Doxy-PEP: Dose-Ranging Study of Persons Receiving Doxycycline

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PROTOCOL TITLE: Doxy-PEP: Dose-Ranging Study of Persons Receiving Doxycycline

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External collaborator will submit designated protocol to The Centers for Disease Control and Prevention IRB for review and approval.

VERSION: 7.0 dated 03 Jul 2024

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REVISION HISTORY

Revision #	Version Date	Summary of Changes
2.0	23Jan2023	• Clarified participants who are “enrolled” vs. counting towards the study “n” • Removed English-speaking from inclusion criteria • Added statement regarding list linking study codes to IHI
3.0	20Mar2023	• Added Certificate of Confidentiality language per CDC requirement
4.0	26Apr2023	• Added Emory and Grady EeMR as a recruitment method
5.0	10Aug2023	• Updated Inclusion/Exclusion Criteria to remove CrCL and hepatitis virus and liver disease
6.0	21May2024	• Updated in Section 1, Study Summery, Study Population to remove “sex” and “not using gender affirming hormone therapy”
7.0	03Jul2024	• Updated minimum anticipated sample size to 12 AMAB and 12 AFAB • Updated that at least 6 participants will complete ARM A prior to moving to ARM B

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1. Study Summary

Project Title	Dose-Ranging Study of Persons Receiving Doxycycline
Project Design	To determine tissue pharmacology of multiple doses of doxycycline for sexually transmitted infection (STI) post-exposure prophylaxis (PEP), investigators at Emory University will collaborate with the Centers for Disease Control and Prevention (CDC) to conduct a clinical trial of up to 40 people aged 18-59 (at least 12 people assigned male sex at birth (AMAB) and 12 people assigned female sex at birth (AFAB)), with measurement of doxycycline concentrations in the rectum and vagina at study follow-up visits. Enrolled participants will take a total of 5 doses of doxycycline over a 3-week period.
Primary Objective	To determine dose-ranging tissue penetration of doxycycline for STI prevention strategies.
Secondary Objective(s)	N/A
Research Intervention(s)/Interactions	Doxycycline & Biological Specimen Collection
Study Population	Healthy people assigned male or female at birth and are willing to undergo study procedures.
Sample Size	40 participants total • Arm A (100mg Doxycycline): at least 6 AFAB and 6 AMAB with a target sample size of 10 in each group • Arm B (200mg Doxycycline): at least 6 AFAB and 6 AMAB with a target sample size of 10 in each group
Study Duration for individual participants	8 weeks
Study Specific Abbreviations/ Definitions	AFAB — Assigned female sex at birth AMAB —Assigned male sex at birth CDC — Centers for Disease Control and Prevention CRAI — Condomless receptive anal intercourse DOX — Doxycycline ED-PrEP —Event-driven pre-exposure prophylaxis HIV — Human Immunodeficiency Virus IDS — Investigational Drug Services MSM — Men who have sex with men PrEP — Pre-exposure prophylaxis PEP — Post-exposure prophylaxis STI — Sexually transmitted infection WHO —World Health Organization
Funding Source (if any)	Centers for Disease Control and Prevention

2. Objectives

The purpose of this study is to collect data regarding the ability of various oral doses of doxycycline to penetrate mucosal tissues in people AMAB and AFAB to inform future studies of combinations of doxycycline to protect against bacterial STIs.

3. Background

Recent studies have demonstrated the potential utility of single-dose oral doxycycline post-exposure prophylaxis (Doxy-PEP) against bacterial sexually transmitted infections (STIs)[1,2]. New dosing strategies are being explored that would allow for a single event-driven oral dose of medications that protect from HIV as well as other bacterial STIs. However, the ability of doxycycline to penetrate mucosal tissues and provide protection from STIs remains underexplored. A previous pilot study conducted by the DHP Laboratory Branch at CDC examined the ability of a 200mg oral dose of doxycycline to penetrate the vaginal and rectal mucosa. However, data regarding alternative doxycycline doses and accumulation of doxycycline with multiple doses are lacking[1,2].

The purpose of this project is to collect data regarding the ability of various oral doses of doxycycline to penetrate mucosal tissues in people AMAB and AFAB to inform optimization of doxycycline for STI prevention strategies. Results from this study will be compared to results of the previous pilot study conducted by the DHP Laboratory Branch at CDC. The objectives of this project are to conduct a clinical study investigating the pharmacokinetics of two different doses of doxycycline in people AMAB and AFAB where biological specimens are provided to the DHP Laboratory Branch for doxycycline measurement and analysis. Data regarding mucosal drug exposure will help inform development of STI prevention strategies.

Public Health Relevance: Incidence of bacterial STIs are increasing and studies have recently shown that Doxy-PEP can reduce incidence of bacterial STIs among men who have sex with men (MSM) and Doxy-PEP is being explored for STI prevention among women[3,4]. A better understanding of mucosal drug penetration of doxycycline will inform the design of future studies to prevent STIs in various populations.

4. Study Endpoints

Primary Study Endpoints

1. To compare doxycycline concentrations in rectal tissues collected 24 hours after T^1 dose of 100 mg or 200 mg of doxycycline in AMAB participants.
2. To compare doxycycline concentrations in vaginal tissues collected 24 hours after T^1 dose of 100 mg or 200 mg of doxycycline in AFAB participants.
3. To compare doxycycline concentrations in rectal tissues collected 24 hours after T^5 dose (visit 8) of 100 mg or 200 mg of doxycycline in AMAB participants.
4. To compare doxycycline concentrations in vaginal tissues collected 24 hours after T^5 dose (Visit 8) of 100 mg or 200 mg of doxycycline in AFAB participants.

Exploratory Endpoint

To assess longitudinal doxycycline concentrations in blood, urine, throat, vaginal, penile, and rectal secretions over the 3-week study period in people taking 5 doses of 100mg vs. 200mg of doxycycline.

5. Study Intervention/Investigational Agent

Study Product Description

Doxycycline is used to treat or prevent infections that are strongly suspected to be caused by bacteria; it is an antimicrobial drug indicated for bacterial infections such as sexually transmitted infections.

It will be purchased from the manufacturer and stored at the Emory Investigational Drug Services (IDS).

Dosage, Preparation and Administration of Study Product

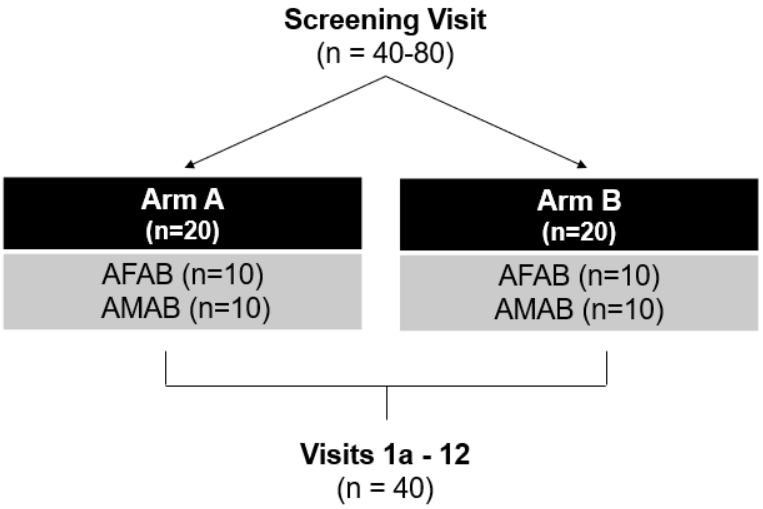
Doxycycline (DOX) will be given orally at 100 and 200 mg doses. Pharmacy packages will be prepared by an IDS Pharmacist and delivered to the participant by a study team member. Prior to drug dispensing, the clinician will assess participant's medical history, and ensure the participant has no known allergies to the study drug. If a participant reports an allergy and a suitable alternative is not available, then the clinician may opt to not enroll the participant into the study.

Accountability Procedures for the Study Product

The IDS pharmacist will maintain accurate accountability logs at the Hope Clinic.

6. Procedures Involved

Study Schema



Study Visits

All study visits described below apply to both Arms A & B. The only difference between the two will be the dose participants receive (100 mg v. 200 mg). Study participants will be assigned to dosing arms in a sequential manner. Arm A will enroll at least 6 participants AFAB and at least 6 participants AMAB at 100mg prior to proceeding to Arm B. Target enrollment will be n=10 in each group. Arm B will enroll at least 6 participants AFAB and at least 6 participants AMAB at 200mg. Target enrollment will be n=10 in each group.

