WeExPAnd: PrEP Demonstration Project Among Women at Risk for HIV Infection - Preexposure Prophylaxis (PrEP)

Study Protocol & Statistical Analysis Plan

NCT04373551

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STATEMENT OF COMPLIANCE

The trial will be conducted in accordance with International Conference on Harmonisation Good Clinical Practice (ICH GCP) and applicable United States (US) Code of Federal Regulations (CFR). The Principal Investigator will assure that no deviation from, or changes to, the protocol will take place without prior documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial subjects. All personnel involved in the conduct of this study have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all subject materials will be submitted to the local Institutional Review Board (IRB) for review and approval. Approval of both the protocol and the consent form must be obtained before any subject is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from subjects who provided consent, using a previously approved consent form.

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title:	WeExPAnd: PrEP Demonstration Project Among Women at Risk for HIV Infection - Preexposure Prophylaxis (PrEP)
Study Description:	This is a prospective, mixed-methods pilot demonstration study using a pre-/post-intervention design to assess the feasibility, acceptability, and preliminary impact of a culturally adapted patient-provider communication tool on PrEP uptake among cisgender women receiving care at federally qualified health centers (FQHCs) in Alabama. The study employs an iterative implementation process guided by the Exploration, Preparation, Implementation, and Sustainment (EPIS) framework and Dynamic Adaptation Process (DAP).
Objectives:	**Primary:** To assess the feasibility, acceptability, and preliminary impact of an adapted patient-provider communication intervention on PrEP uptake among cisgender women **Secondary:** To evaluate PrEP medication adherence and clinic visit adherence
Endpoints:	**Primary:** PrEP uptake rates, intervention feasibility metrics (recruitment numbers, enrollment rate (proportion of eligible participants consenting), participant retention (proportion completing 3-month follow-up), PrEP referral acceptance rate, and intervention delivery completion rate), and intervention acceptability measures (patient satisfaction surveys) **Secondary:** PrEP adherence (self-report via Visual Analogue Scale), clinic visit adherence (attendance rates)
Study Population:	Cisgender, HIV-uninfected women aged 18 years or older who are English-speaking and report sexual activity or anticipate sexual activity within 6 months.
Phase:	N/A

Description of Study Intervention:	Participants receive a brief patient-provider communication intervention using an adapted flip-book communication tool, optionally preceded by a 3-minute PrEP informational video. The intervention facilitates structured conversations about HIV risk assessment and PrEP as a prevention option, with referrals to PrEP services for interested participants.
Study Duration:	Approximately 18 months for enrollment and intervention implementation, with a 12-month follow-up for outcome assessment
Subject Duration:	Up to 3 months active participation (baseline assessment, intervention visit, 3-month follow-up), with medical record data abstraction at 3 months and 12 months post-intervention

1.2 SCHEDULE OF ACTIVITIES (SOA)

Study Activity	Screening	Baseline (Day 0)	Intervention Visit	3-Month Follow-up	12-Month Data Collection
Eligibility Assessment	x				
Informed Consent		x			
Demographics		x			
Baseline Assessments*		x			
PrEP Video (optional)			x		
Patient-Provider Communication Tool			x		
PrEP Referral (if interested)			x		
Patient Satisfaction Survey			x		
3-Month Assessments**				x	
Qualitative Interview				x	

Medical Record Abstraction***				x	x
Adverse Event Assessment		x	x	x	

Notes:

*Baseline Assessments include: intimate partner violence, depression, anxiety, substance use, sexual behaviors, HIV knowledge, PrEP awareness, social support, spirituality/religiousness, PTSD screening

**3-Month Assessments include: depression, anxiety, substance use, sexual behaviors, HIV knowledge, intimate partner violence, PrEP adherence (if applicable), stage of change

***Medical record data abstraction includes PrEP initiation and clinic visit attendance

2 INTRODUCTION

2.1 STUDY RATIONALE

Cisgender women, particularly women of color living in the rural southeastern United States, remain persistently at risk for HIV infection. Pre-exposure prophylaxis for HIV (PrEP) is a highly effective HIV prevention tool that may overcome barriers experienced by women when using traditional HIV prevention tools, such as condoms, which are primarily used and controlled by male partners. However, we know very little about how to facilitate effective access and use of PrEP for women at high risk for HIV infection. This project seeks to understand how to make PrEP more accessible to these women, which may ultimately affect HIV incidence in this population.

Suboptimal healthcare provider communication about sexual health, HIV/STI risk, and preventive measures like PrEP represents a significant barrier to widespread PrEP uptake. Provider awareness of PrEP for women and willingness to prescribe PrEP to patients is alarmingly low. A collaborative effort among providers and PrEP-eligible women is needed to develop culturally tailored interventions supporting PrEP uptake among women at risk of HIV infection.

