Study Protocol

Study Title: Supporting Oral Pre-exposure Prophylaxis Decision Making Among Pregnant Women in Lilongwe, Malawi: A Pilot Study

NCT number NCT06394323
Document Date 02/23/2024

Proposal Title: Supporting oral pre-exposure prophylaxis decision making among pregnant women in Lilongwe, Malawi: a pilot study

PI: Lauren Hill, PhD MSPH (UNC-Chapel Hill, USA)

Co-Investigators Friday Saidi, MBBS, MMed (UNC Project-Malawi)

Benjamin Chi, MD MSc (UNC-Chapel Hill, USA)

Carol Golin, MD (UNC-Chapel Hill, USA)

Suzanne Maman, PhD (UNC-Chapel Hill, USA)

Lisa Pearce, PhD (UNC-Chapel Hill, USA)

Country Contact: Friday Saidi, UNC Project-Malawi

Email: fsaidi@unclilongwe.org

Study contact phone number: +265 1 755 056

Duration: 2 Years

TABLE OF CONTENTS

TABLE OF ABBREVIATIONS 1
1. ABSTRACT 1
2. BACKGROUND, PROBLEM STATEMENT AND JUSTIFICATION 1
3. LITERATURE REVIEW 2
3.1 HIV risk during pregnancy and breastfeeding 2
3.2 PrEP in pregnancy and breastfeeding 2
3.3 The importance of shared decision-making for appropriate PrEP use 3
3.4 Our formative work 4
4. STUDY OBJECTIVES AND OUTCOMES 5
4.1 Objective and Aims 5
4.2 Study Outcomes 5
4.2.1 Primary outcomes 5
4.2.2 Secondary outcome 5
4.2.3 Exploratory outcomes 5
5. METHODOLOGY 6
5.1 Study design 6
5.3 Standard of care (control arm) 7
5.4 Eligibility criteria 8
5.5 Place of study 8
5.6 Target population 8
5.7 Recruitment and enrollment procedures 9
5.7.1 Recruitment procedures 9
5.7.2 Enrolment procedures 9
5.8 Study follow-up 9
5.9 Assessment of study outcomes 10
5.9.1 Assessment of primary outcomes 10
5.9.2 Assessment of secondary outcomes 10
5.9.3 Assessment of exploratory outcomes 11
5.10 Retention 12
5.11 Safety Monitoring 12
5.12 Biological specimen collection and testing 12
5.13 Quality control and quality assurance procedures 13
5.14 Data Management and Storage 13
5.15 Sample size 13
5.15.1 Precision calculations for continuous outcomes 13

5.15.2 Precision calculations for binary outcomes 14
5.16 Data Analysis 15
5.16.1 Analysis of primary endpoints 15
5.16.2 Analysis of secondary endpoints 15
5.16.3 Quantitative analysis of exploratory endpoints 16
5.16.4 Qualitative analysis of IDIs (exploratory outcomes) 17
6. ETHICAL CONSIDERATIONS 18
6.1 Ethical approval 18
6.2 Informed consent 18
6.3 Data storage 18
6.4 Confidentiality 18
6.5 Potential risks to participants 18
6.6 Protection Against Risks 19
6.7 Potential Benefits of Proposed Research to Human Subjects and Others 20
6.8 Inclusion of children, sub-populations, and vulnerable populations 20
6.9 Reimbursement/compensation 20
6.10 Dissemination of findings 20
7. WORK PLAN 20
REFERENCES 21

TABLE OF ABBREVIATIONS

Abbreviation	Definition
ANC	Antenatal care
DBS	Dried blood spot
HIV	Human immunodeficiency virus
IDI	In-depth interview
NHSRC	National Health Science Research Committee
PrEP	Pre-exposure prophylaxis
SDM	Shared decision making
SOC	Standard of care
SOP	Standard Operating Procedure
STI	Sexually transmitted infection
TDF-FTC	Tenofovir disoproxil fumarate and emtricitabine
TFVdp	Tenofovir diphosphate
WHO	World Health Organization

1. ABSTRACT

An estimated 45% of mother-to-child HIV transmission in Malawi is attributable to acute maternal HIV infection during pregnancy and breastfeeding, indicating a critical need to address HIV risk during this period. Pre-exposure prophylaxis (PrEP) is a promising tool for the prevention of HIV acquisition during pregnancy and the postpartum period and is a recommended component of a comprehensive package of prevention of mother-to-child HIV transmission services. Yet, few strategies exist to promote person-centered shared decision-making about PrEP use during pregnancy and breastfeeding despite the complexity of this decision and the importance of shared decision-making for medication adherence. To be able enable pregnant women to make shared decisions about PrEP use with their health care providers, person-centered counseling approaches are needed to help women determine if PrEP or an alternative HIV prevention method is most appropriate based on their values. Therefore, we propose a pilot study to evaluate a novel shared decision-making counseling approach for tailored to the needs of pregnant and breastfeeding women in Malawi. This intervention was developed on the basis of a previous formative study conducted in Lilongwe (NHSRC Protocol 20/01/2465), which consisted of a mixed methods study to understand women's values and decision-making needs regarding PrEP uptake, and to refine the intervention through and participant feedback. In this pilot study we aim to evaluate the feasibility, acceptability, and appropriateness of the shared decision-making (SDM) intervention to support oral PrEP decision making among pregnant and breastfeeding women in Lilongwe. This pilot will inform a future efficacy trial to determine the effect of the SDM intervention on decisional satisfaction and adherence to PrEP. Thus, this study will ultimately contribute meaningfully to the successful delivery of PrEP in the context of antenatal care in Malawi to ensure that decision-making regarding PrEP use by pregnant and breastfeeding women is person-centered to encourage appropriate and adherent use.

2. BACKGROUND, PROBLEM STATEMENT AND JUSTIFICATION

Pre-exposure prophylaxis (PrEP) is a promising strategy to prevent HIV acquisition among pregnant and breastfeeding women; however, realizing this promise will require effective strategies to promote adherence. Prevention of HIV acquisition during pregnancy and the postpartum period is critical to preventing both horizontal and vertical transmission of HIV in sub-Saharan Africa. Women are at elevated HIV risk during this period[1], and one-third to one-half of mother-to-child transmission of HIV is attributable to acute maternal infection[2–4]. Oral PrEP with daily tenofovir-emtricitabine is highly effective in preventing HIV infection

when taken with high adherence[5–7]. WHO guidelines recommend offering oral PrEP to individuals at-risk for acquiring HIV, including pregnant and breastfeeding women[8]. To realize the potential of PrEP, strategies to promote adherence are urgently needed because of the sensitivity of PrEP's effectiveness to user error: for protective drug levels during vaginal sex, a minimum of 85% adherence is required[10]. Women in PrEP trials have generally fallen short of this effective level, in some studies achieving a mean of only 24% adherence[11–13].

Ensuring user fit and motivation prior to PrEP initiation may be an important complement to conventional adherence support strategies. Poor adherence among women in the aforementioned PrEP trials was observed despite the inclusion of adherence counselling and support for participants[14]. Documented barriers to PrEP adherence among women have included poor fit with user lifestyles[15–17], women's difficulty using PrEP in the context of romantic relationships [15,18–20], and low motivation for PrEP use[16]. These findings highlight the fact that ensuring the appropriateness of PrEP for each potential user from the outset is essential. We need to help women decide which HIV prevention method best fits their needs and preferences, as this will be the method they will be most likely to use effectively [21]. Strategies to support women's decision-making about PrEP initiation are needed to ensure that it is informed and person-centred.

Actively engaging women considering PrEP in shared decision-making may ensure user fit and promote adherence. Shared decision-making (SDM) is strongly recommended for *preference-sensitive* medical decisions for which multiple options are available with no distinctly superior option[22]. The SDM model provides a patient-centred approach to encourage an informed and active patient role in these decisions. By providing patients with knowledge about the options available to them, and helping them to clarify their needs and values relevant to the decision, SDM may improve adherence by ensuring user fit and promoting motivation and self-efficacy to adhere to the choice taken[23–27]. While SDM has been shown to promote adherence to other medications[28], this promising approach needs to be evaluated for PrEP use. For novel tools like PrEP, decision support aids are particularly critical as clinicians often lack the skills or training to guide their patients through SDM.

Problem statement: Pre-exposure prophylaxis (PrEP) represents an opportunity to dramatically reduce the elevated risk of HIV in pregnant and breastfeeding women in sub-Saharan Africa, but shared decision making (SDM) about its use is essential to identify appropriate users and promote adherent use. No evidence-based approaches for PrEP shared decision making in pregnancy exist. Thus, we aim to fill this gap in the proposed pilot study to determine the feasibility, acceptability, and appropriateness of a novel SDM intervention and associated study procedures to inform a future efficacy trial.

3. LITERATURE REVIEW

3.1 HIV risk during pregnancy and breastfeeding

Prevention of HIV infection during pregnancy and breastfeeding is a major HIV prevention priority because of the increased biological and behavioural risk factors for infection during this period[29–32] and the danger that acute maternal HIV infection poses for transmission to the infant[2,33–37]. Indeed, in Malawi an estimated 45% of mother-to-child HIV transmission in Malawi is attributable to acute maternal HIV infection during pregnancy and breastfeeding, indicating a critical need to address HIV risk during this period[38].

3.2 PrEP in pregnancy and breastfeeding

Following evidence that oral PrEP with daily tenofovir-emtricitabine effectively prevents HIV transmission[5–7], and is safe during pregnancy and breastfeeding[39], WHO and Malawi national guidelines recommend offering PrEP in standard PMTCT practice[10]. To date, however, little is known about how to identify appropriate PrEP users in antenatal settings and determine the appropriate PrEP method for each patient. The PrEP choice is highly preference sensitive[22]as

a given product may not be the right fit for every woman. Though many pregnant women in sub-Saharan Africa would be candidates for PrEP use according to HIV risk criteria (e.g., partner HIV status knowledge, STI history)[33,40], women in PrEP trials who met HIV risk criteria and expressed an interest in PrEP often had low adherence[11–13]. This suggests that evaluated HIV risk alone is not in itself a sufficient motivator for women to adhere to PrEP.