Recruitment

Potential participants will be identified from one of the recruitment methods (e.g., flyers, social media, advertisements, etc.) mentioned in the recruitment methods section below.

Phone Screening

Once a potential participant is identified via recruitment methods, study staff may administer a pre-screening questionnaire via phone to assess preliminary eligibility. If the results of the pre-screening questionnaire indicate that the potential participant may be eligible for this study, they will be invited to the clinic to complete the screening visit.

Screening Visit

At this visit, the informed consent will be reviewed, and all questions answered. The participant will sign the consent form prior to completing any study activities. Once the participant signs the informed consent, a study identification number will be assigned. Eligibility will then be determined for each participant based primarily on information gathered during the screening visit. Procedures conducted during the screening visit may include:

- Collection of demographic information
- Collection of medical history
- Collection of current medications
- Physical exam
- Pregnancy test for women of childbearing potential
- Self-collected vaginal and/or rectal swab test for gonorrhea and chlamydia
- Urine specimen to test for gonorrhea and chlamydia
- Blood sample collection - up to 17 mL
    - HIV testing
    - CBC
    - Coagulation Tests
    - Creatinine

Timing of the first doxycycline dose will be denoted at T^1 = 0hr. All subsequent visits should be calculated from this time point. Additional doses will be denoted as T^2, T^3, T^4 and T^5.

Visit 1a (Day 0) – Enrollment, Pre-T[1] Dose & T[1] Dosing

This visit should occur ≤ 42 days after the Screening Visit. Participants will count towards the total n of the study upon completion of this visit.

Procedures conducted PRIOR TO DOSING may include:

- Blood Sample Collection **–** up to 10 mL
- Urine Sample Collection – Urinalysis
- Self-Administered Swab Collection
  - Rectal (x3)
  - Vaginal (x3) – for participants with a vagina only
  - Throat (x2)

Dosing

Doxycycline (Arm A – 100mg; Arm B – 200 mg) will be administered to the participant. This dose should take place while the participant is in the clinic.

Visit 1b (Hour 2-4/Day 0) – Post-T[1] Dose

This visit will take place 2-4 hours after the first dose (T^1 = 0 hr).

Procedures conducted at this visit may include:

- Blood Sample Collection **–** up to 10 mL
- Self-Administered Swab Collection
  - Rectal (x3)
  - Vaginal (x3) – for participants with a vagina only
  - Throat (x2)

Visit 2 (Hour 24/Day 1) – Biopsy Visit

This visit will take place 24 hours after the first dose (T^1 = 0 hr). For participants who menstruate, this visit should take place 7-10 days after their last menstrual cycle.

Participants will be asked to abstain from receptive anal and/or vaginal intercourse for 3 days prior to this visit.

Procedures conducted at this visit may include:

- Review of medical history
- Review of current medications
- Symptom-guided physical exam
- Evidence-based HIV/STI risk reduction counseling
- Rapid HIV test (if risk behavior has changed since screening)
- Blood Sample Collection **–** up to 10 mL
- Urine Sample Collection

  - Urinalysis
  - Urine pregnancy test – for women of childbearing potential
- Staff-Assisted Swab Collection
  - Urethral (x1)
  - Glans (x1)
- Self-Administered Swab Collection
  - Rectal (x3)
  - Vaginal (x3) – for participants with a vagina only
  - Throat (x2)
- Rectal Biopsy – *Required for participants who DO NOT have a vagina. This is an optional, additional biopsy for those who do have a vagina.*
  - Rigid sigmoidoscopy
  - Biopsies (2-4 tissue samples)
- Vaginal/Cervical Biopsy – *Required for participants who DO have a vagina.*
  - Speculum insertion
  - Vaginal Biopsies (1-2 tissue samples)
  - Cervical Biopsies (1-2 tissues samples)

All participants will be instructed to place nothing in the rectum and/or vagina and to abstain from intercourse for 7 days after the biopsy procedure to allow the mucosa to heal.

Visit 3 (Hour 48/Day 2)

This visit will take place 48 hours after the first dose (T^1 = 0 hr).

Procedures conducted at this visit may include:

- Blood Sample Collection **–** up to 10 mL
- Urine Sample Collection – Urinalysis
- Self-Administered Swab Collection
  - Rectal (x3)
  - Vaginal (x3) – for participants with a vagina only
  - Throat (x2)

Visit 4 (Hour 72/Day 3) – Pre-T^2 Dose & T^2 Dosing

This visit will take place 72 hours (3 days) after the first dose (T^1 = 0 hr).

Procedures conducted PRIOR TO DOSING may include:

- Blood Sample Collection **–** up to 10 mL
- Urine Sample Collection – Urinalysis
- Staff-Assisted Swab Collection
  - Urethral (x1)
  - Glans (x1)
- Self-Administered Swab Collection

- Rectal (x3)
- Vaginal (x3) – for participants with a vagina only
- Throat (x2)

Dosing

Doxycycline (Arm A – 100mg; Arm B – 200 mg) will be administered to the participant. This dose should take place while the participant is in the clinic.

Visit 5 (Hour 168/Day 7) – T^3 Dosing at Home

Participant will take dose (Arm A – 100mg; Arm B – 200 mg) at home and provide proof of dosing as described in study-specific procedures.

Visit 6 (Hour 240/Day 10) – T^4 Dosing at Home

Participant will take dose (Arm A – 100mg; Arm B – 200 mg) at home and provide proof of dosing as described in study-specific procedures.

Study Drug Dispensation Visit (if needed)

If, due to scheduling constraints, menses, holidays, etc., Visit 8 (Biopsy) cannot be completed per protocol, study staff may delay Visits 7a – 12 for up to 4 weeks. In this case, participants would continue to take doxycycline twice a week until the visits could be scheduled. An additional drug dispensation visit may be needed so the participant can pick up study drug.

Visit 7a (Hour 336/Day 14) – Pre-Dose & T^5 Dosing

This visit will take place 336 hours (14 days) after the first dose (T^1 = 0 hr).

Procedures conducted at this visit may include:

- Blood Sample Collection **–** up to 10 mL
- Urine Sample Collection – Urinalysis
- Self-Administered Swab Collection
  - Rectal (x3)
  - Vaginal (x3) – for participants with a vagina only
  - Throat (x2)

Dosing

Doxycycline (Arm A – 100mg; Arm B – 200 mg) will be administered to the participant. This dose should take place while the participant is in the clinic.

Visit 7b (Hour 338-340/Day 14) – Post-T^5 Dose

This visit will take place 2-4 hours after the T^5 dose and 338-340 hours (14 days) after the first dose (T^1 = 0 hr).

Procedures conducted at this visit may include:

- Blood Sample Collection **–** up to 10 mL
- Self-Administered Swab Collection
    - Rectal (x3)
    - Vaginal (x3) – for participants with a vagina only
    - Throat (x2)

Visit 8 (Hour 360/Day 15) – Biopsy Visit

This visit will take place 360 hours (15 days) after the first dose (T^1 = 0 hr) and 24 hours after T^5 dose.

Participants will be asked to abstain from receptive anal and/or vaginal intercourse for 3 days prior to this visit.

- Review of medical history
- Review of current medications
- Symptom-guided physical exam
- Evidence-based HIV/STI risk reduction counseling
- Rapid HIV test (if risk behavior has changed since screening)
- Blood Sample Collection **–** up to 10 mL
- Urine Sample Collection
    - Urinalysis
    - Urine pregnancy test – for participants who are able to bear children
- Staff-Assisted Swab Collection
    - Urethral (x1)
    - Glans (x1)
- Self-Administered Swab Collection
    - Rectal (x3)
    - Vaginal (x3) – for participants with a vagina only
    - Throat (x2)
- Rectal Biopsy – *Required for participants who DO NOT have a vagina. This is an optional, additional biopsy for those who do have a vagina.*
    - Rigid sigmoidoscopy
    - Biopsies (8-12 tissue samples)
- Vaginal/Cervical Biopsy – *Required for participants who DO have a vagina.*
    - Speculum insertion
    - Vaginal Biopsies (1-2 tissue samples)
    - Cervical Biopsies (1-2 tissues samples)

All participants will be instructed to place nothing in the rectum and/or vagina and to abstain from sex for 7 days after the biopsy procedure to allow the mucosa to heal.