2.2 BACKGROUND

Despite representing a minority of the US female population, African American (AA) women bear a disproportionate burden of new HIV diagnoses among women each year. These disparities are especially glaring in the Southeast where HIV prevalence and incidence is among the highest in the nation.

Traditional HIV prevention efforts, such as abstinence-only education approaches prevalent in the rural South, have failed to reduce rates of STI and HIV infections. 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. 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.

Although PrEP can curb incident HIV infection among high-risk individuals, research on its promotion and use among women – particularly in the US South – is limited. Multiple studies indicate that, regardless of geographic location, women as well as staff members at healthcare clinics are unfamiliar with PrEP as an HIV prevention tool and express concern about the broad lack of awareness of its availability to women. However, women, particularly women of color, expressed being generally interested in using PrEP if available, especially if recommended by a trusted healthcare provider.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

It is unlikely that patient participants will be at any risk for physical harm because of study participation. Participants may find some of the questions covered in the assessments to be emotionally upsetting.

Participating in qualitative interviews may also be distressing, as the interview may involve discussing personal matters. The most common risks for providers include asking patients uncomfortable sexual health questions.

2.3.2 KNOWN POTENTIAL BENEFITS

The potential benefits of the research include improved service delivery, which aims to maximize benefits for patients and minimize adverse health effects. Participants may benefit from receiving information about PrEP as well as referrals to appropriate services if needed.

3 STUDY DESIGN

3.1 OVERALL DESIGN

This is a prospective, mixed-methods pilot demonstration study using a pre-/post-intervention design to assess the feasibility, acceptability, and preliminary impact of a culturally adapted patient-provider communication tool on PrEP uptake among cisgender women receiving care at federally qualified health centers (FQHCs) in Alabama. The study employs an iterative implementation process guided by the Exploration, Preparation, Implementation, and Sustainment (EPIS) framework and Dynamic Adaptation Process (DAP).

Following formative qualitative research with patients and providers (Phase 1), this protocol focuses on Phase 2 implementation activities. Enrollment occurs in iterative cycles with continuous feedback from an Implementation Resource Team (IRT) to refine the intervention throughout the study period. The study uses a single-arm design without randomization, as this is a pilot feasibility study evaluating intervention implementation rather than comparative effectiveness.

4 STUDY POPULATION

4.1 INCLUSION CRITERIA

Cisgender women; age 18 years or older; HIV-uninfected according to self-report; report any sex with male partners in the past 6 months OR anticipate sexual activity with male partners in the next 6 months; primary language English; willing and able to give informed consent; receiving care at one of the participating clinic study sites.

4.2 EXCLUSION CRITERIA

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.

4.3 STRATEGIES FOR RECRUITMENT AND RETENTION

Recruitment Methods: Patient recruitment occurs through three approaches: (1) research assistant pre-screening of electronic medical records to identify potentially eligible patients with upcoming clinic visits; (2) recruitment flyers posted in clinic waiting areas; and (3) direct referral by healthcare providers at participating clinics.
Patients recruited through EMR pre-screening are formally screened during routine clinic visits. Patients recruited via flyers or provider referral either contact the research assistant directly using the phone number on flyers or provide permission to be contacted by study staff for telephone screening.

Retention Strategies: Participants receive compensation at each study visit ($30 baseline, $30 intervention, $40 three-month follow-up). Reminder calls are conducted 24 hours before scheduled visits. Flexible scheduling options are provided for follow-up assessments, including in-person or telephone completion.

5 STUDY INTERVENTION

5.1 STUDY INTERVENTION(S) ADMINISTRATION

5.1.1 STUDY INTERVENTION DESCRIPTION

The study intervention consists of a brief patient-provider communication session using a culturally adapted flip-book communication tool, optionally preceded by a 3-minute PrEP informational video. The intervention facilitates structured conversations about HIV risk assessment and PrEP as a prevention option.

During the intervention visit, participants may first watch the informational video about PrEP. The trained study provider then follows up on video content and uses the flip-book communication tool to guide discussion about HIV risk, PrEP candidacy, and prevention options. The session concludes with referral to PrEP services for interested participants or discussion of alternative risk-reduction strategies for those not interested in PrEP.

5.2 STUDY INTERVENTION COMPLIANCE

Intervention compliance is assessed through the providers' completion of content checklists, which document the use of communication tool components during each patient session. Providers complete brief feedback surveys weekly to assess intervention delivery fidelity and implementation challenges.

6 STUDY INTERVENTION DISCONTINUATION AND SUBJECT DISCONTINUATION/WITHDRAWAL

6.1 SUBJECT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Subjects are free to withdraw from participation in the study at any time upon request.
An investigator may discontinue or withdraw a subject from the study for the following reasons:

- Significant study intervention non-compliance
- If any clinical adverse event (AE), laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the subject

Subjects who withdraw or are discontinued from the study will not be replaced, as this is a pilot feasibility study.

