Self-sampling to Optimize anal Lesion Outcomes (SOLO) Pilot

Short Title
SOLO Pilot

Pilot Study Principal Investigator
Alan G. Nyitray, PhD

ClinicalTrials.gov Number
NCT07085845

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Proprietary and Confidential

PILOT STUDY INVESTIGATORS' CONTACT INFORMATION

Project Long Title: Self-sampling to Optimize anal Lesion Outcomes (SOLO) Pilot

MCW Protocol No.: PRO00054186 (for parent SOLO study)

Principal Investigator:
Alan G. Nyitray, PhD
Associate Professor Epidemiology
Center for Cancer Discovery
Division of Community Health and Intervention Research
Department of Psychiatry and Behavioral Medicine
Medical College of Wisconsin
8701 Watertown Plank Road, N4643
Milwaukee WI 53189
Phone: 414-955-7701
Email: anyitray@mcw.edu

PILOT STUDY FUNDING

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VERSION HISTORY

Date Submitted	Date Approved	Version Revisions Author
22MAY2025	15JUL2025	1.0 Pilot None: This is the initial pilot protocol sent to the MCW IRB. Nyitray AG
25JUL2025	30JUL2025	Amendment to the ICF, protocol, and smartform to notify individuals that we will collect their street address to support payment using the MCW visa card.
10SEP2025	12SEP2025	-Add letter to participants who receive inadequate / unsatisfactory results -Modify letter to participants who receive an abnormal cytology result with HPV test results. -Change address of PI to new office address

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PILOT PROTOCOL SUMMARY

Title	Self-sampling to Optimize anal Lesion Outcomes (SOLO) Pilot
Principal Investigator	Alan G. Nyitray, PhD
Pilot Study Site	Milwaukee, WI a. Medical College of Wisconsin (MCW) Cancer Center / MCW Center for AIDS Intervention Research will enroll, randomize, collect data, and analyze all pilot data. b. Wisconsin Diagnostic Labs will perform cytopathology and HPV reflex testing for anal cytology swabs collected. Tampa, FL – Moffitt Cancer Center will conduct HPV genotyping on all swabs used in the pilot.
Clinical Trial Phase	Phase I
Pilot Study Population	Sexual and gender minorities (SGM) who have sex with men living with and without HIV.
Primary Objective	To ensure the use of a swab in SOLO that is comparable to the originally proposed swab for SOLO, determine the preliminary performance characteristics of the new NF swab in a feasibility study.
Primary Endpoints	1. A comparison of the proportions of individuals who collect squamocolumnar cells when using a NF swab with a 5 cm vs. a 3 cm insertion depth. 2. A comparison of the proportions of individuals who collect cytologically adequate specimens when using a NF swab with a 5 cm vs. a 3 cm insertion depth. 3. A comparison of the proportions of individuals who collect adequate specimens for molecular genotyping when using the new NF swab vs. the original swab used in the PAC Self-Swab Study. 4. A comparison of the acceptability and pain performance of the new NF swab vs. the original swab and the 5 cm and 3 cm insertion depth.
Pilot Study Design	Two-arm, randomized controlled trial
Eligibility Criteria	Eligibility See section 3.0
Pilot Study Intervention	Swabbing with a new nylon-flocked swab with an insertion depth of 5 cm.

Number of Subjects	60 participants
Estimated Time to Complete Accrual	Approximately 2 months
Subject Participation Duration	Approximately 30 minutes
Estimated Time to Primary Completion	Approximately 4 months
Estimated Time to Pilot Study Completion	Within 6 months of accrual initiation.

LIST OF ABBREVIATIONS

AE	adverse event
CASI	computer-assisted self-interview
HPV	human papillomavirus
IRB	institutional review board
NF	nylon-flocked
PHI	protected health information
PAC	Prevent Anal Cancer
SAE	serious adverse event
SCJ	squamocolumnar junction
SGM	sexual and gender minorities
SOLO	self-sampling to optimize anal lesion outcomes
UPIRSO	unanticipated problem involving risk to subject or other

A Background and Rationale

An important component of SOLO is the testing of two different kinds of swabs, nylon-flocked and Dacron, for molecular and cytological adequacy and end user acceptability within a self-sampling and clinician-sampling context. We chose a nylon-flocked (NF) swab for use in SOLO given its high adequacy in our prior study: the Prevent Anal Cancer (PAC) Self-Swab Study (R01 CA215403, PI: Nyitray); however, this NF swab is unlikely to be available for clinical use in the future due to recent changes in the manufacturer's priorities. Since SOLO results need to be widely generalizable and relevant to anal cancer screening, we need to use a different NF swab model and assess its cytological and molecular performance characteristics in a pilot study before beginning SOLO. Given our prior success with a NF swab developed by Copan Italia s.p.a. (Brescia, Italy) we will test the feasibility of a new Copan swab developed for anal cancer screening.

We will test the cytological performance of the swab at two insertion depths, 3 cm and 5 cm, to determine which insertion depth is better at collecting cells from the squamocolumnar junction (SCJ), an anatomic site that is particularly vulnerable to carcinogenic transformation. We hypothesize that the 5 cm insertion will result in a higher quality specimen with cells from the SCJ. However, the deeper swab insertion may affect end user acceptability without increasing adequacy or quality.

