sampling kit with the instructions, the colorectal cancer self-sampling kit with the instructions, a Penn State Heath Clinical lab Pathology Services Special Account Requisition form, educational materials regarding the use of home cancer screening kits, and an intervention cover letter.

The package will also include a prepaid and labeled mailing to send the kits and Pathology Services Special Account Requisition documents to the Penn State Heath Clinical lab. Participants will need to include the date and time of sample collection on the requisition form.

7.4.6.4 Return or Destruction of the Test Article

HPV self-sampling kits will not be returned to participants. The samples will be analyzed and the kits will be destroyed by the Penn State Heath Clinical lab once analysis is complete.

Colorectal cancer self-sampling kits will not be returned to participants. The samples will be analyzed and the kits will be destroyed by the Quest Diagnostics once analysis is complete.

7.4.6.5 Prior and Concomitant Therapy

Not applicable.

8.0 Subject Numbers and Statistical Plan

8.1 Number of Subjects

We plan to contact 500 potentially-eligible women via mail and email using the initial invitation letter. Of these, 220 are planned to consent and complete the baseline survey. From this 220, 110 will be randomized to the control group and 110 will be randomized to the intervention group. We expect about 10% loss to follow-up over the study period.

8.2 Sample size determination

This is a pilot study to approximate the rates of colorectal and cervical screening in the two study arms. Should the intervention yield a screening rate of 40% and the control arm a screening rate of 20%, then the proposed sample sizes yield 80% power based on a two-sided Fisher's exact test and a 2.5% type-1 error rate (allowing for two co-primary endpoints). The results of this pilot study will inform us with more accurate assessments of these screening rates so that future, more accurately powered studies can be conducted.

8.3 Statistical methods

The statistical analysis of study outcomes will primarily be descriptive. Outcomes will be assessed via the baseline and follow-up surveys, and whether or not self-sampling kits were returned by participants in the intervention arm. The main outcome is the differences in overall cervical cancer screening rate and the overall colorectal cancer screening rate at the end of the study between the two arms. Analysis of the main outcomes will be evaluated with a Fisher's exact test. Demographics of the patients in the two groups will be compared.

9.0 Data and Safety Monitoring Plan

9.1 Periodic evaluation of data

Not applicable.

9.2 Data that are reviewed

Not applicable.

9.3 Method of collection of safety information

Not applicable.

9.4 Frequency of data collection

Not applicable.

9.5 Individuals reviewing the data

Not applicable.

9.6 Frequency of review of cumulative data

Not applicable.

9.7 Statistical tests

Not applicable.

9.8 Suspension of research

Not applicable.

10.0 Risks

The greatest potential risk to participants is psychological harm of cancer screening. Some participants may experience anxiety while collecting the screening samples or awaiting screening results. Studies have demonstrated that this anxiety is transient[10]. Financial, legal, or other risks are not anticipated.

For participants who complete the self-sampling test for cervical cancer, there is a risk of minor internal damage that may occur when collecting the sample. The minor internal damage is transient and resolves itself. There are no foreseeable physical risks for completing the self-sampling test for colorectal cancer. For participants who screen positive on HPV test or FIT, additional risks are possible. Among 100 participants ages 50-65, we anticipate that up to 6 will screen positive on the HPV test [11] and up to 4 will screen positive on the FIT[12].

For participants with abnormal results on their screening tests, test results will be communicated to the participant via their medical provider at the FQHC following the standard of care, including encouraging her to seek follow-up care (e.g., additional screenings) at the FQHC or elsewhere. In addition, educational materials mailed to those in the intervention group will include recommended follow-up steps for women who receive abnormal results, specifically, seeking additional screening or diagnostic tests. These materials will encourage participants to reach out to their medical provider at the FQHCs for these tests (or for referral to specialists). Test results will be mailed to both the study team and the participating FQHC to ensure proper follow-up. These procedures should minimize the time it takes for participants to seek follow-up for abnormal screening results, therefore lowering the potential risks from an abnormal screening result. Should any participants be diagnosed with cervical or colorectal cancer, potential treatments for individuals with screen-detected versus symptomatic cancers are theoretically less risky.