6.2 LOST TO FOLLOW-UP

A subject will be considered lost to follow-up if he or she fails attend 2 scheduled visits and is unable to be contacted by the study site staff. A subject will also be lost to follow-up if they fail to complete the 3-month follow-up assessment and cannot be contacted by study staff after documented attempts. Before a subject is deemed lost to follow-up, the research assistant will make at least 3 telephone contact attempts. Contact attempts will be documented in the subject's study file.

7 STUDY ASSESSMENTS AND PROCEDURES

7.1 STUDY ASSESSMENTS

Baseline Assessments (completed prior to intervention): Demographics, intimate partner violence (Abuse Assessment Screen), depression (CES-D-10), anxiety (State-Trait Anxiety Inventory), substance use (Addiction Severity Index-Lite), sexual behaviors, HIV transmission knowledge, PrEP awareness, social support (MOS Social Support Survey), spirituality/religiousness (Ironson-Woods Scale), and trauma screening.

Post-Intervention Assessments: Patient satisfaction with intervention (Client Satisfaction Questionnaire CSQ-8) completed immediately following the intervention session.

3-Month Follow-up Assessments: Repeat measures of depression, anxiety, substance use, sexual behaviors, HIV knowledge, intimate partner violence, PrEP adherence (if applicable), and stage of change. Qualitative interview exploring study experience and PrEP decision-making.

Medical Record Data Collection: PrEP initiation and clinic visit attendance abstracted at 3 months and 12 months post-intervention.

7.2 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

7.2.1 DEFINITION OF ADVERSE EVENTS (AE)

An adverse event is defined as a harmful occurrence to study participants, either study-related or non-study-related. As a result of participation in the PrEP uptake intervention or qualitative interviews, study staff may become aware of an adverse event, including participant distress, suicidal ideation, or disclosure of violence or abuse.

7.2.2 DEFINITION OF SERIOUS ADVERSE EVENTS (SAE)

Given the minimal risk of the patient-provider communication intervention, serious adverse events are not anticipated.

7.2.3 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

Study staff will assess for adverse events during study visits and interviews. Events will be monitored from informed consent through 7 days after the last study visit.

7.2.4 ADVERSE AND SERIOUS ADVERSE EVENT REPORTING

Because study participation may reflect a unique opportunity to provide referrals for social services and because we are collecting data on depressive symptoms and intimate partner violence, any participant endorsing significant symptoms on either of these measures (or a participant who spontaneously reports these problems) will be provided with a referral for services. Study staff will be trained to make appropriate referrals for clinical care in consultation with the PI and clinic site investigators, including participant distress, suicidal ideation, or disclosure of violence or abuse.

Adverse events will be reported to all relevant IRBs as soon as any study staff member discovers them and consistent with site reporting guidelines, and these will be discussed on weekly calls/in-person meetings between Dr. Kempf and the research team.

7.3 UNANTICIPATED PROBLEMS

7.3.1 DEFINITION OF UNANTICIPATED PROBLEMS (UP)

Unanticipated problems are incidents, experiences, or outcomes that are unexpected, possibly related to study participation, and suggest greater risk than previously known.

7.3.2 UNANTICIPATED PROBLEM REPORTING

Unanticipated problems will be reported to the UAB Institutional Review Board (IRB) within 10 working days of the investigator becoming aware of the problem

8 STATISTICAL CONSIDERATIONS

8.1 STATISTICAL HYPOTHESES

Primary Hypotheses:

- The adapted patient-provider communication intervention will demonstrate feasibility as measured by successful recruitment, enrollment, and retention rates
- The intervention will demonstrate acceptability as measured by patient satisfaction scores
- The intervention will show a preliminary impact on PrEP uptake rates among participants

Secondary Hypotheses:

- Participants who initiate PrEP will demonstrate adequate medication adherence and clinic visit adherence

8.2 SAMPLE SIZE DETERMINATION

The target sample size of N=125 patient participants provides reasonable precision for estimating feasibility and acceptability measures in this pilot study. For instance, assuming 25% of participants initiate PrEP, the 95% confidence interval width for this proportion would be approximately 15.8%. This sample size is adequate for a pilot study aimed at informing the design of a future larger-scale trial rather than testing definitive efficacy hypotheses.

8.3 STATISTICAL ANALYSES

8.3.1 GENERAL APPROACH

Quantitative data will be analyzed using SPSS or R. Descriptive statistics will summarize all collected data. As this is a pilot feasibility study, analyses will focus on estimation rather than hypothesis testing, with emphasis on confidence intervals for key parameters.