Visit 9 (Hour 384/Day 16)

This visit will take place 384 hours (16 days) after the first dose (T^1 = 0 hr).

Procedures conducted at this visit may include:

- Blood Sample Collection **–** up to 10 mL
- Urine Sample Collection – Urinalysis
- Self-Administered Swab Collection
    - Rectal (x3)
    - Vaginal (x3) – for participants with a vagina only
    - Throat (x2)

Visit 10 (Hour 408/Day 17)

This visit will take place 408 hours (17 days) after the first dose (T^1 = 0 hr).

Procedures conducted at this visit may include:

- Blood Sample Collection **–** up to 10 mL
- Urine Sample Collection – Urinalysis
- Staff-Assisted Swab Collection
    - Urethral (x1)
    - Glans (x1)
- Self-Administered Swab Collection
    - Rectal (x3)
    - Vaginal (x3) – for participants with a vagina only
    - Throat (x2)

Visit 11 (Hour 432hr/Day 18)

This visit will take place 432 hours (18 days) after the first dose (T^1 = 0 hr).

Procedures conducted at this visit may include:

- Blood Sample Collection **–** up to 10 mL
- Urine Sample Collection – Urinalysis
- Swab Collection
    - Rectal (x3)
    - Vaginal (x3) – for participants with a vagina only
    - Throat (x2)

Visit 12 (Hour 504/Day 21)

This visit will take place 504 hours (21 days) after the first dose (T^1 = 0 hr).

Procedures conducted at this visit may include:

- Blood Sample Collection **–** up to 10 mL
- Urine Sample Collection – Urinalysis
- Swab Collection
    - Rectal (x3)
    - Vaginal (x3) – for participants with a vagina only
    - Throat (x2)

Study-Specific Procedures

Visit Windows

Windows for all study visits are provided in Table 1. Study staff should make efforts to stay within these windows, however, study procedures done outside the provided windows will not be considered a protocol deviation.

Dosing

Participants will be asked not to eat or drink anything except water after midnight the day before their scheduled dose. Study personnel will dispense study drug to participant. Doses 1, 2 and 5 will take place in the clinic. Participants will take doses 3 and 4 at home according to the schedule of activities.

Proof of Home Dosing

Photos and videos taken with smartphones automatically include a timestamp. Study staff will instruct participants to bring the photo/video to their next clinic visit as proof of dosing. Participants will also have the option to send a text study staff at a specified number at the time of dosing if their phone does not have video/photo capabilities.

HIV Testing

Participants who are presumed HIV negative but test positive on study will be referred for confirmatory testing. Study staff will also assist any HIV positive participant in accessing healthcare for HIV infection as needed.

Evidence-based HIV/STI Risk Reduction Counseling

Topics covered in this counseling should include increasing condom use, reducing number of partners, addressing substance abuse, PrEP, undetectable=untransmissible, etc. Counseling will be provided by the study coordinator or clinician with provision of condoms and lubricant available for free at the Hope Clinic.

HIV negative participants will also be educated about HIV pre-exposure prophylaxis during the study by the coordinator and/or study clinician. After completion of the study, individuals who are interested in PrEP for HIV prevention will be linked to community services.

Vaginal/Cervical Mucosal Sampling Procedures

A trained, delegated clinician will be performing all vaginal/cervical mucosal sampling procedures with the assistance of the study coordinator utilizing a disposable speculum, light source, and sterilized Tischler biopsy forceps.

Once the speculum is inserted, additional swabs will be inserted into the vagina. Then, 1 to 2 vaginal and 1 to 2 cervical biopsies will be collected. Monsel's paste or similar product may be used to stop sites of active bleeding. All participants will be informed not to place anything into the vagina and abstain from intercourse for 7 days after the procedure to allow the mucosa to heal.

Vaginal and cervical tissue samples will not be collected in women who are menstruating, pregnant, or have possible cervical or vaginal infection. A pregnancy test will be administered to women of childbearing potential to ensure they are not pregnant. The first vaginal/cervical biopsy will be scheduled 7 to 10 days after their last menstrual cycle.

Twenty-four to forty-eight hours after the procedure, study personnel will call the participants who donated biopsy samples and inquire about symptoms, complications, or adverse events related to study procedures. Participants who report symptoms suggestive of any significant complications will receive advice on seeking care and will be given referrals to appropriate healthcare professionals as needed. This follow-up may be completed over the phone or through electronic communication.

Rectal Mucosal Sampling Procedures

A trained, delegated clinician will be performing all rectal mucosal sampling procedures with the assistance of the study coordinator utilizing a disposable anoscope, rigid sigmoidoscope, light source, and jumbo biopsy forceps.

Then, without the administration of any previous enemas or other preparation, a rigid sigmoidoscope will be inserted and 2-4 (first biopsy) or 8-12 (second biopsy) adequate ~1.0 mm thick biopsy specimens will be taken from normal-appearing rectal mucosa approximately 10 cm above the external anal aperture using flexible sigmoidoscopic forceps mounted on a semi-flexible rod. All biopsy specimens will be coded with a unique numeric identifier such that the laboratories that receive the specimens will be unable to link them back to the study participants. Two to three biopsy specimens will be placed immediately into cryotubes for testing of drug levels at CDC. The remaining biopsy specimens will be placed in media and transported to Dr. Kelley's lab where the specimens will be processed for various laboratory protocols (e.g., bulk and spatial transcriptomics, exogenous hormone treatment for bulk and spatial transcriptomics and explant challenge experiments, or flash-frozen for subsequent quantification of HIV within rectal tissue).

Twenty-four to forty-eight hours after the procedure, study personnel will call the participants who donated rectal biopsy samples and inquire about symptoms, complications, or adverse events related to study procedures. Participants who report symptoms suggestive of any significant complications will receive advice on seeking care and will be given referrals to appropriate healthcare professionals as needed. This follow-up may be completed over the phone or through electronic communication.

Table 1. Study Schema – Arm A & B

	Screening Visit	Visit 1a	Visit 1b	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7a	Visit 7b	Visit 8	Visit 9	Visit 10	Visit 11	Visit 12
Timepoint (Days)	-42 to 0	0	0	1	2	3	7	10	14	14	15	16	17	18	21
Timepoint (Hours)	-	0	2-4	24	48	72	168	240	336	338-340	360	384	408	432	504
Window	-	-	±2 hr	±2 hr	± 2hr	±2 hr	±2hr	±2hr	±2hr	±2hr	±2hr	±2hr	±2hr	±72hr	±72hr
Informed Consent	X														
Physical Exam	X			X[1]							X[1]				
Medical History	X			X[1]							X[1]				
Current Medications	X			X[1]							X[1]				
Screening Labs[2]	X														
Pregnancy Test	X			X							X				
Eligibility	X														
Dose Administration		X				X	X[3]	X[3]	X						
Biopsy				X							X				
Urine Sample	X	X		X	X	X			X		X	X	X	X	X
Rectal & Vaginal[4] Swab		X	X	X	X	X			X	X	X	X	X	X	X
Throat Swab		X	X	X	X	X			X	X	X	X	X	X	X
Urethral & Glans Swab				X		X					X		X		
Blood Volume	17 mL	10 mL	10 mL	10 mL	10 mL	10 mL			10 mL	10 mL	10 mL	10 mL	10 mL	10 mL	10 mL

[1]Abbreviated/symptom-directed/review during non-screening visits.
[2]Includes CBC, coagulation, creatinine, HIV testing, urine, and self-collected swab for chlamydia & gonorrhea.
[3]Dose taken at home.
[4]Vaginal swabs done only on participants with vaginas.

7. Statistical Analysis Plan

Primary Outcomes

Comparisons between time points will be conducted with a non-parametric statistical test of differences in median doxycycline concentrations between the two dosing regimen arms, stratified by sex assigned at birth. P-values less than 0.05 will be considered significant.

Exploratory Outcomes

Exploratory outcomes will be analyzed with various statistical methods to examine changes over time in doxycycline concentrations between the dosing arms, stratified by sex assigned at birth.