We will test the new swab with 60 individuals who were participants in the PAC Self-Swab Study and who agreed be contacted for follow-up studies. Individuals will be randomized to use the new NF swab with either a 3 cm or 5 cm insertion depth. After consenting, individuals will receive written instructions and then conduct the self-sampling in private. Staff will take the swab in PreservCyt to the Medical College of Wisconsin Tissue Bank where it will be aliquoted for assessment of cytology and reflex HIV testing at Wisconsin Diagnostic Labs and HPV genotype at Moffitt Cancer Center. We have one objective: To ensure the use of a swab in SOLO that is comparable to the originally proposed swab for SOLO, determine the preliminary performance characteristics of the new NF swab. We have three hypotheses within the objective:

- **H1**: A higher proportion of the new NF swabs with 5 cm insertion will have SCJ cells compared to the NF swab for 3 cm insertion.
- **H2:** A higher proportion of the new NF swabs with 5 cm insertion will be adequate for cytopathology interpretation compared to the NF swab for 3 cm insertion.
- **H3**: The new NF swab will have molecular adequacy that is commensurate with the original NF swab used in the PAC Self-Swab Study.
- **H4:** The new NF swab will have acceptability/pain performance commensurate with the originally proposed NF swab and the 5 cm insertion depth will have similar acceptability/pain performance as the 3 cm insertion depth.

Our ***expected outcomes*** are cytological and molecular preliminary performance characteristics of the new NF swab in addition to user acceptability. These outcomes will help ensure the use of a viable swab in SOLO that is relevant in future anal cancer screening programs.

B Pilot Study Objective and Endpoints

B.1 Pilot Study Objective

To ensure the use of a swab in SOLO that is comparable to the originally proposed swab for SOLO, determine the preliminary performance characteristics of the new NF swab.

B.2 Pilot Study Endpoints

1. A comparison of the proportions of individuals who collect squamocolumnar cells when using a NF swab with a 5 cm vs. a 3 cm insertion depth.

2. A comparison of the proportions of individuals who collect cytologically adequate specimens when using a NF swab with a 5 cm vs. a 3 cm insertion depth.

3. A comparison of the proportions of individuals who collect adequate specimens for molecular genotyping when using the new NF swab vs. the original swab used in the PAC Self-Swab Study.

4. A comparison of the acceptability and pain performance of the new NF swab vs. the original swab and the 5 cm and 3 cm insertion depth.

C Pilot Study Eligibility

The pilot study team will evaluate eligibility according to the following criteria. Individuals must meet all inclusion and none of the exclusion criteria to be registered on to the pilot study. Any questions or concerns regarding eligibility should be directed to the PI, Dr. Nyitray (anyitray@mcw.edu).

C.1 Inclusion Criteria

A potential pilot study subject who meets all of the following inclusion criteria is eligible to participate in the pilot study. Note that these criteria apply regardless of HPV vaccination status or disability status.

1. Aged ≥ 35 years.

2. Must be either:

   a) A cisgender or transgender sexual minority man, or

   b) A transgender woman who has sex with men.

3. Resides in the Milwaukee metropolitan area.

4. Speak and understand English.

5. Ability to understand a written informed consent document, and the willingness to sign it. NOTE: this inclusion criterion is mandatory unless a waiver of the informed consent process and document is being requested.

C.2 Exclusion Criteria

A potential pilot study subject who meets any of the following exclusion criteria is ineligible to participate in the pilot study.

1. Presence of any contraindicating severe anal disease or condition, e.g., anal stenosis.

D Pilot Study Accrual Goals and Study Duration

A total of 60 SGM will be recruited from the greater Milwaukee metropolitan area. Accrual will last for approximately 2 months.

The pilot study will reach pilot study completion within 4 months of the beginning of accrual.

E Subject Recruitment and Registration

E.1 Recruitment

Potential SGM participants will be recruited first from the group of individuals who consented into the PAC Self-Swab Study (PRO00032999) and then indicated an interest in a follow-up study (n=126). We will enroll those aged ≥ 35 years. Persons reporting no sex with men during the last five years will be included if they identify as an SGM individual.

If the initial recruitment results in fewer than 60 people, we will recruit by other means:

1. Advertising on geo-located social/dating apps commonly used by older SGM, e.g., Scruff, Growlr, and Jack'd. We will run advertisements on the apps using a 25-mile radius from the city center in Milwaukee to reach people throughout the city's metro area.
2. The use of print materials in gay-friendly business and a website (mindyourbehind.org) used in the PAC Self-Swab Study. The material will mention the study is recruiting for an anal cancer screening study.

Recruitment material will be approved by an MCW Institutional Review Board (IRB). The SOLO Study Coordinator in Milwaukee will oversee recruitment activity. We will record recruitment activities.

E.2 Consenting

Potential participants will be screened using an online computer-assisted self-interview (CASI). Those who are eligible will be asked to leave contact information. Study staff will contact eligible individuals, provide an overview of the pilot study, and invite the individual to a schedule a consenting session which will be followed by the cytology screening at the Curative Building on the MCW campus. Those who are not eligible will be thanked for their interest and provided links to vetted anal cancer education websites. Minimal Protected Health Information (PHI) will be collected in the eligibility survey.

At the consenting session staff will first ask the eligible individual to confirm their email address, name, and birthdate. The session will occur in a closed office and include information about 1) high rates of anal cancer in SGM, 2) anal cancer screening and the role of swabbing, 3) pilot study activities, and 4) the potential harms and benefits of participation. The staff member obtaining consent will emphasize that participation is voluntary and that participants can choose to join and,

if desired, leave the pilot study at any point without any repercussions. The ICF will also notify individuals that we will collect their street address to support payment using the MCW visa card.

Prior to obtaining their signature, the staff member will ask the individual if they have any questions and, if not, to briefly review their understanding of their participation by asking simple questions about the pilot study to be sure the information was clearly understood.

Individuals agreeing to provide consent will sign an ICF hard copy. It will be photocopied with the copy given to the participant.

F Pilot Study Design and Intervention

F.1 Study Design

This pilot feasibility study will use a randomized controlled trial design. **Figure 1** illustrates the pilot study design.