8.3.2 ANALYSIS OF THE PRIMARY EFFICACY ENDPOINT(S)

Intervention feasibility: Feasibility will be assessed using descriptive statistics (i.e., counts and proportions) for: recruitment numbers (number of participants screened), enrollment rate (proportion of eligible participants consenting), participant retention (proportion completing 3-month follow-up), PrEP referral acceptance rate (proportion accepting referral among those offered), and intervention delivery completion rate (proportion receiving complete intervention). Reasons for non-participation, referral decline, and incomplete intervention delivery will be summarized using frequency distributions and percentages.

Intervention acceptability. Acceptability will be assessed using descriptive statistics (mean and standard deviation) for CSQ-8 scores among patient participants. Missing item responses will be handled according to each instrument's scoring guidelines.

PrEP uptake changes. PrEP uptake rates will be compared between the 7-month pre-intervention period and the post-period using binomial logistic regression. Time period (pre-intervention vs. post) will serve as the primary predictor. Uptake proportions (i.e., patients who initiate PrEP over eligible patients referred) and 95% confidence intervals will be calculated to estimate the change in uptake rates between periods.

8.3.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

PrEP adherence. PrEP adherence will be measured with Visual Analog Scale scores from the ACTG Adherence Questionnaire among participants who initiate PrEP. Adherence will be evaluated through descriptive statistics (i.e., counts) of patients' self-perceived PrEP prescription regimen adherence and descriptive statistics (i.e., means and standard deviation) of patients' estimated PrEP dosage adherence. Adherence scores are collected at the 3-month timepoint.

Clinic visit adherence. Clinic visit adherence will be assessed using descriptive statistics (i.e., mean and standard deviation) for the ratio of PrEP visits attended to PrEP visits scheduled among patients who initiate PrEP. Adherence ratios were collected at 3-month and 12-month follow-up timepoints.

8.3.4 BASELINE DESCRIPTIVE STATISTICS

Baseline characteristics of enrolled participants will be summarized using appropriate descriptive statistics (means and standard deviations for continuous variables, frequencies and percentages for categorical variables) to characterize the study population and inform future trial design.

9 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

9.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

9.1.1 INFORMED CONSENT PROCESS

9.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO SUBJECTS

The consent form includes all study procedures, information about potential risks and benefits of participation, and information regarding whom they can contact for further questions. It also states that participation is voluntary. Participants can refuse to answer any question, they can withdraw from the study at any time, and study participation is in no way related to their health care, including receipt of PrEP services.

9.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Patients will be given an iPad by the Research Assistant (RA) prior to their baseline assessment that will contain an e-form consent linked to REDCap. The RA will be available to answer any questions the patient may have about the consent form. For patients requiring remote baseline assessment, patients will be emailed or texted a link to REDCap where they will read and sign an e-form consent. For patients who do not have computer access and/or literacy to complete the consent via REDCap, patients can provide verbal consent over the phone with study staff using a telephone script.

9.1.2 CONFIDENTIALITY AND PRIVACY

All data will be kept confidential and accessible only to trained study staff. An ID number only will identify participants' data, and a link between names and ID numbers will be kept separately in an encrypted, password-protected computer file. Interview recordings will be kept on encrypted, password-protected computer file and deleted at the end of the study.

All research activities will be conducted in as private a setting as possible.

9.1.3 QUALITY ASSURANCE AND QUALITY CONTROL

The site will perform internal quality management of study conduct, data collection, documentation and completion. Quality control (QC) procedures will be completed by study staff after data entry. Any missing data or data anomalies will be communicated to the PIs for clarification/resolution.

Study staff will verify that the study is conducted and data are generated are collected, documented (recorded), and reported in compliance with the protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), and applicable regulatory requirements.

The site will provide direct access to all study-related sites, source data/documents, and reports for the purpose of monitoring and inspection by local and regulatory authorities.

9.1.4 DATA HANDLING AND RECORD KEEPING

9.1.4.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection is the responsibility of the study staff at the UAB and the partnering clinical sites under the supervision of the Principal Investigator. Informed consent and assessments will be captured via iPad and directly entered into REDCap. All computers or iPads used to collect, store, and manipulate data will be password protected with access to a secure REDCap server provided by UAB Department of Medicine.

9.1.4.2 STUDY RECORDS RETENTION

Investigators will maintain all paper records pertaining to this protocol for a period of 3 years after close of the study, after which all records will be destroyed with permission from the principal investigator.

9.1.5 PROTOCOL DEVIATIONS

It is the responsibility of the Principal Investigator to use continuous vigilance to identify and report deviations within 10 working days of identification of the protocol deviation. Protocol deviations must be sent to the reviewing Institutional Review Board (IRB) per their policies.