8. Data and/or Specimen Banking

Data and biological specimens collected for this study will be stored at the Hope Clinic. Identifiable data will be kept in a separate, locked cabinet at Hope Clinic and only accessible by MPIs and study staff. Electronic data will be stored in a secure database only accessible to study staff. Data and biological specimens will be stored with a unique study code number to maintain the blinding of the identity of the participant. After the study is completed, the de-identified, archived data and specimens may be stored for use by other researchers including those outside of the study. Only the PI and study staff will have access to a list that links a participants' unique study code to their identifiable information.

Leftover specimens from all study participants will be stored indefinitely and may be used for future use including laboratory assay development, unless a participant requests that specimens be destroyed or if required by IRB or other regulatory authority. Other use of specimens may apply to studies not covered by the protocol or the informed consent form for the main study.

De-identified data from this study may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. Any personal information that could identify participants will be removed or coded before the information is shared. Despite these measures, we cannot guarantee anonymity of participant personal data.

9. Sharing of Results with Participants

Study results, including results of laboratory tests, will not be shared with participants. If abnormalities deemed to be clinically significant are discovered during the procedure and/or from the safety labs, such as positive STI tests, these results will be discussed with the participant and a referral will be made to a primary care physician or specialist, as needed.

10. Study Timelines

- Participants will be considered on study for no more than 7 weeks .
- The duration anticipated to enroll all study participants is 1 years.
- This study is expected to take 2 years to complete.

11. Inclusion and Exclusion Criteria

Inclusion Criteria

1. Aged 18-59 years
2. Assigned male sex or female sex at birth
3. In good general health
4. Not currently taking doxycycline or other tetracycline-derived antibiotics and no plans to initiate during the study
5. For HIV positive people, on stable antiretroviral therapy with an undetectable viral load and CD4 count> 300ul/ml
6. Willing to use condoms consistently for the duration of the study
7. Able to provide informed consent
8. No plans for relocation in the next 4 months
9. Not pregnant and does not plan on getting pregnant for the duration of the study
10. Willing to undergo peripheral blood, urine, rectal or vaginal secretion collection, and a rectal or vaginal and cervical biopsy procedure
11. Willing to use study products as directed

Exclusion Criteria

1. Current or chronic history of liver disease
2. Continued need for, or use during the 90 days prior to enrollment, of the following medications:
    a. Systemic immunomodulatory agents
    b. Supraphysiologic doses of steroids (short course steroids less than 7 days duration, allowable at the discretion of the investigators)
    c. Chemotherapy or radiation for treatment of malignancy
    d. Experimental medications, vaccines, or biologicals
3. Intent to use doxycycline or other tetracycline-derived antibiotics during the course of the study, outside of the study procedures
4. Any other clinical condition or prior therapy that, in the opinion of the investigator, would make the patient unsuitable for the study or unable to comply with the study requirements
5. Known allergic reaction to study drugs.
6. Significant laboratory abnormalities at baseline visit for rectal biopsies, including but not limited to:
    a. Hgb ≤ 10 g/dL
    b. PTT > 1.5x ULN or INR > 1.5x ULN

c. Platelet count <100,000

12. Population

This study will not include any of the vulnerable populations listed below.

- Adults unable to consent
- Individuals who are not yet adults (infants, children, teenagers)
- Pregnant women
- Prisoners
- Cognitively impaired or
- Individuals with Impaired Decision-Making Capacity

At the time of enrollment, participants will be asked to complete a demographic form in which they will indicate their sex assigned at birth (male/female), gender identity, ethnicity (Hispanic/Latinx or non-Hispanic/Latinx) and race with which they identify (White, Black/African American, American Indian/Alaska Native, Asian, Native Hawaiian/Other Pacific Islander, and/or Other). Other than sex assigned at birth, this information will be used for descriptive statistics only and not as a variable to explain differences between participants.

13. Vulnerable Populations

This research will not involve human fetuses, neonates, prisoners, minors or cognitively impaired adults.

14. Local Number of Participants

This study will accrue a total of 40 participants (20 AMAB and 20 AFAB). In order to reach this number, it is anticipated that 80 will sign consent and be screened.

Our goal will be to enroll approximately 50% AMAB and 50% AFAB. We will include participants from all races and ethnicities in the study. Every effort will be made to include data from diverse individuals. Based on similar studies previously conducted at the Hope Clinic, we expect a nearly 1:1 ratio AMAB: AFAB and a race/ethnicity distribution of approximately 45% Caucasian, 50% Black/African American, and 5% Hispanic/Latinx.

15. Recruitment Methods

Databases
The Hope Clinic maintains an extensive database of people who have previously expressed interest in participating in future research. Additionally, the study team will use existing Emory University databases, including Research Match and the Emory Healthcare Clinical Data Warehouse, which have agreed to be contacted about research opportunities. Email blasts and phone calls will be made to potential participants from these databases.

Electronic Medical Records
The Emory Healthcare and Grady EeMR systems will be utilized to identify patients who are living with HIV. Once a potential participant is identified, the study team will communicate with their care provider. The care provider will then reach out to the participant and ask if the

study team may contact them. If the patient agrees, a member of the study team will reach out directly to that patient.

Face- to-face Engagements
Participants may be actively or passively recruited at community venues listed below and engaged with limited information about the study and study qualifications. A site contact sheet or a tablet will be used to populate name, phone number, and email address of interested participants. Examples of locations used for face-to-face engagement are listed below:

a. Community annual events attended by study population
b. Bars and Night Clubs
c. Community organizations serving study population
d. Sporting events
e. Community venues

Online Engagements
Potential participants will be engaged and supplied with limited information about the study and study qualifications via free & paid advertisements on social media sites and dating apps.

a. Dating Sites (Tinder, Bumble, Jack'd, Adam4Adam, Grindr, etc.)
b. Social Network (Facebook, Snapchat, Instagram, etc.)
c. Other online social media platforms and websites where study population might visit/patronize
d. Craigslist

Management of the social media sites will be the responsibility of approved and trained clinical recruitment research staff members. Site log-in credentials are kept in a locked document, to which access is only granted after a full review of expectations and training. Upon registration for potential social media sites, the research team plans to review and screen content for adherence to site specific terms of use and advertising, privacy and prohibited content policies of the social media sites to be used for recruitment. A team supervisor will conduct regular reviews of posted material to ensure continued compliance to both social media site and IRB-communication guidelines. Team members will continuously monitor media for posts and comments that may need to be addressed as a result of involving PHI, study specific information, or any other inappropriate content. Those staff members engaging with the community through approved social media accounts will abide by the following guidelines:

- When action is supported by the site's platform, interested participants will click a posted ad with an embedded hyperlink, which will redirect them to a short screener. This screener will capture information regarding eligibility, including HIV status, name, phone number and email. Recruiters will use information obtained from online screener to contact and schedule participant visits.
- When posting in site user groups/discussion boards, research staff will seek permission from creator/ moderator of the private website/ group, etc. before entering an interaction if possible.
- If a potential participant reaches out to the team via social media site, the team will respond providing contact info for the clinic and requesting their information and consent to be contacted via phone. To avoid a potential violation of privacy, the team will not request any PHI via direct message and after responding, delete any unsolicited private information that the potential participant may have sent.

Print Ads and Listservs
In order to reach a wider audience, print ads will be placed around Emory and other community settings. Study staff will also utilize listservs run by our community partners to disseminate recruitment materials.

Text Messaging
This method will only be used for participants who have indicated they are willing to receive messages via text. This information will be collected in sign in sheets or via questionnaires. For texting, an initial text message will be sent asking if the participant consents to receiving text messages. Consent to message via text will be stored in Clinical Conductor. Participants who have already consented to text messages via previous recruitment efforts, will receive a message asking if they're still interested in participating and for the best time and date to contact them if so.

16. Withdrawal of Participants

A study participant may elect to discontinue participation in the study at any time. The study may be discontinued at any time by the IRB, the OHRP, or other government agencies as part of their duties to ensure that research subjects are protected. Participants are free to withdraw from participation in the study at any time upon request. Under certain circumstances, an individual participant may be terminated from participation in this study. Specific events that will result in early termination include:

- Participant refuses further participation
- Participant relocates prior to completion of the biopsy visit
- If any laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant
- If the participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation

The reason for participant discontinuation or withdrawal from the study will be recorded on the appropriate Case Report Form (CRF).

17. Risk to Participants

Phlebotomy

Risks include discomfort, pain, bruising, bleeding, dizziness, fainting and possibility of infection. Only qualified and trained staff using sterile technique will perform the procedure.