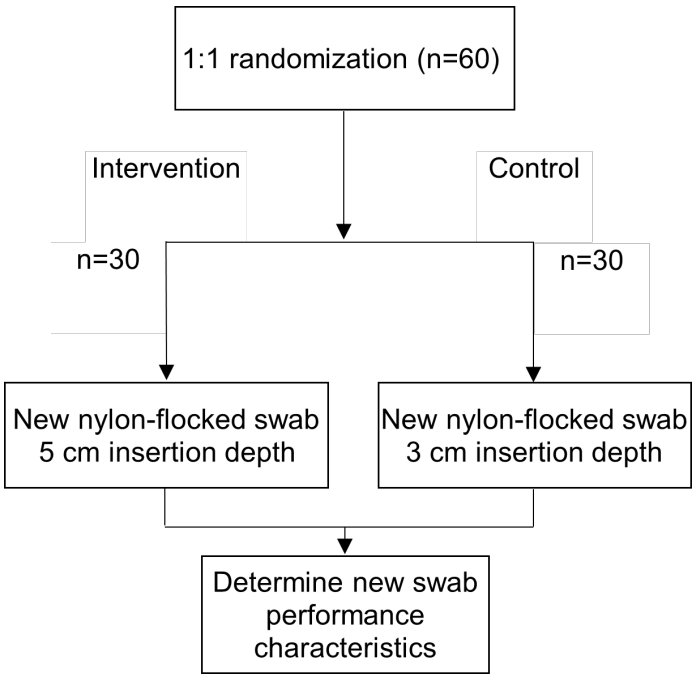


Figure 1. Pilot study schema.

F.2 Randomization

Consented individuals will be randomized to either the intervention (5 cm insertion depth) or the control (3 cm insertion depth) arm using a number generator in REDCap. If the number is .0000 to .4999, the individual will be assigned to the intervention condition. If the number is .5000 to .9999, the individual will be assigned to the control condition.

The participant is considered enrolled in the pilot study when they sign a consent form and are randomized to either the intervention or control arm.

F.3 Cytology Sampling

The cytology sampling will occur immediately after randomization. In preparation, staff will have created two cytology collection kits (labeled as Kit A or Kit B) each containing swabbing instructions, a swab, ThinPrep vial, and gloves. Kit A and Kit B will have identical contents except that Kit A will have a swab with a colored mark 5 cm from the swab tip and Kit B will have a swab with a colored mark 3 cm from the swab tip.

Clinical staff will review the sampling instructions with the individual and then show them to a bathroom in Curative with a locking door where they will do the self-sampling with sampling instructions available. Individuals will be instructed to take the cap off the vial, put on gloves, remove the swab from the packaging, hold the swab at the marker on the shaft of the swab (which corresponds to either 3 cm or 5 cm), get in a comfortable position, insert the swab gently all the way to the mark, begin to twirl the swab clockwise and counterclockwise, and apply pressure to the anal canal walls, while removing the swab as they count slowly to 10.

After swabbing, the participant will put the swab in 20 mL of PreservCyt® solution, agitate and twirl it in the solution for 10 seconds, and then remove the swab while pressing against the sides of the vial. The swab will be discarded, the vial cap replaced, and the vial inserted back into the Kit and returned to the staff member. Participants will be instructed to wash their hands.

Participants will complete a short CASI in the consenting office in private on their phone (or hard copy if they prefer) immediately after their self-sampling to assess the swabbing experience, including discomfort and pain, using validated questions. Clinic staff will assist individuals with technology limitations. Participants will then receive $40.

For those who do not show up for their consenting and cytology appointment, a member of the study team will contact them twice to reschedule within 2 months of their original appointment date.

F.4 Kit Processing, Cytopathology, and Genotyping

Staff will walk the cytology kit to the MCW Tissue Bank who will process the PreservCyt liquid by removing a 0.5 mL aliquot for HPV genotyping. The remaining specimen will be kept in the original vial for cytopathology.

The remaining specimen will be delivered to Wisconsin Diagnostic Labs (Milwaukee, Wisconsin) which uses the COBAS 4800 system for cytology reading. Cytology findings will use the Bethesda System[39] with classification as follows: negative for intraepithelial lesions; atypical squamous cells of undetermined significance (ASCUS) or atypical squamous cells, cannot rule out high-grade squamous intraepithelial lesion; low-grade squamous intraepithelial lesion; or high-grade squamous intraepithelial lesion. Reflex HPV testing will be conducted for all abnormal (i.e., ≥ ASCUS) specimens.

Anal cytology is approved for use in anal cancer screening. Thus, individuals will be given the cytopathology results (either abnormal, normal, or inadequate/unsatisfactory) and any HPV reflex testing results through the individual's preferred mode of communication; however, regardless of the result, all individuals will be encouraged to seek medical advice about their results. Currently, there is no FDA approval for anal self-sampling, thus, the cytology results should not be used to guide care or referrals.

The 0.5 mL aliquot will be batch-shipped to the Moffitt Cancer Center for HPV genotyping. Moffitt will extract DNA from the 0.5 mL aliquot (MDx Media Kit, QIAGEN) and then use the SPH_{10}-$LiPA_{25}$ kit according to the manufacturer's instructions to first test for adequacy of the specimen, defined by the presence of human RNase P, and second to test for HPV DNA, and HPV genotypes.[34]

HPV genotyping results from Moffitt will not be available for several months after the cytology screening since the specimens will be batched shipped only after all 60 individuals complete the screening. In addition, participants with abnormal cytology results will also have HPV reflex testing which would indicate if a high-risk HPV type is detected in the cytology specimen. Thus, the results of the HPV genotyping will not be provided to the participant after genotyping is completed and results are available.

F.5 Subject Withdrawal Criteria

F.5.1 Subject-initiated Withdrawal

A participant may decide to withdraw from the study at any time.

F.5.2 Investigator-initiated Withdrawal

The investigator may withdraw a participant whenever continued participation is no longer in their best interests. Reasons for withdrawing a participant include, but are not limited to, a participant's noncompliance, or simply significant uncertainty on the part of the investigator that continued participation is prudent.