In randomized trials, oral pre-exposure prophylaxis (PrEP), in the form of daily tenofovir disoproxil fumarate and emtricitabine (TDF-FTC) has been shown to be effective for prevention of HIV acquisition[5–7,41], including in women[13,42]. This intervention may be particularly well-suited for pregnancy and breastfeeding. Not only are HIV incidence rates exceedingly high during pregnancy but features that characterize this period may lead to greater PrEP adherence: high levels of institutional healthcare[43], altruistic motivations towards the unborn fetus [44–46], a tradition of male partner engagement[47], and a window of concentrated risk. In order to be effective, however, adherence is critical.

TDF-FTC has been used in the context of pregnancy for both HIV and hepatitis B therapy, and has a strong track record for maternal and infant safety[39]. Data from PrEP trials have shown that TDF-FTC in the first trimester did not result in adverse outcomes at birth or in infant growth[49]. A smaller, open-label study—where women were given the option of continuing PrEP once they became pregnant—demonstrated similarly encouraging outcomes[50]. Studies in Kenya and Uganda suggest that PrEP can be safely used during breastfeeding with minimal infant drug exposure[51]. In settings with high HIV incidence during pregnancy (i.e., greater than 3.0 infections per 100 person-years), oral PrEP has been shown to be highly cost-effective across a range of modelling assumptions.[52] TDF-FTC is approved by the Malawi ministry of health and available through standard of care.

3.3 The importance of shared decision-making for appropriate PrEP use

Because of the promise of PrEP for HIV prevention in pregnancy and breastfeeding and for PMTCT, there is a critical need to develop interventions to engage pregnant and breastfeeding women in PrEP use in ways that promote adherence to PrEP. To date, however, very little is known about how to engage pregnant women in PrEP use and how to identify appropriate PrEP users in this population. Though many pregnant women in sub-Saharan Africa would be candidates for PrEP use according to HIV risk criteria (e.g., partner HIV status knowledge, STI history)[33,40], women in PrEP trials who met HIV risk criteria and expressed an interest in PrEP often had low adherence[11–13]. This suggests that evaluated HIV risk alone is not in itself a sufficient motivator for women to adhere to PrEP.

User fit and motivation for PrEP use are integral to promoting adherence; a shared decision-making process can help to ensure this fit and motivation. Unlike antiretroviral therapy, the decision to use PrEP is a highly preference-sensitive decision[22]; despite the advantage of PrEP as a woman-controlled method for HIV prevention, PrEP may not be the right HIV prevention fit for every woman. To promote this fit, a shared decision-making (SDM) process can be used to encourage values-congruent choices, or said otherwise, to reduce *decisional conflict*, defined as uncertainty about the best choice among competing options and discomfort with the decision taken[53]. SDM can reduce decisional conflict by increasing one's sense of being informed about alternatives, benefits, and risks and by clarifying relevant personal values. The SDM model is both theoretically intended and empirically shown to promote values-congruent choices (low decisional conflict)[23], as well as adherence to ART[25–27], and treatments for depression and diabetes[54,55]. Shared decision-making in HIV care is well accepted and strongly desired by patients [56–58], and is associated with enhanced adherence to ART be promoting patient engagement, adherence self-efficacy, confidence in the treatment regimen, and satisfaction with the patient-provider relationship[25,26]. This effect on adherence can be understood by the fact that SDM is highly conducive to real and perceived choice autonomy, which is an essential precursor to intrinsic motivation for a behavior[59]. Decision-making theory suggests that adherence is more than a result of but rather a manifestation of real and perceived choice autonomy, which is optimally promoted through

shared decision-making[21]. This evidence points to the need for shared decision-making to identify appropriate PrEP users and to promote PrEP adherence.

Antenatal care provides a unique opportunity to engage women in HIV prevention and PrEP use and is a context in which structured and guided decision aids are particularly needed. While women are engaged and motivated during pregnancy[60], they are little engaged in health care outside of pregnancy. Because they usually lack previous exposure to healthcare and medical decision-making, women in ANC may feel poorly equipped to make decisions about HIV prevention options, making structured and guided decision processes particularly important[61–63]. For their part, ANC clinicians may feel poorly equipped to counsel women about potential PrEP use. In a recent formative study conducted by our team, ANC-based nurses expressed the need for additional training and communication materials to effectively counsel women about the decision to use PrEP. To overcome these communication barriers, SDM is specifically recommended for complex HIV prevention decisions[64]. Moreover, shared decision-making has been shown to be a feasible low-cost intervention, particularly when implemented using structured decision support aids[65].

To be able to implement the WHO guidelines to offer PrEP as a standard PMTCT service, we must ensure that limited resources for PrEP are targeted to those who are most likely to benefit. PrEP is a highly cost-effective HIV prevention strategy in low-resource settings[52], yet funds to provide PrEP to pregnant and breastfeeding women are limited. Understanding how best to deliver PrEP to this population will be increasingly critical to inform policy in these settings. Given the limited resources available for PrEP, it will be essential that its provision be targeted to those women most likely to benefit from its use, as demonstrated by adherent use.

3.4 Our formative work

We have completed extensive formative research with pregnant women, male partners, and clinicians from the study site to develop the intervention for this pilot study. Formative evidence (regarding women's values for PrEP decision making, the implications of these values for feelings regarding PrEP use, and preferences for partner involvement[66]) as well as key guidelines (Ottawa Decision Support Framework[67] and International Patient Decision Aid Standards[68]) informed the PrEP SDM intervention, known as My Choice for HIV Prevention (MYCHOICE). In the formative study [66], we assessed women's key values (motivations and concerns) for PrEP use. All participants wanted to protect themselves and their babies from HIV infection, 81% believed they were at risk for HIV, and 73% expressed concern about their partner's risk behaviours. Concerns included worries about potential harm to their babies (36%), themselves (32%), and being perceived as HIV-positive (24%). Qualitative insights highlighted motivations for PrEP use, such as protection for themselves and their unborn babies, while concerns encompassed potential harm to infants, side effects, stigma, and confusion about PrEP versus antiretroviral therapy. Participants often made autonomous choices and frequently disclosed them to partners. Limited family involvement was attributed to apprehensions about stigma and misunderstandings. Nevertheless, despite their varied concerns, participants overwhelmingly expressed enthusiasm for the HIV prevention benefits offered by PrEP. These formative findings along with SDM guidelines informed the content of the MYCHOICE intervention. The intervention has been refined through an iterative process of clinician and stakeholder feedback followed by feedback from 15 participants to refine the tool ahead of the proposed feasibility pilot study. During feedback interviews, women's understanding of the intervention content was good. Scores for comprehension of HIV risk factors and prevention averaged 8.5 (range 5-10), 9.7 (range 7-10) for PrEP information, and 9.2 for male and female condoms. The values clarification section had a mean comprehension score of 9.4. Furthermore, participants viewed the intervention content to be highly for decision-making (mean score of 10) and reported they would be likely to accept counselling using this tool during an ANC appointment (mean score of 9.7, range 7-10). Additionally, qualitative feedback revealed that all participants found the SDM tool acceptable and highly appropriate to support PrEP decision making. Additional Constructive feedback informed

improvements to enhance comprehension and utilization of the tool during pregnancy, and make the counselling content more efficient and acceptable (see 5.2 for full description of intervention content).

4. STUDY OBJECTIVES AND OUTCOMES

4.1 Objective and Aims

The overall objective of this pilot study is to:

> Evaluate the feasibility (score of ≥4 among ≥80% of participants), acceptability (score of ≥4 among ≥80% of participants), and appropriateness (score of ≥4 among ≥80% of participants) of a shared decision-making intervention (MyChoice) to support personally appropriate decision making about oral PrEP use during pregnancy among 100 women in antenatal care at Bwaila Hospital by the end of 2025.

We will achieve this objective through three Specific Aims which will be completed through the pilot study:

> Aim 1: Evaluate the acceptability, appropriateness, and feasibility of the oral PrEP shared decision-making intervention.
>
> Aim 2: Assess the plausibility of intervention effects on a proximal cognitive endpoint (decisional conflict) in preparation for a future efficacy trial.
>
> Aim 3: Describe exploratory behavioral outcomes to better understand participant experiences during and following the intervention (PrEP uptake, PrEP adherence, Intervention fidelity, qualitative assessment of participant and implementer experiences).

4.2 Study Outcomes

Corresponding to the primary, secondary, and exploratory study objectives (above), we will assess the following primary secondary, and exploratory outcomes in this feasibility pilot study.

4.2.1 Primary outcomes

Primary outcomes will include participant reports of the perceptions regarding the intervention (assessed through questionnaire self-report):

- *Intervention acceptability* (extent to which participants perceive the intervention to be agreeable, palatable, or satisfactory)
- *Intervention appropriateness* (perceived relevance and usefulness to support decision making)
- *Intervention feasibility* (extent to which the intervention is feasible or practical)

4.2.2 Secondary outcome

- Decisional Conflict assessed through validated scale (measure assessing perceptions of decision uncertainty, satisfaction, clarity of personal values, and support for decision-making)

4.2.3 Exploratory outcomes

- *PrEP uptake* (receipt of prescription as applicable)
- *Retention with functional PrEP adherence* at month 2 (through study records and pharmacologic assessment)
- *Intervention fidelity* (independent review of intervention sessions)
- *Qualitative perceptions of intervention and study procedure feasibility* (from the perspective of participants, male partners, and study staff)

5. METHODOLOGY

5.1 Study design

We propose a pilot feasibility study of a shared decision making (SDM) intervention for pregnant women considering PrEP. 100 women will be randomized to receive either the SDM intervention addressing daily oral PrEP and alternative HIV prevention methods (condoms), or standard of care counselling addressing the same prevention methods. We will evaluate the feasibility, acceptability, and appropriateness of the intervention and associated study procedures. Women expressing interest in oral PrEP will be referred to government PrEP services. See Table 1 for a summary of the study design and Section 6 below further details of the study procedures.

