BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2023-075250
Article Type:	Protocol
Date Submitted by the Author:	01-May-2023
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Keywords:	HIV & AIDS < INFECTIOUS DISEASES, Feasibility Studies, Health Equity, Health Education, SEXUAL MEDICINE, Primary Prevention

Protocol for WeExPAnd: PrEP Demonstration Project among Women Vulnerable to HIV Infection in the US South

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Abstract

Introduction: African American women (AA), particularly those living in the southeastern United States (US), experience disproportionately high rates of HIV infection. Pre-exposure prophylaxis (PrEP) is a highly effective HIV prevention tool that may circumvent barriers to traditional HIV prevention tools, such as condom use; however, very little is known about how to improve PrEP access and uptake among AA women who may benefit from PrEP use. This project aims to understand how to increase PrEP access among AA women in the rural US South, which may ultimately affect HIV incidence in this population.

Methods and Analysis: The goal of the current study is to systematically adapt a patient-provider communication tool to increase PrEP uptake among AA women receiving care at a federally qualified health center (FQHC) in Alabama. We will use an iterative implementation process, by assessing the feasibility, acceptability, and preliminary impact of the tool on PrEP uptake, using a pilot pre-/post-intervention design (N=125). We will evaluate women's reasons for declining a referral to a PrEP provider, reasons for incomplete referrals, reasons for not initiating PrEP after a successful referral, and ongoing PrEP use at 3 and 12 months after PrEP initiation among our sample. The proposed work will significantly contribute to our understanding of factors impacting PrEP uptake and use among AA women, particularly in underserved areas in the Deep South that are heavily impacted by the HIV epidemic and experience worse HIV-related health outcomes relative to other areas in the US.

Ethics and Dissemination: This protocol has been approved by the Institutional Review Board (IRB) at University of Alabama at Birmingham (UAB; Birmingham, AL; protocol 300004276). Results will be disseminated through peer-reviewed manuscripts, reports, and local, national, and international presentations.

Strengths and limitations of this study

- Application of an implementation science framework facilitates rapid implementation, evaluation, and modification of a novel patient-provider communication intervention to increase PrEP awareness and potential uptake for women in an U.S. region where HIV transmission remains comparatively high.
- Provides data on PrEP uptake and key social, behavioral, and cultural factors associated with PrEP uptake among African American women in the South, who remain under-represented in PrEP research despite being disproportionately affected by HIV.
- Expands knowledge base on PrEP attitudes and experiences among health care providers within a Federally Qualified Health Care Center (FQHC) in the South, where many women who may benefit from PrEP enter the health care system.
- Challenges and barriers identified by participants and providers throughout the adaptation process may include contextual, structural, and system-level factors that are beyond the scope of this communication intervention.

Introduction

The Deep South region of the United States (US) bears the greatest burden of the HIV epidemic in the US, with rural counties disproportionately affected and underserved by both HIV care and prevention services.[1,2] Of the more than 1.1 million people living with HIV in the US in 2018, women accounted for nearly a quarter (23%) of all cases and a significant portion (19%) of new cases, with most new cases attributed to heterosexual contact (85%).[3] Despite representing just 13% of the US female population, African American (AA) women accounted for 55% of new HIV diagnoses among all women in the US in 2019.[2] In 2016, the rate of new HIV diagnoses among AA women was 15 times higher than that of White women,[3] and in

2018, HIV infection ranked in the top eight leading causes of death among AA women aged 20-44 in the US.[4] The elevated HIV risk profile among AA women in the South may reflect factors unique to rural areas, such as the prevalence of small sexual networks resulting in cyclical HIV transmission patterns,[5] in addition to barriers to HIV prevention rooted in structural racism such as high incarceration rates among male AA populations, limited awareness of and access to effective contraception and sexual health interventions, higher rates of concurrent partnerships among AA men in AA women's sexual networks, and financial and transportation-related barriers to accessing HIV/STI screening, prevention, and treatment.[6-11]

Traditional HIV prevention efforts, such as abstinence-only education approaches that are prevalent in the rural South, have been insufficient to control high rates of sexually transmitted infections (STIs) and HIV infections. Abstinence-only education does not provide women with comprehensive information critical for maintaining sexual health.[12,13] Moreover, interventions promoting condom use, partner-based testing, and/or monogamous relationships are dependent on behaviors of women's sexual partners and, therefore, may be outside each woman's direct control. AA women experiencing financial challenges may be financially dependent on male partners; they may also be experiencing intimate partner violence, further complicating their ability to make independent sexual health decisions.[14,15] Given disproportionate diagnoses and mortality among AA women, along with limitations to non-biomedical HIV prevention methods, novel and more effective approaches to HIV prevention are necessary.

Biomedical HIV prevention tools, including pre-exposure prophylaxis (PrEP) are promising as they hold the potential to minimize barriers to traditional means of HIV prevention among groups who are persistently vulnerable to HIV infection. Oral PrEP has over 90% efficacy demonstrated across numerous trials, including cisgender women, but efficacy

depends on consistent daily adherence as prescribed.[16] Long-acting injectable PrEP is also highly efficacious for cisgender women and is now available for use in the U.S.[17,18] Although overall oral PrEP prescriptions in the US increased substantially between 2012 and 2017, PrEP uptake among AA women has remained low. While biomedical prevention efforts have historically focused on men who have sex with men (MSM), women have not received equitable attention reflective of the epidemiology.[19] Indeed, 94% of PrEP users in 2017 were male, indicating a substantial unmet need among PrEP-eligible women.[18] In 2016, only 11% of all PrEP users with available race/ethnicity data were from AA communities.[20]

Regardless of geographic location, most women in the US remain unaware of PrEP, and PrEP uptake among AA women remains low, particularly in rural areas of the US where women may have less access to healthcare and more limited knowledge of PrEP than women in urban areas.[21] In several studies, the majority of women participating in PrEP focus groups, as well as staff at health services organizations, were unfamiliar with PrEP as an HIV prevention tool and expressed concern about a broad lack of awareness within their communities; of the 10% of women who had previously heard of PrEP, none were aware of its availability and efficacy for women.[22,23] However, AA women expressed being generally interested in using PrEP if available,[24] especially if recommended by a trusted health-care provider.[25]

Suboptimal patient-provider communication has been identified as a barrier to PrEP uptake among AA women,[26] as has limited provider knowledge of PrEP. Historically, the most common reported barriers to prescribing PrEP include a perceived lack of clinical training and experience in PrEP delivery, greater time investment to monitor patients on PrEP, and insufficient structural support from clinic sites.[27] In a 2022 survey of 359 health care providers across the US, 100% of respondents were aware of PrEP, about 97% reported willingness to

prescribe PrEP, and around 80% had prescribed PrEP;[28] however, these statistics varied by region of practice and by race, with a higher number of providers prescribing PrEP in the West and a disproportionate number of PrEP prescriptions provided to White individuals.[28] A recent qualitative study among providers in Alabama indicated uncertainty about offering PrEP to AA heterosexual, cis-gender adolescent or young adult females in the absence of transactional sex or a known HIV positive partner.[29]

Existing literature highlights numerous barriers to effective patient-provider communication about sexual health, including time constraints, embarrassment or shame surrounding these topics, patient confidentiality concerns, and both language and cultural barriers.[30-33] Moreover, PrEP services are less routinely implemented in settings where many patients who may benefit from PrEP use may receive care, such as Federally Qualified Health Centers (FQHCs).[34] In rural areas and small metropolitan areas in particular, FQHCs offering a variety of health services, ranging from primary care to family planning, have been central to the provision of primary and preventive care to underserved populations.[35] Almost 6 million women of reproductive age received care from FQHCs in 2012.[36] Of the 30 million patients served by FQHCs in 2021, 65% were racial and/or ethnic minorities and 42% lived in rural areas.[37] FQHCs are thus an important treatment setting for research geared toward increasing PrEP access among AA women in the rural South.

Study Aims

This paper describes the second phase of a two-phase study. The aim of the first phase was to conduct qualitative interviews exploring preferences around patient-provider communication about HIV and PrEP services to address the needs of AA women. Participants (N=41) included FQHC patients – AA women who reported current and/or recent PrEP use

(N=6) or had clinical indications for PrEP use (N=15) – as well as providers (N=20).[38]

The primary aims of this second phase of the study are: (1) to systematically adapt a patient-provider PrEP communication tool developed by the Centers for Disease Control and Prevention (CDC)[39] to increase PrEP uptake at an FQHC serving a small metropolitan area as well as rural Alabama, using an iterative implementation process, and (2) to assess the feasibility, acceptability, and preliminary impact of the patient-provider communication tool on PrEP uptake among AA women and their providers using a pilot pre-/post-intervention design (N=125).

Methods

Study Design

During this second phase of the study, the qualitative data collected in the first phase has been used to adapt a patient-provider communication tool focusing on the first steps of the PrEP care cascade, notably identifying as a person who may benefit from PrEP use and being interested in using PrEP, among AA women receiving care at an FQHC in Alabama. For interested women, referrals to PrEP services within the health center will be facilitated. The protocol will be evaluated in real-time for acceptability and feasibility using both quantitative and qualitative data. The protocol will be iteratively updated until satisfactory procedures have been designed and simultaneously tested for preliminary impact on PrEP uptake. We anticipate conducting three waves of assessments (approximately every three to five months). Each wave will consist of 25-40 participants at one enrollment (clinic) site with a target total of N=125. This protocol will be tested for effectiveness, including cost-effectiveness, in a larger R01 cluster randomized implementation trial at primary care and reproductive health centers serving AA women vulnerable to HIV infection in the Deep South.

Population and Setting

Participants will include both patients (up to N=125) and healthcare providers (up to N=20) recruited from one FQHC in Alabama. The participating FQHC offers PrEP services, so all PrEP referrals are handled internally at the clinic. Participants will attend a total of two assessment visits (baseline and 3-month assessment) and an intervention visit following the baseline assessment.

Eligibility Criteria

Inclusion criteria for patients include: (1) self-identified cisgender women; (2) AA race; (3) age 18 or older; (4) not living with HIV according to self-report (5) any sex with male partners in past six months or anticipated sex in the next 6 months; (6) primary language English; and (7) willing and able to give informed consent. Inclusion criteria for healthcare providers includes: (1) fluency in English; (2) identifies as a physician, nurse practitioner, physician assistant, nurse, medical assistant, social worker/counselor or other potential PrEP service provider; and (3) willing and able to give informed consent. Potential participants may be excluded if the principal investigators determine, on a case-by-case basis, that their participation would be medically unsafe, complicate interpretation of study findings, or otherwise interfere with achieving study objectives.

Theoretical Framework

The Exploration, Preparation, Implementation, and Sustainment (EPIS) Implementation Framework[40] is a meta-theoretical framework that incorporates components from multiple evidence-based implementation process theories and provides a platform to guide intervention planning, adaptation and implementation (Figure 1). The EPIS has guided the development and evaluation of multiple implementation trials[41,42] and will be used as the overarching

methodological framework to guide intervention adaptation in this study. EPIS is segmented into four stages: *Exploration* (i.e., organization, provider, and client-level factors that identify potential barriers/facilitators for PrEP uptake); *Preparation* (i.e., adapting intervention to enhance PrEP uptake); *Implementation* (i.e., training, coaching, and active facilitation of patient-provider communication intervention); and *Sustainment* (i.e., PrEP uptake and adherence).