F.5.3 Replacement Policy and Data Usage

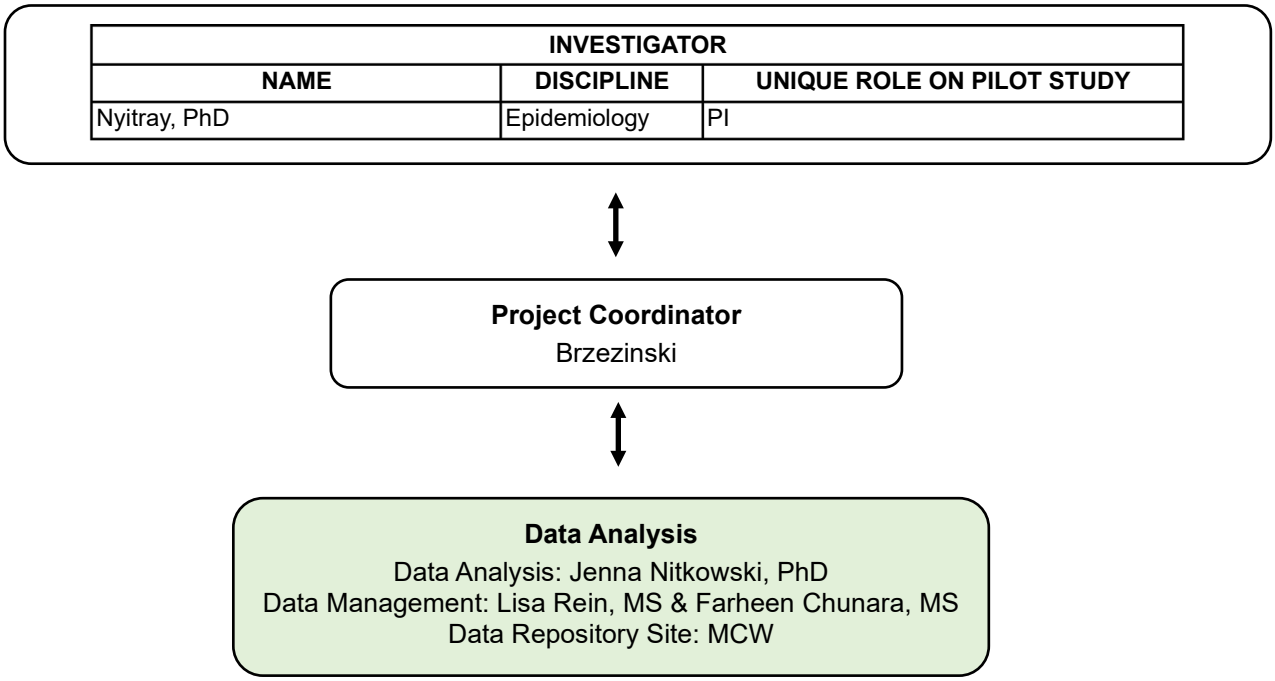
Individuals who sign the informed consent form and are randomized, but subsequently withdraw, will be replaced. Data collected from individuals that withdraw or discontinue from the study will be used.

F.6 End of Pilot Study Definition

An individual is considered to have completed the study if they have completed the post-cytology survey. Those who participated in the pilot study will not be eligible or involved in the parent SOLO study.

G Pilot Study Team, Assessments, and Procedures

G.1 Pilot Study Team Structure



G.2 Pilot Study Schedule of Events

Procedures and Events	Recruitment	Consent & Cytology Appointment	End of Pilot Study
Eligibility Screening	X		
Informed Consent		X	
Randomization and Enrollment[1]		X	
INTERVENTION			
Self-sampling with a 5 cm nylon-flocked swab		X	
CONTROL			
Self-sampling with a 3 cm nylon-flocked swab		X	
RESEARCH PROCEDURES			
Adverse Events Collection[2]	(SAEs only)	AEs collected from the start of the intervention to 30 days after the end of the intervention	
Cytology Appointment Computer-Assisted Self-Interview (CASI)[3]			X

[1] After an individual has signed the informed consent form and been randomized to one of the study arms, they are considered enrolled in the study.

[2] Refer to Section 7.2 for adverse event (AE) collection and reporting requirements.

[3] The cytology CASI will be given to participants immediately after they complete cytology collection.

G.3 Pilot Study Procedures to be Conducted by Site

Activity	Milwaukee		Tampa
	Medical College of Wisconsin	Wisconsin Diagnostic Labs	Moffitt Cancer Center
Funding	Primary Award	Service contract	Service contract
Recruitment	X	-	-
Consenting	X	-	-
Randomization	X	-	-
Participant interaction	X	-	-
Obtaining PHI	X	-	-
Surveying	X	-	-
Access to PHI	X	X	-
Supplying cytology kits	X	-	-
Cytology reading	-	X	-
HPV genotyping	-	-	X

Activity	Milwaukee		Tampa
	Medical College of Wisconsin	Wisconsin Diagnostic Labs	Moffitt Cancer Center
Key personnel	X	-	-

H Statistical and Epidemiological Considerations

H.1 Pilot Study Primary Endpoints

1. A comparison of the proportions of individuals who collect squamocolumnar cells when using a NF swab with a 5 cm vs. a 3 cm insertion depth.

2. A comparison of the proportions of individuals who collect cytologically adequate specimens when using a NF swab with a 5 cm vs. a 3 cm insertion depth.

3. A comparison of the proportions of individuals who collect adequate specimens for molecular genotyping when using the new NF swab vs. the original swab used in the PAC Self-Swab Study.

4. A comparison of the acceptability and pain performance of the new NF swab vs. the original swab.

H.2 Power for Endpoints

This pilot feasibility study does not have the power to make conclusive statements about the study endpoints.