Table 1. Study design summary

n	100 women
Intervention	SDM counseling with choice of oral PrEP and/or condoms
Follow-up duration	3 months
Primary endpoints	Intervention acceptability Intervention appropriateness Intervention feasibility
Secondary endpoints	Decisional Conflict

5.2 Study intervention

The study intervention, My Choice for HIV Prevention (MyChoice), is a counselor-delivered shared decision-making approach for pregnant women considering PrEP. The intervention counseling will be delivered by trained study staff with a background in psychosocial counseling. The intervention consists of counseling facilitated by a SDM tool, following the steps in Table 2. The woman's partner may be present depending on her preference. It begins with a review of HIV risk in pregnancy/breastfeeding including discussion of population-specific risk factors which may apply to the participant. After understanding participant HIV risk and desire for HIV protection, the counselor presents HIV prevention options including oral PrEP, and internal and external condoms (discussing attributes and potential advantages and disadvantages of each method). This is followed by a values clarification exercise to identify which features of the competing options matter most to the participant (product attributes and personal and interpersonal implications of each method). The counselor reviews information about these valued features for each offered method. This information and checks to understand and address any unmet participant decision support needs serve as the basis for structured deliberation to collaboratively identify participant preferred method(s). The participant may defer or decline the decision, and may request a follow-up counseling visit to take more time to consider her preference or return with a partner or other supporter. If and when a decision is made, the counselor provides post-decision counseling including adherence counseling and disclosure counseling if desired.

Table 2. Shared Decision-Making Intervention Content

Counselling component	Content
Pre-counseling	• Overview of counseling content • Discuss participant's desire to include partner in counseling
MYCHOICE Counseling	
HIV info & risk assessment	• HIV risk in pregnancy and breastfeeding Evaluation of HIV risk criteria according to Malawian national guidelines
HIV prevention options	• Present oral PrEP, & condoms Features attributes and potential advantages and disadvantages of each
Values clarification	• Identify and discuss participant-valued features of available options (attributes, personal & interpersonal implications of each method)
Structured deliberation	• Assess and address unmet decision making needs • Collaboratively determine if participant is ready to make a decision, identify preferred method(s)
Post-decision counseling	• Persistence/adherence counseling • Disclosure coaching if desired
PrEP referral	• If oral PrEP selected, referral to SOC services
Post-counseling	• Adherence counseling for selected HIV prevention method • Disclosure support • Partner ART adherence counseling (if applicable)

Before the counseling visit, women will receive information about the content of the counseling and discuss whether or not they wish to have their partner or someone else (e.g., family member) participate in the counseling with them. The MyChoice counseling may be completed with or without the partner or another person they choose present depending on the participant's preference. After completion of the main counseling, participants will receive brief adherence counseling for the HIV prevention method they have selected and additional post-decision counseling as appropriate: for participants choosing PrEP, they will be asked if they hope to tell anyone about their decision. If yes, they will be offered coaching to support disclosure; for participant who have a partner living with HIV present, they will receive brief counseling on the continued importance of ART adherence and mutual support for ART and PrEP adherence (if applicable). While the counseling is intended to take place over one day, if the participant requests follow-up counseling (e.g., want more time to make a decision, wish to come back with a partner for a future session), reasonable accommodations will be made for the MyChoice counselor to meet with the participant a second time.

Women choosing oral PrEP during the intervention counseling session will be referred to government services to initiate PrEP.

5.3 Standard of care (control arm)

Participants randomized to the control arm will PrEP counseling as based on the current standard of care (SOC). The SOC counseling will be delivered by a trained study staff member. The SOC counselor PrEP counseling according to national guidelines.

Per current guidelines, the SOC counseling may include the following elements: An HIV risk assessment according to PrEP eligibility criteria; discussion of a combination prevention approach (PrEP and condoms) and risk reduction strategies. The women will receive comprehensive education on both the advantages and limitations of PrEP, including guidance on managing potential side effects. Subsequently, the counselor will assess the woman's eligibility, willingness, and readiness to start using PrEP.[69]

Women choosing oral PrEP during the SOC counseling session will be referred to government services to initiate PrEP.

5.4 Eligibility criteria

The criteria for pregnant women participants is as follows:
Inclusion criteria

- Age 18 or older
- Documented pregnancy by urine pregnancy test or physical exam
- Documented negative HIV status within the past three months
- Identified factor(s) for elevated risk for HIV acquisition per PrEP national eligibility guidelines
- Willingness to remain in the study site's catchment area over the course of study follow-up and to comply with visit schedule
- Ability and willingness to provide informed consent

Exclusion criteria

- Positive HIV test at time of screening
- No identified HIV risk factors per national PrEP guidelines
- Risk for intimate partner violence or social harms as a result of participation, in the judgement of the study personnel

We will also conduct interviews with male partners and study staff to assess exploratory qualitative outcomes. All study staff will be eligible to participate in an interview. Male partners will be eligible to participate if they meet the following criteria:

- Referred by a study participant as her romantic partner
- Age 18 or older
- Able and willing to provide informed consent

5.5 Place of study

The study will take place at a government health facility, Bwaila Hospital, a high-volume district facility run by the Malawi Ministry of Health. Approximately 1,500 babies are delivered each month at Bwaila and approximately 500 women present each month for immunization visits for their babies at 9 months after delivery. Bwaila Hospital has been providing PMTCT services since April 2002 and promoting male participation since 2007.

5.6 Target population

The primary population to be recruited for this study is HIV-negative pregnant women. For qualitative data collection only, we will also recruit male partners of these participants, and PrEP counselors and health care workers. We focus on pregnant women because of the elevated HIV risk faced by women in the perinatal period.

We will recruit 100 women to participate in the pilot study. A subset of these participants will participate in qualitative interviews. Up to 20 male partners and up to 15 study staff will be recruited to participate in qualitative in-depth interviews. See a summary of the sample size by participant group below in Table 3. Qualitative sampling will continue until saturation is reached.

Table 3. Sample size summary of by Study by type participant type

Type of Participant	**n**
Pregnant women	100 (up to 30 complete IDIs)
Male partners of PrEP users (*IDIs only*)	Up to 20
PrEP counsellors/Health care workers (*IDIs only*)	Up to 15

5.7 Recruitment and enrollment procedures

5.7.1 Recruitment procedures

Staff will provide interested participants with study information and referral to the study. Potential participants will be identified at any point in their pregnancy. All women attending the study site who meet the eligibility criteria (section 5.4) will be invited to participate in the study. All participants will undergo an informed consent procedure to ensure they are well-informed about the study, its objectives, and its requirements (section 6.2). We will obtain locator information from the participant, including phone numbers, addresses, and directions.

5.7.2 Enrolment procedures

HIV-negative pregnant women eligible for the study and interested in participating will be scheduled to return for an enrolment visit within 1-2 weeks. Prospective participants who wish to complete the enrolment visit on the same day as screening or who need more time to return to for the enrolment visit will be reasonably accommodated. Participants will complete informed consent and be formally enrolled. We will collect social, demographic, medical, and behavioural information from all participants. We will obtain from the locator information from the participant, including phone numbers, addresses, and directions. Participants will be randomly assigned to one of two study arms (intervention or comparison). Statistical software will be used to generate a list of random assignments with a 1:1 ratio. To facilitate balance of intervention and SOC arms, permuted block randomization will be used. The randomly generated arm assignments will be placed in opaque sealed envelopes and sequentially numbered with participant identification numbers. Participants will be blinded to their assignment, but study staff will not.

5.8 Study follow-up

Participants choosing oral PrEP during the counselling session in either intervention or comparison arm will receive an assisted referral to government PrEP services at the study site to initiate their selected PrEP method per national guidelines. No study drug will be administered. Initiation of oral PrEP (i.e., receipt of prescription) will be confirmed through clinic or pharmacy records, as well as information on reasons for non-initiation if applicable.

We plan study follow-up visits at month 1, month 2, and month 3. Study visits will be scheduled to align with ANC/pharmacy visits whenever possible to minimize the number of trips needed at the clinic.

Interviewer-administered questionnaires will be completed at the month 1 follow-up and the final follow-up visit (month 3). Questionnaires will assess study outcomes and associated social and behavioural measures to contextualize understanding of primary study outcomes. A subset of participants will complete in-depth qualitative interviews at month 1. Interviews will provide additional understanding of participant experiences with the intervention and experience using PrEP (if applicable).

At each follow-up visit, women who have chosen oral PrEP will undergo adherence assessment through self-report and pill counts. Furthermore, we will collect dried blood spots (DBS) at month 2 to assess adherence among all oral PrEP users.

Table 4. Study visit schedule

Procedure	Screening	Enrollment Visit	Follow-up visits		
			1 mo.	2 mo.	3 mo.
Study introduction	X				

Eligibility assessment	X				
Informed consent		X			
SDM counseling (intervention)		X			
Questionnaires		X	X		X
PrEP assisted referral		X			
Qualitative interviews			X		X
Adherence measurement (PrEP adopters only)					
Pill count/self-report			X	X	X
DBS				X	X

5.9 Assessment of study outcomes

5.9.1 Assessment of primary outcomes

Primary study outcomes will be assessed in participant questionnaires at the enrollment visit. The outcomes will be assessed at the final follow-up visit to as well to understand how perceptions of the intervention have changed over time.