Loss of confidentiality is a risk of participation. Disclosure of responses to survey items will not place participants at risk of criminal or civil liability or be damaging to their finances, employability, or reputation.

Protection against risks.
To protect against psychological risks associated with cancer screening, we will include information in the educational materials about (1) what screening tests examine, (2) what potential abnormal results could indicate, and (3) recommendations for follow-up after abnormal results.

In order to protect participant privacy (including survey responses and results of cancer screening tests), data will be maintained on a password-protected database on a secure network. A password-protected dataset containing participant identifying information will also be maintained on the secure network, but only the study team will have access to this dataset; this dataset will be destroyed after the study is complete.

11.0 Potential Benefits to Subjects and Others

11.1 Potential Benefits to Subjects

No direct benefits to subjects.

11.2 Potential Benefits to Others

The findings of this study can provide benefits to others in that they will inform future interventions, public health programs, and clinical practice to promote screening, earlier diagnosis, and increased survival of cervical and colorectal cancer, especially in vulnerable communities. In addition, the proposed research will benefit participants and others by contributing to scientific knowledge about the fields of health behaviors and cancer prevention. This knowledge has implications for improving clinical and public health generally, as well as specifically increasing cancer screening and, in the long-term, reducing disparities in, and the overall burden of, cervical and colorectal cancers.

12.0 Sharing Results with Subjects

Study findings will not be directly shared with participants by the study team. However, participants will be notified of their self-sampling results by their medical provider at the FQHC. Research study team members will receive the results of the self-sampling kit from the lab and communicate these results to a central administrative employee at the FQHC via Penn State Kiteworks. This individual will share the results with the participants' medical provider at the FQHC. The medical provider will then share these results with the participants via the standard of care as determined by the provider. PHN's policy regarding sharing test results with patients is as follows:
Once the results are received, the ordering providers must personally acknowledge receipt of the results with a signature and date and indicated if further action is needed.

a. Depending on the type of the test result, the ordering providers may communicate results to the patients or may request that a clinical staff member contact the patient with results and any follow-up instructions. All patient communication is to be documented in the EMR.
b. When the patient must take action in response to the results, direct verbal communication should be used. Documentation should reflect that the information was received and understood by the patient. If the patient cannot be reached, reasonable attempts should be made, this includes using phone outreach and mailed letter attempts. All attempts should be documented in the medical record.

For abnormal results:
1. An attempt to communicate results to the patient must be initiated within 14 days of receiving results. Follow up instructions should be provided via verbal communication.
2. If the patient is not able to reached in person or by phone, a standard 'test result' letter found in our EMR, indicating the need for the patient to contact the office will be mailed to the patient.

13.0 Subject Payment and/or Travel Reimbursements

The study team has received an exception from using Greenphire ClinCards from the Controller. Physical or electronic retailer gift cards to reimburse participants will be purchased through Shop OnLion.

Subjects will receive a total of $50 in Walmart gift cards for their participation. A $20 Walmart gift card will be provided upon completion of the baseline survey and a $30 Walmart gift card will be provided upon completion of the follow-up survey, regardless of whether the self-sampling kits are returned. All gift cards will be electronic unless a physical gift card is requested by the participant.

14.0 Economic Burden to Subjects

14.1 Costs

There are no costs that subjects may be responsible for because of participation in this research. All necessary costs will be covered by the research study.

14.2 Compensation for research-related injury

Not applicable.

15.0 Resources Available

15.1 Facilities and locations

Participants will be recruited through collaborating FQHCs in eligible counties. These counties include: Crawford, Lawrence, Greene, Forest, Clarion, McKean, Clearfield, Indiana, Somerset, Huntingdon, Union, Northumberland, Schuylkill, and Wayne. FQHCs have been identified by the Pennsylvania Association of Community Health Centers. A letter of support that states participating clinic locations, provided by the partner FQHC, is available for review in the attached letters of agreement.