H.3 Analysis Plan

H.3.1 Preliminary analyses

We will assess the success of randomization. For surveys, we will calculate item response rates for each arm of the study and for subgroups based on HIV status, race/ethnicity, and education.[43]

After evaluating missing survey data, we will use multiple imputation[44] to maintain the maximum sample size if data are missing at random. Sensitivity analyses will compare results if data are not missing at random.[45]

In each study arm, we will analyze frequencies of survey items, demographics, other domains, adverse events, and serious adverse events.

H.3.2 Primary Endpoint 1

The presence of cells from the squamocolumnar junction will be assessed in each specimen (Yes/No). Proportions of specimens with squamocolumnar cells will be compared for the 5 cm and 3 cm swabs.

H.3.3 Primary Endpoint 2

Cytologic adequacy is defined as the presence of ~2000-3000 nucleated squamous cells. Proportions of adequate specimens will be compared for the 5 cm and 3 cm swabs.

H.3.4 Primary Endpoint 3

The PAC Self-Swab Study molecular adequacy estimates, given study size, were quite precise with narrow confidence limits. The estimates derived from this pilot study will have wider confidence limits. The original and new swabs will be considered to have commensurate molecular adequacy if the exact confidence limits of the original PAC Self-Swab Study swab are covered by the exact confidence limits of the piloted swab.

H.3.5 Primary Endpoint 4

Each participant will receive a short cytology CASI immediately after the cytology screening to rate their acceptability of the cytology screening on a Likert scale and pain on a visual scale.[37] Proportions of individuals' ratings for adequacy and pain will be compared for

1) the 5 cm and 3 cm swabs, and
2) the new NF swab vs the original swab.

The Exact 95% confidence limits surrounding proportions for acceptability and pain will be compared for overlap for 5 cm vs 3 cm insertion depths.

The comparison of acceptability/pain between the new NF swab and the original swab will be analyzed as in H.3.4.

I ADVERSE EVENTS AND OTHER REPORTABLE INCIDENTS

This study is low risk to participants due to its design and the nature of the intervention being tested (i.e., cancer screening and behavioral interventions). No investigational drugs or devices are involved.

Even though this study does not test a therapeutic intervention, this study will follow the Cancer Therapy Evaluation Program (CTEP) guidelines for reporting of adverse events. All expedited adverse event reports are required to be submitted to the MCW Institutional Review Board (IRB).

I.1 Definitions

I.1.1 Adverse Event (AE)

Any untoward medical occurrence in an individual or clinical investigation subject administered an interventional product and which does not necessarily have to have a causal relationship with this intervention.

This study will utilize the NCI Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, located on the CTEP web site:

https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm

AEs may be spontaneously reported by the subject and/or in response to an open question from study personnel or revealed by observation, physical examination or other diagnostic procedures.

I.1.2 Serious Adverse Event (SAE)

Serious Adverse Event (SAE) means any untoward medical occurrence that results in any of the following outcomes:

- **Death.** Results in death.
- **Life-threatening**. Is life-threatening (refers to an AE in which the participant was at risk of death at the time of the event. It does not refer to an event which hypothetically might have caused death if it were more severe).
- **Hospitalization**. Requires inpatient hospitalization ≥24 hours or prolongation of an existing hospitalization.
- **Disability/incapacity**. Results in persistent or significant disability or incapacity. (Disability is defined as a substantial disruption of a person's ability to conduct normal life functions).
- **Pregnancy**
- **Medically important event**. This refers to an AE that may not result in death, be immediately life-threatening, or require hospitalization, but may be considered serious when, based on appropriate medical judgment, may jeopardize the participant, require medical or surgical intervention to prevent one of the outcomes listed above, or involves suspected transmission via a medicinal product of an infectious agent. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse; any organism, virus, or infectious particle (*e.g.*, prion protein transmitting transmissible spongiform encephalopathy), pathogenic or nonpathogenic, is considered an infectious agent.

I.1.3 Attribution of an Adverse Event

An assessment of the relationship between the adverse event and the medical intervention, using the following categories:

- **Definitely Related**: *The AE is clearly related to the intervention*. There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out.
- **Probably Related:** *The AE is likely related to the intervention.* There is evidence to suggest a causal relationship, and the influence of other factors is unlikely.
- **Possibly Related:** *The AE may be related to the intervention.* There is some evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after administration of the trial medication). However, the influence of other factors may have contributed to the event (*e.g.*, the subject's clinical condition, other concomitant events).
- **Unlikely:** *The AE is doubtfully related to the intervention.* A clinical event, including an abnormal laboratory test result, whose temporal relationship to drug administration makes a causal relationship improbable (*e.g.*, the event did not occur within a reasonable time after administration of the trial medication) and in which other drugs or chemicals or underlying disease provides plausible explanations (*e.g.*, the subject's clinical condition, other concomitant treatments).

- **Unrelated:** *The AE is clearly NOT related to the intervention.* The AE is completely independent of study drug administration, and/or evidence exists that the event is definitely related to another etiology.

I.2 Expectedness of an Adverse Event

The study investigator will be responsible for determining whether an AE is expected or unexpected as indicated in the protocol. 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.

I.3 Collection and Reporting Requirements for Adverse and Serious Adverse Events

AEs that are Grade 3 or higher and are related (possibly, probably, or definitely) to the intervention will be collected from the time the subject starts the intervention through conclusion of the intervention, which comprises the cytology self-sampling and CASI. AEs will be tracked and followed until resolution, the subject withdraws consent or is lost to follow-up (including individuals who discontinue early). SAEs that occur after the subject has signed the consent form through 30 days after the conclusion of the intervention will be collected. Adverse events collected per the protocol should be followed with appropriate medical management.