Collection of Rectal and Vaginal Fluid

This swab procedure is a non-invasive sample collection method. Brief discomfort is the only foreseeable risk.

Collection of Rectal Fluid

This swab procedure is a non-invasive sample collection method. Brief discomfort is the only foreseeable risk.

Rigid Sigmoidoscopy

Risks associated with lower gastrointestinal endoscopy performed for clinical purposes include colitis from chemicals for endoscope sterilization, bowel perforation, bleeding, diverticulitis, and infection. Colonoscopy has been shown to be associated with a still low, but significantly greater risk of complications than rectosigmoidoscopy[5]. The frequency of serious complications after flexible sigmoidoscopy is extremely low and complications from rigid sigmoidoscopy are presumably even lower, but unknown. All sigmoidoscopy procedures will be performed by a trained, delegated clinician who will utilize disposable rigid sigmoidoscopes and forceps for the procedures.

Rectal Biopsies

To minimize risks in this study, the number of biopsies taken will be limited to 12. In two studies on rectal biopsies[6,7], serious complications occurred at a rate of 0.33%. More relevant to the present protocol, in a study of subjects undergoing endoscopic procedures exclusively for research purposes[8], there were no major complications. Minor risks include self-limited bleeding and pain, which were not related to the number of biopsies. Thus, the risk of serious complications from the proposed study procedures, even with up to 12 biopsy specimens, is expected to be very low. Of note, Dr. Kelley's team has performed >400 such procedures for other research protocols at the Hope Clinic with zero complications.

There is theoretical risk of increased acquisition of HIV or other infection if an HIV negative study participant is exposed soon after the rectal biopsy procedure (i.e., while the mucosal surface is damaged). Similarly, transmission risk from an HIV positive participant to sexual partners may also be heightened with mucosal bleeding. Therefore, study subjects will be counseled not to engage in anal intercourse for 1 week after the procedure.

Any abnormalities discovered during the procedure and/or from the safety labs conducted will be discussed with the participant, and a referral will made to a primary care physician, gastroenterologist or other specialist as needed.

Vaginal and Cervical Biopsies

To minimize the risks in this study, the number of vaginal and cervical biopsies taken will be limited to 2 each. Risks of vaginal and cervical biopsies include pain, discomfort, a persistent odor, bleeding, and infection. If bleeding occurs that cannot be stopped by applying pressure, medication will be used, such as Monsel's solution and paste, to stop it. When applied, Monsel's solution will produce silver nitrate. Silver nitrate has a gray color that can cause gray flecks in the vaginal discharge after the biopsy is completed. All female participants will be notified of this expected side effect. Subjects will be instructed on how to care for the area and to contact the PI or their medical care provider if any of the aforementioned risks occur and persist.

Doxycycline

Doxycycline (DOX) is a medication used to treat or prevent infections that are strongly suspected to be caused by bacteria[9-11]. DOX is an antimicrobial drug indicated for bacterial infections such as sexually transmitted infections. The most common adverse reaction reported is diarrhea. Other adverse reactions include vomiting, nausea, dysphagia, and inflammatory lesions. Additional adverse reactions that are rare and not expected to occur with the short course regimen prescribed in this protocol include hepatotoxicity, exfoliative

dermatitis (skin), rise in BUN levels, hypersensitivity reactions, hemolytic anemia, neutropenia, and eosinophilia[9-11].

The medication provided in this study is not for treatment or prevention of HIV and other STI infections. Participants who are interested in pre-exposure prophylaxis (PrEP) or STI PEP after this study ends, will be referred to a medical provider who can prescribe these.

To protect against possible side effects of the study drug, women who are pregnant or nursing a child may not take part in this study. If a female participant becomes pregnant, there may be risks to the participant, the embryo, or fetus. These risks are not yet known. Women of childbearing potential will be asked to provide a urine pregnancy test to ensure they are not pregnant, prior to administering drug. Women of childbearing ability will discuss contraceptive methods to use throughout the study and may be asked to abstain throughout the duration of the study. If the participant becomes pregnant during the study, they must inform the study doctor immediately. Pregnant women will be excluded or removed from the study.

18. Potential Benefits to Participants

There is no anticipated direct benefit to participants.

19. Compensation to Participants

Participants will be compensated according to the schedule below:

- Screening Visit: $50
- In Clinic Follow-Up Visits: $50 x 10 visits = $500
- Biopsy Visit: $100 x 2 visits = $200
- Total Compensation: $750
- Optional Rectal Biopsy (Participants with Vaginas Only): $100 x 2 visits = $200
- Unscheduled/Drug Dispensation Visit (if needed): $20

If they do not finish the study, they will be compensated for the visits they have completed. Participants may also receive an additional $25 for peer referrals to the study if the peer referral enrolls in the study and identifies the enrolled participant as the referral source.

Compensation will be provided via Emory ClinCard.

20. Data Management and Confidentiality

The principal investigator, Dr. Colleen Kelley, will be ultimately responsible for receipt and transmission of the data and biospecimens. Biospecimens may be transported by local courier or shipping.

Participants will be assigned a unique study-specific identification number after they sign the consent form. All collected data and specimens will be associated with this number (excluding demographic intake forms). Data will be recorded on paper Case Report Forms (CRFs) and entered into a study-specific REDCap Database. Data entered in REDCap will only be linked to a participant by a unique study identification number. Paper forms will be

stored in a locked cabinet at Hope Clinic. Only study staff will have access to identifiable data.

Biologic specimens will be labeled with a unique study identification number at stored at the Hope Clinic prior to processing or shipment to another lab for assays. Laboratory staff will be unable to link the specimen identifier number with identifiable information.

Data and specimens will be stored indefinitely. However, once the IRB protocol is closed, deidentified electronic data will be exported from the REDCap database for long-term storage on Emory OneDrive. Paper records will be destroyed no sooner than 1 year after IRB close out.

Certificate of Confidentiality

Consistent with Section 301(d) of the Public Health Service Act, a Certificate of Confidentiality (CoC) applies to this research because this research is funded, conducted, or supported by CDC and the following is true:

The activity constitutes biomedical, behavioral, clinical, or other research; AND

1. Individually identifiable (including coded) information or biospecimens will be obtained or used for research purposes or as defined at 45 CFR 46.102(e); and/or
2. Biospecimens are collected or used as part of the research, and is there a small risk that some combination of the biospecimen and other available data sources could be used to deduce the identity of an individual; and/or
3. The research involves information about an individual for which there is at least a very small risk, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual

Therefore, CDC and any of its collaborators, contractors, grantees, investigators or collaborating institutions that receive “identifiable, sensitive information” as defined by subsection 301(d) of the Public Health Service Act shall not:

- Disclose or provide, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding “identifiable, sensitive information” that was created or compiled for purposes of the research, unless such disclosure or use is made with the consent of the individual to whom the information, document, or biospecimen pertains; or
- Disclose “identifiable, sensitive information” or provide ISI to any other person not connected with the research.

Disclosure is permitted only when:

- Required by Federal, State, or local laws (e.g., as required by the Food, Drug and Cosmetic Act or required by state laws requiring the reporting of communicable diseases to State and local health departments), excluding instances of disclosure in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding;

- Made with the consent of the individual to whom the information, document, or biospecimen pertains; or
- Made for the purposes of other scientific research that is in compliance with applicable Federal regulations governing the protection of human subjects in research.

CDC and its collaborators and contractors conducting this research will establish and maintain effective internal controls (e.g., policies and procedures) that provide reasonable assurance that the research is managed in compliance with subsection 301(d) of the Public Health Service Act. CDC will ensure: 1) that any investigator or institution not funded by CDC who receives a copy of identifiable, sensitive information protected by this Certificate, understands that it is also subject to the requirements of the Certificate; and 2) that any subrecipient that receives CDC funds to carry out part of this research involving a copy of identifiable, sensitive information protected by a Certificate understands that it is subject to subsection 301(d) of the PHS Act. Therefore, all study staff will receive training on the importance of protecting the confidentiality of human research subjects and of personal information acquired, including the collection of biological specimens.

All research subjects will be informed of the protections and the limits to protections provided by this Certificate through the informed consent process. All study staff who obtain consent from study subjects will be trained on how the Certificate protects the information collected and the limitations of the Certificate's protections.