Furthermore, the Dynamic Adaptation Process (DAP) framework, which is part of the *Preparation* and *Implementation* phases of EPIS, will be used in the adaptation of the patient-provider communication tool (Figure 1). The DAP provides direction for activities during each EPIS phase and a continuously iterative, data-informed approach to support intervention implementation.[43] Developed for the adaptation of evidence-based interventions (EBIs), it provides a model framework that includes adaptations tailored to specific subgroups. The DAP provides a process for pre-assessment, convening an "implementation resource team" to guide the implementation process, and use of audit and feedback data to help guide appropriate EBI adaptation.

Outcome Variables

Primary outcomes will include intervention feasibility, acceptability, and PrEP uptake. Secondary outcomes will include PrEP adherence; and clinic visit adherence. Psychosocial factors will also be measured to characterize the sample and assess potential mediating and moderating factors associated with the outcome measures. All measures and timing of assessments are provided in Table 1.

Feasibility. We will measure the number of individuals screened, the number of eligible individuals enrolled, and the number of enrolled participants who initiate PrEP and adhere to their prescribed regimen. We will also track reasons for declining enrollment, prematurely

leaving the study, declining a referral, not attending a PrEP clinic visit, and/or discontinuing PrEP. Recruitment and scheduling strategies, participant contact, and feasibility of administering instruments (e.g., assessment duration), will be documented.

Acceptability. Acceptability will be assessed through in-depth, individual, qualitative exit interviews at the end of the study. Interviews will explore participants' experiences with and perceptions of the study, as well as their evaluations of the patient-provider communication tool to facilitate PrEP uptake. Patient and provider satisfaction with the intervention will be assessed via the Client Satisfaction Questionnaire (CSQ-8)[44] and the Behavioral Interventionist Satisfaction Survey (BISS).[45]

PrEP Uptake. PrEP uptake will be measured by calculating the ratio of patients initiating PrEP to the number of patients eligible for the study who enrolled and were referred to PrEP services.

PrEP Adherence. Self-report (i.e., Visual Analog Scale) will be used to assess patients' adherence to taking PrEP as prescribed, as is currently the standard practice in the participating clinics.[46] Reasons for discontinuing PrEP use, as applicable, will also be tracked. Participants will also be asked to rate, on a 6-point Likert scale, their ability to take all medications as prescribed.

Clinic Visit Adherence. Attendance at clinic visits will be defined as the number of PrEP visits attended divided by the number of visits scheduled. Adherence will be assessed at 3-month follow-up and 12-months via electronic medical record abstraction.

Psychosocial Factors. Psychosocial factors will include assessments of intimate partner violence, depression, anxiety, post-traumatic stress disorder (PTSD), sexual behaviors, HIV

transmission knowledge, substance use, social support, and spirituality/religiousness.

Intervention Adaptation

Adaptation Activities. Based on the formative evaluation in the first phase of this study, involving qualitative interviews with patients and providers (i.e., *Exploration* phase), a first draft of the patient-provider communication tool was produced. An adaptation plan as described by Aarons and colleagues[40] was used to document changes (i.e., new activities and materials to be included) to the protocol and reasons for such changes or additions. Given the minority status of our target population, it was anticipated that cultural adaptations would include process and content changes relevant to AA women vulnerable to HIV infection.[64,65] Adaptation was considered on the patient, provider, and organizational levels as per the EPIS.

During the *Preparation* phase, an Implementation Resource Team (IRT) was convened to review the first draft of the adapted patient-provider communication tool. The IRT was comprised of experts in implementation science and PrEP delivery, representatives of the clinic administration/staff (at both the FQHCs and the PrEP clinics), potential PrEP candidates and PrEP users, providers, and members of the research team. A second draft of the adapted communication tool integrated the recommendations made and measures added by the IRT, again maintaining the core elements of the patient-provider communication tool and considering the limitations and needs of the study sites.

Intervention Implementation

Provider Recruitment and Training. Provider participants will be identified by the partnering clinic's study research assistant (RA). The study RA will contact study research staff on participating providers' behalf. Recruited providers will complete an informed consent form and baseline assessment online. Links to the assessment battery will be sent to providers via

email by research team members. Signed consent forms and baseline assessment responses will be directly entered into and stored in a secure Research Electronic Data Capture (REDCap) database.

Enrolled providers will receive training in the use of the patient-provider communication tool and best practices for prescribing PrEP. Training will be directed by health care practitioners with extensive experience in PrEP prescribing, training providers in PrEP prescribing, and/or managing PrEP-related logistics. Provider training will consist of two parts: first, providers will watch two training videos, which will include an overview of PrEP basics and the study's patient-provider communication tool; second, providers will participate in a live training session (in-person or via virtual platform) with trainers, which will involve an interactive roleplay using parts of the patient-provider communication tool, all of which has been piloted during phase I. Additional trainings and preparation sessions may be held in-person at the clinic site or by phone on an as-needed basis.

Patient Recruitment. Patient participants will be recruited in three ways: (1) the study RA will pre-screen potential participants through their electronic medical records (EMR) and flag any patients with upcoming clinic visits who meet study eligibility criteria; (2) flyers will be posted in clinic waiting areas; and (3) health care providers at the participating clinic will directly refer interested patients who may be eligible to participate in the study. If a patient is recruited through EMR pre-screen, they will be formally screened by the study RA during their routine clinic visit. If a patient is recruited via flyer or provider referral, they will either contact the study RA by phone (using the phone number listed on the flyer) or may provide permission to be contacted by the study RA directly, who will then screen the prospective participant by

phone. All individuals who meet inclusion criteria will be invited to complete the informed consent process at the baseline visit (Figure 2).

Informed Consent. All participants will complete a baseline assessment visit either in-person or by phone, in which they will review an informed consent form, which will include a detailed explanation of all study procedures, information about potential risks and benefits of participation, and contact information for the study team in the event of further questions. The consent form will also state that participation is voluntary, that they can withdraw from the study at any time, and that study participation is in no way related to their health care, including receipt of PrEP services. Written or verbal consent will be obtained, and a copy of the signed consent form will be provided to participants for their records.

Study Assessments and Intervention. Enrolled patients will complete a quantitative assessment during the baseline visit, administered via REDCap,[66] which will include sociodemographics and measures of anxiety, depression, interpersonal violence, substance use, PrEP awareness, sexual behaviors, PTSD as well as spiritual/emotional support. Patients will then be scheduled to meet with a provider, who will use the newly adapted PrEP patient-provider communication tool. Patients who are interested in receiving a referral for PrEP after completing the intervention will be referred to the in-house PrEP clinic; this referral will include a "warm hand-off" by a provider or PrEP navigator. Providers will document the visit in patients' electronic health records per standard clinic practice. Referrals will be made if domestic or intimate partner violence, and/or suicidal ideation are indicated in the risk assessment portion of the quantitative baseline assessment.

Patients and providers at the local PrEP clinic will then jointly decide whether to initiate PrEP after referral. Providers at the PrEP clinics will be responsible for all aspects of PrEP care,

including reviewing lab results, reinforcing educational messages around adherence and additional HIV/STI prevention options, and conducting patient examinations as needed, consistent with their current PrEP delivery practices. Regardless of PrEP initiation, patients will be scheduled for the 3-month follow-up study visit which will be conducted via phone call. During implementation, quarterly feedback will be provided by the IRT (or more frequently if needed), who will evaluate whether further adaptations are needed to the patient-provider communication intervention. IRT members will be comprised of experts in implementation science and PrEP delivery, representatives of the clinic administration and staff at local FQHCs, potential PrEP candidates and users, providers, and members of the investigative team. Best practices for intervention delivery process, type, and frequency of communication with AA women vulnerable to HIV infection will also be assessed.

Remuneration. Patients will be remunerated a total of $100 for their participation and transportation costs, independent of PrEP uptake. Providers will receive $50 for their time and 1.5 credit hours of continuing education credit for their participation in the study training.

Patient and Public Involvement. Patient and PrEP healthcare provider involvement is incorporated into the design and conduct of this implementation science trial. The Implementation Resource Team described above is comprised of FQHC patients and PrEP navigators/providers as well as research team members. The IRT guides and informs the intervention design and implementation of the trial throughout the study, including the interpretation and dissemination of results.

Data Analyses

The feasibility, acceptability, and preliminary impact of this intervention will be assessed among patients and providers using this pre-/post-intervention design. Quantitative data will be

analyzed using SPSS or R. Feasibility will be determined by evaluation of recruitment and retention, number of PrEP referrals, PrEP initiation, PrEP adherence, and clinic visit adherence. Acceptability will be measured using in-depth, individual, qualitative exit interviews and satisfaction surveys. Continuous feedback from participants and experts relevant to the population and outcomes studied will assure feasibility, acceptability, and appropriateness of the adapted intervention. Structural and content related changes of the intervention will be based on the feedback provided by patients and providers.

Primary and secondary outcomes will be assessed by characterizing the sample using descriptive statistics, computing confidence intervals on these measures, and exploring patient and implementation characteristics as possible moderators of these outcomes in order to inform the design of our future trial. Measures of effect size (e.g., Cohen's d, Cohen's r, Cramer's V, R^2, etc.) will be used to determine the characteristics that individually appeared to be relevantly associated with PrEP uptake and secondary outcomes in the sample.

To examine impact of the protocol adaptation, we will use calendar quarter of entry in the study as a possible moderator. Multivariable exploratory analyses will be conducted using non-parametric methods[67] including penalized regression (LASSO) and Random Forest, to determine if the sample data suggest a smaller set of relevant characteristics based on their cross-validated predictive ability of each outcome. These data will be useful in tailoring our implementation approach based on empirical observation. On *a priori* conceptual considerations, we expect age, intimate partner violence and sexual risk behavior to be supported by the data as moderators of PrEP uptake. In addition, exploratory mediation analyses will be conducted based on conceptual considerations using the procedures outlined by Hayes.[68]

Clinics' electronic medical record data be used to estimate PrEP uptake, based on the number of PrEP-eligible AA women who have been referred to PrEP in the three years pre- and post-implementation of the protocol (i.e., pre-/post-test design). Binomial logistic models (events/trials syntax) will be fitted with time-period and clinic as main effects to estimate the differences in uptake proportions between pre- and post-protocol time periods. To determine specific impact of the iterative process of protocol adaptation during the year of implementation, we will fit a logistic model for uptake with bi-monthly assessment wave number (3 waves) as categorical predictor. *A priori*, we expect a positive relationship between the assessment wave number and the odds of uptake, indicating that as the protocol became more refined during the year, PrEP uptake increased.

Ethics and Dissemination

The study was a single-IRB (sIRB) at the University of Alabama at Birmingham (UAB) with reliant sites at Massachusetts General Hospital and Beth Israel Deaconess Medical Center. Ethics approval was obtained for all aspects of this study by the IRB at UAB (UAB; protocol 300004276), where the work is being conducted. Study updates, preliminary findings, and final results will be disseminated through publication of manuscripts in peer-reviewed journals, as well as through reports to the National Institutes of Health, and through local, national, and international presentations at HIV-focused conferences and meetings.

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Authors' Contributions

C.P. and **M.C.K.** conceived and designed the demonstration project and its protocol and directed protocol activities. **G.R.G.** drafted the protocol manuscript and designed several manuscript tables. **V.M.**, **C.O.**, **A.B.**, and **A.R.** contributed to drafting, editing, and finalizing the protocol manuscript and the design of the overall project protocol. **L.S.** planned and edited the statistical methods section of the manuscript. **M.C.** and **E.U.** advised on the protocol methods and provided comments on manuscript. **D.K.**, **L.E.**, **K.K.**, and **K.S.** advised on the structure and implementation of the protocol and provided comments on the protocol manuscript.

Funding Statement: This work is supported by the National Institute of Mental Health (NIMH; grant number 5R34MH118044-03).