AEs will be collected as reported. In the case of an adverse event, participants will be instructed to contact study staff and/or investigators as soon as possible, ideally within 24 hours. All Grade 3 and higher adverse events will be discussed with the PI and appropriate study staff. The PI will oversee that all AEs, SAEs, and UPIRSOs, are reported appropriately. Information about adverse events experienced by study individuals will be monitored by the following means:

- Report given by study participants to study staff, either in person or by telephone.
- Report given to study staff by study participants' family or friends, either in person or by telephone.
- Report by the participant's physician or other health care provider involved in the subject's care.
- Report from a hospital or other healthcare facility where the study participant is being treated for the serious adverse event.
- Other persons who may have knowledge of such a serious adverse event.

The PI will consult with other investigator(s) to assign event attribution category (unrelated, unlikely, possible, probable, or definite).

I.4 Institutional

Adverse and serious adverse events are not expected. If such events occur, AEs and SAEs will be reported per MCW Institutional Review Board (IRB) guidelines and the MCWCC Data and Safety Monitoring Plan (DSMP).

Institutional Review Board (IRB). For routine reporting, the events will be reported to the IRB as part of the annual continuing progress report. Events requiring expedited reporting to the IRB include: 1) any AE or SAE that is unexpected, related (possibly, probably, or definitely) to the

research, and places research participants or others at a greater risk of physical or psychological harm than was previously known or recognized, and 2) unanticipated problems or any incident, experience, or outcome that are unexpected with reference to the procedure and risks defined in the initial IRB application, related (possibly, probably, or definitely) to participation in the research project, and suggests the research places participants or others at greater risk or harm than was previously known or recognized. Events that meet expedited reporting requirements must be reported to the IRB no later than five calendar days after the study team becomes aware of the event.

Data Safety and Monitoring Committee (DSMC). The study team will report AEs and SAEs to the DSMC according to **Table 1**. For routine reporting, the events will be reported at the time of scheduled monitoring. For expedited reporting, the study team must notify the DSMC via email (DSMC_MCWCC@mcw.edu) within five days of the team's knowledge. This email should include the subject ID, date of event, grade, relatedness, expectedness, and a short narrative.

Table 1. DSMC AE and SAE Reporting Requirements

Attribution	SAE				AE			
	Grade 1, 2 & 3		Grade 4 and 5		Grade 3		Grade 4	
	Expected	Unexpected	Expected	Unexpected	Expected	Unexpected	Expected	Unexpected
Possible Probable Definite	Routine Review	Expedited: Within 5 calendar days	Expedited: Within 5 calendar days	Expedited: Within 5 calendar days	Routine Review	Expedited: Within 5 calendar days	Expedited: Within 5 calendar days	Expedited: Within 5 calendar days

I.5 Unanticipated Problem Involving Risk to Subject or Other (UPIRSO)

Unanticipated problems will be submitted to the IRB of record according to local policies and procedures. An unanticipated problem is one that is unexpected, possibly, probably, or definitely related to the research described in the paragraph above and suggests the research places research participants or others at a greater risk of physical or psychological harm than was previously known or recognized.

Since this is an investigator-initiated study, the principal investigator is responsible for reporting unanticipated problems to any regulatory agency and to the IRB. Any unanticipated problems detected will be promptly documented by the study coordinator and submitted to the IRB within five calendar days of study staff's knowledge. These reviews would pick up any unanticipated negative trends among participants.

I.6 Participant Complaints

If a complaint is received by anyone on the study staff, it will be discussed with the study staff and will be addressed on a case-by-case basis. The PI will be notified of any complaints. Complaints will be reported to the IRB if indicated.

If the subject has questions about their rights as a study subject, wants to report any problems or complaints, obtain information about the study or offer input, the subject can call the Medical College of Wisconsin/Froedtert Hospital research subject advocate at 414-955-8844. This information is provided to the subject in their consent.

I.7 Protocol Deviations

This pilot is a study of swab performance characteristics.

I.7.1 Definitions

- **Protocol Deviations.** A protocol deviation is any change, divergence, or departure from the study design or procedures of a research protocol that is under the investigator's control and that has not been approved by the IRB.
- **Significant Protocol Deviations.** Significant protocol deviations are those that increase the risk to participants or others, decrease potential benefits of the project, undermine the scientific integrity of the project, or occur more than once.
- **Planned Protocol Deviations.** Planned protocol deviations are any temporary protocol deviation acknowledged by the IRB prior to its initiation. Any permanent change to the protocol constitutes an amendment that must be submitted to the IRB for approval prior to initiation.

I.7.2 Reporting Protocol Deviations

Any deviations from the protocol must be fully documented in the source documents. A summary of all protocol deviations must be reported to the DSMC at the time of scheduled monitoring. Per the most recent MCW Office of Research SOP, the following events meet the MCW IRB expedited reporting criteria; any other deviation is to be reported in a timely manner.

- Significant Protocol Deviations. Examples include but are not limited to the following:
    - Any departure from the protocol (deviation or violation) where participants or others were harmed or might be at increased risk of harm.
    - Any departure from the protocol that compromises the integrity of the research data.
    - Any change made to the research without prior IRB approval in order to eliminate apparent immediate harm.
- Planned Protocol Deviations. Planned protocol deviations that increase the risk to participants or others, decrease potential benefits of the project, or undermines the scientific integrity of the project are considered events that meet MCW's prompt reporting criteria. For example, enrolling an individual who does not meet the eligibility criteria.

J DATA AND SAFETY MONITORING PLAN

The Medical College of Wisconsin (MCW) Cancer Center (MCWCC) places the highest priority on ensuring the safety of patients participating in clinical trials. Every cancer interventional trial conducted at MCW includes a plan for safety and data monitoring.

More information can be found related to the MCWCC Data and Safety Monitoring Plan at the MCWCC website: https://cancer.mcw.edu/.