21. Plans to Monitor the Data to Ensure Safety of Participants and Data Integrity

X **More than minimal risk** – Continue below.

Select one of the following:
☐ Medium Complexity
☐ High Complexity Category A
☒ High Complexity Category B *If choosing this category for a study under an IND or IDE because you believe the study intervention does not significantly impact morbidity or mortality, please provide your rationale:*

DSMP Requirement	How this Requirement is Met	Frequency	Responsible Party(ies)
Site Monitoring at pre-determined intervals: The Principal Investigator has a responsibility to ensure that the study is following all aspects of the protocol.	*There should be a standard operating procedure to review data (whether a sample or 100%) at pre-determined intervals to ensure that there is adequate documentation of critical elements such as eligibility criteria. Monitoring is required at*	*At a minimum, a review is required annually when no one has been enrolled or the study is in long term follow up. Additional risk-*	*Delegate a responsible party for each requirement below.* Self-assessment is acceptable.* *Self-assessment*: a process for self-

DSMP Requirement	How this Requirement is Met	Frequency	Responsible Party(ies)
	the following timepoints (but may be done more frequently): • *study initiation* • *at least every six months while participants are receiving intervention and* • *annually while participants are in follow-up*	*based interim monitoring may be required at least once every 12-24 weeks based on the site activity, to include the possibility of remote monitoring. A longer frequency could be acceptable with justification about risk to participants.*	assessment of protocol compliance and data integrity which can be part of an overall DSMP. See Emory's self-assessment tool on this page.
Real-time review of participant data during initial data collection.	After data collection for a visit is complete, another study coordinator or nurse reviews the visit documentation.	Following each study visit	Everyone on the study team responsible for primary data collection.
100% review of regulatory files	A review of the study regulatory binder will be conducted.	At study initiation and IRB close out.	Hope Clinic Quality Management Staff
100% review of consent forms	The Hope Clinic consenting SOP requires real time verification of all consents by a staff member other than who obtained consent.	Real time	Hope Clinic Staff
Review of credentials, training records, the delegation of responsibility logs (if applicable)	The Hope Clinic Regulatory Core maintains a spreadsheet of all non-study specific trainings/documents and their expiration dates. This spreadsheet is reviewed on a weekly basis. The Regulatory Coordinator maintains a study-specific spreadsheet tracking all study staff, DOA start and stop dates as well as training dates. This spreadsheet is reviewed any time an update is needed and on a monthly basis.	Monthly	Study Regulatory Coordinator
Comparison of case report forms (CRF) to source documentation for accuracy and completion	After data collection for a visit is complete, another study coordinator or nurse reviews the visit documentation and compare to the EDC.	Following each study visit	Everyone on the study team responsible for primary data collection.
Review of documentation of all adverse events	After data collection for a visit is complete, another study coordinator or nurse reviews the visit documentation.	Following each study visit	Everyone on the study team responsible for primary data collection.
Monitoring of critical data points (eligibility, study endpoints, etc.)	Self-assessment tool will be completed by study staff twice annually while subjects are still active on study.	Twice annually while subjects are still active on study.	Lead Study Coordinator/Nurse
Laboratory review of processing and storage of specimens	Self-assessment tool will be completed by study staff twice annually while subjects are still active on study.	At study initiation, twice annually while subjects are still on study and at IRB close out.	Hope Clinic Laboratory Manager

DSMP Requirement	How this Requirement is Met	Frequency	Responsible Party(ies)
Assessment of laboratory specimens stored locally	Self-assessment tool will be completed by study staff twice annually while subjects are still active on study.	Twice annually while subjects are still active on study.	Hope Clinic Laboratory Manager
Test article accountability review	Self-assessment tool will be completed by study staff twice annually while subjects are still active on study.	At study initiation, twice annually while subjects are still on study and after the last subject has completed all dosing visits.	Investigational Drug Services (IDS) Pharmacist
Accountability logs, dispensing records, and other participant records	Self-assessment tool will be completed by study staff twice annually while subjects are still active on study.	Twice annually while subjects are still active on study.	Investigational Drug Services (IDS) Pharmacist
For FDA regulated studies, the following requirements apply:	**How this Requirement is Met**	**Timing, frequency, and intensity of monitoring**	**Responsible Party(ies)**
Monitoring methods (may include centralized, on-site, and self-assessment)	N/A	N/A	N/A

Subject Safety

Physical exam, medical history, and safety labs will be checked prior to each biopsy visit to ensure no increased risk for complications. Biopsy procedures will be conducted with all disposable materials in a private clinic room. Case report forms will be completed in a timely fashion so as to be reviewed by the PI, study staff, etc. The participant will be contacted 1-2 days after biopsy procedures to collect any adverse events. Once an unanticipated event is recognized and reported, the event will be investigated to determine if the event represents an unreasonable risk to the subject so as to terminate all or part of the study.

The investigators will review all data in real time and resolve any inconsistencies. Adverse events associated with rectal biopsy will be reported per local IRB/EC requirements.

22. Provisions to Protect the Privacy Interest of Participants

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be stored in locked cabinets at the Hope Clinic or on a secure online database. Electronic data will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by the Hope Clinic research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived.

Authorized representatives of the sponsor, Emory Institutional Review Board (IRB), and/or regulatory agencies may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and

pharmacy records for the participants in this study. The clinical study site will permit access to such records.

23. Economic Burden to Participants

There will be no costs to subjects for participating in this study, other than basic expenses like transportation.

24. Informed Consent

The protocol informed consent form documents that a participant (1) has been informed about the potential risks, benefits, and alternatives to participation, and (2) is willing to participate in the study. Informed consent encompasses all written or verbal study information study staff provide to the participant, before and during the trial. Study staff will obtain informed consent of participants according to applicable policies and procedures.

The informed consent process will continue throughout the study. Key study concepts will be reviewed periodically with the participant and the review will be documented. At each study visit, study staff will consider reviewing the procedures and requirements for that visit and for the remaining visits.

Additionally, if any new information is learned that might affect the participants' decisions to stay in the trial, this information will be shared with trial participants. If necessary, participants will be asked to sign revised informed consent forms.

Process to Document Consent in Writing

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Consent forms will be Institutional Review Board (IRB)-approved.

The investigator or his/her designee will explain the research study to the participant and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. Participants must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the participants for their records. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

Non-English-Speaking Participants: If any non-English speaking participants plan to be enrolled, the study team will first use the Emory IRB provided short forms. Then, have the consent translated into the language the participant is proficient in, per IRB policy.

Participants who are not yet adults (infants, children, teenagers): Not applicable

Cognitively Impaired Adults: Not applicable

Adults Unable to Consent: Not applicable

Waiver or Alteration of Consent Process:
Per IRB guidance (http://www.irb.emory.edu/forms/consent_toolkit/index.html) studies that are not covered by HIPAA and are not conducting any procedures during pre-screening do not require an oral consent. Therefore, we will not be obtaining oral consent prior to the phone screening questionnaire.

25. Setting

All participant procedures will be completed in a clinic setting at the Emory Hope Clinic, except the at home doses. Emory Healthcare and Grady will only be utilized for identifying potential participants through EeMR. No study activities will take place at Emory Healthcare or Grady.

26. Resources Available

The Hope Clinic routinely meets enrollment goals. Over the years, we've developed a large pool of people interested in participating in our studies as well as strong partnerships that serve as resources for new potential participants. The Hope Clinic has been highly successful in recruiting subjects who are either at lower or higher risk of acquiring HIV infection and the LGBT community. The study team does not anticipate any issues recruiting for this study.

The Hope Clinic is a research-only facility in Decatur, with approximately 50 ongoing studies at a time. The facility has 8 clinic rooms on the top floor in which to see participants. The bottom floor houses the sample processing and storage lab. At all times there is a clinician in the clinic available to study staff (all clinicians are on all studies). Should a medical emergency arise, the clinician will manage the immediate situation. The Hope Clinic is located across the street from Emory Decatur Hospital. If needed, Hope Clinic staff would call 911 and have the participant transported there.

All Hope Clinic research staff have completed all Emory University institutional required research training. Prior to working on the study, each staff member is trained thoroughly on each protocol and it's supporting documents. There is a dedicated regulatory coordinator who ensures all training and delegation is completed appropriately for each study.