Competing interests: None declared.

Word Count: 3,666

Protocol issue date: 07 Mar 2022

Protocol number: 01

Table 2. WeExPAnd trial registration data

Data category	Information
Primary registry and trial identifying number	ClinicalTrials.gov NCT04373551
Date of registry in primary registry	May 4, 2020
Secondary identifying numbers	300003885, 1R34MH118044-01A1
Source(s) of monetary or material support	National Institute of Mental Health
Primary sponsor	National Institute of Mental Health
Secondary sponsor	N/a
Contact for public queries	Mirjam-Colette Kempf, PhD [mkempf@uab.edu]
Contact for scientific queries	Mirjam-Colette Kempf, PhD University of Alabama at Birmingham
Public title	PrEP Demonstration Project Among Women at Risk for HIV Infection
Scientific title	N/a
Countries of recruitment	United States
Health condition(s) or problem(s) studied	HIV-infection/AIDS
Intervention(s)	Behavioral: Cultural adaptation of a patient-provider communication tool
Key inclusion and exclusion criteria	Ages eligible for study: ≥ 18 years Sexes eligible for study: cisgender female Gender-based eligibility: yes Accepts health volunteers: no
	Patients Inclusion criteria: African American cisgender women aged 18 years or older without HIV; report HIV risk and/or recent PrEP use; English-speaking
	Providers Inclusion criteria: Physicians, nurse practitioners, physician assistants, nurses, medical assistants, social workers/counselors or other potential/actual PrEP service providers; English-speaking
Study type	Interventional (Clinical Trial)
	Allocation: N/a
	Primary purpose: Health Services Research
	Phase: N/a
Study start date	April 14, 2020
Target sample size	125 participants
Recruitment status	Enrolling by invitation
Primary outcome(s)	PrEP uptake changes [Time Frame: baseline, 3 months, and 12 months] Intervention feasibility changes [Time Frame: baseline, 3 months, and 12 months] Intervention acceptability [Time Frame: Through study completion, an average of 12 months]
Secondary outcome(s)	PrEP adherence [Time Frame: 3 months and 12 months] Clinic visit adherence changes [Time Frame: 3 months and 12 months] Biological measures of HIV, STIs and pregnancy [Time Frame: baseline, 3 months, and 12 months]

Appendix A

Patient Consent

Please complete the survey below.

Thank you!

Title of Research: We ExPAnd: PrEP Demonstration Project among Women at Risk for HIV Infection

UAB IRB Protocol #: IRB-300004276

Principal Investigator: Dr. Mirjam-Colette Kempf

Sponsor: National Institutes of Health (NIH)

General Information You are being asked to take part in a research study. This research study is voluntary, meaning you do not have to take part in it. The procedures, risks, and benefits are fully described further in the consent form.

Purpose The purpose of the study is to develop a better understanding of how to make HIV prevention medication, PrEP (known as pre-exposure prophylaxis which is action taken to prevent diseases before it happens), more accessible to African American women in Alabama.

Duration & Visits You will be in this study for 3 months. Visits will include a baseline visit, intervention visit, and 3-month follow-up visit.

Overview of Procedures This study will include a baseline assessment, a discussion with your provider using a patient-provider communication tool, and a 3-month follow-up assessment.

Risks The most common risk is feeling uncomfortable answering sexual health questions.

Benefits You may or may not benefit from participating in this study. However, this study may help us better understand how to optimize HIV prevention efforts and improve care in the future.

Alternatives The alternative is to not participate in this study.

Purpose of the Research Study We are asking you to take part in a research study of cis-gender women (individuals who were assigned the female sex at birth and identify as women) who are HIV-negative and potentially at risk for HIV. The purpose of the study is to develop a better understanding of how to make HIV prevention medication, PrEP (known as pre-exposure prophylaxis which is action taken to prevent diseases before it happens), more accessible to African American women in Alabama. It is hoped that the information gained from this study will help us understand the barriers and facilitators of PrEP use. You will receive information about PrEP during this study but will not receive PrEP medication as part of this research study. We anticipate recruitment of up to 250 participants from 2 clinics.

Study Participation & Procedures If you agree to join the study:

You agree that study staff can contact you to schedule study visits. You will be asked to participate in a baseline assessment at your baseline visit. During this visit you will be asked to provide demographic information (5-10 mins) and complete baseline assessments (50-70 mins) You will discuss PrEP with your provider using a new patient-provider communication tool (10-15 mins). This tool will be used by your provider to discuss your sexual health and to help you make informed decision about your sexual health. You will participate in a 3-month follow-up assessment about your health and study participation (75-90 mins). Assessments conducted at baseline and 3-months will be completed in-person on a tablet. You do not have to agree to start a PrEP regiment in order to participate in this study. Baseline and 3-month assessments will be asking you questions about HIV stigma, abuse, depression, anxiety, Posttraumatic distress, addiction, religiousness, and sexual risk. Additionally, the 3-month assessment will include questions about your satisfaction in the study.

As mentioned, during the baseline visit, you will also be asked to complete a few demographic questions. These questions will include contact information so that the study staff can contact you regarding appointments. These questions will also include information regarding insurance coverage, annual income, and the location of your place of residence. It is important to understand exactly what this information will be used for so that you can make an informed decision to participate in this portion of the study.

We are asking you to give UAB researchers the authorization to use your address so that we can examine how you and your neighborhood influence your health and wellness. A member of the study staff will match your address to a geographic area called a census block group (CBG), which is large enough so that your exact address cannot be determined. CBG's are used by the US Census to report on demographic characteristics of entire communities. The community demographic data - and not your address- will be used by researchers to help them better understand how neighborhood and community factors relate to health and wellness. This process is called spatial mapping. Your actual address will not be reported, published or shared with anyone else.

You can choose to opt-out of the spatial mapping portion of the study. You can still participate in the study if you choose to opt-out of this part of the study. If you choose to opt-out of this part of the study, the study staff will make a note of this in your participant file.

○ I agree to allow spatial mapping
○ I do not agree to allow spatial mapping

Additional Information

Your de-identified private information may be used for future research studies or distributed to another researcher for future research studies without additional informed consent.

Risks and Discomforts

It is unlikely that you will be at risk for physical harm as a result of your study participation. You may find some of the questions asked in the assessments emotionally upsetting. You may decline to answer questions which upset you.

Benefits

You may or may not benefit directly from taking part in this study. However, this study may help us better understand how to optimize HIV prevention efforts and improve care in the future.

Alternatives

The alternative is to not participate in this study.

Confidentiality and Authorization to Use and Disclose Information for Research Purposes

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.

All participants are assigned a study identification number. In this study, information with your name is stored separately from information that we collect for the study, which will be stored with a study identification number. The information with your name is used for tracking purposes and for contacting you or others you have given us permission to contact. Only study staff who are trained in confidentiality and research ethics, are allowed access to this information.

What protected health information may be used and/or given to others?

All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of any kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills; any other information related to or collected for use in the research study, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes; records about any study drug you received or about study devices used; and consent forms from past studies that might be in your medical record.

A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Who may use and give out this information?

Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study.

Who might get this information?

All individuals/entities listed in the informed consent document(s), including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere). Your information may also be given to the sponsor of this research. "Sponsor" includes any persons or companies that are working for or with the sponsor, or are owned by the sponsor, or are providing support to the sponsor (e.g., contract research organization).

Information about you and your health which might identify you may be given to:

The Office for Human Research Protections (OHRP) The U.S. Food and Drug Administration (FDA) Department of Health and Human Services (DHHS) agencies Governmental agencies in other countries Governmental agencies to whom certain diseases (reportable diseases) must be reported The University of Alabama at Birmingham - the physicians, nurses and staff working on the research study (whether at UAB or elsewhere); the UAB IRB and its staff The billing offices of UAB and UAB Health Systems affiliates and/or Children's of Alabama and its billing agents

Why will this information be used and/or given to others?

Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the NIH which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of such as child abuse and neglect, or harm to self or others.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

Information obtained during the course of the study which, in the opinion of the investigator(s), suggests that you may be at significant risk of harm to yourself or others will be reportable to a third party in the interest of protecting the rights and welfare of those at potential risk.

What if I decide not to give permission to use and give out my health information?

By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research.

May I review or copy the information obtained from me or created about me?

You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?

Yes, but this permission will not stop automatically. The use of your personal health information will continue until you cancel your permission.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?

If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others. Including others outside of UAB, without your permission.

Voluntary Participation and Withdrawal

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in it. If you decide not to be in the study, you will not lose any benefits you are otherwise owed.

You are free to withdraw from this study at any time. Your choice to leave the study will not affect your relationship with this institution. Contact [redacted] or [redacted] if you want to withdraw from the study.

You may be removed from the study without your consent if the sponsor ends the study or if you are not following the study rules.

Cost of Participation

There will be no cost to you for taking part in this study.

Payment for Participation

You will be paid $100 if you complete each stage of this study: $30 baseline, $30 intervention visit, and $40 for 3-month follow-up. If you withdraw from the study you are only paid for the portions you completed. Ask the study staff about the method of payment that will be used for this study (e.g., check, cash, gift card, direct deposit).

New Findings

You will be told by the study doctor or the study staff if new information becomes available that might affect your choice to stay in the study.

Optional

Future Research Use of Identifiable Private Information and/or Identifiable Biospecimens

We would like your permission to keep your private information (data containing personal information) collected in this study for future research. The future research may be similar to this study or may be completely different. Your private information will be stored indefinitely or until used.

You can take part in this study even if you decide not to let us keep your identifiable private information for future research.

If you give us permission now to keep your identifiable private information, you can change your mind later and ask us to destroy it. However, once we have analyzed your private information, we may not be able to take it out of our future research.

We may share your identifiable private information, so that others can use it in their research. Their research may be similar to this study or may be completely different. Once we have shared your identifiable private information with other researchers, we will not be able to get it back.

Future research use of your identifiable private information will be conducted in compliance with applicable regulatory requirements.

You will not find out the results of the future research. Allowing us to do future research on your identifiable private information will not benefit you directly.

Select your choice below:

○ I agree to allow my identifiable private information to be kept and used for future research on HIV prevention studies
○ I do not agree to allow my identifiable private information to be kept and used for future research.

Questions

If you have any questions, concerns, or complaints about the research or a research-related injury including available treatments, please contact the study doctor. You may contact Dr. Mirjam-Colette Kempf at [redacted]

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday.

Legal Rights

You are not waiving any of your legal rights by signing this consent form.