15.2 Feasibility of recruiting the required number of subjects

Community Health Centers see thousands of patients annually. Our partner FQHC sees close to 85,000 patients annually across all clinics, and sees roughly 1,800 women in our target population (women ages 50-65) at participating clinics. We seek to recruit 220 members of this target population.

15.3 PI Time devoted to conducting the research

The PI will utilize dedicated research time to conduct this research.

15.4 Availability of medical or psychological resources

Any participant requiring medical or psychological resources as a result of participating in this study will be referred to the Primary Health Network clinic where they receive care. These resources might include follow-up procedures or any other preventive/screening services they need."

15.5 Process for informing Study Team

The research team will meet regularly to discuss this study, study procedures, and any issues that may arise. All team members will receive in-depth protocol training before performing any study-related tasks.

16.0 Other Approvals

16.1 Other Approvals from External Entities

This research proposal has been reviewed by the National Institutes of Health, which is the funding agency for the study, during the grant review process. Each FQHC has provided approvals to confirm their participation in this study as noted in the attached letters of agreement.

16.2 Internal PSU Committee Approvals

Check all that apply:

☐ Anatomic Pathology – **Penn State** Health **only** – Research involves the collection of tissues or use of pathologic specimens. Upload a copy of "HRP-902 - Human Tissue For Research Form" in CATS IRB.

☐ Animal Care and Use – **All campuses** – Human research involves animals and humans or the use of human tissues in animals

☐ Biosafety – **All campuses** – Research involves biohazardous materials (human biological specimens in a PSU research lab, biological toxins, carcinogens, infectious agents, recombinant viruses or DNA or gene therapy).

☒ Clinical Laboratories – **Penn State Health only** – Collection, processing and/or storage of extra tubes of body fluid specimens for research purposes by the Clinical Laboratories; and/or use of body fluids that had been collected for clinical purposes but are no longer needed for clinical use. Upload a copy of "HRP-901 - Human Body Fluids for Research Form" in CATS IRB.

☐ Clinical Research Center (CRC) Advisory Committee – **All campuses** – Research involves the use of CRC services in any way.

☐ Conflict of Interest Review – **All campuses** – Research has one or more of study team members indicated as having a financial interest.

☐ Radiation Safety – **Penn State Health only** – Research involves research-related radiation procedures. All research involving radiation procedures (standard of care and/or research-related) must upload a copy of "HRP-903 - Radiation Review Form" in CATS IRB.

☐ IND/IDE Audit – **All campuses** – Research in which the PSU researcher holds the IND or IDE or intends to hold the IND or IDE.

☒ Scientific Review – **Penn State Health only** – All investigator-written research studies requiring review by the convened IRB must provide documentation of scientific review with the IRB submission. The scientific review requirement may be fulfilled by one of the following: (1) external peer-review process; (2) department/institute scientific review committee; or (3) scientific review by the Clinical Research Center Advisory committee. NOTE: Review by the Penn State Health Cancer Institute (PSCI) Protocol Review Committee or the PSCI Disease Team is required if the study involves cancer prevention studies or cancer patients, records and/or tissues. For more information about this requirement see the IRB website.

17.0 Multi-Site Study

17.1 Other sites
Not applicable.

17.2 Communication Plans
Not applicable.

17.3 Data Submission and Security Plan
Not applicable.

17.4 Subject Enrollment
Not applicable.

17.5 Reporting of Adverse Events and New Information
Not applicable.

17.6 Audit and Monitoring Plans
Not applicable.

18.0 Adverse Event Reporting

18.1 Reporting Adverse Reactions and Unanticipated Problems to the Responsible IRB
In accordance with applicable policies of The Pennsylvania State University Institutional Review Board (IRB), the investigator will report, to the IRB, any observed or reported harm (adverse event) experienced by a subject or other individual, which in the opinion of the investigator is determined to be (1) unexpected; and (2) probably related to the research procedures. Harms (adverse events) will be submitted to the IRB in accordance with the IRB policies and procedures.