Intervention Acceptability

We will evaluate intervention acceptability, defined as the extent to which participants perceive the intervention to be agreeable, palatable, or satisfactory. Acceptability will be assessed through participant self-report using a validated 4-item scale. This scale measures how agreeable and satisfactory women find the intervention (responses rated on a 5-point Likert scale ranging from "Completely Disagree" to "Completely Agree"). This assessment will be conducted at both month 0 and month 2 using the Acceptability of Intervention Measure (AIM) scale [70]

Intervention Appropriateness

We will also evaluate participant perceptions of Intervention appropriateness, defined as the perceived relevance and usefulness of the intervention to support decision making about HIV prevention methods. Appropriateness will be assessed through self-report using a validated 4-item scale to measure women's perceptions of its relevance and usefulness (responses rated on a 5-point Likert scale ranging from "Completely Disagree" to "Completely Agree")[70].

Intervention Feasibility

We will also evaluate participant perceptions of Intervention appropriateness, defined as the extent to which the intervention is deemed feasible or practical from their perspective. This Feasibility of Intervention Measure will be administered at both month 0 and month 2. The items on the scale will be measured using a 5-point Likert scale, and individual responses will be averaged to create a score for each measure. Higher scores will indicate a greater level of feasibility[70].

5.9.2 Assessment of secondary outcomes

Secondary outcomes will be assessed through study questionnaires and study records.

Decisional Conflict

The Decisional Conflict Scale (DCS) will be utilized to gauge women's' perceptions of decision uncertainty, satisfaction, clarity of personal values, and support for decision-making. This 16-item scale assesses these aspects on a 5-point scale, with scores totalling 100 points (mean rating multiplied by 25)[70 717273,74]A "low" DCS score will be identified using a cut-off of 25 out of 100, which has been linked to reduced decisional regret and enhanced choice retention.

DCS scores will be computed based on women's responses to statements, where higher scores indicate greater decisional conflict, while lower scores indicate diminished conflict and heightened certainty in decision-making. The scale will be administered at the enrolment visit following completion of study counselling.

5.9.3 Assessment of exploratory outcomes

PrEP uptake

We will assess PrEP uptake (i.e., receipt of oral PrEP prescription) among participants choosing PrEP during the intervention session. This will be assessed through clinic or pharmacy records.

Retention with functional adherence

Our clinical exploratory endpoint to be measured among participants taking up PrEP is retention in care with functional adherence to PrEP at two months. Retention will be assessed through study records. For participants taking up oral PrEP, functional adherence will be measured categorically according to Tenofovir diphosphate (TFVdp) quantified in dried blood spot (DBS) samples at the 2-month visit.

Intervention Fidelity

Intervention sessions will be digitally audio recorded with participant consent. A random subset of sessions will be reviewed by a study team member using a structured tool to assess intervention fidelity. Study staff will use recordings to evaluate the quality of counseling delivered (adherence to intended components and quality of counseling delivered) using a structured tool. Raters will score each section of the counseling and overall, with elements rated on a 5-point scale (0 "no effort" to 4 "exemplary effort").

Qualitative assessment of intervention & study procedure perceptions

Qualitative in-depth interviews (IDIs) with study participants will be conducted at the visits designated above to explore women's satisfaction with study counseling, session quality, and feeling about their decision. Follow-up interviews will evaluate women's experience using their selected HIV prevention method and the perceive impact of the study counseling on their current use of the selected product. Additional feedback on the intervention and study procedures will be gathered.

Additional IDIs will be conducted with male partners and study staff to gather insights into their experiences with the intervention, different procedures, perceptions of integrating Shared Decision-Making (SDM) into routine care, and suggestions for procedural improvements.

IDIs will be conducted by a locally recruited and trained research assistant fluent in Chichewa and English using semi-structured interview guides. Interviews will be digitally audio-recorded, transcribed, and translated to English for analysis.

Table 5. Schedule of Evaluations

	Screening	Enrollment	Month 1	Month 2	Month 3
Eligibility assessment					
Pregnancy status	X				
HIV status	X				
Additional eligibility criteria	X				
Participant-reported assessments					
Questionnaires					
Demographic information		X			
Intervention assessment		X		X	
Decisional conflict		X			
Partner information		X	X	X	X
Social harms		X	X	X	X

Qualitative interviews			X		X
Adherence assessments					
PrEP uptake assessment			X		
Oral PrEP					
Pill count			X	X	X
Self-report			X	X	X
DBS				X	

5.10 Retention

Once participants are enrolled in the trial, the study team will make efforts to retain them in follow-up to minimize bias associated with loss to follow-up. The study team will closely monitor retention rates and address any issues prospectively. Strategies to minimize attrition include:

- Thorough explanation of the study visit schedule and procedures during informed consent.
- Collection of detailed locator information at enrolment.
- Use of appropriate and timely visit reminder mechanisms (including phone calls and text messages, if participants specifically agree).
- Follow-up after missed visits, including home or alternative, off-site visits where possible.
- Mobilization of trained outreach workers to complete in-person contact with participants at their homes and/or other locations.

If participants elect to discontinue their involvement in the study, we will document their stated reason(s). These will be reported in any reports about the study cohort.

5.11 Safety Monitoring

At each study visit, study staff will evaluate participants for social harms and adverse events (AEs). A social harm will be defined as a non-medical untoward consequence of study participation, including: difficulties in personal relationships, stigma, or discrimination from family or community. An AE will be defined as any untoward medical occurrence in a study participant including any abnormal sign (e.g., abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the individual's participation in the research, whether or not considered related to participation in the research.

All adverse events and social harms will be documented, assessed for seriousness / severity, expectedness, and relatedness, and carefully monitored. The severity of events will be graded using the National Institute of Health's Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events. We will also record information on all serious adverse events (SAEs) occurring in participants whether or not they are related to study participation, including AEs that:

1. Result in hospital admission (unless hospitalization is preplanned, i.e. for delivery) or prolongation of existing hospitalization
2. Are immediately life-threatening, including drug reactions that necessitate discontinuation of study participation,
3. Cause significant, persistent, or permanent harm or disability, either physical or psychological,
4. Result in death to mother or infant, or
5. Are congenital anomalies or birth defects

5.12 Biological specimen collection and testing

To assess quantify drug concentrations to assess PrEP adherence among participants taking up oral PrEP, a participant blood specimen will be collected via venipuncture at the for applicable participants (those using oral PrEP). This specimen will be used to create a dried

blood spot (DBS) specimen at the local designated laboratory, prior to storage and shipment to the reference pharmacology laboratory for testing.

All samples will be obtained from study participants by trained study staff according to approved standard operating procedures. All samples will be processed according to the assay manufacturers' specifications. Specimens will be transported, processed, and temporarily housed at UNC Project Malawi (Lilongwe, Malawi) and shipped to UNC Chapel Hill for analysis. All laboratory testing will be performed by trained staff using standard operating procedures and according to specific assay manufacturers' specifications.

5.13 Quality control and quality assurance procedures
Standard Operating Procedures (SOPs) following manufacturer's protocols and detailing technical procedures involved (e.g. sample collection, processing and storage, assay procedures and how to interpret test results) will be developed and used by the study team. Tests will only be performed by certified laboratory personnel. Site coordinators will complete annual recertification. The certification process is an opportunity to ensure the highest specimen quality and standardize collection techniques.

5.14 Data Management and Storage
Data collected from each participant will include sociodemographic information, cognitive and behavioural self-reported information, qualitative transcripts, and relevant HIV and obstetrical history. Study data management (e.g., data transmission, query resolution, etc.) will follow site data management standard operating procedures. Study identification numbers will be used on all forms and communications related to the study. A separate confidential register will link study identification numbers and participant names. All data instruments and registers will be securely stored. Data will be entered into a custom-built database and, where possible, will be validated via double entry. Computers and tablets will be encrypted and password protected and their access restricted to authorized study personnel. Backups of the data will be made on a weekly basis. Data may be transmitted electronically to the study investigators through secure cloud-based servers. Study information will not be released without written permission of the participant, except when necessary for monitoring by the relevant ethical committees or their designees. Data will be disposed of after completion of the study per country guidelines. At that time, electronic records, including linkage codes and identifiers, will be deleted. Paper records will be shredded prior to disposal.

All interviews will be digitally audio recorded, unless participants ask not to be recorded. The recording will be transcribed and translated to English for analysis. All identifiers will be redacted from the interview transcripts prior to analysis. Participants will be assigned a unique study ID number that will be used to capture data. Data will be kept in an encrypted computer with a password known only to the study staff. Audio files will be erased from the recorders after data are transferred into the computer. All study materials will be kept in a locked, fireproof safe cabinet in locked offices at the study sites. No participants will be identified in any report or publication about this study.

5.15 Sample size
In this pilot study, the primary objective is to understand intervention acceptability, feasibility, and appropriateness. As such, the sample sizes are based on feasibility considerations. Despite this general approach, we provide estimated precision calculations for primary outcomes.

5.15.1 Precision calculations for continuous outcomes
For continuous measures, such as mean acceptability, appropriateness, and feasibility scores, or mean decisional conflict score, we used the t-distribution to estimate the level of precision we can expect to achieve given our various sample sizes and an expected 10% loss to follow-up over the course of the study. Table 6 shows the precision we can expect for estimates of 95% confidence intervals for mean acceptability, appropriateness, or feasibility at baseline

and at follow-up If we assume a common standard deviation of 0.9, we can expect a margin of error of ±0.256 points at baseline and ±0.270 points at follow-up on a 4-point scale. Likewise, Table 7 shows estimates of precision for 95% confidence intervals around mean decisional conflict score (DCS), except means will be estimated overall and by each arm. Here, if we assume a common standard deviation of 13.26, we can expect the margin of error for the 95% CI around the means to range from ±2.6 (pooled at baseline) to ±4.0 (by arm at follow-up) points on a 100-point scale.