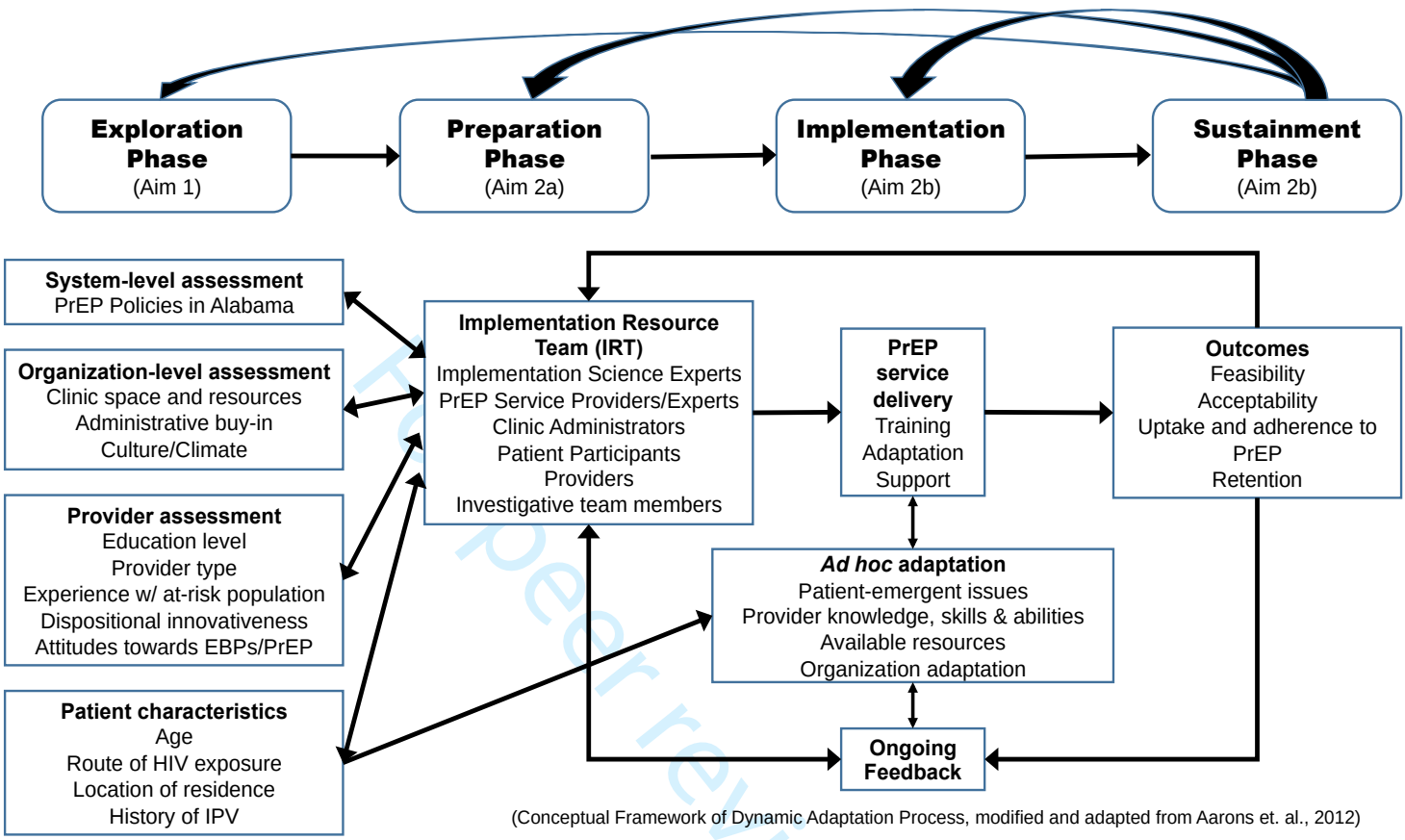
Signatures

Your signature below indicates that you have read (or been read) the information provided above and agree to participate in this study. You will receive a copy of this signed consent form.

Full name of the participant _____

Signature of Participant _____

Figure 1: Measurement framework of EPIS stages



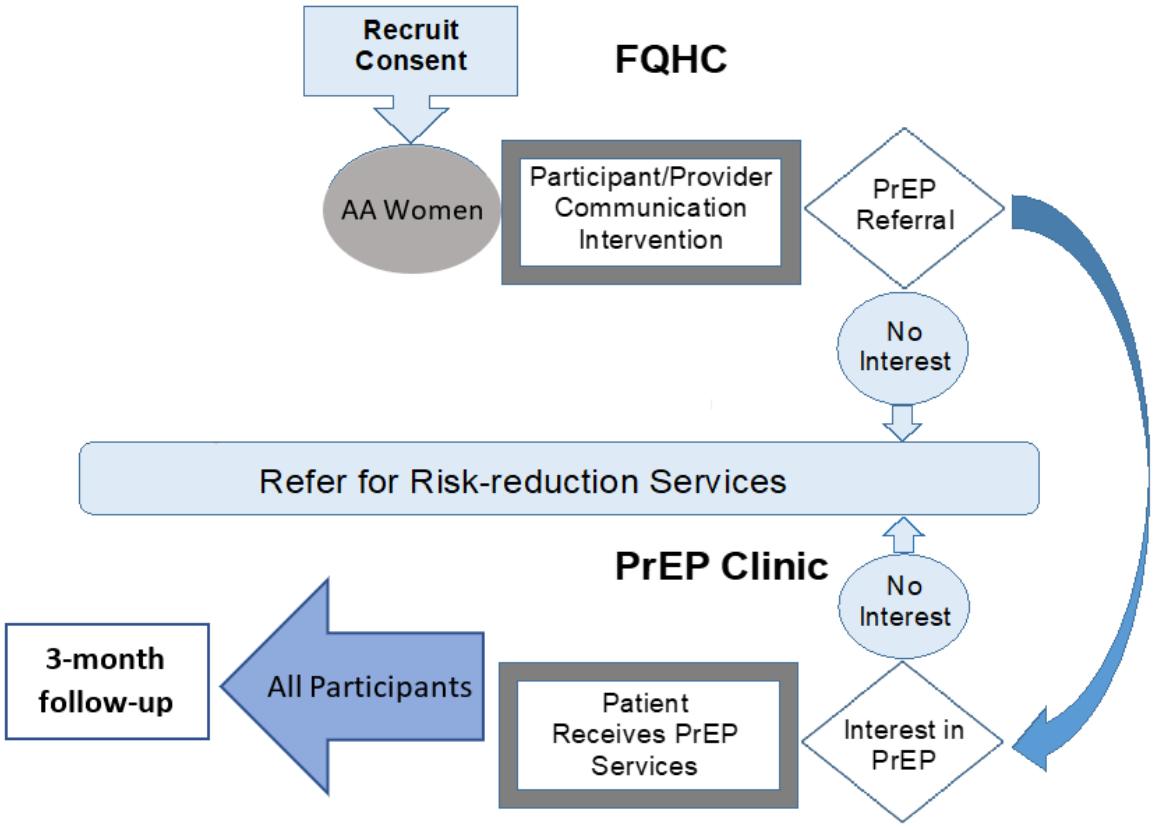
(Conceptual Framework of Dynamic Adaptation Process, modified and adapted from Aarons et. al., 2012)

Table 1. Measures to be Administered at Each Assessment Visit.

Patients	BL	PT	3M	12M
Recruitment: Number screened; number of eligible individuals enrolled; reasons for declining enrollment or leaving study; participant contact throughout study; recruitment/scheduling strategies; feasibility of administering instruments/questions	X		X	
PrEP referral: Number of patients referred; number of patients accepting referral; reasons for declining referral; reasons for unsuccessful or incomplete referral		X	X	X
PrEP uptake: Ratio of patients initiating PrEP to the number eligible patients screened and referred (measured throughout)			X	X
PrEP adherence: Self-report via Visual Analog Scale[47]; reasons for discontinuing PrEP	X		X	
Clinic visit adherence: Calculated as PrEP visits adhered to divided by PrEP visits scheduled			X	X
Satisfaction with intervention: Client Satisfaction Questionnaire (CSQ-8) [44]		X		
Perceptions of study and evaluation of intervention: Qualitative interview			X	
Intimate partner violence: Abuse Assessment Screen (AAS)[48]	X		X	
Depression: Center for Epidemiologic Studies Depression (CES-D)[49]	X		X	
Spiritual support: Ironson-Woods Spirituality/Religiousness (SR)[50]	X			
Social Support: Medical Outcomes Study (MOS) Social Support Survey[51]	X			
Substance use: Addiction Severity Index-Lite (ASI-Lite)[52]	X		X	
Trauma experience: Adapted from items within Project BRIgHT[53]	X		X	
Anxiety: State-Trait Anxiety Inventory State Form (STAI-S)[54]	X		X	
Identification with organization: Items drafted by study team	X			
Stage of change: Adapted from Stage of Change measures[55,56]	X	X	X	
PrEP knowledge and experience: Adapted from PrEP Awareness and Willingness[57]	X			
HIV transmission knowledge: Adapted from the HIV Risk Knowledge Test[58]	X		X	
Sexual behavior: Number of sexual partners; alcohol/drug use before sex; vaginal/anal sex; knowledge of partners' HIV status; condom use	X		X	
Reflecting and evaluating: Quantitative and qualitative feedback about progress and quality of implementation, accompanied with regular personal and team debriefing about progress and experience.	Continuous			
Proposed intervention modifications: Both structural and didactic	Continuous			
Providers	**BL**	**PT**	**3M**	**12M**
Sociodemographics: Age, race, ethnicity, education, clinic position	X			
Implementation readiness: Adapted from the Implementation Climate Scale (ICS)[59]	X			
Dispositional innovativeness: Physician-Motivation-Adoption (PMA)[60]	X			
Culture: Organizational Culture Assessment Instrument (OCAI)[61]	X			
Patient needs and clinic resources: Adapted subscales from Texas Christian University Organizational Readiness for Change Scale (TCU-ORC-D4)[62]	X			
Stigma: Adapted from the Attitude Toward People Living with HIV Scale[63]	X			
Satisfaction with intervention: Behavioral Interventionist Satisfaction Survey (BISS)[45] (12M only) and Short Survey (PT only)		X		X
Identification with organization: Qualitative interview				X
Stage of change: Qualitative interview				X
Perceptions of study and evaluation of intervention: Qualitative interview				X
Reflecting and evaluating: Quantitative and qualitative feedback about progress and quality of implementation, accompanied with regular personal and team debriefing about progress and experience.				X
Proposed intervention modifications: Both structural and didactic	Continuous			

Note: BL = baseline; PT = post-treatment; 3M = 3-month assessment visit; 12M = 12-month data abstraction from EMR (patients) or assessment visit (provider)

Figure 2: Participant flow in PrEP intervention



Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

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		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	28
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	28
Protocol version	#3	Date and version identifier	27
Funding	#4	Sources and types of financial, material, and other support	27
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1 & 27

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	1
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	n/a; This funding source and sponsor had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	n/a; IRB has designated the study minimal risk; all aspects of the trial are overseen by the co-PIs and research team
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	n/a; Single Group Assignment
Objectives	#7	Specific objectives or hypotheses	6
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	7
Methods:			

Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	8
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	8
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	14
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	14
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	15
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	n/a; No restrictions or specific allowances made on any health-related care or interventions during study participation.
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event),	9

		method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	14
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	7
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	13
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	n/a; This study uses a single group assignment with no randomization or masking.
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until	n/a; This study uses a single group assignment with no randomization or masking.

		interventions are assigned	
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	n/a; This study uses a single group assignment with no randomization or masking.
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	n/a; This study uses a single group assignment with no randomization or masking.
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a; This study uses a single group assignment with no randomization or masking.
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	15
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data	14

		entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	15
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	16
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	16
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	n/a; IRB designated study minimal risk; all data monitoring occurs internally by the co-principle investigators.
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	n/a; Plans for interim analyses are detailed in the IRB-approved data safety monitoring plan and are not described fully in the protocol manuscript.
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events	n/a; Plans for adverse events are detailed in the IRB-approved data safety

		and other unintended effects of trial interventions or trial conduct	monitoring plan and are not described fully in the protocol manuscript.
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n/a; Plans for trial conduct audits are detailed in the IRB-approved data safety monitoring plan and are not described fully in the protocol manuscript.
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	17
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	15
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	14
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	29
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	17; IRB approval has been obtained for all aspects of the study, including the collection and protection of participant confidentiality and personal information
Declaration of	#28	Financial and other competing interests	27

interests		for principal investigators for the overall trial and each study site	
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	n/a; Data access enumerated in the IRB-approved Data Safety Monitoring Plan and protocol
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	n/a; This trial has been designated as minimal risk by the UAB IRB.
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	17
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	n/a; Author contributions detailed on page 27 and no professional writers were used
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a; No current plans exist for granting public access to full protocol, participant dataset, or statistical code.
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	29
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a; This study collects no biological specimen.