19.0 Study Monitoring, Auditing and Inspecting

19.1 Auditing and Inspecting
The investigator will permit study-related monitoring, audits, and inspections by the Penn State quality assurance program office(s), IRB, the sponsor, and government regulatory bodies, of all study related

documents (e.g., source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g., pharmacy, diagnostic laboratory, etc.).

20.0 Future Undetermined Research: Data and Specimen Banking

20.1 Data and/or specimens being stored

Not applicable.

20.2 Location of storage

Not applicable.

20.3 Duration of storage

Not applicable.

20.4 Access to data and/or specimens

Not applicable.

20.5 Procedures to release data or specimens

Not applicable.

20.6 Process for returning results

Not applicable.

21.0 References

1 Siegel, R. L., Miller, K. D. & Jemal, A. Cancer statistics, 2018. *CA Cancer J Clin* **68**, 7-30, doi:10.3322/caac.21442 (2018).

2 U. S. Preventive Services Task Force. *Final recommendation statement: Cervical cancer: Screening*, <https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/cervical-cancer-screening2> (2018).

3 U. S. Preventive Services Task Force. *Final recommendation statement: Colorectal cancer: Screening*, <https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/colorectal-cancer-screening2> (2016).

4 Blake, K. D., Moss, J. L., Gaysynsky, A., Srinivasan, S. & Croyle, R. T. Making the case for investment in rural cancer control: An analysis of rural cancer incidence, mortality, and funding trends. *Cancer Epidemiol Biomarkers Prev* (2017).

5 Cole, A. M., Jackson, J. E. & Doescher, M. Urban–rural disparities in colorectal cancer screening: cross-sectional analysis of 1998–2005 data from the Centers for Disease Control's Behavioral Risk Factor Surveillance Study. *Cancer medicine* **1**, 350-356 (2012).

6 Coughlin, S. S., King, J., Richards, T. B. & Ekwueme, D. U. Cervical cancer screening among women in metropolitan areas of the United States by individual-level and area-based measures of socioeconomic status, 2000 to 2002. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology* **15**, 2154-2159, doi:15/11/2154 [pii] (2006).

7 Bandura, A. Social cognitive theory. *Handbook of social psychological theories*, 349-373 (2011).

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9 Moss, J. L., Ehrenkranz, R., Perez, L. G., Hair, B. Y. & Julian, A. K. Geographic disparities in cancer screening and fatalism among a nationally representative sample of US adults. *J Epidemiol Community Health* **73**, 1128-1135, doi:10.1136/jech-2019-212425 (2019).

10 Wardle, J. *et al.* Psychological impact of colorectal cancer screening. *Health Psychol* **22**, 54-59, doi:10.1037//0278-6133.22.1.54 (2003).

11 Datta, S. D. *et al.* Human papillomavirus infection and cervical cytology in women screened for cervical cancer in the United States, 2003-2005. *Ann Intern Med* **148**, 493-500, doi:10.7326/0003-4819-148-7-200804010-00004 (2008).

12 Shin, H. Y. *et al.* Performance of the Fecal Immunochemical Test for Colorectal Cancer Screening Using Different Stool-Collection Devices: Preliminary Results from a Randomized Controlled Trial. *Gut Liver* **10**, 925-931, doi:10.5009/gnl15479 (2016).

22.0 Confidentiality, Privacy and Data Management

IMPORTANT: The following section is required for all locations EXCEPT Penn State Health and the College of Medicine. Penn State Health and College of Medicine should skip this section and complete "HRP-598 Research Data Plan Review Form." In order to avoid redundancy, for this section state "See the Research Data Plan Review Form" if you are conducting Penn State Health research. Delete all other sub-sections of section 22.

See the Research Data Plan Review Form.