This study will be reviewed by the MCWCC Data and Safety Monitoring Committee (DSMC). A summary of the MCWCC DSMC activities are as follows:

1. Periodically review progress reports and evaluate the clinical trial for safety and data integrity.
2. Provide recommendations on trial continuation, suspension, or termination.

This study was categorized as low risk by the MCW Cancer Center Scientific Review Committee. The DSMC will perform scheduled monitoring at a frequency commensurate with the risk level (at least annually), and the study will be subject to review by Cancer Center Quality Assurance staff according to the MCWCC Data and Safety Monitoring Plan.

All DSMC letters will be submitted to the IRB of record as required.

K REGULATORY COMPLIANCE, ETHICS, AND STUDY MANAGEMENT

K.1 Ethical Standard

This pilot study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, consistent with Good Clinical Practice (GCP) and all applicable regulatory requirements.

K.2 Regulatory Compliance

This pilot study will be conducted in compliance with:

- The protocol.
- Federal regulations, as applicable, including 21 CFR 50 (Protection of Human Subjects/Informed Consent); 21 CFR 56 (Institutional Review Boards) and 45 CFR 46 Subparts A (Common Rule), B (Pregnant Women, Human Fetuses and Neonates), C (Prisoners), and D (Children), GCP/ICH guidelines, and all applicable regulatory requirements. The IRB must comply with the regulations in 21 CFR 56 and applicable regulatory requirements.

K.3 Staff Training

K.3.1 Informed Consent Process

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the pilot study and continues throughout the individual's pilot study participation. Extensive discussion of risks and possible benefits of this therapy will be provided to the subjects and their families. Informed consent forms (ICF) describing in detail the pilot study intervention, pilot study procedures, and risks are given to the subject and written documentation of informed consent is required prior to starting intervention/administering pilot study product.

ICFs will be IRB-approved and the subject (and legally authorized representative, if necessary) will be asked to read and review the document. Upon reviewing the document, the investigator will explain the research pilot study to the subject and answer any questions that may arise. In accordance with 46 CFR 46.111, the subject will sign and date the informed consent document prior to any procedures being done specifically for the pilot study.

K.4 Subject Confidentiality and Access to Source Documents and Data

Subject confidentiality is strictly held in trust by the principal investigator and staff. This confidentiality includes the information relating to participating individuals, as well as any genetic or biological testing.

The pilot study protocol, documentation, data and all other information generated will be held in strict confidence. No information concerning the study data will be released to any unauthorized third party without the prior written approval of the principal investigator.

The conditions for maintaining the confidentiality of the individuals' records are required for the life of the data. These rules apply equally to any and all MCW Cancer Center (MCWCC) projects.

The principal investigator will allow access to all source data and documents for the purposes of monitoring, audits, IRB review and regulatory inspections.

The study monitor or other authorized representatives of the principal investigator may inspect all documents and records required to be maintained by the investigator.

K.5 Risk-Benefit Assessment

K.5.1 Potential Risks

HIV and anal cancer screening information is sensitive. All staff will have adequate training to appropriately handle participant data. The packaging of any needed mailings will comply with confidentiality standards. CASI data collection will use a web platform by REDCap with data stored on a secure web-based server at the Medical College of Wisconsin.

Potential risks to participants can be divided into three areas: 1) data collection using CASI, 2) concerns about disclosure of confidential, sensitive information, and 3) collection of anal canal cells and test results. These risks are described below.

1. CASI. This pilot study will ask sensitive questions of participants that may make some participants uncomfortable.

2. Potential disclosure of confidential, sensitive information. Some people may fear that unauthorized persons who may discriminate might obtain personal medical information or otherwise cause a change in the participant's social status or access to benefits to which participants would otherwise be entitled.

3. Collection of anal canal cells and test results. Some persons may feel embarrassed about inserting a swab into the anal canal. The swab can be uncomfortable, and occasionally there can be minor bleeding. Individuals will be notified of cytology results.
4.

There are no alternative screening procedures that are FDA-approved for anal cancer; however, cytology is now recommended by national and international bodies.

K.5.2 Potential Benefits

There is no benefit of this research to participants. However, they will learn about anal cancer and receive anal cytology results. Thus, the risk of discomfort during study procedures (either physical discomfort during clinical procedures or psychological discomfort due to sensitive survey

questions) is reasonable within the context of important educational and personal health information gained by the participant. The knowledge gained by this research will benefit science by determining the utility of a 3 cm or 5 cm swab for use in the parent SOLO study. If SOLO finds that self-sampling supports clinic attendance, that will benefit the performance of anal cancer screening procedures in society. For these reasons, the potential benefits of the pilot study are reasonable in relation to the anticipated benefits to the pilot study participants.

K.6 Protection of Human Subjects

K.6.1 Protection from Unnecessary Harm

MCW is responsible for protecting all individuals involved in human experimentation. This is accomplished through the IRB mechanism and the informed consent process. The IRB reviews all proposed studies involving human experimentation and ensures that the subject's rights and welfare are protected and that the potential benefits and/or the importance of the knowledge to be gained outweigh the risks to the individual. The IRB also reviews the informed consent document associated with each study to ensure that the consent document accurately and clearly communicates the nature of the research to be done and its associated risks and benefits.

K.6.2 Protection of Privacy

To ensure confidentiality, each participant is assigned an anonymous study ID, which is then used on all pilot study forms that collect participant data. Study IDs are linked to participant names and other private identifiable information in only one location, on an encrypted, firewall-protected, electronic document housed on MCW's server. All study forms are kept on the MCW server or HIPAA-compliant MCW data-sharing platform and access is restricted to authorized study personnel.