Notes:

- 5c: n/a; This funding source and sponsor had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.
- 5d: n/a; IRB has designated the study minimal risk; all aspects of the trial are overseen by the co-PIs and research team
- 6b: n/a; Single Group Assignment
- 11d: n/a; no restrictions or specific allowances made on any health-related care or interventions during study participation.
- 16a: n/a; This study uses a single group assignment with no randomization or masking.
- 16b: n/a; This study uses a single group assignment with no randomization or masking.
- 16c: n/a; This study uses a single group assignment with no randomization or masking.
- 17a: n/a; This study uses a single group assignment with no randomization or masking.
- 17b: n/a; This study uses a single group assignment with no randomization or masking.
- 21a: n/a; IRB designated study minimal risk; all data monitoring occurs internally by the co-principle investigators.
- 21b: n/a; Plans for interim analyses are detailed in the IRB-approved data safety monitoring plan and are not described fully in the protocol manuscript.
- 22: n/a; Plans for adverse events are detailed in the IRB-approved data safety monitoring plan and are not described fully in the protocol manuscript.
- 23: n/a; Plans for trial conduct audits are detailed in the IRB-approved data safety monitoring plan and are not described fully in the protocol manuscript.
- 26b: n/a; ancillary study consent not included in protocol manuscript
- 27: 17; IRB approval has been obtained for all aspects of the study, including the collection and protection of participant confidentiality and personal information
- 29: n/a; Data access enumerated in the IRB-approved Data Safety Monitoring Plan and protocol
- 30: n/a; This trial has been designated as minimal risk by the UAB IRB.
- 31b: n/a; author contributions detailed on page 27 and no professional writers used
- 31c: n/a; no current plans exist for granting public access to full protocol, participant dataset, or statistical code.

- 33: n/a; This study collects no biological specimen. The SPIRIT Explanation and Elaboration paper is distributed under the terms of the Creative Commons Attribution License CC-BY-NC. This checklist was completed on 19. April 2023 using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai

BMJ Open

Protocol for WeExPAnd: a prospective, mixed-methods pilot demonstration study to increase access to pre-exposure prophylaxis among women vulnerable to HIV infection in the US South

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2023-075250.R1
Article Type:	Protocol
Date Submitted by the Author:	19-May-2023
Complete List of Authors:	Psaros, Christina; Massachusetts General Hospital Department of Psychiatry; Harvard Medical School Department of Psychiatry Goodman, Georgia; Massachusetts General Hospital Department of Psychiatry; Brigham and Women's Hospital Department of Emergency Medicine McDonald, Victoria; The University of Alabama at Birmingham School of Nursing, Ott, Corilyn; The University of Alabama at Birmingham School of Nursing; The University of Alabama at Birmingham Heersink School of Medicine Blyler, Abigail; University of Pennsylvania School of Arts and Sciences Rivas, Alexa; Massachusetts General Hospital Department of Psychiatry Shan, Liang; The University of Alabama at Birmingham School of Nursing Campbell, Marquetta; Whatley Health Services, Inc. - Maude L. Whatley Health Center Underwood, Eric; Whatley Health Services, Inc. - Maude L. Whatley Health Center Krakower, Douglas; The Fenway Institute at Fenway Health; Beth Israel Deaconess Medical Center Elopre, Latesha; The University of Alabama at Birmingham Heersink School of Medicine Kudroff, Kachina; The University of Alabama at Birmingham Heersink School of Medicine Sherr, Kenneth H.; University of Washington Department of Global Health Kempf, Mirjam-Colette ; The University of Alabama at Birmingham School of Nursing; The University of Alabama at Birmingham Heersink School of Medicine
Primary Subject Heading:	HIV/AIDS
Secondary Subject Heading:	Infectious diseases, Sexual health, Communication, Epidemiology, Evidence based practice
Keywords:	HIV & AIDS < INFECTIOUS DISEASES, Feasibility Studies, Health Equity, Health Education, SEXUAL MEDICINE, Primary Prevention

Protocol for WeExPAnd: a prospective, mixed-methods pilot demonstration study to increase access to pre-exposure prophylaxis among women vulnerable to HIV infection in the US South

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Abstract

Introduction: African American women (AA), particularly those living in the southeastern United States (US), experience disproportionately high rates of HIV infection. Pre-exposure prophylaxis (PrEP) is a highly effective HIV prevention tool that may circumvent barriers to traditional HIV prevention tools, such as condom use; however, very little is known about how to improve PrEP access and uptake among AA women who may benefit from PrEP use. This project aims to understand how to increase PrEP access among AA women in the rural US South, which may ultimately affect HIV incidence in this population.

Methods and analysis: The goal of the current study is to systematically adapt a patient-provider communication tool to increase PrEP uptake among AA women receiving care at a federally qualified health center (FQHC) in Alabama. We will use an iterative implementation process, by assessing the feasibility, acceptability, and preliminary impact of the tool on PrEP uptake, using a pilot pre-/post-intervention design (N=125). We will evaluate women's reasons for declining a referral to a PrEP provider, reasons for incomplete referrals, reasons for not initiating PrEP after a successful referral, and ongoing PrEP use at 3 and 12 months after PrEP initiation among our sample. The proposed work will significantly contribute to our understanding of factors impacting PrEP uptake and use among AA women, particularly in underserved areas in the Deep South that are heavily impacted by the HIV epidemic and experience worse HIV-related health outcomes relative to other areas in the US.

Ethics and dissemination: This protocol has been approved by the Institutional Review Board (IRB) at University of Alabama at Birmingham (Birmingham, AL; protocol 300004276).

All participants will review a detailed informed consent form approved by the IRB and will provide written or verbal informed consent prior to enrollment. Results will be disseminated through peer-reviewed manuscripts, reports, and local, national, and international presentations.

Study registration: ClinicalTrials.gov, NCT04373551.

Strengths and limitations of this study

- Application of an implementation science framework facilitates rapid implementation, evaluation, and modification of a novel patient-provider communication intervention to increase pre-exposure prophylaxis (PrEP) awareness and potential uptake for women in a US region where HIV transmission remains comparatively high.
- Provides data on PrEP uptake and key social, behavioral, and cultural factors associated with PrEP uptake among African American women in the US South, who remain under-represented in PrEP research despite being disproportionately affected by HIV.
- Expands knowledge base on PrEP attitudes and experiences among health care providers within a Federally Qualified Health Care Center (FQHC) in the US South, where many women who may benefit from PrEP enter the health care system.
- Challenges and barriers identified by participants and providers throughout the adaptation process may include contextual, structural, and system-level factors that are beyond the scope of this communication intervention.

Introduction

The Deep South region of the United States (US) bears the greatest burden of the HIV epidemic in the US, with rural counties disproportionately affected and underserved by both HIV care and prevention services.[1,2] Of the more than 1.1 million people living with HIV in the US in 2018, women accounted for nearly a quarter (23%) of all cases and a significant portion (19%) of new cases, with most new cases attributed to heterosexual contact (85%).[3] Despite representing just 13% of the US female population, African American (AA) women accounted for 55% of new HIV diagnoses among all women in the US in 2019.[2] In 2016, the rate of new HIV diagnoses among AA women was 15 times higher than that of White women,[3] and in 2018, HIV infection ranked in the top eight leading causes of death among AA women aged 20-44 in the US.[4] The elevated HIV risk profile among AA women in the South may reflect factors unique to rural areas, such as the prevalence of small sexual networks resulting in cyclical HIV transmission patterns[5] and barriers to HIV prevention rooted in structural racism such as high incarceration rates among male AA populations, limited awareness of and access to effective contraception and sexual health interventions, higher rates of concurrent partnerships among AA men in AA women's sexual networks, and financial and transportation-related barriers to accessing HIV/STI screening, prevention, and treatment.[6-11]

Traditional HIV prevention efforts, like abstinence-only education approaches that are prevalent in the rural South, have been insufficient to control high rates of sexually transmitted infections (STIs) and HIV infections. Abstinence-only education does not provide women with comprehensive information critical for maintaining sexual health.[12,13] Moreover, interventions promoting condom use, partner-based testing, and/or monogamous relationships are dependent on behaviors of women's sexual partners and, therefore, may be outside each woman's direct

control. AA women experiencing financial challenges may be financially dependent on male partners; they may also be experiencing intimate partner violence, further complicating their ability to make independent sexual health decisions.[14,15] Given disproportionate diagnoses and mortality among AA women, along with limitations to non-biomedical HIV prevention methods, novel and more effective approaches to HIV prevention are necessary.

Biomedical HIV prevention tools, including pre-exposure prophylaxis (PrEP) are promising as they can potentially minimize barriers to traditional means of HIV prevention among groups who are persistently vulnerable to HIV infection. Oral PrEP has over 90% efficacy demonstrated across numerous trials, including cisgender women, but efficacy depends on consistent daily adherence as prescribed.[16] Long-acting injectable PrEP is also highly efficacious for cisgender women and is now available for use in the U.S.[17,18] Although overall oral PrEP prescriptions in the US increased substantially between 2012 and 2017, PrEP uptake among AA women has remained low. While biomedical prevention efforts have historically focused on men who have sex with men (MSM), women have not received equitable attention reflective of the epidemiology.[19] Indeed, 94% of PrEP users in 2017 were male, indicating a substantial unmet need among PrEP-eligible women.[18] In 2016, only 11% of all PrEP users with available race/ethnicity data were from AA communities.[20]

Regardless of geographic location, most women in the US remain unaware of PrEP, and PrEP uptake among AA women remains low, particularly in rural areas of the US where women may have less access to healthcare and more limited knowledge of PrEP than women in urban areas.[21] In several studies, the majority of women participating in PrEP focus groups and staff at health services organizations were unfamiliar with PrEP as an HIV prevention tool and expressed concern about a broad lack of awareness within their communities; of the 10% of

women who had previously heard of PrEP, none were aware of its availability and efficacy for women.[22,23] However, AA women expressed being generally interested in using PrEP if available,[24] especially if recommended by a trusted health-care provider.[25]

Suboptimal patient-provider communication has been identified as a barrier to PrEP uptake among AA women,[26] as has limited provider knowledge of PrEP. Historically, the most common reported barriers to prescribing PrEP include a perceived lack of clinical training and experience in PrEP delivery, greater time investment to monitor patients on PrEP, and insufficient structural support from clinic sites.[27] In a 2022 survey of 359 health care providers across the US, 100% of respondents were aware of PrEP, about 97% reported willingness to prescribe PrEP, and around 80% had prescribed PrEP;[28] however, these statistics varied by region of practice and by race, with a higher number of providers prescribing PrEP in the West and a disproportionate number of PrEP prescriptions provided to White individuals.[28] A recent qualitative study among providers in Alabama indicated uncertainty about offering PrEP to AA heterosexual, cis-gender adolescent or young adult females in the absence of transactional sex or a known HIV positive partner.[29]

Existing literature highlights numerous barriers to effective patient-provider communication about sexual health, including time constraints, embarrassment or shame surrounding these topics, patient confidentiality concerns, and both language and cultural barriers.[30-33] Moreover, PrEP services are less routinely implemented in settings where many patients who may benefit from PrEP use may receive care, such as Federally Qualified Health Centers (FQHCs).[34] In rural areas and small metropolitan areas in particular, FQHCs offering a variety of health services, ranging from primary care to family planning, have been central to the provision of primary and preventive care to underserved populations.[35] Almost 6 million

women of reproductive age received care from FQHCs in 2012.[36] Of the 30 million patients served by FQHCs in 2021, 65% were racial and/or ethnic minorities and 42% lived in rural areas.[37] FQHCs are thus an important treatment setting for research geared toward increasing PrEP access among AA women in the rural South.