For primary outcomes, mean AIM, IAM, and FIM, assumed SD=0.9 for all measures based on Lavoie et al. Mean AIM, IAM, and FIM calculated among intervention arm only.

Table 6. Expected precision for mean acceptability, appropriateness, or feasibility score among intervention arm

	Precision Estimate for 95% CI of Mean*
Baseline (n=50)	±0.256
Follow-up (n=45)†	±0.270

*Assume SD=0.9 for mean acceptability, appropriateness, and feasibility scores (4-point scale); precision estimates for 95% confidence intervals obtained using t-distribution.
†Assume 10% loss to follow-up by the end of study

For secondary outcome, mean DCS, assumed SD=13.26 for each arm based on Vlemmix et al. Mean DCS will be calculated and compared by arm.

Table 7. Expected precision for mean decisional conflict score, overall and by study arm

	Precision Estimate for 95% CI of Mean*
Overall	
Baseline (n=100)	±2.631
Follow-up (n=90)†	±2.777
By arm	
Baseline (n=50)	±3.768
Follow-up (n=45)†	±3.984

*Assume SD=13.26 for mean decisional conflict score (100-point scale); precision estimates for 95% confidence intervals obtained using t-distribution.
†Assume 10% loss to follow-up by the end of study

5.15.2 Precision calculations for binary outcomes

To estimate the expected precision of our binomial outcomes, we used the normal approximation confidence limit approach and calculated the exact binomial 95% CI as a sensitivity approach. For our calculations we looked at both baseline and follow-up measurements, assuming 10% loss to follow-up over the course of the study. Table 8 presents the precision achieved for the outcomes of acceptability, appropriateness, or feasibility scores of 4 or greater with an expected proportion between 60-90% achieving mean scores above that threshold. The proportion of women with mean acceptability, appropriateness, and feasibility score ≥4 will be calculated only among women that received the intervention. By our estimates, we can expect to achieve a precision level levels in Table 8 below if 80% have high mean scores. Similarly, Table 9 shows estimates of precision for women with low vs. high mean decisional conflict scores (DCS, ≤25 vs. >25) with expected proportion of women with low DCS ranging from 50-90%. In this analysis, women will be assessed overall and by arm (intervention vs SOC). For example, we expect a ±7.8% precision if 80% of women in both arms (n=100) have DCS ≤25 at baseline with a 95% CI of 69-89%; at the end of study, we expect ±8.3% precision if we observe that 80% have a DCS of ≤25 (95% CI: 69-89%).

Table 8. Expected precision for proportion of participants with high mean acceptability, appropriateness, or feasibility scores

	Observed Proportion with ≥4 Mean Score			
	0.6	**0.7**	**0.8**	**0.9**
Baseline (n=50)†				
Approximate precision	0.45-0.74	0.55-0.92	0.66-0.90	0.78-0.97

	Exact binomial 95% CI	±0.136	±0.127	±0.111	±0.083
Follow-up (n=45)*†					
	Approximate precision	0.44-0.74	0.53-0.82	0.65-0.90	0.76-0.96
	Exact binomial 95% CI	±0.143	±0.134	±0.117	±0.088
*Assume 10% loss to follow-up; precision calculated using a normal distribution. †Estimates among intervention arm only. Pooled estimates include participants receiving intervention from (n=100 enrolled, 1:1 randomization)					

Table 9. Expected precision for proportion of participants with low mean decisional conflict score (DCS)

	Observed Proportion with ≤25 Mean DCS				
	0.5	**0.6**	**0.7**	**0.8**	**0.9**
Baseline (n=100)†					
Approximate precision	0.39-0.62	0.48-0.71	0.58-0.79	0.69-0.88	0.82-0.96
Exact binomial 95% CI	±0.098	±0.096	±0.090	±0.078	±0.059
Follow-up (n=90)*†					
Approximate precision	0.38-0.63	0.47-0.72	0.58-0.81	0.69-0.89	0.80-0.96
Exact binomial 95% CI	±0.103	±0.101	±0.095	±0.083	±0.062
By arm at baseline (n=50)†					
Approximate precision	0.36-0.64	0.45-0.74	0.55-0.92	0.66-0.90	0.78-0.97
Exact binomial 95% CI	±0.139	±0.136	±0.127	±0.111	±0.083
By arm at follow-up (n=45)*†					
Approximate precision	0.34-0.64	0.44-0.74	0.53-0.82	0.65-0.90	0.76-0.96
Exact binomial 95% CI	±0.146	±0.143	±0.134	±0.117	±0.088
*Assume 10% loss to follow-up; precision calculated using a normal distribution. †Estimates overall (n=100, 1:1 randomization), or by arm (n=50 per arm).					

5.16 Data Analysis

Initial analysis will include descriptive analyses to characterize the sample on features such as demographics (e.g., age, marital status, income, education) and each outcome of interest. We will examine whether key sociodemographic features (age, income, education, marital status, gestational age, parity, perceived HIV risk, and experience of IPV) differ by study arm. Any characteristics differing significantly by arm will be included as covariates in sensitivity analyses comparing study arms; otherwise, primary analyses will be unadjusted

Given the pilot nature of the study, emphasis will be put on estimation and precision of measured effects, rather than null hypothesis testing. An alpha=0.05 will be used throughout to compute 95% confidence intervals (CIs), with no adjustment for multiplicity. In the case of small cell counts or analyses of continuous data with n<30, exact statistical methods (e.g., exact CI for a risk difference) will be used. Given potential for precision loss with exact CI methods and the pilot nature of these studies, we will use large-sample methods (e.g., Wald CIs) when the nominal CI coverage level is tenable.

Specific analyses for each study outcome are described in detail below. Detailed statistical analysis plans will be finalized prior to study outcome analysis.

5.16.1 Analysis of primary endpoints

Descriptive statistics will be calculated for primary outcomes of intervention acceptability, appropriateness, and feasibility among intervention arm participants. For each 4-item scale, item scores will be averaged to produce a composite score for each participant (range 1-5). Higher scores will indicate a greater level of acceptability, appropriateness, or feasibility, respectively. We will estimate the mean differences between arms for each primary outcome with a corresponding 95% confidence interval and p-value.

5.16.2 Analysis of secondary endpoints

Decisional Conflict
Decisional Conflict Scale (DCS) will be calculated according to published methods. A mean of the 16-item scale (rated on a 5-point scale) will be taken and multiplied by 25 to produce summary scores ranging from 0-100 points [71,74] Descriptively, summary scores will be presented descriptively (mean and SD across participants in each arm by study). We will compare DCS scores across in the SDM intervention condition to the SOC counselling control condition in an exploratory manner. We hypothesize that the intervention will be superior to the control, with intervention participants reporting at least an 8-point lower decisional conflict score on average than control participants. An intent-to-treat approach will be used to evaluate the effect of treatment on decisional conflict. We will first compare group means of decisional conflict scores by study arm and then examine the intervention's effect on this outcome using a two-sample Welch's t-test. If demographic variables related to decisional conflict differ substantively by study arm, we will instead use augmented inverse probability weights (AIPW) to perform doubly robust estimation of the average intervention effect to compare intervention vs. control (e.g., using the CAUSALTRT procedure in SAS software). Missing (unevaluable) data are anticipated to be uncommon (≤10%). Multiple imputation methods will be applied to address missing data if appropriate.

Exploratory analyses will also be conducted with a dichotomous coding of DCS score according to published thresholds. A "low" DCS score will be identified using a cut-off of 25 out of 100, which has been linked to reduced decisional regret and enhanced choice retention. DCS scores will be computed based on women's responses to statements, where higher scores indicate greater decisional conflict, while lower scores indicate diminished conflict and heightened certainty in decision-making.

5.16.3 Quantitative analysis of exploratory endpoints
We will examine the intervention effect on retention and PrEP adherence in an exploratory fashion. In order to evaluate effectiveness, analyses will be conducted using an intention-to-treat approach, with women analysed according to the arm they were randomly assigned.

Given the pilot nature of these studies, emphasis will be put on estimation and precision of measured effects, rather than null hypothesis testing. An alpha=0.05 will be used throughout to compute 95% confidence intervals (CIs), with no adjustment for multiplicity. In the case of small cell counts (<5), 95% CI coverage properties of large-sample methods will be evaluated using exact statistical methods (e.g., exact CI for a risk difference) in sensitivity analyses. Given potential for precision loss with exact CI methods and the pilot nature of these studies, we will use large-sample methods (e.g., Wald CIs) when the nominal CI coverage level is tenable.

Missing (unevaluable) data are anticipated to be uncommon (≤10%). The primary analyses are based on a composite endpoint of being retained in care with functional PrEP use, and thus complete case analyses will be conducted. Women who are not retained in care will be counted in the denominator for the primary analysis. Sensitivity analyses will exclude women who were not retained in care.

PrEP uptake
Uptake of oral PrEP will be described as the proportion of participants with record of receipt of an oral PrEP prescription.

Retention + Functional Adherence
Our clinical exploratory endpoint to be measured among participants taking up PrEP is retention in care with functional adherence to PrEP at two months. We will assess adherence to oral PrEP among participants taking it up through Tenofovir diphosphate (TFVdp) concentrations in participant dried blood spot (DBS) samples. TFVdp will be measured using

established liquid-chromatography tandem mass spectrometry methods[75] Using published thresholds[76], TFVdp concentrations will be categorized as in Table 10 below. Emtricitabine triphosphate (FTCtp) concentrations will also be quantified and may be interpreted in an exploratory manner (e.g., in the event that TFVdp is below the level of quantification). Participants will be considered for this composite outcome if they have any record of oral PrEP initiation following study assisted referral. Participants retained at two months meeting the relevant definition of functional adherence (below) will be categorized as retained with functional adherence.