27. References

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7. Rutter MD, Saunders BP, Wilkinson KH, et al. Thirty-year analysis of a colonoscopic surveillance program for neoplasia in ulcerative colitis. Gastroenterology 2006;130:1030-8.
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28. Protocol Checklist

Please note that protocol sections with an asterisk (*) should always be included in the protocol; if the section does not have an asterisk, and you have not included the section in the protocol, the IRB will consider it your attestation that the section does not apply to your study.

Protocol Section	Added to the protocol?
External Collaborators- if applicable, add each external collaborator information and indicate whether that institution's IRB will review (or has already reviewed) that individual's engagement in human participants research activities)	☒ **Yes**
Funding Source*: Include the information for the funding entity for this study. Please explain if this study is covered by a sub-award or other pertinent information. Say "department" if you do not have any other funding.	☒ **Yes**
Objectives*: Describe the purpose, specific aims, or objectives and state the hypotheses to be tested	☒ **Yes**
Background*: Describe the relevant prior experience and gaps in current knowledge. Describe any relevant preliminary data. Provide the scientific or scholarly background for, the rationale for, and significance of the research based on the existing literature and how will it add to existing knowledge	☒ **Yes**
Study Endpoints*: Describe the primary and secondary study endpoints. Describe any primary or secondary safety endpoints.	☒ **Yes**
Study Intervention/Investigational Agent*: Describe the study intervention and/or investigational agent (e.g., drug, device) that is being evaluated.	☒ **Yes**
Drug/Device Handling: If the research involves drugs or devices, describe your plans to store, handle, and administer those drugs or devices so that they will be used only on participants and be used only by authorized investigators.	☒ **Yes**

If using a drug, explain if the control of the drug is managed by IDS (or VA/Grady/CHOA research pharmacies). If not, provide IDS exemption document. If a device, explain how the device is being stored and managed.	
If the drug is under an FDA REMS, plan to complete the REMS checklist found here, on the IRB website.	☐ **Yes**
If the drug is considered a controlled substance, make sure you have filled out this form.	☐ **Yes**
If applicable, identify the holder of the IND/IDE/Abbreviated IDE. An Emory investigator who holds an IND or IDE is considered to be a Sponsor-Investigator (S-I). If the study is under an S-I, review this section of our website for additional requirements.	☒ **Yes**
Procedures involved*: Describe and explain the study design and include a study schema. Describe all research procedures being performed and when they are performed, including procedures being performed to monitor participants for safety or minimize risks	☒ **Yes**
Procedures-Minimizing risk*: describe the procedures performed to lessen the probability or magnitude of risks.	☒ **Yes**
Procedures- Drug/Device Use: describe all drugs and devices used in the research and the purpose of their use and their regulatory approval status	☒ **Yes**
Procedures-Source Records*: describe source records that will be used to collect data about participants. Attach all surveys, scripts, and data collection forms to the submission.	☒ **Yes**
Procedures-Data collection*: describe what data will be collected during the study and how that data will be obtained	☒ **Yes**
Procedures- Long Term Follow Up*: once all research-related procedures are complete, what data will be collected during this period. If no data is collected after procedures are completed, please state in the submission.	☒ **Yes**
Data and Specimen Banking: describe where the specimens will be stored, how long they will be stored, how the specimens will be accessed, and who will have access to the specimens. Depending on the volume and nature of the collection, this may require a separate repository-specific IRB submission. The VA Data Repository SOP is required if the study is creating a data repository at the Atlanta VA. List the data to be stored or associated with each specimen. Describe the procedures to release data or specimens, including the process to request a release, approvals required for release, who can obtain data or specimens, and the data to be provided with specimens.	☒ **Yes**

Sharing of Results with Participants*: Describe whether results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) will be shared with participants or others (e.g., the participant's primary care physicians) and if so, describe how the results will be shared If applicable (e.g. for studies involving scans and/or panels of exploratory testing on specimens) Plan for managing the types of findings that might arise. This should include any secondary findings that are being sought actively, findings that might be anticipatable, and findings that might be un-anticipatable. Plan for recognizing, analyzing, and handling incidental findings and how incidental findings will be communicated to participants during the consent process. If the plan is not to disclose any findings, then this should be included. This plan might include the option for participants to opt-out of receiving incidental findings. Description of the research team's responsibilities following disclosure of a finding. This should detail educational information about the nature of the finding, how to seek care from a clinician or specialist, obtaining health insurance to secure treatment, and/or referral to a clinical specialist, if one is required. Reminder to include language in the consent form to let the participants know your plans for this – see Modular Language for Informed Consent Forms on IRB website)	**☒ Yes**
Study timelines*: describe the duration of an individual participant's participation in the study; anticipated time to enroll all study participants and the estimated date for the investigators to complete this study (complete primary analyses)	**☒ Yes**
Inclusion and Exclusion Criteria*: describe how individuals will be screened for eligibility and the criteria that define who will be included or excluded in your final study sample	**☒ Yes**
Population*: describe the study popualation and indicate specifically whether you will include or exclude each of the following special populations: • Adults unable to consent • Individuals who are not yet adults (infants, children, teenagers) • Pregnant women • Prisoners Note: you cannot exclude people with limited English proficiency unless you can demonstrate the scientific need for such exclusion. Community Participation: For studies aimed at addressing issues that affect a certain community or group: How, if at all, will this study involve people from the target community in the design of the study? Conduct of the study? How will the results of the research be shared with the participants and/or the target community/ies? **If studying Race or Ethnicity, have you defined these terms, and explained their proposed mechanism of action if these characteristics will be used in an explanatory model?**	**☒ Yes**

Research with pregnant women, fetuses, or neonates: review this checklist to verify you have provided enough information to ensure the safety and well-being of this population.	☒ **Yes**
Research with neonates of uncertain viability: review this checklist to verify you have provided enough information to ensure the safety and well-being of this population.	☒ **Yes**
Research involving prisoners: review this checklist to verify you have provided enough information to ensure the safety and well-being of this population.	☒ **Yes**
Research involving children: review this checklist to verify you have provided enough information to ensure the safety and well-being of this population.	☒ **Yes**
Research involving cognitively impaired adults: review this checklist to verify you have provided enough information to ensure the safety and well-being of this population.	☒ **Yes**
Research involving economically or educationally disadvantaged persons: describe the additional safeguards that have been included in the study to protect the rights and welfare of these subjects	☒ **Yes**
Local Number of Participants*: Indicate the total number of participants to be accrued locally. If applicable, distinguish between the number of participants who are expected to be enrolled and screened, and the number of participants needed to complete the research procedures (i.e., numbers of participants excluding screen failures.) Provide your projected enrolling goals, including the percentage of participants according to sex and race.	☒ **Yes**
Recruitment Methods*: Describe when, where, and how potential participants will be recruited. Describe the source of participants. Describe the methods that will be used to identify potential participants. Describe materials that will be used to recruit participants. Attach copies of these documents with the application. If including advertisements, attach the final copy of them. When advertisements are taped for broadcast*, attach the final* audio/videotape. You may submit the wording of the advertisement before taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/videotape. Describe the amount and timing of any payments to participants. Reimbursement for expenses/travel? If using contests or raffles as incentive, you must offer entry to all potential participants, not just those who enroll in the study/complete study-related procedures, per Georgia State Law. All research recruitment through social media needs to follow this guidance, which does not allow the use of personal social media accounts for some recruitment activities.	☒ **Yes**
Withdrawal of Participants*: Describe anticipated circumstances under which participants will be withdrawn from the research without their consent. Describe any procedures for orderly termination. Describe procedures that will be followed when participants withdraw	☒ **Yes**

from the research, including partial withdrawal from procedures with continued data collection.	
Risk to Participants*: List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the participants related to the participant's participation in the research. Include as may be useful for the IRB's consideration, a description of the probability, magnitude, duration, and reversibility of the risks. Consider physical, psychological, social, legal, and economic risks. If applicable, indicate which procedures may have risks to the participants that are currently unforeseeable. If applicable, indicate which procedures may have risks to an embryo or fetus should the subject be or become pregnant. If applicable, describe risks to others who are not participants.	**☒ Yes**
Potential Benefits to Participants*: Describe the potential benefits that individual participants may experience from taking part in the research. Include as may be useful for the IRB's consideration, the probability, magnitude, and duration of the potential benefits. Indicate if there is no direct benefit. Do not include benefits to society or others.	**☒ Yes**
Compensation to Participants*: Describe if/how subjects will be compensated for participation in this study. Indicate what method compensation will be delivered (e.g. cash, gift card, school credit). Describe the amount and timing of any payments to participants. How much? What kind? Is tax information required? (if so, must be reflected in the informed consent form). Will payments be pro-rated if a participant withdraws early?	**☒ Yes**
Data Management and Confidentiality*: Describe the data analysis plan, including any statistical procedures or power analysis. Describe the steps that will be taken to secure the data (e.g., training, authorization of access, password protection, encryption, physical controls, certificates of confidentiality, and separation of identifiers and data) during storage, use, and transmission. Describe any procedures that will be used for the quality control of collected data.	**☒ Yes**
Describe how data or specimens will be handled study-wide*: What information will be included in that data or associated with the specimens?	**☒ Yes**
• Where and how data or specimens will be stored? • How long the data or specimens will be stored? • Who will have access to the data or specimens? • Who is responsible for receipt or transmission of the data or specimens? • How data or specimens will be transported?	
Data Monitoring and Participants Safety (if this study is more than minimal risk, this section is required):	**☒ Yes**
Ensure that you review our Data and Safety Monitoring plan guidance for specific details about this section, and examples of what the IRB will be requiring according to the level of risk.	