Study aims

This paper describes the second phase of two-phased prospective, mixed-methods pilot demonstration study. The aim of the first phase was to conduct qualitative interviews exploring preferences around patient-provider communication about HIV and PrEP services to address the needs of AA women. Participants (N=41) included FQHC patients – AA women who reported current and/or recent PrEP use (N=6) or had clinical indications for PrEP use (N=15) – as well as providers (N=20).[38]

The primary aims of this second phase are: (1) to systematically adapt a patient-provider PrEP communication tool developed by the Centers for Disease Control and Prevention (CDC)[39] to increase PrEP uptake at an FQHC serving a small metropolitan area as well as rural Alabama, using an iterative implementation process, and (2) to assess feasibility, acceptability, and preliminary impact of the patient-provider communication tool on PrEP uptake among AA women (up to N=125) and their providers (up to N=20) using a pilot pre-/post-intervention design.

Methods and analysis

Study design

During this second phase of the study, the qualitative data collected in the first phase has been used to adapt a patient-provider communication tool focusing on the first steps of the PrEP care cascade, notably identifying as a person who may benefit from PrEP use and being interested in

using PrEP, among AA women receiving care at an FQHC in Alabama. For interested women, referrals to PrEP services within the health center will be facilitated. The protocol will be evaluated in real-time for acceptability and feasibility using both quantitative and qualitative data. The protocol will be iteratively updated until satisfactory procedures have been designed and simultaneously tested for preliminary impact on PrEP uptake. We anticipate conducting three waves of assessments (approximately every three to five months). Each wave will consist of 25-40 participants at one enrollment (clinic) site with a target total of N=125. This protocol will be tested for effectiveness, including cost-effectiveness, in a larger R01 cluster randomized implementation trial at primary care and reproductive health centers serving AA women vulnerable to HIV infection in the Deep South.

Population and setting

Participants will include both patients (up to N=125) and healthcare providers (up to N=20) recruited from one FQHC in Alabama. The participating FQHC offers PrEP services, so all PrEP referrals are handled internally at the clinic. Participants will attend a total of two assessment visits (baseline and 3-month assessment) and an intervention visit following the baseline assessment.

Eligibility criteria

Inclusion criteria for patients include: (1) self-identified cisgender women; (2) AA race; (3) age 18 or older; (4) not living with HIV according to self-report (5) any sex with male partners in past six months or anticipated sex in the next 6 months; (6) primary language English; and (7) willing and able to give informed consent. Inclusion criteria for healthcare providers includes: (1) fluency in English; (2) identifies as a physician, nurse practitioner, physician assistant, nurse, medical assistant, social worker/counselor or other potential PrEP service provider; and (3)

willing and able to give informed consent. Potential participants may be excluded if the principal investigators determine, on a case-by-case basis, that their participation would be medically unsafe, complicate interpretation of study findings, or otherwise interfere with achieving study objectives.

Theoretical framework

The Exploration, Preparation, Implementation, and Sustainment (EPIS) Implementation Framework[40] is a meta-theoretical framework that incorporates components from multiple evidence-based implementation process theories and provides a platform to guide intervention planning, adaptation, and implementation (Figure 1). The EPIS guided the development and evaluation of multiple implementation trials[41,42] and will be used as the overarching methodological framework to guide intervention adaptation in this study. EPIS is segmented into four stages: *Exploration* (i.e., organization, provider, and client-level factors that identify potential barriers/facilitators for PrEP uptake); *Preparation* (i.e., adapting intervention to enhance PrEP uptake); *Implementation* (i.e., training, coaching, and active facilitation of patient-provider communication intervention); and *Sustainment* (i.e., PrEP uptake and adherence).

Furthermore, the Dynamic Adaptation Process (DAP) framework, which is part of the *Preparation* and *Implementation* phases of EPIS, will be used in the adaptation of the patient-provider communication tool (Figure 1). The DAP provides direction for activities during each EPIS phase and a continuously iterative, data-informed approach to support intervention implementation.[43] Developed for the adaptation of evidence-based interventions (EBIs), it provides a model framework that includes adaptations tailored to specific subgroups. The DAP provides a process for pre-assessment, convening an "implementation resource team" to guide

the implementation process, and use of audit and feedback data to help guide appropriate EBI adaptation.

Outcome variables

Primary outcomes will include intervention feasibility, acceptability, and PrEP uptake. Secondary outcomes will include PrEP adherence and clinic visit adherence. Psychosocial factors will also be measured to characterize the sample and assess potential mediating and moderating factors associated with the outcome measures. All measures and timing of assessments are provided in Table 1.

Feasibility

We will measure the number of individuals screened, number of eligible individuals enrolled, and number of enrolled participants who initiate PrEP and adhere to their prescribed regimen. We will also track reasons for declining enrollment, prematurely leaving the study, declining a referral, not attending a PrEP clinic visit, and/or discontinuing PrEP. Recruitment and scheduling strategies, participant contact, and feasibility of administering instruments (e.g., assessment duration), will be documented.

Acceptability

Acceptability will be assessed through individual in-depth qualitative interviews at the end of the study. Interviews will explore participants' experiences with and perceptions of the study, and their evaluations of the patient-provider communication tool to facilitate PrEP uptake. Patient and provider satisfaction with the intervention will be assessed via the Client Satisfaction Questionnaire (CSQ-8)[44] and the Behavioral Interventionist Satisfaction Survey (BISS).[45]

PrEP uptake

Table 1. Measures to be administered at each assessment visit

Patients	BL	PT	3M	12M
Recruitment: Number screened; number of eligible individuals enrolled; reasons for declining enrollment or leaving study; participant contact throughout study; recruitment/scheduling strategies; feasibility of administering instruments/questions	X		X	
PrEP referral: Number of patients referred; number of patients accepting referral; reasons for declining referral; reasons for unsuccessful or incomplete referral		X	X	X
PrEP uptake: Ratio of patients initiating PrEP to the number eligible patients screened and referred (measured throughout)			X	X
PrEP adherence: Self-report via Visual Analog Scale[46]; reasons for discontinuing PrEP	X		X	
Clinic visit adherence: Calculated as PrEP visits adhered to divided by PrEP visits scheduled			X	X
Satisfaction with intervention: Client Satisfaction Questionnaire (CSQ-8) [44]		X		
Perceptions of study and evaluation of intervention: Qualitative interview			X	
Intimate partner violence: Abuse Assessment Screen (AAS)[47]	X		X	
Depression: Center for Epidemiologic Studies Depression (CES-D)[48]	X		X	
Spiritual support: Ironson-Woods Spirituality/Religiousness (SR)[49]	X			
Social Support: Medical Outcomes Study (MOS) Social Support Survey[50]	X			
Substance use: Addiction Severity Index-Lite (ASI-Lite)[51]	X		X	
Trauma experience: Adapted from items within Project BRIgHT[52]	X		X	
Anxiety: State-Trait Anxiety Inventory State Form (STAI-S)[53]	X		X	
Identification with organization: Items drafted by study team	X			
Stage of change: Adapted from Stage of Change measures[54,55]	X	X	X	
PrEP knowledge and experience: Adapted from PrEP Awareness and Willingness[56]	X			
HIV transmission knowledge: Adapted from the HIV Risk Knowledge Test[57]	X		X	
Sexual behavior: Number of sexual partners; alcohol/drug use before sex; vaginal/anal sex; knowledge of partners' HIV status; condom use	X		X	
Reflecting and evaluating: Quantitative and qualitative feedback about progress and quality of implementation, accompanied with regular personal and team debriefing about progress and experience.	Continuous			
Proposed intervention modifications: Both structural and didactic	Continuous			
Providers	**BL**	**PT**	**3M**	**12M**
Sociodemographics: Age, race, ethnicity, education, clinic position	X			
Implementation readiness: Adapted from the Implementation Climate Scale (ICS)[58]	X			
Dispositional innovativeness: Physician-Motivation-Adoption (PMA)[59]	X			
Culture: Organizational Culture Assessment Instrument (OCAI)[60]	X			
Patient needs and clinic resources: Adapted subscales from Texas Christian University Organizational Readiness for Change Scale (TCU-ORC-D4)[61]	X			
Stigma: Adapted from the Attitude Toward People Living with HIV Scale[62]	X			
Satisfaction with intervention: Behavioral Interventionist Satisfaction Survey (BISS)[45] (12M only) and Short Survey (PT only)		X		X
Identification with organization: Qualitative interview				X
Stage of change: Qualitative interview				X
Perceptions of study and evaluation of intervention: Qualitative interview				X
Reflecting and evaluating: Quantitative and qualitative feedback about progress and quality of implementation, accompanied with regular personal and team debriefing about progress and experience.				X
Proposed intervention modifications: Both structural and didactic	Continuous			

PrEP uptake will be measured by calculating the ratio of patients initiating PrEP to the number of patients eligible for the study who enrolled and were referred to PrEP services.

Note: BL = baseline; PT = post-treatment; 3M = 3-month assessment visit; 12M = 12-month data abstraction from EMR (patients) or assessment visit (provider)

PrEP adherence

Self-report (i.e., Visual Analog Scale) will be used to assess patients' adherence to taking PrEP as prescribed, as is currently standard practice in the participating clinics.[63] Reasons for discontinuing PrEP use, as applicable, will also be tracked. Participants will also be asked to rate, on a 6-point Likert scale, their ability to take all medications as prescribed.

Clinic visit adherence

Attendance at clinic visits will be defined as the number of PrEP visits attended divided by the number of visits scheduled. Adherence will be assessed at 3-month follow-up and 12-months via electronic medical record abstraction.

Psychosocial factors

Psychosocial factors will include assessments of intimate partner violence, depression, anxiety, post-traumatic stress disorder (PTSD), sexual behaviors, HIV transmission knowledge, substance use, social support, and spirituality/religiousness.

Intervention adaptation

Adaptation activities

Based on the formative evaluation in the first phase of this study, involving qualitative interviews with patients and providers (i.e., *Exploration* phase), a first draft of the patient-provider communication tool was produced. An adaptation plan as described by Aarons and colleagues[40] was used to document changes (i.e., new activities and materials to be included) to the protocol and reasons for such changes or additions. Given the minority status of our target population, it was anticipated that cultural adaptations would include process and content changes relevant to AA women vulnerable to HIV infection.[64,65] Adaptation was considered on the patient, provider, and organizational levels as per the EPIS.

During the *Preparation* phase, an Implementation Resource Team (IRT) was convened to review the first draft of the adapted patient-provider communication tool. The IRT was comprised of experts in implementation science and PrEP delivery, representatives of the clinic administration/staff (at both the FQHCs and the PrEP clinics), potential PrEP candidates and PrEP users, providers, and research team members. A second draft of the adapted communication tool integrated recommendations made and measures added by the IRT, maintaining the core elements of the patient-provider communication tool and considering the limitations and needs of the study sites.

Intervention implementation

Provider recruitment and training

Provider participants will be identified by the partnering clinic's study research assistant (RA). The study RA will contact study research staff on participating providers' behalf. Recruited providers will complete an informed consent form and baseline assessment. Links to the assessment battery will be sent to providers via email by research team members. Signed consent forms and baseline assessment responses will be directly entered and stored in a secure Research Electronic Data Capture (REDCap) database.