Table 10. Adherence interpretation of TFVdp concentration levels

	DBS TFVdp fmol/punch	
Interpretation	*Pregnant participants*	*Postpartum participants**
~7 doses/week	≥650	≥1050
2-6 doses/week	200-649	300-1049
<2 doses/week	<200	<300

**participants will be enrolled during pregnancy but may deliver prior to the month 2 visit when this outcome is assessed*

Treatment effect on PrEP adherence among participants adopting PrEP will be explored as sample size and rates of adoption permit. We will compare the proportion of the sample retained in care with functional PrEP adherence at 2-month follow-up between the two randomization arms using a linear-binomial model. Women who are not retained for 2-month follow-up will be counted as failures and will contribute to the analysis denominator. From the linear-binomial model, the site-adjusted risk difference of being retained and in care with functional PrEP for the intervention arm versus the control arm will be calculated, along with a corresponding 95% CI.

In addition to the primary analysis, assessing functional PrEP adherence as binary outcome, secondary analyses will compare the adherence categories between the study arms using a Wilcoxon rank-sum test. This analysis will be restricted to women with an evaluable adherence score.

Intervention Fidelity

To assess intervention fidelity, we will quantify intervention fidelity in a series of items rated by a study team member on a 5-point scale. A random subset (~20%) of these sessions will be audited by a study team member using a fidelity assessment tool that includes objective and subjective measures. These assessments will help to characterize the quality of implementation over the course of study participation. Fidelity to the intervention will be assessed through study staff audits of counseling sessions on including quality of counseling delivered (adherence to intended components and quality of counseling delivered), for of each section of the counseling and overall, with elements rated on a 5-point scale (0 “no effort” to 4 “exemplary effort”). Ratings for each section of the scoring instrument tool will be averaged and summarized descriptively (including mean scores and standard deviations) to report fidelity to the intervention.

5.16.4 Qualitative analysis of IDIs (exploratory outcomes)

Thematic analysis will be used to analyse the qualitative data. The transcripts will be transcribed and translated into English. Analysis will consist of: 1) Reading for Content: We will read the data until content becomes intimately familiar. As data are reviewed emergent themes will be noted. 2) Coding: A list of codes will be created and documented in a codebook based on identified themes in addition to structural codes corresponding to initial interview questions. Two coders will independently code each transcript. To ensure inter-coder reliability, 10% of data will be double-coded; 3) Data reduction: We will review the data related to each code to identify principal sub-themes that reflect finer distinctions in the data. This entails taking an inventory of what is related to a given code, observing the variation or

richness of each theme, and noting differences between individuals or among subgroups; 4) Data display and comparison: Matrices that categorize and display data will be used to help facilitate comparisons across the sampling groups.

6. ETHICAL CONSIDERATIONS

6.1 Ethical approval

All study participants will be fully informed of the study procedures described above. Prior to study activation, for each participating site, ethical approval will be sought from the relevant institutional review boards / research ethics committees, national authorities, and other regulatory authorities.

6.2 Informed consent

All participants will be consented prior to participation and during the consent process they will be reminded that their participation is voluntary. Discussions with prospective participants and informed consent procedures will be conducted in private to protect patient confidentiality. We will obtain written informed consent from all participants. The study procedures, risks, and benefits will be discussed and we will answer all questions prior to obtaining consent. The consent forms will be translated into relevant local languages and back-translated into English to assure accurate translation. For illiterate participants, a literate impartial witness will be present during the entire consent process to ensure that all of the relevant information has been provided and the participant voluntarily gives consent. Eligible women who do not wish to participate in this study will continue to receive ANC care according to local clinical standards. We will obtain signed permission from the pregnant woman to collect locator information, including phone numbers, addresses, and directions. Permission for collection of locator information and contract tracing will be per usual practice at the clinic.

6.3 Data storage

The confidentiality of all study records will be safeguarded to the extent legally possible. To maintain participant confidentiality, all laboratory specimens, reports, study data and administrative forms will be identified by a coded number only. All databases will be secured with password-protected access systems, and computer entries will be identified by coded number only. Forms, lists, logbooks, appointment books, and any other listings or data forms that link participant ID numbers to other identifying information will be stored in a separate, locked fireproof safe cabinet in a locked local office. For the data collected through audio recordings, all audio files will be deleted from the recorders after data are transferred into a computer. Study-related computers, tablets, audio tapes, field notes, and other study materials will be kept in a locked cabinet in a locked local office. All data analysis will be performed using datasets which have only study ID numbers as unique identifiers.

6.4 Confidentiality

Measures will be taken to ensure safety of data and confidentiality of all our study participants. All participants will be assigned a unique study ID number. The interview guides will not capture names of the participants but only their ID number. No study participant will be identified in any report or publication about this study. However, for quality control and safety purposes, data that we collect may be reviewed by the sponsor of this study (i.e. United States National Institute of Health), the ethical and regulatory committees in Malawi and at the University of North Carolina at Chapel Hill. Clinical information with individual identifiers will not be released without the written permission of the participant. We expect these procedures to adequately protect participant confidentiality.

6.5 Potential risks to participants

No study drug will be administered thus all risks to participants relate to risks relevant to counseling and study assessment procedures. The risk to participants in this study is minimal. The main risk is possible discomfort to participants in answering question about themselves

and their decisions or actions related to PrEP. All participants will be asked to provide written informed consent before participation in the study. During the consent process, we will inform all participants that they may stop at any time and may ask the interviewer to skip any questions they do not feel comfortable answering.

Participation in clinical research includes the risks of loss of confidentiality and discomfort with the personal nature of questions, particularly when discussing HIV infection or sexual behaviors. At each step in the study, we will protect participant privacy and confidentiality to reduce these risks (e.g., consenting participants in a private setting, not including names on case report forms, etc.). Although investigators will make every effort to protect participant privacy and confidentiality, it is possible that participant involvement in the study could become known to others, and that social harms may result (i.e., as participants could become known as HIV-positive). Participants will be given a phone number they can call at any time if they need assistance or feel they are at risk of harm.

Venipuncture is sometimes associated with discomfort. Venipuncture may lead to discomfort, dizziness, bruising, swelling, and rarely, an infection at the venipuncture site.

6.6 Protection Against Risks

Risks to the participant will be minimized by thorough training and supervision of all staff. Participants' privacy will be assured by conducting interviews, surveys, and other forms of data collection in a private location, for example, in a private room at the health facility. The confidentiality of all study records will be safeguarded to the extent legally possible. All study data, reports, and administrative forms will be identified by a coded number only to maintain participant confidentiality. All databases will be secured with password-protected access systems, and computer entries will be identified by coded number only. Forms, lists, logbooks, appointment books, audio-recordings, and any other data forms that link participant ID numbers to other identifying information will be stored in a separate, locked cabinet. All data analysis will be done on transcripts which have only the study number as a unique identifier. Clinical information with individual identifiers will not be released without the written permission of the participant.

Participant name and contact information are the only individually identifiable private information that will be collected specifically for our project. Data will be entered into a protected electronic database and all analytic datasets will have only the study number as a unique identifier. Forms, logbooks, appointment books, and any other data forms that link participant ID numbers to other identifying information will be stored in a separate, locked file cabinet. Clinical information with individual identifiers will not be released without the written permission of the participant. Data collection forms, electronic databases, and printed data will only be supplied to appropriate study staff on an as-needed basis. Any publication about this research study will omit names and any other identifying information.

Paper copies of consent forms, observation forms, exit interviews, and surveys will be kept in a locked room at the UNC Project office in Lilongwe. Only staff and researchers directly involved in processing and analyzing data will have access and will be allowed to transfer the data to electronic databases. Voice recordings and electronic databases will be stored in computers with password protection. Any computers used will also be encrypted. Each participant will be assigned a unique identification number, which will be used in databases and on transcriptions instead of any identifying information. Paper copies and original voice recordings will be stored for 3 years after the completion of the publications from this research.

We expect these procedures to adequately protect participant confidentiality. However, it is possible that a participant's study participation could become known to people in the community and may result in stigma or discrimination. Should that occur, study staff will work

with the participant and their family as appropriate to resolve the situation in whatever manner is preferred. All study procedures carry minimal risks.

6.7 Potential Benefits of Proposed Research to Human Subjects and Others

Participants will not benefit personally from participating in this research. The results of this study may benefit society as the results can be used to develop a decision-making aid to help pregnant women, their partners, and clinicians make decisions about PrEP use. An improved decision-making process may lead to more appropriate and adherence PrEP use, which may ultimately serve to prevent HIV infection during pregnancy and mother-to-child transmission of HIV.

6.8 Inclusion of children, sub-populations, and vulnerable populations

This study focuses on the outcomes of pregnant and breastfeeding women; as such, they must be included in our study population. Prisoners will be excluded as they receive care at separate facilities.

6.9 Reimbursement/compensation

There is no cost to participate in the study. Participants will be provided with transport reimbursement for each study visit, according to local research standards.

6.10 Dissemination of findings

Study findings will be disseminated through appropriate local channels, including academic and public health research symposia. We will report findings to relevant local authorities in Malawi. One or more publications will also be submitted to a peer-reviewed journal. Our study team plans to publish the study results whether positive or negative. The study participants' privacy and confidentiality will be strictly maintained in all results dissemination or publication activities.