K.6.3 Protection Against Additional Risks

All procedures in the proposed pilot study involve minimal risk. The SOLO pilot uses very similar procedures as did our prior Prevent Anal Cancer Self-Swab Study. When a participant provides consent, they will be thoroughly informed of all pilot study procedures, potential risks, and benefits, and that they can discontinue participation in the study at any time without risk to subsequent care at the place(s) they receive health care. The participant, in a confidential space, will complete the consent in-person. The PI will do the initial consents while being observed by the study coordinator and other study staff; thereafter, the study coordinator and other trained study staff will perform the consents. Before signing, we will ask participants to answer three simple questions that will indicate the participant has understood the consent.

ICFs will be documented in hard copy with participant signatures kept on file in a locked cabinet at the Medical College of Wisconsin.

1. Self-swabbing. When the participant performs a self-swabbing, they will be provided instructions written at a 6th grade reading level, modeled after already-tested self-sampling instructions in the Prevent Anal Cancer Self-Swab Study.[17]
2. Sensitive nature of questions. This pilot study will ask sensitive questions about, sexual behavior and disease status during the computer-assisted self-interviews. Thus, names will be kept separate from coded identifiers. All computers will require a password to access files. Computer-assisted self-interviewing will be used so participants can confidentially report sensitive behaviors while minimizing feelings of shame or embarrassment discussing sexual histories. The survey items will mainly come from the

PAC Self-Swab Study surveys, which, in turn, were adapted from validated cervical cancer screening instruments.

3. PHI access. Access to all PHI-protected pilot study data will be limited to the PI, study coordinator, other trained and CITI-certified study staff, and clinicians. Data will be destroyed after the pilot study is completed according to federal regulations.

Persons with HIV may be vulnerable; thus, we will ensure that the highest ethical standards will be respected and followed so that benefits are maximized for a diverse set of persons while harms are minimized for all participants. For example, we include a very wide age range of people in enrollment, i.e., 35 years and older.

K.7 Required Education on the Protection of Human Subjects

In accordance with federal guidelines, all research personnel involved in these studies have completed and will periodically complete coursework in the Protection of Human Subjects as mandated by the Medical College of Wisconsin. These programs meet NIH requirements.

This study will be submitted for review to the Medical College of Wisconsin IRB prior to implementation. The IRB will oversee any human participants' concerns during the study.

K.8 Changes in the Protocol

Once the protocol has been approved by the MCW IRB, any changes to the protocol must be documented in the form of an amendment. The amendment must be signed by the investigator and approved by the IRB prior to implementation.

If it becomes necessary to alter the protocol to eliminate an immediate hazard to individuals, an amendment may be implemented prior to IRB approval. In this circumstance, however, the investigator must then notify the IRB in writing within five working days after implementation.

The IRB may provide expedited review and approval/favorable opinion for minor change(s) in ongoing studies that have the approval /favorable opinion of the IRB. The investigator will submit substantial protocol modifications to the NIH in accordance with the governing regulations. Changes to the protocol may require approval from the NIH.

K.9 Investigator Compliance

The investigator will conduct the study in compliance with the protocol given approval/favorable opinion by the IRB.

Onsite Audits: Auditing is essential to ensure that research conducted at the Medical College of Wisconsin (MCW) Cancer Center is of the highest quality and meets MCW and regulatory agency standards.

Regulatory authorities, the IRB, and/or sponsor may request access to all source documents, data capture records and other study documentation for onsite audit or inspection. Direct access to these documents must be guaranteed by the investigator, who must always provide support for these activities.

The PI will follow the procedures as outlined above, which will serve as part of the quality control procedure. To ensure the validity and integrity of pilot study data, the PI will discuss data management with the research team on a regular basis.

L DATA HANDLING AND RECORD KEEPING

The study team, including the PI, study coordinator, and other study staff will have weekly meetings. At each weekly meeting after enrollment starts, the study coordinator will provide the following information: number of participants entering the pilot study and completing cytology self-sampling, the number of dropouts, and reasons for dropout. Information about any adverse events also will be presented, including potential anxiety from cytology results. These participants will be managed using standard-of-care practices. By examining this information, the team will keep abreast of critical issues regarding reconsenting and data integrity.

- *Participant Records*. The computer-assisted self-interviews themselves will be identified only by ID number and do not contain personal identification information. Information linking the participants' identity to the study data will be kept on password-protected secure servers, while signed ICFs will be archived separately at the Medical College of Wisconsin.

- *Computer records*. Passwords and dual authentication will be used to limit access to computer records and pilot study data. No information that could lead to personal identification of participants will be included in any of the reports or given to any non-authorized person.

All raw data, data figures, data interpretation, models, and conclusions drawn from this pilot study will be managed by the principal investigator. The findings from this study may be presented at relevant conferences/meetings, published in a respectable peer-reviewed journal, or used as preliminary data in a grant application to justify extramural funding.

For any manuscript that is to be published in a journal, the role of authors/contributors, the disclosure of financial/non-financial relationships and activities, and the report of perceived conflicts of interest should largely adhere to the recommended guidelines set forth by the International Committee of Medical Journal Editors (ICMJE; Defining the Role of Authors and Contributors, Disclosure of Financial and Non-Financial Relationship and Activities and Conflicts of Interest). The PI, in consultation with the study co-investigators, should determine who will be listed as first, senior, corresponding authors, and co-authors. Study team members who have made substantial and significant intellectual contributions to the study and its findings should be listed as co-authors or, in certain circumstances, acknowledged. Funding sources and any conflict of interests, perceived or actual, should be disclosed and stated within the appropriate section of the manuscript at submission.

In accordance with the MCW Human Research Protection Program and Federal regulations FDAAA 801 and 42 CFR Part 11 (per the Final Rule, effective 1/18/2017), information about and results collected from this study are registered on ClinicalTrials.gov under NCT07085845, the clinical trial registry and results data bank operated by the National Library of Medicine (NLM) of the National Institutes of Health (NIH). All informed consent documents include a specific statement relating to the posting of study information in ClinicalTrials.gov.