Enrolled providers will receive training in use of the patient-provider communication tool and best practices for prescribing PrEP. Training will be directed by health care practitioners with extensive experience in PrEP prescribing, training providers in PrEP prescribing, and/or managing PrEP-related logistics. Provider training will consist of two parts: first, providers will watch two training videos, which will include an overview of PrEP basics and the study's patient-provider communication tool; second, providers will participate in a live virtual training session with trainers, including an interactive roleplay using parts of the patient-provider

communication tool, all of which has been piloted during phase I. Additional trainings and preparation sessions may be held in-person at the clinic site or by phone as-needed.

Patient recruitment

Patient participants will be recruited in three ways: (1) study RA will pre-screen potential participants through their electronic medical records (EMR) and flag any patients with upcoming clinic visits who meet study eligibility criteria; (2) flyers will be posted in clinic waiting areas; and (3) health care providers at the participating clinic will directly refer interested patients who may be eligible to participate in the study. If a patient is recruited through EMR pre-screen, they will be formally screened by the study RA during their routine clinic visit. If a patient is recruited via flyer or provider referral, they will either contact the study RA by phone (using the phone number listed on the flyer) or may provide permission to be contacted by the study RA directly, who will then screen the prospective participant by phone. All individuals who meet inclusion criteria will be invited to complete the informed consent process at the baseline visit (Figure 2).

Informed consent

All participants will complete a baseline assessment visit either in-person or by phone, in which they will review an informed consent form, including a detailed explanation of all study procedures, information about potential risks and benefits of participation, and contact information for the study team in the event of further questions. The consent form will also state that participation is voluntary, that they can withdraw from the study at any time, and that study participation is in no way related to their health care, including receipt of PrEP services. Written or verbal consent will be obtained, and a copy of the signed consent form will be provided to participants.

Study assessments and intervention

Enrolled patients will complete a quantitative assessment during the baseline visit, administered via REDCap,[66] which will include sociodemographics and measures of anxiety, depression, interpersonal violence, substance use, PrEP awareness, sexual behaviors, PTSD as well as spiritual/emotional support. Patients will then be scheduled to meet with a provider, who will use the newly adapted PrEP patient-provider communication tool. Patients who are interested in receiving a referral for PrEP after completing the intervention will be referred to the in-house PrEP clinic; this referral will include a "warm hand-off" by a provider or PrEP navigator. Providers will document the visit in patients' electronic health records per standard clinic practice. Referrals will be made if domestic or intimate partner violence, and/or suicidal ideation are indicated in the baseline assessment.

Patients and providers at the local PrEP clinic will then jointly decide whether to initiate PrEP after referral. Providers at the PrEP clinics will be responsible for all aspects of PrEP care, including reviewing lab results, reinforcing educational messages around adherence and additional HIV/STI prevention options, and conducting patient examinations as needed, consistent with their current PrEP delivery practices. Regardless of PrEP initiation, patients will be scheduled for a 3-month follow-up study visit conducted via phone. During implementation, quarterly feedback will be provided by the IRT (or more frequently if needed), who will evaluate whether further adaptations are needed to the patient-provider communication intervention. IRT members will be comprised of experts in implementation science and PrEP delivery, representatives of the clinic administration and staff at local FQHCs, potential PrEP candidates and users, providers, and members of the investigative team. Best practices for intervention delivery process, type, and frequency of communication with AA women vulnerable to HIV infection will also be assessed.

Remuneration

Patients will be remunerated a total of $100 for their participation and transportation costs, independent of PrEP uptake. Providers will receive $50 for their time and 1.5 credit hours of continuing education credit for their participation in the study training.

Patient and public involvement

Patient and PrEP healthcare provider involvement is incorporated into the design and conduct of this implementation science study. The Implementation Resource Team described above is comprised of FQHC patients and PrEP navigators/providers as well as research team members. The IRT guides and informs the intervention design and implementation of the study throughout, including the interpretation and dissemination of results.

Data analyses

The feasibility, acceptability, and preliminary impact of this intervention will be assessed among patients and providers using this pre-/post-intervention design. Quantitative data will be analyzed using SPSS or R. Feasibility will be determined by evaluation of recruitment and retention, number of PrEP referrals, PrEP initiation, PrEP adherence, and clinic visit adherence. Acceptability will be measured using in-depth, individual, qualitative exit interviews and satisfaction surveys. Continuous feedback from participants and experts relevant to the population and outcomes studied will assure feasibility, acceptability, and appropriateness of the adapted intervention. Structural and content related changes of the intervention will be based on the feedback provided by patients and providers.

Primary and secondary outcomes will be assessed by characterizing the sample using descriptive statistics, computing confidence intervals on these measures, and exploring patient and implementation characteristics as possible moderators of these outcomes in order to inform

the design of our future trial. Measures of effect size (e.g., Cohen's d, Cohen's r, Cramer's V, R^2, etc.) will be used to determine the characteristics that individually appeared to be relevantly associated with PrEP uptake and secondary outcomes in the sample.

To examine impact of the protocol adaptation, we will use calendar quarter of entry in the study as a possible moderator. Multivariable exploratory analyses will be conducted using non-parametric methods[67] including penalized regression (LASSO) and Random Forest, to determine if the sample data suggest a smaller set of relevant characteristics based on their cross-validated predictive ability of each outcome. These data will be useful in tailoring our implementation approach based on empirical observation. On *a priori* conceptual considerations, we expect age, intimate partner violence and sexual risk behavior to be supported by the data as moderators of PrEP uptake. In addition, exploratory mediation analyses will be conducted based on conceptual considerations using the procedures outlined by Hayes.[68]

Clinics' electronic medical record data be used to estimate PrEP uptake, based on the number of PrEP-eligible AA women who have been referred to PrEP in the three years pre- and post-implementation of the protocol (i.e., pre-/post-test design). Binomial logistic models (events/trials syntax) will be fitted with time-period and clinic as main effects to estimate the differences in uptake proportions between pre- and post-protocol time periods. To determine the specific impact of the iterative process of protocol adaptation during the year of implementation, we will fit a logistic model for uptake with bi-monthly assessment wave number (three waves) as a categorical predictor. *A priori*, we expect a positive relationship between the assessment wave number and the odds of uptake, indicating that as the protocol became more refined during the year, PrEP uptake increased.

Sample size

To examine differences in PrEP uptake rates in the participating clinic comparing three years before and the year after the implementation of the protocol, we estimate that there are at least 3,500 AA PrEP-eligible women serviced annually. Assuming an uptake proportion of 0.0125 (44/3500 = 1.25%) estimated retrospectively in the three years prior to study implementation and a within-subject correlation of 0.65, at a significance level of 0.01, a sample size of 3,500 provides 90% power to detect an increase in proportion of uptake of .007 (.7%=25/3500); however, though power is high, interpretation of this inference would be restricted to the particular clinic in the study or clinics with similar characteristics.

The target sample size of N=125 is informative to provide reasonable range estimates (in the form of 95% confidence intervals) for the measures of interest in this study. For instance, assuming that 25% (n=31/125) of the in-study clients referred to PrEP in fact initiate PrEP, the width of the confidence interval for this percentage is 15.8%, and assuming that age has a standard deviation of 5 years and age moderates PrEP uptake, the confidence interval width for the mean difference in age between those who initiate PrEP (n=31) and those who do not (n=94) is 4.1 years (computations conducted using PASS 23 software). Given that this is an exploratory study with several primary and secondary outcomes, we do not have an expected effect size, but our study is nonetheless powered to detect a moderate effect.

Ethics and dissemination

The study will be conducted under a single IRB (sIRB) at the University of Alabama at Birmingham (UAB), with reliant sites at Massachusetts General Hospital and Beth Israel Deaconess Medical Center. Ethics approval was obtained for all aspects of this study by the IRB at UAB (UAB; protocol 300004276), where the work is being conducted. All participants will receive detailed written information on the purpose and procedures of the study and will provide

Table 2. WeExPAnd trial registration data

Data category	Information
Primary registry and trial identifying number	ClinicalTrials.gov NCT04373551
Date of registry in primary registry	May 4, 2020
Secondary identifying numbers	300003885, 1R34MH118044-01A1
Source(s) of monetary or material support	National Institute of Mental Health
Primary sponsor	National Institute of Mental Health
Secondary sponsor	N/a
Contact for public queries	Mirjam-Colette Kempf, PhD [mkempf@uab.edu]
Contact for scientific queries	Mirjam-Colette Kempf, PhD University of Alabama at Birmingham
Public title	PrEP Demonstration Project Among Women at Risk for HIV Infection
Scientific title	N/a
Countries of recruitment	United States
Health condition(s) or problem(s) studied	HIV-infection/AIDS

written or verbal informed consent prior to enrollment. Study updates, preliminary findings, and final results will be disseminated through publication of manuscripts in peer-reviewed journals, as well as through reports to the National Institutes of Health, and through local, national, and international presentations at HIV-focused conferences and meetings. The study is registered at ClinicalTrials.gov, NCT04373551 (Table 2).

Study status

At the time of writing, a total of 49 patients and nine providers have been enrolled in the study; screening and enrollment is ongoing. The PIs determined that a single FQHC site, rather than the two FQHCs initially identified, would both provide sufficient data to pilot test the patient-provider communication tool and allow for better concentration of implementation resources; as such, only one site has been activated with a target enrollment of N=125. The study will be completed by June 2024.

Intervention(s)	Behavioral: Cultural adaptation of a patient-provider communication tool
Key inclusion and exclusion criteria	Ages eligible for study: ≥ 18 years Sexes eligible for study: cisgender female Gender-based eligibility: yes Accepts health volunteers: no
	Patients Inclusion criteria: African American cisgender women aged 18 years or older without HIV; report HIV risk and/or recent PrEP use; English-speaking
	Providers Inclusion criteria: Physicians, nurse practitioners, physician assistants, nurses, medical assistants, social workers/counselors or other potential/actual PrEP service providers; English-speaking
Study type	Interventional (Clinical Trial)
	Allocation: N/a
	Primary purpose: Health Services Research
	Phase: N/a
Study start date	April 14, 2020
Target sample size	125 participants
Recruitment status	Enrolling by invitation
Primary outcome(s)	PrEP uptake changes [Time Frame: baseline, 3 months, and 12 months] Intervention feasibility changes [Time Frame: baseline, 3 months, and 12 months] Intervention acceptability [Time Frame: Through study completion, an average of 12 months]
Secondary outcome(s)	PrEP adherence [Time Frame: 3 months and 12 months] Clinic visit adherence changes [Time Frame: 3 months and 12 months] Biological measures of HIV, STIs and pregnancy [Time Frame: baseline, 3 months, and 12 months]

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Contributors: C.P. and M.C.K. conceived and designed the pilot demonstration study and its protocol and directed protocol activities. G.R.G. drafted the protocol manuscript and designed several manuscript tables. V.M., C.O., A.B., and A.R. contributed to drafting, editing, and finalizing the protocol manuscript and the design of the overall project protocol. L.S. planned and edited the statistical methods section of the manuscript. M.C. and E.U. advised on the protocol methods and provided comments on manuscript. D.K., L.E., K.K., and K.S. advised on

the structure and implementation of the protocol and provided comments on the protocol manuscript.

Funding: This work is supported by the National Institute of Mental Health (NIMH; grant number 5R34MH118044-03).

Competing interests: None declared.