7. WORK PLAN

In the table below, we show our proposed timeline for the study activities (2 year study period)

		Y1				Y2			
		Q1	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**
Study startup	Study site & data systems setup	**X**							
	Protocol training	**X**							
	Instrument piloting	**X**							
Pilot study	Enrollment & intervention		**X**	**X**					
	Follow up			**X**	**X**				
	Fidelity assessment			**X**	**X**				
Analysis & Reporting					**X**	**X**	**X**		
Data cleaning					**X**	**X**			
Quantitative analysis						**X**	**X**		
Qualitative analysis							**X**	**X**	
Results dissemination (local meetings, conferences)								**X**	**X**
Publications								**X**	**X**

REFERENCES

1. Drake AL, Wagner A, Richardson B, John-Stewart G. Incident HIV during pregnancy and postpartum and risk of mother-to-child HIV transmission: a systematic review and meta-analysis. *PLoS Med*. 2014;11(2):e1001608. doi:10.1371/journal.pmed.1001608

2. Johnson NB, Hayes LD, Brown K, Hoo EC, Ethier KA, Centers for Disease Control and Prevention (CDC). CDC National Health Report: leading causes of morbidity and mortality and associated behavioral risk and protective factors--United States, 2005-2013. *MMWR Suppl*. 2014;63(4):3-27.

3. Dinh T-H, Delaney KP, Goga A, et al. Impact of Maternal HIV Seroconversion during Pregnancy on Early Mother to Child Transmission of HIV (MTCT) Measured at 4-8 Weeks Postpartum in South Africa 2011-2012: A National Population-Based Evaluation. *PLoS ONE*. 2015;10(5):e0125525. doi:10.1371/journal.pone.0125525

4. Lu L, Motswere-Chirwa C, Legwaila K. Abstract 15: HIV incidence in women during the first postpartum year: implications for PMTCT programs Francistown, Botswana, 2010. *3rd International Workshop on HIV Pediatrics Rome, Italy: Reviews in Antiviral Therapy and Infectious Diseases 2011_8*. 17.

5. Baeten JM, Donnell D, Ndase P, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med*. 2012;367(5):399-410. doi:10.1056/NEJMoa1108524

6. Thigpen MC, Kebaabetswe PM, Paxton LA, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. *N Engl J Med*. 2012;367(5):423-434. doi:10.1056/NEJMoa1110711

7. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med*. 2010;363(27):2587-2599. doi:10.1056/NEJMoa1011205

8. World Health Organization. Preventing HIV during pregnancy and breastfeeding in the context of PrEP. Accessed September 13, 2023. https://www.who.int/publications/i/item/WHO-HIV-2017.09

9. Delany-Moretlwe S, Hughes JP, Bock P, et al. Cabotegravir for the prevention of HIV-1 in women: results from HPTN 084, a phase 3, randomised clinical trial. *Lancet*. 2022;399(10337):1779-1789. doi:10.1016/S0140-6736(22)00538-4

10. Cottrell ML, Yang KH, Prince HMA, et al. A translational pharmacology approach to predicting outcomes of preexposure prophylaxis against HIV in men and women using tenofovir disoproxil fumarate with or without emtricitabine. *J Infect Dis*. 2016;214(1):55-64. doi:10.1093/infdis/jiw077

11. Marrazzo JM, Ramjee G, Richardson BA, et al. Tenofovir-Based Preexposure Prophylaxis for HIV Infection Among African Women. *Obstet Gynecol Surv*. 2015;70(7):444-446. doi:10.1097/01.ogx.0000466878.37011.6f

12. Van Damme L, Corneli A, Ahmed K, et al. Preexposure prophylaxis for HIV infection among African women. *N Engl J Med*. 2012;367(5):411-422. doi:10.1056/NEJMoa1202614

13. Thomson KA, Baeten JM, Mugo NR, Bekker L-G, Celum CL, Heffron R. Tenofovir-based oral preexposure prophylaxis prevents HIV infection among women. *Curr Opin HIV AIDS*. 2016;11(1):18-26. doi:10.1097/COH.0000000000000207

14. Amico KR, Mansoor LE, Corneli A, Torjesen K, van der Straten A. Adherence support approaches in biomedical HIV prevention trials: experiences, insights and future directions from four multisite prevention trials. *AIDS Behav*. 2013;17(6):2143-2155. doi:10.1007/s10461-013-0429-9

15. Corneli A, Perry B, McKenna K, et al. Participants' Explanations for Nonadherence in the FEM-PrEP Clinical Trial. *J Acquir Immune Defic Syndr*. 2016;71(4):452-461. doi:10.1097/QAI.0000000000000880

16. van der Straten A, Stadler J, Montgomery E, et al. Women's experiences with oral and vaginal pre-exposure prophylaxis: the VOICE-C qualitative study in Johannesburg, South Africa. *PLoS ONE*. 2014;9(2):e89118. doi:10.1371/journal.pone.0089118

17. Madrasi K, Chaturvedula A, Haberer JE, et al. Markov mixed effects modeling using electronic adherence monitoring records identifies influential covariates to HIV preexposure prophylaxis. *J Clin Pharmacol*. 2017;57(5):606-615. doi:10.1002/jcph.843

18. Amico KR, Wallace M, Bekker L-G, et al. Experiences with HPTN 067/ADAPT Study-Provided Open-Label PrEP Among Women in Cape Town: Facilitators and Barriers Within a Mutuality Framework. *AIDS Behav*. 2017;21(5):1361-1375. doi:10.1007/s10461-016-1458-y

19. Ware NC, Wyatt MA, Haberer JE, et al. What's love got to do with it? Explaining adherence to oral antiretroviral pre-exposure prophylaxis for HIV-serodiscordant couples. *J Acquir Immune Defic Syndr*. 2012;59(5):463-468. doi:10.1097/QAI.0b013e31824a060b

20. Roberts ST, Haberer J, Celum C, et al. Intimate Partner Violence and Adherence to HIV Pre-exposure Prophylaxis (PrEP) in African Women in HIV Serodiscordant Relationships: A Prospective Cohort Study. *J Acquir Immune Defic Syndr*. 2016;73(3):313-322. doi:10.1097/QAI.0000000000001093

21. Sandman L, Granger BB, Ekman I, Munthe C. Adherence, shared decision-making and patient autonomy. *Med Health Care Philos*. 2012;15(2):115-127. doi:10.1007/s11019-011-9336-x

22. Elwyn G, Frosch D, Rollnick S. Dual equipoise shared decision making: definitions for decision and behaviour support interventions. *Implement Sci*. 2009;4:75. doi:10.1186/1748-5908-4-75

23. Shay LA, Lafata JE. Where is the evidence? A systematic review of shared decision making and patient outcomes. *Med Decis Making*. 2015;35(1):114-131. doi:10.1177/0272989X14551638

24. Street RL, Makoul G, Arora NK, Epstein RM. How does communication heal? Pathways linking clinician-patient communication to health outcomes. *Patient Educ Couns*. 2009;74(3):295-301. doi:10.1016/j.pec.2008.11.015

25. Beach MC, Duggan PS, Moore RD. Is patients' preferred involvement in health decisions related to outcomes for patients with HIV? *J Gen Intern Med*. 2007;22(8):1119-1124. doi:10.1007/s11606-007-0241-1

26. García PR, Côté JK. Factors Affecting Adherence to Antiretroviral Therapy in People Living with HIV/AIDS. *Journal of the Association of Nurses in AIDS Care*. 2003;14(4):37-45. doi:10.1177/1055329003252424

27. Enriquez M, McKinsey DS. Strategies to improve HIV treatment adherence in developed countries: clinical management at the individual level. *HIV AIDS (Auckl)*. 2011;3:45-51. doi:10.2147/HIV.S8993

28. Guadagnoli E, Ward P. Patient participation in decision-making. *Soc Sci Med*. 1998;47(3):329-339. doi:10.1016/s0277-9536(98)00059-8

29. Morrison C, Fichorova RN, Mauck C, et al. Cervical inflammation and immunity associated with hormonal contraception, pregnancy, and HIV-1 seroconversion. *J Acquir Immune Defic Syndr*. 2014;66(2):109-117. doi:10.1097/QAI.0000000000000103

30. MacIntyre DA, Chandiramani M, Lee YS, et al. The vaginal microbiome during pregnancy and the postpartum period in a European population. *Sci Rep*. 2015;5:8988. doi:10.1038/srep08988

31. Businge CB, Longo-Mbenza B, Mathews V. Risk factors for incident HIV infection among antenatal mothers in rural Eastern Cape, South Africa. *Glob Health Action*. 2016;9:29060. doi:10.3402/gha.v9.29060

32. Peltzer K, Mlambo G. Sexual HIV risk behaviour and associated factors among pregnant women in Mpumalanga, South Africa. *BMC Pregnancy Childbirth*. 2013;13:57. doi:10.1186/1471-2393-13-57

33. Pintye J, Drake AL, Kinuthia J, et al. A risk assessment tool for identifying pregnant and postpartum women who may benefit from preexposure prophylaxis. *Clin Infect Dis*. 2017;64(6):751-758. doi:10.1093/cid/ciw850

34. Liang X, Garland S, Hartley S, et al. Attitudes and acceptance of potential changes in cervical screening: Views of obstetricians and gynaecologists. *BJOG-AN INTERNATIONAL JOURNAL OF OBSTETRICS AND GYNAECOLOGY*. 2015;122:80.

35. Humphrey JH, Marinda E, Mutasa K, et al. Mother to child transmission of HIV among Zimbabwean women who seroconverted postnatally: prospective cohort study. *BMJ*. 2010;341:c6580. doi:10.1136/bmj.c6580

36. Dunn DT, Newell ML, Ades AE, Peckham CS. Risk of human immunodeficiency virus type 1 transmission through breastfeeding. *Lancet*. 1992;340(8819):585-588. doi:10.1016/0140-6736(92)92115-v

37. Van de Perre P, Simonon A, Msellati P, et al. Postnatal transmission of human immunodeficiency virus type 1 from mother to infant. A prospective cohort study in Kigali, Rwanda. *N Engl J Med*. 1991;325(9):593-598. doi:10.1056/NEJM199108293250901

38. HIV/AIDS Joint United Nations Programme on. Improving UNAIDS'paediatric and adolescent estimates. *Geneva, Swizerland: UNAIDS*. 2019.