If a DSMB is needed, please describe the composition of the board (if not already detailed in the protocol). Review this guidance for more information. If the sponsor protocol does not contain all required information, please in this section. Describe the plan to periodically monitor the data at the site level according to risk level. Include the appropriate completed monitoring table, if applicable. Description of the plan for notifying the IRB of reportable events, whether the sponsor requires reporting above and beyond the Emory IRB reporting requirements, and if so, a description of the requirements and plan for meeting them. Please address the specific details below. If deemed not applicable, please provide rationale: Subject safety: • Specific subject safety parameters • Frequency of subject safety observations • Individual responsible for safety monitoring • Subject stopping rules – under what conditions will a subject be removed from study participation and who will make the decision? • Study stopping rules - under what conditions will the study be modified or stopped and who will make the decision? • Reporting mechanisms (i.e. Deviations, adverse events, UPs) Data Integrity: • Specific data elements to be reviewed • Frequency of monitoring data, points in time, or after a specific number of participants • Individual responsible for data monitoring Additional considerations for FDA regulated trials Depending on the procedures affecting risks to participants, the site monitoring plan should specify: • Categorization of activities done centrally and those on-site if applicable • Monitoring methods (may include centralized/remote, on-site, and self-monitoring) • Reference to any tools used (i.e. checklists) • Identification of events that may trigger changes • Identification of deviations or failures that would be critical to study integrity	
Provisions to Protect the Privacy Interests of Participants*: • Describe the steps that will be taken to protect participants' privacy interests. "Privacy interest" refers to a person's desire to place limits on whom they interact with or whom they provide personal information. • Describe what steps you will take to make the participants feel at ease with the research situation in terms of the questions being asked and the procedures being performed. "At ease" does not refer to physical discomfort, but the sense of intrusiveness a participant might experience in response to questions, examinations, and procedures. • Indicate how the research team is permitted to access any sources of information about the participants.	**☒ Yes**
Economic Burden to Participants*: Describe any costs that participants may be responsible for because of participation in the research.	**☒ Yes**

Consent Process*: Describe where the consent process will take place, any waiting period available between informing the prospective subject and obtaining the consent; and the process to ensure ongoing consent. Describe the role of the individuals listed in the application as being involved in the consent process; the time that will be devoted to the consent discussion; steps that will be taken to minimize the possibility of coercion or undue influence; and steps that will be taken to ensure the participants' understanding. **Note**: If you are planning to obtain consent via electronic signature, please review this document. Additional guidance on consent documentation and process can be found on our website, under the consent toolkit.	☒ **Yes**
Consent Process-Non-English-Speaking Participants*: Indicate what language(s) other than English are understood by prospective participants or representatives. If participants who do not speak English will be enrolled, describe the process to ensure that the oral and written information provided to those participants will be in that language. Indicate the language that will be used by those obtaining consent. If you checked N/A, please provide reasoning of why subjects with limited English proficiency are excluded. **Note**: if you stated that subjects with LEP will be enrolled, you are approved for the use of the Emory IRB short forms. Please read the guidance about the use of short forms here.	☒ **Yes**
Consent Process-Children: After determining if the subject is a child per GA law (or if enrolled outside GA, per state/country law), please describe whether parental permission will be obtained from: • Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. • One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child. Describe whether permission will be obtained from individuals other than parents, and if so, who will be allowed to provide permission. Describe the process used to determine these individuals' authority to consent to each child's general medical care. When assent of children is obtained describe whether and how it will be documented per Emory Policies and Procedures	☒ **Yes**
Consent Process-Cognitively Impaired Adults: describe the process to determine whether an individual is capable of consent. The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require assent documents and does not routinely require children to sign assent documents.	☒ **Yes**
Consent Process-Adults Unable to Consent: List the individuals from whom permission will be obtained in the order of priority. (E.g., durable power of attorney for health care, a court-appointed guardian for health care decisions, spouse, and adult child.)	☒ **Yes**

For research conducted in the state, review "46 LEGALLY AUTHORIZED REPRESENTATIVES AND SURROGATE CONSENT" to be aware of which individuals in the state meet the definition of "legally authorized representative." For research conducted outside of the state, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the procedure(s) involved in this research. Describe the process for the assent of the participants. Indicate whether: • Assent will be required of all, some, or none of the participants. If some, indicated, which participants will be required to assent and which will not. • If assent will not be obtained from some or all participants, an explanation of why not. Describe whether the assent of the participants will be documented and the process to document assent. The IRB allows the person obtaining assent to document assent on the consent document and does not routinely require assent documents and does not routinely require participants to sign assent documents	
Waiver or Alteration of Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception) Review the Emory IRB waiver document to ensure you have provided sufficient information for the IRB to make these determinations. If the research involves a waiver of the consent process for planned emergency research, please review the "CHECKLIST: Waiver of Consent for Emergency Research (HRP-419)" to ensure you have provided sufficient information for the IRB to make these determinations.	**☒ Yes**
Setting*: Describe the sites or locations where your research team will conduct the research including where the subject will be identified and recruited, where the research procedures will be performed, and if you will involve a community advisory board. For research conducted outside the organization and its affiliates describe the site-specific regulations or customs affecting the research outside the organization and the local scientific and ethical review structure outside the organization.	**☒ Yes**
Resources Available*: Describe the resources available to conduct the research such us the feasibility of recruiting the required number of suitable participants within the agreed recruitment period; describe the time that you will devote to conducting and completing the research; describe the availability of medical or psychological resources that participants might need as a result of an anticipated consequences of the human research; describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.	**☒ Yes**
Multi-Site Research when Emory is the Lead Site: Study -Wide Number of Participants: indicate the total number of participants to be accrued across all sites. Study-Wide Recruitment Methods: If this is a multicenter study and participants will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements) describe those methods. Describe when, where, and how potential participants will be recruited.	**☒ Yes**

Describe the methods that will be used to identify potential participants. Describe materials that will be used to recruit participants. Describe the processes to ensure communication among sites. See “WORKSHEET: Communication and Responsibilities (HRP-830).” All sites have the most current version of the protocol, consent document, and HIPAA authorization. All required approvals (initial, continuing review and modifications) have been obtained at each site (including approval by the site’s IRB of record). All modifications have been communicated to sites and approved (including approval by the site’s IRB of record) before the modification is implemented. All engaged participating sites will safeguard data, including secure transmission of data, as required by local information security policies. All local site investigators conduct the study in accordance with applicable federal regulations and local laws. All non-compliance with the study protocol or applicable requirements will reported in accordance with local policy Describe the method for communicating to engaged participating sites (see “WORKSHEET: Communication and Responsibilities (HRP-830)”):	
• Problems (inclusive of reportable events). • Interim results. • The closure of a study	
If this is a multicenter study where you are a participating site/investigator, describe the local procedures for maintenance of confidentiality. (See “WORKSHEET: Communication and Responsibilities (HRP-830).”)	
• Where and how data or specimens will be stored locally? • How long the data or specimens will be stored locally? • Who will have access to the data or specimens locally? • Who is responsible for receipt or transmission of the data or specimens locally? • How data and specimens will be transported locally?	