Protocol issue date: 07 Mar 2022

Protocol version number: 01

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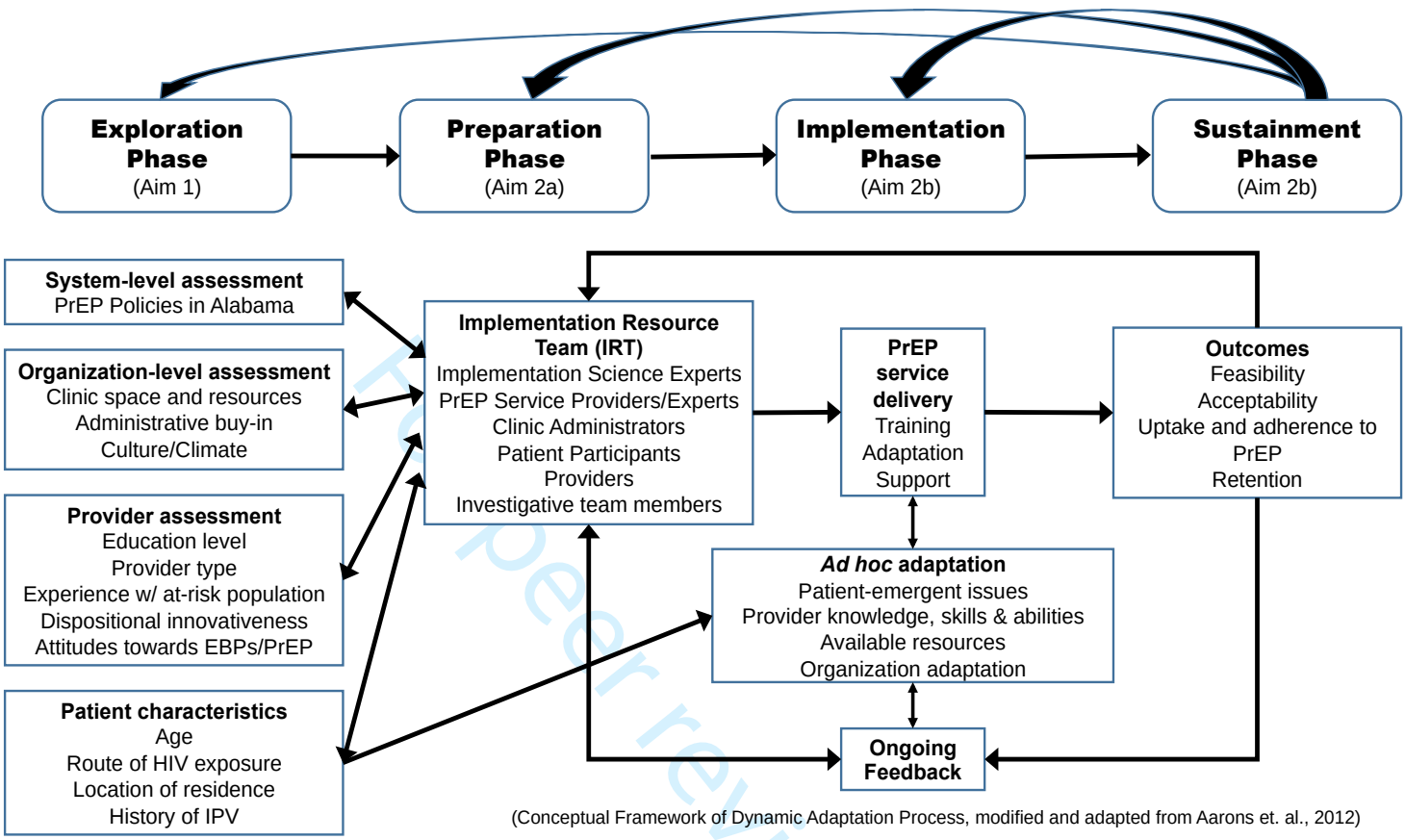
FIGURE TITLES AND LEGENDS

Figure 1. Overview of the Exploration, Preparation, Implementation, and Sustainment (EPIS) Implementation Framework for the study

The EPIS Implementation Framework a meta-theoretical framework incorporating components from multiple implementation process theories to guide intervention planning, adaptation and implementation. EPIS provides the overarching methodological framework to guide intervention adaptation in this study.

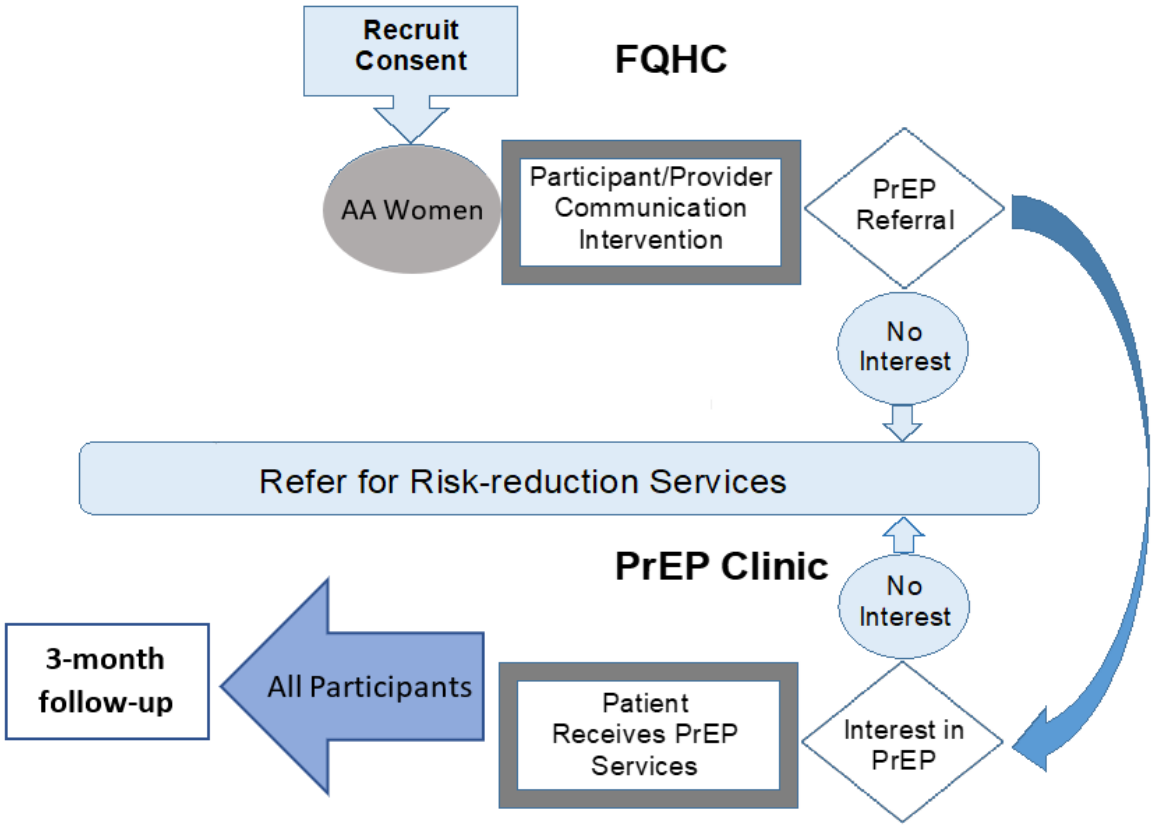
Figure 2. Flowchart of the informed consent, assessment, and intervention process for the study

Figure 1: Measurement framework of EPIS stages



(Conceptual Framework of Dynamic Adaptation Process, modified and adapted from Aarons et. al., 2012)

Figure 2: Participant flow in PrEP intervention



Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	28
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	28
Protocol version	#3	Date and version identifier	27
Funding	#4	Sources and types of financial, material, and other support	27
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1 & 27

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	1
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	n/a; This funding source and sponsor had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	n/a; IRB has designated the study minimal risk; all aspects of the trial are overseen by the co-PIs and research team
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	n/a; Single Group Assignment
Objectives	#7	Specific objectives or hypotheses	6
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	7
Methods:			

Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	8
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	8
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	14
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	14
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	15
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	n/a; No restrictions or specific allowances made on any health-related care or interventions during study participation.
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event),	9

		method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	14
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	7
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	13
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	n/a; This study uses a single group assignment with no randomization or masking.
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until	n/a; This study uses a single group assignment with no randomization or masking.

		interventions are assigned	
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	n/a; This study uses a single group assignment with no randomization or masking.
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	n/a; This study uses a single group assignment with no randomization or masking.
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a; This study uses a single group assignment with no randomization or masking.
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	10
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	15
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data	14

		entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	15
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	16
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	16
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	n/a; IRB designated study minimal risk; all data monitoring occurs internally by the co-principle investigators.
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	n/a; Plans for interim analyses are detailed in the IRB-approved data safety monitoring plan and are not described fully in the protocol manuscript.
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events	n/a; Plans for adverse events are detailed in the IRB-approved data safety

		and other unintended effects of trial interventions or trial conduct	monitoring plan and are not described fully in the protocol manuscript.
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n/a; Plans for trial conduct audits are detailed in the IRB-approved data safety monitoring plan and are not described fully in the protocol manuscript.
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	17
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	15
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	14
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	29
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	17; IRB approval has been obtained for all aspects of the study, including the collection and protection of participant confidentiality and personal information
Declaration of	#28	Financial and other competing interests	27

interests		for principal investigators for the overall trial and each study site	
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	n/a; Data access enumerated in the IRB-approved Data Safety Monitoring Plan and protocol
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	n/a; This trial has been designated as minimal risk by the UAB IRB.
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	17
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	n/a; Author contributions detailed on page 27 and no professional writers were used
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a; No current plans exist for granting public access to full protocol, participant dataset, or statistical code.
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	29
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a; This study collects no biological specimen.

Notes:

- 5c: n/a; This funding source and sponsor had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.
- 5d: n/a; IRB has designated the study minimal risk; all aspects of the trial are overseen by the co-PIs and research team
- 6b: n/a; Single Group Assignment
- 11d: n/a; no restrictions or specific allowances made on any health-related care or interventions during study participation.
- 16a: n/a; This study uses a single group assignment with no randomization or masking.
- 16b: n/a; This study uses a single group assignment with no randomization or masking.
- 16c: n/a; This study uses a single group assignment with no randomization or masking.
- 17a: n/a; This study uses a single group assignment with no randomization or masking.
- 17b: n/a; This study uses a single group assignment with no randomization or masking.
- 21a: n/a; IRB designated study minimal risk; all data monitoring occurs internally by the co-principle investigators.
- 21b: n/a; Plans for interim analyses are detailed in the IRB-approved data safety monitoring plan and are not described fully in the protocol manuscript.
- 22: n/a; Plans for adverse events are detailed in the IRB-approved data safety monitoring plan and are not described fully in the protocol manuscript.
- 23: n/a; Plans for trial conduct audits are detailed in the IRB-approved data safety monitoring plan and are not described fully in the protocol manuscript.
- 26b: n/a; ancillary study consent not included in protocol manuscript
- 27: 17; IRB approval has been obtained for all aspects of the study, including the collection and protection of participant confidentiality and personal information
- 29: n/a; Data access enumerated in the IRB-approved Data Safety Monitoring Plan and protocol
- 30: n/a; This trial has been designated as minimal risk by the UAB IRB.
- 31b: n/a; author contributions detailed on page 27 and no professional writers used
- 31c: n/a; no current plans exist for granting public access to full protocol, participant dataset, or statistical code.

- 33: n/a; This study collects no biological specimen. The SPIRIT Explanation and Elaboration paper is distributed under the terms of the Creative Commons Attribution License CC-BY-NC. This checklist was completed on 19. April 2023 using https://www.goodreports.org/, a tool made by the EQUATOR Network in collaboration with Penelope.ai