39. Mofenson LM, Baggaley RC, Mameletzis I. Tenofovir disoproxil fumarate safety for women and their infants during pregnancy and breastfeeding. *AIDS*. 2017;31(2):213-232. doi:10.1097/QAD.0000000000001313

40. Pintye J, Singa B, Wanyonyi K, et al. Preexposure Prophylaxis for Human Immunodeficiency Virus (HIV) Prevention Among HIV-uninfected Pregnant Women: Estimated Coverage Using Risk-based Versus Regional Prevalence Approaches. *Sex Transm Dis*. 2018;45(12):e98-e100. doi:10.1097/OLQ.0000000000000898

41. Fonner VA, Dalglish SL, Kennedy CE, et al. Effectiveness and safety of oral HIV preexposure prophylaxis for all populations. *AIDS*. 2016;30(12):1973-1983. doi:10.1097/QAD.0000000000001145

42. Murnane PM, Celum C, Mugo N, et al. Efficacy of preexposure prophylaxis for HIV-1 prevention among high-risk heterosexuals: subgroup analyses from a randomized trial. *AIDS*. 2013;27(13):2155-2160. doi:10.1097/QAD.0b013e3283629037

43. Malawi. Malawi Demographic and Health Survey, 2010. *Malawi Demographic and Health Survey, 2010*. 2011.

44. Mellins CA, Chu C, Malee K, et al. Adherence to antiretroviral treatment among pregnant and postpartum HIV-infected women. *AIDS Care*. 2008;20(8):958-968. doi:10.1080/09540120701767208

45. Vaz MJR, Barros SMO, Palacios R, et al. HIV-infected pregnant women have greater adherence with antiretroviral drugs than non-pregnant women. *Int J STD AIDS*. 2007;18(1):28-32. doi:10.1258/095646207779949808

46. Sullivan KM, Ford ES, Azrak MF, Mokdad AH. Multivitamin Use in Pregnant and Nonpregnant Women: Results from the Behavioral Risk Factor Surveillance System. *Public Health Rep*. 2009;124(3):384-390. doi:10.1177/003335490912400307

47. Ambia J, Mandala J. A systematic review of interventions to improve prevention of mother-to-child HIV transmission service delivery and promote retention. *J Int AIDS Soc*. 2016;19(1):20309. doi:10.7448/IAS.19.1.20309

48. *Guidelines on Long-Acting Injectable Cabotegravir for HIV Prevention*. World Health Organization; 2022.

49. Mugo NR, Hong T, Celum C, et al. Pregnancy incidence and outcomes among women receiving preexposure prophylaxis for HIV prevention: a randomized clinical trial. *JAMA*. 2014;312(4):362-371. doi:10.1001/jama.2014.8735

50. Heffron R, Mugo N, Hong T, et al. Pregnancy outcomes and infant growth among babies with in-utero exposure to tenofovir-based preexposure prophylaxis for HIV prevention. *AIDS*. 2018;32(12):1707-1713. doi:10.1097/QAD.0000000000001867

51. Mugwanya KK, Hendrix CW, Mugo NR, et al. Pre-exposure Prophylaxis Use by Breastfeeding HIV-Uninfected Women: A Prospective Short-Term Study of Antiretroviral Excretion in Breast Milk and Infant Absorption. *PLoS Med*. 2016;13(9):e1002132. doi:10.1371/journal.pmed.1002132

52. Price JT, Wheeler SB, Stranix-Chibanda L, et al. Cost-Effectiveness of Pre-exposure HIV Prophylaxis During Pregnancy and Breastfeeding in Sub-Saharan Africa. *J Acquir Immune Defic Syndr*. 2016;72 Suppl 2(Suppl 2):S145-53. doi:10.1097/QAI.0000000000001063

53. Decision making: A psychological analysis of conflict, choice, and commitment. *Eval Program Plann*. 1978;1(2):167. doi:10.1016/0149-7189(78)90042-3

54. Loh A, Simon D, Wills CE, Kriston L, Niebling W, Härter M. The effects of a shared decision-making intervention in primary care of depression: a cluster-randomized controlled trial. *Patient Educ Couns*. 2007;67(3):324-332. doi:10.1016/j.pec.2007.03.023

55. Schoenthaler AM, Schwartz BS, Wood C, Stewart WF. Patient and physician factors associated with adherence to diabetes medications. *Diabetes Educ*. 2012;38(3):397-408. doi:10.1177/0145721712440333

56. Kumar R, Korthuis PT, Saha S, et al. Decision-making role preferences among patients with HIV: associations with patient and provider characteristics and communication behaviors. *J Gen Intern Med*. 2010;25(6):517-523. doi:10.1007/s11606-010-1275-3

57. Kremer H, Ironson G, Schneiderman N, Hautzinger M. "It's my body'': does patient involvement in decision making reduce decisional conflict? *Med Decis Making*. 2007;27(5):522-532. doi:10.1177/0272989X07306782

58. Deber RB, Kraetschmer N, Urowitz S, Sharpe N. Do people want to be autonomous patients? Preferred roles in treatment decision-making in several patient populations. *Health Expect*. 2007;10(3):248-258. doi:10.1111/j.1369-7625.2007.00441.x

59. Ryan RM, Deci EL. Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being. *Am Psychol*. 2000;55(1):68-78. doi:10.1037/0003-066X.55.1.68

60. Zambia. Zambia: Demographic and Health Survey, 2013-14. *Zambia: Demographic and Health Survey, 2013-14*. 2015;1.

61. Watson-Jones D, Balira R, Ross DA, Weiss HA, Mabey D. Missed opportunities: poor linkage into ongoing care for HIV-positive pregnant women in Mwanza, Tanzania. *PLoS ONE*. 2012;7(7):e40091. doi:10.1371/journal.pone.0040091

62. Kalichman SC, Cherry C, Kalichman MO, et al. Randomized clinical trial of HIV treatment adherence counseling interventions for people living with HIV and limited health literacy. *J Acquir Immune Defic Syndr*. 2013;63(1):42-50. doi:10.1097/QAI.0b013e318286ce49

63. Williams S, Renju J, Ghilardi L, Wringe A. Scaling a waterfall: a meta-ethnography of adolescent progression through the stages of HIV care in sub-Saharan Africa. *J Int AIDS Soc*. 2017;20(1):21922. doi:10.7448/IAS.20.1.21922

64. Seidman DL, Weber S, Cohan D. Offering pre-exposure prophylaxis for HIV prevention to pregnant and postpartum women: a clinical approach. *J Int AIDS Soc*. 2017;20(Suppl 1):21295. doi:10.7448/IAS.20.2.21295

65. Stacey D, Légaré F, Lewis K, et al. Decision aids for people facing health treatment or screening decisions. *Cochrane Database Syst Rev*. 2017;4(4):CD001431. doi:10.1002/14651858.CD001431.pub5

66. Hill LM, Golin CE, Saidi F, et al. Understanding PrEP decision making among pregnant women in Lilongwe, Malawi: A mixed-methods study. *J Int AIDS Soc*. 2022;25(9):e26007. doi:10.1002/jia2.26007

67. O'Connor AM, Drake ER, Fiset V, Graham ID, Laupacis A, Tugwell P. The Ottawa patient decision aids. *Eff Clin Pract*. 1999;2(4):163-170.

68. Elwyn G, O'Connor A, Stacey D, et al. Developing a quality criteria framework for patient decision aids: online international Delphi consensus process. *BMJ*. 2006;333(7565):417. doi:10.1136/bmj.38926.629329.AE

69. Malawi National Oral Pre-Exposure Prophylaxis (PrEP) Guidelines - Malawi National PrEP Guidelines - Document Management System. Accessed September 13, 2023. https://dms.hiv.health.gov.mw/dataset/malawi-national-oral-pre-exposure-prophylaxis-prep-guidelines/resource/f5be8a13-c3a9-46e8-afb6-fef0a0912c2f

70. Weiner BJ, Lewis CC, Stanick C, et al. Psychometric assessment of three newly developed implementation outcome measures. *Implement Sci*. 2017;12(1):108. doi:10.1186/s13012-017-0635-3

71. O'Connor AM. Validation of a decisional conflict scale. *Med Decis Making*. 1995;15(1):25-30. doi:10.1177/0272989X9501500105

72. Garvelink MM, Boland L, Klein K, et al. Decisional Conflict Scale Use over 20 Years: The Anniversary Review. *Med Decis Making*. 2019;39(4):301-314. doi:10.1177/0272989X19851345

73. Knops AM, Goossens A, Ubbink DT, Legemate DA, Stalpers LJ, Bossuyt PM. Interpreting patient decisional conflict scores: behavior and emotions in decisions about treatment. *Med Decis Making*. 2013;33(1):78-84. doi:10.1177/0272989X12453500

74. Sun Q. *Predicting Downstream Effects of High Decisional Conflict: Meta-Analyses of the Decisional Conflict Scale*. 2005.

75. Schauer AP, Sykes C, Cottrell ML, Prince H, Kashuba ADM. Validation of an LC-MS/MS assay to simultaneously monitor the intracellular active metabolites of tenofovir, emtricitabine, and lamivudine in dried blood spots. *J Pharm Biomed Anal*. 2018;149:40-45. doi:10.1016/j.jpba.2017.10.030

76. Stranix-Chibanda L, Anderson PL, Kacanek D, et al. Tenofovir Diphosphate Concentrations in Dried Blood Spots From Pregnant and Postpartum Adolescent and Young Women Receiving Daily Observed Pre-exposure Prophylaxis in Sub-Saharan Africa. *Clin Infect Dis*. 2021;73(7):e1893-e1900. doi:10.1093/cid/ciaa1872